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Atlas of Sexually Transmitted Diseases

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Atlas of Sexually Transmitted Diseases

Clinical Aspects and Differential Diagnosis



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Foreword

In these days of Internet with facial recognition tools spreading from airports to banks and social media with photo sharing apps, do we still need a bound paper reference book? Yes, we do! We need a solid academic book, easy to search, with good pictures and sound practical tips. Professor Mauro Romero Leal Passos and his team of Brazilian leading scientists have created such a reference book. The differential diagnosis of sexually transmitted diseases is an art combining questionnaire, risk evaluation, physical examination, laboratory tests selection as well as counseling. The physical examination is still the most important stepping stone to proper patient management. With so many diseases with features overlapping we need a solid reference book. We may be a few years before we can take a picture and wait few seconds for a diagnosis to come in through Internet but before it becomes a reality I do suggest you acquire Professor Mauro's reference book for your practice either in dermatology, venereology, urology, family medicine, or gynecology-obstetrics. Your management skills and your teaching will improve, your students will gain experience faster, and, even more important, the well-being of your patients will improve more rapidly.

Have a great reading and viewing.

Marc Steben Québec National Public Health Institute, Clinique A rue McGill, Montreal, QC, Canada

Preface

What a Professional Involved in STD Should Know

Treating STD/genital infections should consider immediate actions and should not be trivialized, for simpler the case may seem.

In latest epidemiological data published by the international literature, the syndromic approach on STD is not supported by the medical perspective with scientific evidence and etiologies' epidemiology involving the main syndromes. Nevertheless, there may be good results in specific situations in the short term.

We believe the main purpose of professionals working in any Science field is to treat other people the way they would like to be treated.

One fact is to treat a patient with a syndromic approach methodology in a specific situation. Another one is to consider the syndromic approach as the only STD assistance policy for the whole country, not valuing nor implementing specialized centers of public and/or private medical attention for the research and epidemiological surveillance on STD.

Considering that STD is not decreasing in the world and the naive actions-based approaches do not reveal solid and lasting progress. On the contrary, the numbers of STD cases advanced.

In 2000, the World Health Organization (WHO) estimated 340 million new cases of four curable STD per year (*Trichomoniasis* 172 million, *Chlamydia* 92 million, gonorrhea 62 million, syphilis 12 million).

In 2008, the same WHO showed other estimates: 498.8 million of same curable STD (*Trichomoniasis* 276.4 million, *Chlamydia* 105.7 million, gonorrhea 106.1 million, syphilis 10.6 million).

To make this situation more difficult, gonococcal strains resistant to multiple antibiotics, including quinolone, are practically a problem all over the world. Furthermore, we all know (or should know) that combating the antibiotics overuse is one of the main questions in the fight against antimicrobial resistance.

STD Fact Sheet, February 2013, from CDC—Incidence, Prevalence, and Cost of Sexually Transmitted Infections in the United States—reveals:

CDC's estimates of STI (USA, 2008):

- Annual new infections (incidence), 20 million dollars, USA, 2008.
- Total infections (prevalence), 110 billion dollars, USA, 2008.
- Total medical costs: 16 billion dollars, USA, 2010.

Is it possible to imagine what the numbers for South Africa, Brazil, China, India, Russia would be? Just to name a few countries.

In July 9, 2014, during the "2014 STD Prevention Conference/CDC", Atlanta, USA, professor King K. Holmes, in a brilliant lecture entitled *Progress and challengers in the evolution of sexual health and STI prevention*, wrote the first phrase in his last presentation slide: *At First: Just need more and better diagnostic and treatment.*

He did not speak only to Americans; he did it to the entire world. Oddly enough, we are lacking basic actions of medicine in STD area.

Clinical sense, common sense, knowledge of epidemiology in this field (local and global), and individualized service related to a specific time have to be constant in every medical assistance. This is different from not seeking the better standards of medical care routinely. Guessing should be for activities such as theatre, cinema, joking among friends.

Therefore, It Should Not Be Postponed

- Excellent anamnesis.
- Satisfactory physical examination and complementary examinations.
- Counseling (on health education, being available to listen).
- Offering serology for syphilis, HIV, hepatitis markers especially anti-HBS, HBsAg and anti-HCV.
- Emphasizing the adherence to the treatment (supervised therapy in the query or make the medication available at the time of the appointment).
- Emphasizing the importance of appointment/examination/treatment of sexual partners.
- Emphasizing the importance of periodical physical examinations (gynecological/prostate).
- Emphasizing the importance of vaccine schemes available in the country (hepatitis A, hepatitis B, HPV).
- Knowing that medications can be acquired in case they are not available to patients during the appointment. And that the so-called generic medications do not always cost less.
- Providing condoms (male/female).
- Scheduling return to the medical appointment for control/review.
- Being available or provide appointment to sexual partners.
- Asking the patient, especially at the end of the anamnesis, the following question: Is there something I didn't ask or talked about that you would like to tell me?
- Notifying the cases to public health organizations for a proper epidemiological surveillance.
- Claiming, demanding the best human and technical resources available for a good medical
 care, whether public or private. Remember once again that our main objective is to treat
 everyone the way we ourselves would like to be treated.

Major Syndromes to Be Observed in STD/Genital Infections

- Genital ulcers (genital herpes, syphilis).
- Urethral discharge (gonorrhea, Chlamydia).
- Vaginal discharge (bacterial vaginosis, candidiasis, Trichomoniasis).
- Endocervicitis/pelvic pain (gonorrhea, *Chlamydia*).
- Testicular pain/swelling (gonorrhea, Chlamydia).
- Proctitis (gonorrhea, *Chlamydia*).
- Ophthalmia (gonorrhea, Chlamydia).

Notes

There may be more than one agent and/or more than one syndrome concomitantly.

Sometimes, a syndrome simulates another. For example, gonococcal ulcerated balanitis or cervical and/or vaginal wounds causing vaginal discharge.

Many genital changes, even some infectious diseases, do not configure STD.

More than 20% of genital ulcers, even employing good laboratory resources, are undiagnosed. Several cases are autoimmune diseases/unknown origin.

In many situations, systemic diseases can cause genital repercussions, with cutaneous and mucosal rush or genital ulcers.

Caution and good sense should be observed not to exaggerate the use of antibiotics, especially in associations.

The indiscriminate use of antibiotics is an important factor to be combated in order to reduce the microbial resistance to drugs.

Important

People with immunodeficiency (AIDS, malignant neoplasm, use of immunosuppressant) can have atypical and/or exaggerated responses to many infections. For these people, treatment may require increased dose and time of use, and even a change of the administration path of anti-infective medicament. Repeating the scheme and/or hospitalization is not unusual.

Women in their teens, in perimenopause, and young gay men are groups in which there has been a great progress in the incidence of HIV infection in several countries during the last years.

Vaginal discharge (due to inflammatory process or microbiota imbalance) exposes woman to great vulnerability to HIV (susceptibility increases in case she is seronegative) and transmission of the virus (transferability increases in case she is positive). Trivializing the medical care in these cases means trivializing the life quality of a community.

Sensitivity of a Laboratory Test

- Measures the test ability to detect an infection.
- Is the maximum concern about the population with a high prevalence of the disease, as it happens in the STD clinics.
- The sensitivity appraises the proportion of positive individuals among all infected patients.

Specificity of a Laboratory Test

- Measures the test's ability to properly exclude the uninfected individual. It is the maximum
 concern with the tests of the population with a low prevalence of the disease, as is the case
 of the family planning clinics and private clinics in general.
- The specificity appraises the proportion of individuals uninfected with negative test.

Reflection

Finally, the items we have been pointing out and divulging for a long time are the following: When treating (attending) a person suspected STD, perhaps it is easier or more didactic to recommend **what Not to do**:

 A prejudiced attitude towards gender/sexuality, skin color, education, socioeconomic and cultural status, occupation, religious belief, place of habitation or birth.

Preface

- Provide diagnosis and treatments based on assumptions without verifying the epidemiological, laboratory and clinical data, because not all there is in the genitals is sexually transmitted. On the other hand, extragenital signs and symptoms can (co)exist with STD/HIV, especially syphilis, HPV.
- Not invite the patient to think about the attitude towards all situations involved nor provide basic information about the problem.
- A judge attitude (make a judgment of the patient and/or situations involving the case).
- Ignore all emotional and existential story involved in the case.
- Fail to make good use of the meeting with the patient to start/expand the process of health education/prevention of other damages to the health. For example, trying to get to know the vaccination status of the patient (hepatitis A, hepatitis B, HPV, flu).
- Avoid "being ashamed", postpone asking other colleagues' opinion about cases of chronic evolution, recidivism and resistant to treatments already made, especially, but not only, in situations where the diagnosis is not fully established. The well-being and the full recovery of the patient is fundamental. Not the "wisdom" of the doctor.
- Overvalue publications on cost-effectiveness. Generally, these studies are made in very different environments, usually public health units, where most professionals treat STD. Although the medical practice has a broad and collective vision, it is a custom/personal assistance. At least for us, to quantify the value (and welfare) of human beings (and their families) is a task that we are not able to perform. Neither our goal.
- The absolute majority of the actions that have caused (and still cause) great impact to a huge number of people start with a decision/personal attitude.
- We can mention as mere examples: discovery of the tuberculosis *Bacillus*; the discovery of penicillin; proposal of a bill requiring the Federal Government of Brazil to ensure antiretroviral therapy in the public health system; free vaccination scheme against HPV, since 2007, for girls and women up to 26 years of age, and for boys, in 2014, by the Government of Australia.

Niterói, Rio de Janeiro, Brazil

Mauro Romero Leal Passos

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1.1 Introduction

The skin is the largest organ of the human body, and corresponds to 15% of the body's weight. Although there are topographical variations, it is composed of three basic structures layered in the following order: hypodermis (subcutaneous layer), dermis and epidermis.

This covering tissue that bounds the individual of his environment has as vital functions the protection against external aggressions, the maintenance of fluids in the body, and the thermoregulation, besides playing an important sensorial role. Due to its great accessibility to inspection, unlike the viscera, the skin becomes one of the major components of the physical beauty providing self-esteem and social coexistence. Frequently, aesthetic changes cause inferiority feelings and unthinkable social discrimination to people for the rest of their lives.

This inspection easiness requires the knowledge of a number of skin changes related only to aesthetics, in order to differentiate them from those that actually bring harm to health.

The cutaneous integrity is fundamental so that the skin can properly put in practice its prevention function against the access of toxic agents, microorganisms and excess of ultraviolet radiation to the body, impede the loss of fluids, and protect against excess of temperature, mechanical forces and low-voltage electric current.

1.2 Skin Structure and Function (Fig. 1.1)

1.2.1 Epidermis

The epidermis is a stratified, keratinized, not vascularized pavement epithelium of ectodermal origin. The epidermis originates the following cutaneous attachments: pilosebaceous follicle, sudoriparous glands, hair, and nails. Its main functions are the relative impermeability, which prevents the free movement of fluids and molecules in both directions, the protection from the entry of microorganisms, as well as from excessive ultraviolet radiation and low-voltage electric power.

As it is not vascularized, the epidermis depends on the supply of nutrients through the dermis, with which establishes a relationship of interdependence.

The dermis basic element is the keratinocyte, which during its migration towards the surface undergoes a differentiation process, whose goal is the production of keratin. When the keratinocyte reaches the surface, it is transmuted into an inviable and anucleated cell full of keratin, which will then perform the main epidermic functions.

The epidermis is divided into four cell extracts, characterized by degrees of its keratinocytes differentiation and morphology. The nearest layer to the dermis is the basal layer, following towards the surface the spinous extract, the granulous and finally the corneal (Fig. 1.2).

Fig. 1.1 Skin Structure and Function

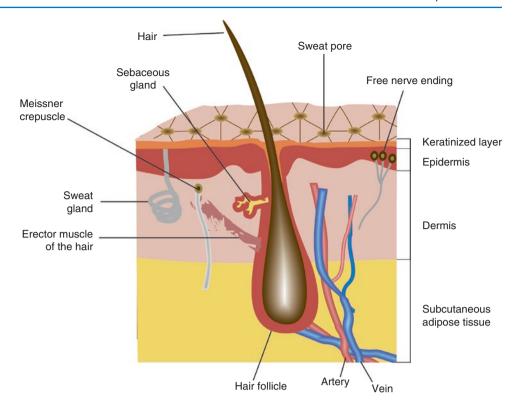
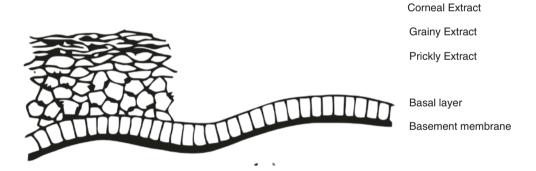


Fig. 1.2 Epidermis



1.2.1.1 Basal or Germinative Layer

As the cornea's cells are continuously removed, the maintenance of the epidermis depends on a permanent replacement of new cells. This replacement is promoted by the keratinocytes mitosis of the basal layer, which are little differentiated, and retain proliferative capacity. The basal layer is composed of a single layer of cylindrical cells, with the largest axis perpendicular to the dermoepidermal junction. In normal skin, around 10% of the basal cells are in mitosis. At any given time this percentage could increase depending on the physiological (repair) or pathological (e.g., psoriasis) needs.

1.2.1.2 Spinous Extract

It consists of several layers of polygonal keratinocytes under differentiation process. These are rich in cytoplasmic tonofilaments, grouped more compactly, as the cell progresses toward the surface. These tonofilaments are the precursors of keratin.

1.2.1.3 Granulous Extract

It consists of variables layers of flattened keratinocytes containing granules of keratohyalin associated with cytoplasmic tonofilaments. These granules seem to contribute to the formation of the cytoplasmic matrix of corneal cells.

1.2.1.4 Corneal Extract

It consists of 8–15 layers of flattened anucleated keratinocytes. The cytoplasm is completely filled with a very resistant and insoluble fibrous protein called keratin.

As it is the final product of the keracinocyte differentiation, the corneal extract is the main responsible for the

protective functions of the epidermis. Although it is not completely impermeable, it is an excellent barrier to the movement of fluids, molecules and microorganisms, and any damage to its integrity harms this function extremely.

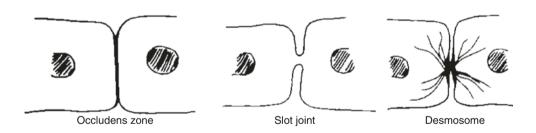
Its low water content is the unique and exclusive feature that raises difficulties to the establishment of microorganisms on the surface of the skin.

The epidermic extracellular space is extremely impermeable, allowing the nutrition of all epidermic layers, except the corneal extract. A water-soluble barrier is located in the boundary between the granulous and the corneal extract. This barrier is probably responsible for the abrupt transformation of the viable cornified cells in not viable ones, because it disables the nutritional supply to those cells located above it. The impermeable property of this region appears to be caused by two factors: a special substance secreted at this level and represented by Odland bodies or lamellar bodies, and a type of intercellular contact found only there, named *zonula occludens*, in which there is an intimate union between the adjacent cytoplasmic membranes.

There are still two other specialized types of epidermal intercellular contact: the gap junction and the desmosome. The gap junction sets a free traffic corridor between the adjacent cells and plays an important role in the differentiation of the epidermis as a whole; only missing in the corneal extract.

The demosomes are the main and most numerous types of epidermal intercellular contact. They occur in all layers, providing stability to the tissue. The hemidesmosomes occur between the basal cells and the basal lamina (Fig. 1.3).

Fig. 1.3 Epidermal intercellular contacts



1.2.1.5 Dermoepidermic Junction

The dermoepidermic junction corresponds to the basal membrane in the optical microscopy. The electronic microscopy is a complex structure comprising the cytoplasmic membrane of the basal cells, the lucid blade (empty space), the basal lamina and the most superficial portion of the papillary dermis. Promoting adhesion between the basal cells and the basal lamina, are the hemidesmosomes, and between this

and the dermis, the anchoring fibrils and microfibrills (Fig. 1.4).

The basal lamina has the following functions: ensure the dermoepidermic adherence, guide the migratory direction of keratinocytes to the surface and work as a system of pores of different sizes, allowing the quick passage of small molecules and making difficult the passage of larger molecules.

Fig. 1.4 Dermoepidermal junction



Basal cells

Lucid blade

Basal blade

Anchoring braces

1.2.1.6 Other Epidermic Cellular Components

Non-keratinocytes cells of the epidermis are called clear cells, as they require special coloring to become evident. We will consider the melanocyte, the Langerhans cell and the Merkel cell.

Melanocyte

The melanocyte is a dendritic cell of neural crest origin (neuroectodermal) located between cells in the basal layer in an approximate proportion of one melanocyte to ten keratinocytes.

Its function is the synthesis of melanin obtained by the action of the enzyme tyrosinase on tyrosine. Melanin is stored in rounded cytoplasmic structures, the melanosomes, which are transferred to the adjacent keratinocytes via phagocytosis of dendritic cytoplasmic portions. Thus, the melanocyte functions as a unicellular exocrine gland.

Melanin is a brown pigment with photoprotection action. Racial variations of skin color depends on the quantity, size and morphology of the melanosome produced, as the melanocytes number and the melanin quality are basically the same.

The exposure to ultraviolet radiation increases the production of melanosome and its transference to the keratinocytes, causing skin pigmentation and providing greater protection against future exposures. White skins are more susceptible to harmful immediate action (burning) and late action (elastosis, keratosis, epitheliomas, melanomas) of this radiation.

Melanocytes are still susceptible to MSH (Melanocyte Stimulating Hormone), as well as to sex hormones, to inflammatory agents and to vitamin D produced in the epidermis.

Langerhans Cell

Is a dendritic cell situated in the basal and granulous layers, containing cytoplasmic granules in the form of a racket. Also originated in the bone marrow, performs an important immune function, presenting the antigen to dermal lymphocytes.

Merkel Cell

It is found in the basal layer of the skin of the fingers, lips, gums and palate, playing a mechanoreceptor sensorial function.

1.2.1.7 Cuttaneous Attachments

Pilosebaceous Follicle

Structure formed by the hair follicle, sebaceous gland, and hair erection muscle.

Hair Follicle

The hair follicle is distributed throughout the skin except in the palmoplantar regions. It is formed in the embryonic life by invagination of the keratinocytes. In the hair follicle ends the sebaceous gland duct, and in certain regions (axilla and genital region) the duct of the apocrine sweat glands also. All these structures are located in the deep dermis.

The hair presents three cyclical and permanent stages: anagen, catagen and telogen, corresponding respectively to growth, regression and resting of the follicle. The growth speed varies according to different parts of the body.

Much more than the aesthetic and the sensorial function, the hair is important for the protection from solar radiation, thermal homeostasis and tissue repair, acting as true reservoir of epidermal stem cells.

Sebaceous Gland

This gland originates in a protuberance of the hair follicle. Vary in number, size, and activity in the parts of the body. Under action of testosterone becomes active from puberty. Their secretion (sebum) is basically composed of liquids, which, together with the lipids derived from the corneal layer, will form the lipid mantle, which is a factor of impermeability (hydrophobic) and antisepticing.

Apocrine Sebaceous Gland

Derives from the same invagination germinal layer, which gives rise to the hair follicle. It is an androgen-dependent scent gland present only in the axillary, genital and periareolar areas, whose secretion is metabolized by the skin saprophytic bacteria, producing characteristic odour that functions as a social and sexual attraction.

Erector Hair Muscle

Smooth muscle positioned at the top of the dermis inside the hair follicle.

Eccrine Sudoriparous Glands

These glands, formed by epidermal sprouting, are distributed throughout the skin. The greater concentrations areas are located in the palmoplantar regions. They are located in the deep dermis and flow directly on the surface of the skin. Their number varies from two to four million, and its total mass is equivalent to a kidney's. An individual can secrete up to 10 L of sweat per day.

Its basic and vital function is the thermoregulation obtained through the sweat evaporation with the consequent cooling of the cutaneous surface.

The composition of the secretion includes water, sodium, calcium, magnesium, iodine, phosphorus, sulfur, iron, zinc, manganese, mercury, urea, amino acids, albumin, types IgA, IgG and IgD alfa globulins and immunoglobulins. However, the serum metabolites depuration is fully held by the kidneys and is not considered a vital function of these glands.

1.2.2 Dermis

The dermis is a soft connective tissue, richly vascularised and innervated. The cellular elements of the normal dermis are the following: fibroblasts (dermal fibres' producers), mast cells, histiocytes, dendritic cells and a small number of lymphocytes. The extracellular matrix is composed of fiber proteins (collagen and elastic fibers) and the essential substance (*proteoglycans*).

It is divided into papillary dermis or superficial (composed of thin collagen fibers arranged vertically), deep or reticular (thick collagen fibers, grouped in dense bundles horizontally compressed), and adventitial (around vessels and attachments).

The dermis performs a protection function against mechanical aggressions due to its viscoelastic property, providing the resistance to tensions and pressures, and becoming recomposed after these movements. Due to this vascular power, it plays an important thermoregulatory role. It has a close relationship with the epidermis, suppressing its nutritional, hormonal, nervous factors, and others.

1.2.3 Hypodermis

The subcutaneous tissue, or hypodermis, is composed of adipocytes' lobules, limited by septa of collagen fibers, which accommodate vessels and nerves. It performs protections functions against mechanical force (pressure) and loss of heat as well, besides storing calories.

1.2.4 Nails

Nails are cytokeratin structures covering the distal phalanges, originated in the nail matrix. Other nails components are the following: eponychium, nail plate, nail bed and hyponychium. Their main function is to protect the ends of the fingers and toes against traumas, keeping the touch of the fingers. It also plays an important role in aesthetics of the hands and feet, particularly for women.

It is a structure of several changes caused by local and systemic diseases, sometimes assisting in the diagnosis conclusion.

1.3 Dematological Diagnosis

The great difficulty of the dermatological diagnosis arises from the small number of possible clinics manifestations due to a wide variety of pathological conditions. However, an accurate analysis of the individual lesions, the arrangement between them, its distribution through the integument associated with systemic manifestations and history, are often enough to the correct diagnostic conclusion. When it does not occur, we make use of the laboratory resources.

The dermatological exam training is like learning to read, and depends on basic theoretical knowledge and a lot of practice.

The dermatological examination routine must always obey the following anamnesis rules: patient identification (full name, age or date of birth, color, marital status, birth-place, and occupation), main complaint, history of present illness, past medical history (including drugs of regular or sporadic use), physiological and pathological history, family background and social history (and also considering conditions of housing, travelling, etc.).

Starting with the observation of the general state of the patient, the examination of the skin, mucous membranes and nails, carried out with the patient preferably entirely naked and under good light conditions. At first, the patient should be inspected at some distance, and considered the distribution of injuries and extension of the manifestation; subsequently examination of the injuries in detail, the type of the lesion, its color, shape and size, arrangement, distribution, and finally, palpation of the consistency, temperature and humidity.

After the physical examination, we can retake the history of the present or pathological disease, and with a diagnostic suspicion already formed, treat it. The following must be necessarily questioned: time and evolution of the disease, subjective symptoms (pruritus, pain sensitivity, etc.), drugs used, description of the initial injury, triggering or aggravating factors and systemic symptoms.

Finally, we can use semiology (sensitivity test, etc.) and laboratory resources, such as specific dermatology procedures (dermatoscopy, biopsy, microbiology, etc.), and the usual (CBC, etc.).

1.3.1 Dermatologic Semiology

The eruptive elements, or cutaneous efflorescence, or elementary lesions can be classified according to the type of injury, shape, arrangement and distribution.

1.3.1.1 According to Type of Lesion

Several classifications of the eruptive elements have already been identified. The most used are the Schulmann's with some changes, as it is didactic and easy to understand.

We can group them into six types, as follows:

- Color-changing lesions.
- Solid lesions.
- Liquid content lesions.
- Lesion with cutaneous thickness change.
- Lesions with continuity solutions.
- Senile lesions.

Color-Changing Lesions (Fig. 1.5)

It is an exclusive change of the skin color, without the modification in the relief or in the consistency of the skin. When the change is limited to an area it is called macula or stain, and receives various names when the process is widespread.

1. Stain

The origin can be vascular, transitory or permanent, or by pigment deposition.

- (a) Transitory Vascular Stains
 - Erythema: various shades of red due to vasodilatation. Characteristically disappears through vitro pressure. There are several subtypes:



Fig. 1.5 Eruptive lesion with <u>color change</u>—erythematous spots (syphilitic roseola)

- Cyanosis: purple, reduced hemoglobin, consequent to the venous congestion.
- Enanthema: erythema located in the mucous membranes.
- Exanthema: generalized erythem.
- Erythrodermia: universal erythema involving all the skin and often accompanied by exfoliation.

(b) Permanent Vascular Stain

- Angioma: red, flat, disappears through vitropressure, caused by vascular neoformation.
- Anemic Nevus: permanent pale.
- Telangiectasia: linear, capillary vasodilation.

(c) Blood Stains

Also called purpura, occurs by extravasation of vases erythrocytes of reddish-violet to purple colour, does not disappears through vitropressure.

- Petechiae: pinpoint.
- · Wound: bigger, in sheet.
- · Víbice: linear.

(d) Pigmentary Stains

Naturaly related to the concentration of melanin in the skin. However, it may occur due to the deposition of other endogenous pigments (e.g. bilirubin) or exogenous (e.g. carotene, tattoo, etc.), causing different colorations related to the provocative element.

- Hypocromic: whitish due to melanin reduction.
- Achromic: porcelain-like, melanin absence.
- Hypercromic: excess of melanin or other pigment.

Solid Lesions

- (a) Papule Fig. 1.6
 - Smaller than 1 cm.
- (b) Plaque
 - Less than 1 cm, with a diameter greater than 1 cm.
 Often it is a consequence of the confluence of papules.
- (c) Nodule (Fig. 1.7)
 - May show or not important changes of the protuberance, in general more palpable than visible, limited, with a diameter between 1 and 3 cm.
- (d) Nodosity or Tumor
 - Limited, with changes of the protuberance or not, bigger than 3 cm in diameter. Normally used for neoplastic lesions.



Fig. 1.6 Eruptive lesion, solid lesions—papule (secondary syphilitic)



Fig. 1.7 Solid eruptive lesion, <u>nodule</u> (cystic inclusion)

(e) Gumma

- Nodule that evolves with infiltration, softening, fistulization, ulceration and scarring.
- (f) Vegetation/Condylomatous (Fig. 1.8)
 - Papule or plaque consisting of small, multiple and grouped elevations.
- (g) Urtiga (seropapule)
 - It is the typical lesion of urticaria, consequent to dermal edema, high, flat and characteristically evanescent, disappearing in a few hours.
- (h) Verrucosity (Fig. 1.9)
 - Papule or plaque with hardened surface due to the peculiar increase of the corneal layer.
- (i) Tubercle
 - Papule or nodule, which usually progresses and leaves a scar.



Fig. 1.8 Eruptive lesion, solid lesions, <u>vegetation/condylomatous</u> aspect (flat condyloma, secondary syphilis)



Fig. 1.9 Eruptive lesion, solid lesions, <u>verrucous</u> aspect(condyloma acuminata— HPV)

Liquid Content Lesions

- (a) Vesicles (Fig. 1.10)
 - Liquid accumulation up to 0.5 cm in diameter.
- (b) Bubble
 - Liquid accumulation over 0.5 cm in diameter.
- (c) Pustule (Fig. 1.11)
 - Superficial purulent accumulation smaller than 0.5 cm in diameter.
- (d) Abscess (Fig. 1.12)
 - Deep purulent accumulation.
- (e) Hematoma
 - Blood accumulation.



Fig. 1.10 Eruptive lesion of liquid content, <u>vesicles</u> (genital herpes)



Fig. 1.11 Eruptive lesion of liquid content, <u>pustule</u> (genital herpes)



Fig. 1.12 Eruptive lesion of liquid content, <u>abscess</u> (lymphogranuloma venereum)

Lesions with Cutaneous Thickness Change

- (a) Keratosis
 - Thickness due to the increase of the corneal layer, dense and inelastic.
- (b) Lichenification
 - Increase of epidermal thickness with accentuation of the skin grooves.
- (c) Infiltration (Fig. 1.13)
 - Resulting from the dermal cell infiltrate, presents increase of the skin consistency with a decrease of its natural groove.
- (d) Esclerosis
 - Increase of skin consistency, which becomes inelastic due to collagen changes.
- (e) Atrophy (Fig. 1.14)
 - Can be epidermic, dermic, or hypodermic; it the first one, the epidermis is thin and transparent, while in the others there is a depression of the skin.
- (f) Scar
 - Residual element of a pathological process. May be atrophic, hypertrophic, or keloidal, where grooves, pores and hair are absent.



Fig. 1.13 Eruptive lesion with changes in cutaneous thickness, <u>infiltration</u> (swelling in vulvitis due to candidiasis)



Fig. 1.14 Eruptive lesion with changes in cutaneous thickness, <u>atro-phic</u> scar (donovanosis sequel)



Fig. 1.16 Eruptive element, solution of continuity, <u>ulcer</u> (chancroid)

Lesions with Continuity Solutions

- (a) Excoriation
 - · Loss of epidermis only.
- (b) Erosion or Exulceration (Fig. 1.15)
 - The loss of substance affects the papillary dermis.
- (c) Ulceration (Fig. 1.16)
 - Loss of substance besides the papillary dermis. The characteristics of its locations and borders (regularity, color, elevation) must be observed, as well as the base consistency, bottom (grainy, purulent, necrotic), pain and associated changes (varices, nodules, sensitivity, etc.).
- (d) Fissures or Rhagades (Fig. 1.17)
 - Consists of the solution of the continuity of the linear format skin, usually around the natural holes.
- (e) Fistula (Fig. 1.18)
 - Ulcerous path that drains a deep focus.



Fig. 1.15 Eruptive lesion, solution of continuity, <u>erosion</u> (genital herpes)



Fig. 1.17 Eruptive element, solution of continuity, <u>fissures</u> (after inflammatory process due to candidiasis



Fig. 1.18 Eruptive lesion, continuity solution, <u>fistula</u> (lymphogranuloma venereum)

Senile Lesions

- (a) Scale
 - Deriving from changes in the keratinization, corresponding to an abnormal corneal layer exfoliation.
- (b) Crusts (Fig. 1.19)
 - Concretions resulting from draining of exudates of the cutaneous surface, blood or pus.

Fig. 1.19 Eruptive lesion, <u>crusts</u> (genital herpes in HIV [+] patient)

(c) Eschar

• Black colored skin segment, resulting in tissue necrosis.

Normally the eruptive elements compose different combinations, allowing several expressions: papular erythema, papulonodular, atrophic squamous, crusted ulcers, vesiculobullous, etc.



1.3.1.2 Shape and Disposition of the Lesions

Each lesion, individually or together, frequently takes special configurations, which can be very important to the diagnosis.

Annular-ring.

Arciform-bow.

Circinate—circular.

Corymboid—central grouping of dense lesions, surrounded by sparse satellite lesions (similar to an explosion).

Discoid—disk shape.

On target—concentric circles.

Gyrate—turnings.

Guttate—drops.

Herpetiformis—grouped in clusters.

Lenticular—lens.

Linear—line.

Miliary—grain.

Nummular—coin.

Punctate—dots.

Reticulated—net.

Serpiginous—sinuous.

Zosteriform—on the path of a nerve.

Lesions Distribution

The distribution of the lesions by the integument is the third component of the semiotic dermatologic triad, and often the elucidative diagnostic.

The lesions may be localized, regional or widespread. The term "universal" is used when there is an involvement of the entire extension of the skin, hair and nails.

The following data should be taken into account due to their importance:

- Symmetry: symmetric lesions are generally of endogenous origin (e.g. virchowian hanseniasis).
- Preferred areas: for example, areas exposed to sunlight (e.g., photodermatoses).
- Intertriginous areas: chafing of adjacent areas (e.g., intertrigo, candidiasis etc.).
- Contact areas in the shape of certain objects (e.g., contact eczema).
- Preferred areas of pathological condition (e.g., hard chancre).

Even when the manifestation is widespread, as in secondary syphilis, the involvement of certain regions (palmoplantar, oral mucosa) can assist in the differential diagnosis (e.g., skin reaction to drugs or pharmaco-dermia). Syphilis 2

2.1 Synonymy

Lues, chancre, protosyphiloma.

2.2 Concept

Syphilis is a chronic and systemic infectious disease that is transmitted sexually or via other intimate contact. It may be transmitted from mother to fetus (intrauterine) or through contact between mother and child during birth.

Data from the World Health Organization (WHO) estimates that around ten million new cases of this disease are reported each year.

2.3 Incubation Period

The incubation period is from 21 to 30 days after contact with an infectious agent. This can vary from 10 to 90 days, however, depends on the number and virulence of the infecting bacteria and the immune response of the individual.

2.4 Etiologic Agent

Treponema pallidum, subspecies pallidum. This is a Gramnegative spirochete that does not grow in artificial media. It is sensitive to heat, detergents and common antiseptics and has difficulty surviving in dry environments. It is an exclusively human pathogen.

2.5 Clinical Presentation

2.5.1 Early Syphilis

Development of lesions:

- 21–30 days: Hard or inoculation chance—a single lesion (and in rare cases multiple) with hardened edges as a result of lymphoplasmacytic inflammation. This lesion is more commonly visible in men, in the balanopreputial groove, than in women. If the chancre is left untreated it can persist for 30–90 days, after which it involutes spontaneously. In women, vulval lesions can be observed in rare cases.
- 30 days: Satellite adenopathy—bilateral (inguinal), painless and uninflamed. The chancre and satellite adenopathy are known as primary syphilis.
- 30–40 days: Seropositive results are obtained.
- 50–180 days: Macular and papular exanthematous legions on the skin and/or genital or oral mucosa. *Treponema* enters the circulation and multiplies, causing the exanthematous stage (roseola) to spread across the body. Macular and papular lesions with a range of clinical appearances then appear (syphilids). This phase is also known as secondary syphilis. All of these lesions involute spontaneously without leaving sequelae, even in the absence of treatment. As a there are a wide variety of possible lesions, it is worth considering any genital lesion to be syphilitic.

2.5.2 Latent Syphilis

This occurs 1–2 years after infection. It is known as the "clinically silent" stage, and may only be diagnosed via serological screening.

This stage is divided into early (up to 1 year) and late.

2.5.3 Late Syphilis

This may start at the end of the latent phase or many years afterwards. Its clinical presentations are divided into:

- A. *Integumentary*: Gums, tuberous syphilids, juxtaarticular nodules and tertiary erythema.
- B. *Extra-integumentary*: Ocular, skeletal, cardiovascular and nervous system.

2.6 Laboratory Diagnosis

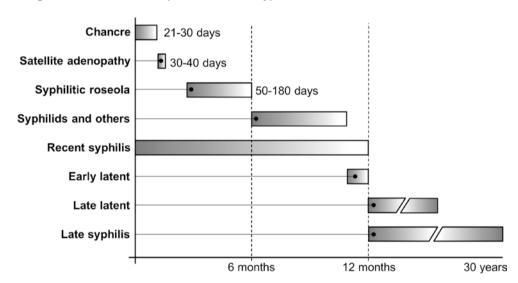
• Chancre and mucocutaneous lesions: Screening for Treponema using darkfield microscopy (this is still the gold standard and should be carried out during consultation as live, moving bacteria can be observed); direct immunofluorescence (excellent technique as it can be sent to a laboratory); silver impregnation (the Fontana-

Tribondeaux technique, although crude and more subject to error, can be carried out after consultation).

All phases of syphilis: Serology: Non-treponemal—VDRL (Venereal Disease Research Laboratory) test and RPR (Rapid Plasma Reagin); Treponemal—FTA-Abs (fluorescent treponemal antibody absorbed), MHA-TP (*Treponema pallidum*-microhemagglutination) and Elisa. In general, a VDRL titer equal to or above 1/16 is considered to demonstrate presence of the disease and indicates that the patient should be treated, except in cases where they are undergoing post-treatment serological monitoring. However, patients with initial-stage (chancre), latent or late-stage syphilis often present low titers in non-treponemal serology.

Graph 2.1 Progression of the clinical presentation of syphilis

Progression of the clinical presentation of syphilis



VDRL may provide a false positive result in low titers as a result of cross reactivity and a false negative result, mainly during the primary and late latent stages. This may also occur with treponemal screening with less frequency.

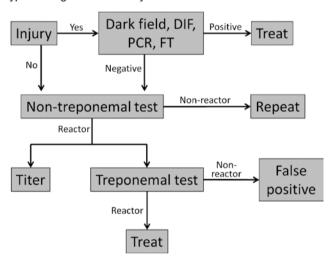
The prozone effect occurs when there is an excess of antibodies in relation to the antigen during VDRL testing, producing a false negative result. Upon dilution of the serum, high titers can be observed. This patient will normally be in the secondary phase.

Carriers of HIV more often have different serological responses, in terms of both false positive results and for very high titers.

Clinical presentations that suggest syphilis should not be underestimated, even when serological screening produces a negative result.

Investigation for neurosyphilis should not be delayed for HIV (human immunedeficiency virus) positive patients presenting neurological symptoms/disease.

Syphilis diagnosis summary



Graph 2.2 Syphilis diagnosis summary. *IF* direct immunofluorescence, *FT* Fontana-Tribondeaux (silver impregnation), *PCR* Polymerase Chain Reaction

2.7 Evaluation of Laboratory Methods

Exam	Sensitivity (%)	Specificity (%)	
Darkfield ^a	85-95	100	
Immunofluorescence ^a	90-95	>98	
VDRL	70-100 ^b	79–98°	
FTA-Abs/Elisa	85-100 ^b	95-100°	
MHA-TP	70-100	95-100	
PCR	>95	>98	

^aVaries according to professional

2.7.1 Treatment and Control

Early (primary/secondary) and latent (up to 1 year) infection: single dose of penicillin G benzathine 2,400,000 IU IM (1,200,000 IU in each gluteal region). We prefer to repeat a second dose after an interval of 1 week, avoiding the administration of a single dose.

Latent (over 1 year) and late infection: penicillin G benzathine 2,400,000 IU IM, once a week for 3 weeks.

- *Neurosyphilis*: Crystalline penicillin G 24,000,000 IU per day (4,000,000 IU every 4 h) IV, for 21 days.
- Criteria of cure: VDRL 3, 6 and 12 months after treatment must present a reduction in four titers or a negative result from 6 months to 1 year. Pregnant women must be monitored on a monthly basis. A reduction of 1 titer per month is to be expected. Treatment should be repeated if serology increases by four titers.
- Alternative drugs: Azithromycin 1 g orally per week for 2 or 3 weeks for cases of syphilis up to 1 year; no studies have been carried out for cases over 1 year. Doxycycline 100 mg orally every 12 h or erythromycin or tetracycline 500 mg orally every 6 h for 14 days for cases of syphilis up to 1 year and for 28 days for cases of syphilis over 1 year.
- Pregnant women: Follow the treatment regimen using penicillin G benzathine. Tetracyclines, doxycycline and erythromycin estolate are contraindicated.
- Children over 1 month old: Should have a cerebrospinal fluid (CSF) examination to exclude neurosyphilis. Review the patient in full to establish if it is a case of congenital or acquired syphilis. Early latent syphilis: penicillin G benzathine 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose. We prefer to repeat a second dose with an interval of 1 week, avoiding the administration of a single dose. Late latent syphilis or latent syphilis of unknown duration: penicillin G benzathine 50,000 units/kg IM, up to the adult dose of 2.4 million units, administered over 3 doses at 1-week intervals (total 150,000 units/kg up to the total adult dose of 7.2 million units)
- HIV positive patients: Perform clinical and serological (VDRL) evaluations 3, 6, 9, 12 and 24 months after treatment. These patients have a higher risk of neurological complications than patients that are not infected with HIV. They may also present more cases of serological failure.

Severe penicillin hypersensitivity is much less frequent than is claimed by both popular and medical myth. Those who think otherwise should seek out well-documented information.

^bVaries according to the stage of the disease

^cVaries according to population

2.7.2 Complications

- Late syphilis: Neurosyphilis, cardiovascular and mucocutaneous (gums).
- Early and late congenital syphilis: Congenital syphilis is a type of watchdog disease for the health system. When it occurs, it shows up errors in the system and the quality of prenatal services. The WHO has established that there should be no more than one case in every 1000 live births. It is known that at least 40% of those conceived by mothers with untreated syphilis during gestation will have serious problems or die. Therefore, pregnant women with syphilis or suspected syphilis should be treated with medical urgency. The incidence of congenital syphilis in many developing countries reflects the disregard, or negligence, of society as a whole (health managers, health professionals, the general population and the media) towards an easily diagnosed disease for which effective treatment is available. However, cases of congenital syphilis can be observed among the disadvantaged communities of developed countries.

Syphilis is considered to be inadequately treated when:

- Treatment is carried out using antibiotics other than penicillin.
- Treatment is incomplete or inadequate during the clinical phase, even if carried out using penicillin.
- Treatment is initiated less than 30 days from birth.
- Serological titers increase after treatment.
- Sexual partners are not treated or this treatment is not documented.

Even in cases where pregnant women are adequately treated for syphilis, newborns must be checked for the disease. Although not common, babies can still contract congenital syphilis from an adequately treated mother.

Positive serological results for newborns of mothers with syphilis may occur up to 18 months after birth.

When evaluating a case of suspected congenital syphilis, the patient's full clinical history must be considered; clinical and serological tests for the mother; serology and bone radiology for the newborn and clinical and serological tests for the mother's sexual partner.

The sexual partner should never be forgotten. The clinical examination, serological tests and adequate treatment of this individual are imperative.

2.7.3 Differential Diagnosis

Herpes simplex, soft chancre, Rollet's mixed chancre (hard + soft chancre), donovanosis, pharmacodermia, exanthematous viruses, fissures and traumatic ulcers.

2.7.4 Observations

- Pregnant women must undergo at least two serological tests, one on their first visit and the other in the 34th–36th week of pregnancy. Any genital lesions must be investigated immediately.
- Request for serology immediately after treatment is not indicated.
- In cases of hypersensitivity to penicillin, desensitization should only be carried out in a safe environment with experienced professionals.
- Serology can present low titers (1:4) for the rest of the patient's life, even after correct treatment.
- Treatment failure can occur with any therapeutic regimen, although there are no reports of resistance of *Treponema* pallidum to penicillin.
- Treatment failure may occur as a result of falsified medicines. Unfortunately this situation can occur in any country.
- In cases where the exact time of infection is unknown, it is better to opt for a treatment regimen of three doses of penicillin G benzathine at weekly intervals.
- A Jarisch-Herxheimer reaction may occur after the first dose of any treponemicidal medication. This will manifest as an exacerbation of skin lesions, fever, headache and arthralgia. This occurs more frequently at the exanthematous stage and responds well to analgesics and antipyretics. However, some professionals recommend betamethasone 12 mg IM and acetylsalicylic acid 500 mg orally before the first dose of antibiotics in patients with severe secondary syphilis mucocutaneous lesions.
- Although azithromycin can be used in pregnant women, it
 is important to remember that this drug does not cross the
 placental barrier. Therefore, after birth the child must be
 evaluated and treated. For this reason, penicillin continues
 to be the first treatment option. Its substitution should be
 analyzed with extreme care.
- As many laboratories no longer perform the FTA-Abs test, we find it practical to request treponemal screening without specifying which type of exam.
- Based on our knowledge of syphilis serology we do not recommend requesting FTA-Abs-IgM, as false positive results are very common.



Fig. 2.1 An adolescent patient who had already sought out health services twice, complaining of this painless lesion that appeared 2 weeks previously. Diagnosis: hard chancre. On one occasion, in a room at the Brazilian College of Surgeons in Rio de Janeiro, I heard Professor Eduardo Rabelo say the following phrase: "Any genital lesion has a 90% chance of being syphilitic; we need to think syphilitically." I had already heard this phrase spoken by various brilliant physicians. Older colleagues affirmed that the phrase was first spoken by Prof. Feijó. Regardless of the author of this phrase, this figure of 90%, is still a challenge for us now in 2011, as we still see many cases of syphilis that pass through various physicians without the hypothesis of infection by *T. pallidum* ever being raised



Fig. 2.2 Similar to the previous case: hard chancre. It has this name as if the lesion is palpated, hardening around the base and the edges can be observed, which is typical of invasion by mononuclear cells



Fig. 2.3 Case of hard chancre identical to the previous examples, representing the location where the *Treponema* entered the patient. This is also called an inoculation chancre. Some time ago it was believed that the disease primarily stayed in the genital area and then spread to the skin and the other organs. Today we know that syphilis is a systemic disease from the beginning, as it rapidly spreads from the point it entered to the satellite lymph nodes and beyond. Therefore, we prefer to classify syphilis as early, latent and late instead of primary, secondary and tertiary. From our point of view, this is physiopathogenically more correct



Fig. 2.4 In this case, the hard chancre looks more like desquamation



Fig. 2.5 As well as the classic single, painless, hardened lesion, we can also observe papillae on the corona of the glans indicated by the *arrows*. Many still confuse these with HPV infection. These are absolutely normal glandular formations



Fig. 2.6 With this case of hard chancre we want to highlight the visible edema on the foreskin, and the detail that upon covering and exposing the glans, the part of the foreskin around the lesion does not fold. This is due to lymphoplasmocytic infiltration, which causes the edges and base of the initial syphilis lesion to harden



Fig. 2.7 Very similar to the previous case and to Fig. 2.15 of this chapter. This patient reported having a fixed non-exclusive partner who was examined and whose clinical examination was normal. Syphilis serology for the partner was negative. After an interval of 30 days, the serology exam was repeated, and on this occasion was positive: VDRL 1:16 and FTA-Abs also positive



Fig. 2.8 In the vast majority of cases, hard chancre lesions in men present in the form of a single painless or relatively painless lesion with a hard base, which even without specific treatment will tend to recede within 30–60 days



Fig. 2.9 You can always count the number of times it has been possible to clearly determine an initial hard chancre lesion in a female patient on one hand. In over 2000 closely followed cases of syphilis, in only four will you be confident enough to affirm that it is a hard chancre. I have four photographs. When the hard chancre is well documented in women, it is more frequently observed on the vulva, as is shown in this case. Syphilis is more often diagnosed in women during the roseola or papular or erosive genital syphilide stage and not during the initial hard chancre stageIt would be logical to believe that initial lesions are found more frequently in the vagina and cervix, which would make diagnosis more difficult. In these situations, the woman generally presents with vaginal discharge and receives topical medicines for vaginitis. As the hard chancre then recedes, many of these are not diagnosed. As the syphilis develops, these cases provide another opportunity for diagnosis at a later stage with the appearance of the mucocutaneous lesions characteristic of secondary syphilis



Fig. 2.10 Attention must be paid to searching for adenopathy, which is generally bilateral and painless, accompanying the hard chancre (*arrow*) in practically 100% of cases. Still a case of hard chancre. One of our partners was consulted without the clinical manifestations of syphilis and negative serological tests (VDRL, FTA-Abs). In such situations, the correct conduct would be to introduce treponemicidal medication



Fig. 2.11 It may be difficult to accept such as case as a hard chancre. However, as a result of diagnostic confirmation, positive results from direct darkfield microscopy, serology (VDRL 1:16) and a bilateral inguinal lymphapolydenomegaly, it was confirmed to be a hard chancre. Observe the prominent edges in the close up



Fig. 2.12 A young patient who presented both a hard chancre on the vulva and vaginal discharge. Highlighted are the base and edges of the hard chancre

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Fig. 2.13 An adolescent who had a hard chancre for over 20 days and was applying a polyvalent cream (antibiotic, antifungal and corticosteroid) because VDRL had been negative and the possibility of syphilis was rejected. It is worth remembering that at the initial hard chancre stage it is common that serology will not react. The diagnostic standard is to look for treponema in the lesion (darkfield microscopy)



Fig. 2.14 A patient with a large and relatively painless ulcerative lesion on the balanopreputial groove, frenulum and penile body, the final diagnosis of which was hard chancre



Fig. 2.15 This type of lesion has already been shown. Note the edema around the hard chancre lesion. The skin around the lesion is so infiltrated that it doesn't have enough elasticity to fold



Fig. 2.16 A patient who was seen at the STD (sexually transmitted disease) clinic at UFF (Universidade Federal Fluminense) with a single, painless ulcerative lesion to the penis. He reported that the lesion appeared approximately 25 days after unprotected sexual contact with a new partner. Upon clinical examination, we found a lesion with a hard base (a), bilateral inguinal micropolyadenomegaly and vegetative lesions (b), also on the shaft of the penis. Material was collected from the lesion (c) for direct darkfield microscopy, which was positive for spirochetal bacteria. An excision was carried out on the condyloma lesions, treatment with penicillin G benzathine was initiated and a vaccine was prescribed for hepatitis B, although the latter was refused by the patient





Fig. 2.16 (continued)

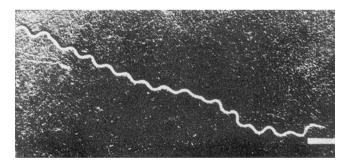


Fig. 2.17 Since cultures of *T. pallidum* still do not exist, the gold standard for diagnosis is still to find bacteria in the lesion through direct microscopy. Some physicians recommend DNA-Tp PCR screening as standard practice. However, this molecular technique is not readily available for most physicians around the world, even in developed countries. The most frequently used technique is dark field microscopy, although silver Impregnation (Fontana-Tribondeaux) and immunofluorescence may also be used. The latter normally provides results just as good as those of darkfield microscopy. A molecular biology technique for the diagnosis of *Treponema pallidum* has been available on the world market for years. One product is being used for the diagnosis of genital ulcers, with which it is possible to detect the DNA of *T. pallidum*, herpesvirus and *H. ducreyi* using the same sample (Multiplex-Roche). This electron micrograph shows a sample of *T. pallidum*



Fig. 2.18 We like to spread the concept of thinking syphilitically, because syphilis is much more common than is realized, especially in developing countries and the vulnerable populations of developed countries. In this figure, we can observe (a) a hard chancre lesion in the balanopreputial groove next to the frenulum. But in (b) the lesions are caused by genital herpes. After receiving advice, the patient agreed to undergo a HIV test. The result was positive. Cases involving more than one STD are common. Avoid ending investigations after the diagnosis of just one STD and seek to check for other possibilities



Fig. 2.19 Initial lesions on the vagina, mouth and anus are not always that same as the typical lesions of the penis. This is a case of a hard chancre on the anus. It is common for multiple lesions to occur in this region

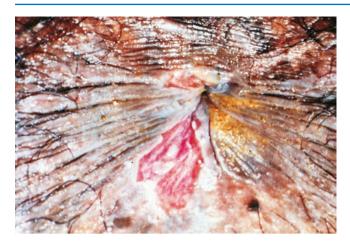


Fig. 2.20 The same situation as shown in the previous figure. Note here that to get a better look at the lesions you need to pull back the anal rim, but take care as these lesions are generally painful. These areas are rich in other bacteria, so proof via the presence of bacteria (*T. pallidum*) is not as easy. Sometimes other non-pathogenic spirochetes with coarse morphology can be found in this area. This may be confusing. Although inguinal adenopathy can exist, it is generally smaller than lesions on the penis or vulva. This is due to the lymphatic drainage of the anus not occurring solely via inguinal lymph nodes



Fig. 2.21 This patient complained mainly of urethral discharge. During the exam, a set of hard chancres was identified on the internal wall of the foreskin when the patient exposed the area further for photography. The patient also reacted positive to hepatitis B serology



Fig. 2.22 A young patient seen at the STD clinic at the Matta Foundation in Manaus, Amazonas State, with a hard chancre on the base of the penis. It is worth remembering that sometimes condoms do not cover this area very well. Some physicians call this "condom chancre" as transmission may occur even using a condom. Following this logic, transmission will not occur using a female condom as it covers a wider area. Lesions in this area are rare, as are those on the scrotum



Fig. 2.23 This figure illustrates the case of a patient with a hard chancre (a), genital herpes lesions (b) and gonococcal urethritis (c). After receiving advice, the patient underwent HIV and hepatitis B testing, the results of both being positive. The partner was examined and presented endocervicitis with a large quantity of pus and pelvic pain. They underwent two HIV exams and tested negative both times. The patient reported being a drug user (nasal cocaine) and having extramarital sexual relations (2 or 3 per year). Edema around the syphilitic lesion on the frenulum can be observed in the close up (a)



Fig. 2.24 The Fontana-Tribondeaux method showing spirochetes using a common microscope (magnified 1.000×). Silver salts attach to the surface of the bacteria, increasing their thickness and making them visible under a microscope. Direct examination of syphilitic lesions using this technique is a viable alternative when a darkfield condenser is not available, although it is not very sensitive and is completely dependent on correct sampling of clinical material

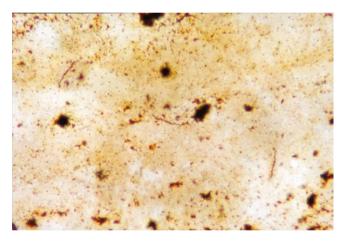


Fig. 2.25 Treponema pallidum impregnated with silver salts using the Fontana-Tribondeaux method. Spirochetes are dark brown against a light brown background (magnified 1.000x). Clinical material must be sampled after cleaning the ulcer with sterile saline solution and using one of the following methods: Apply a drop of commercial sulfuric ether on the clean base of the lesion, wait around 1-2 min for exudate to be produced which will mobilize the treponemes from their sub epithelial position. Then add a drop of sterile saline solution and collect the mixture with a spatula or platinum or plastic loop, using this to place a thin smear on a slide in one direction only, avoiding circular movements. Leave the sample to dry at room temperature before proceeding. Another method is to use a dry gauze to scarify the base of the lesion very carefully in order to avoid bleeding, which may interfere with the final result if this material is observed under a darkfield microscope. If this occurs, dry off the blood and start again, sampling the exudate according to the method described above



Fig. 2.26 Ulcerative lesion, with raised hardened edges and a clean base in a patient who was infected during oral sex, whose clinical diagnosis was confirmed in the laboratory through visualization of *Treponema pallidum* under a darkfield microscope and through histopathological findings of inflammatory infiltrate and periarteritis, confirming the hard chancre as a primary syphilis. Left submandibular inflammatory lymph nodes were palpable



Fig. 2.27 Image showing a slightly irregular depressed area with loss of papillae in the median region of the tongue, characterizing erythematous candidiasis. On the anterior portion there is an irregular ulcerative hard chancre with hardened edges (see *arrow*). This patient had HIV. The submental lymph nodes were palpable

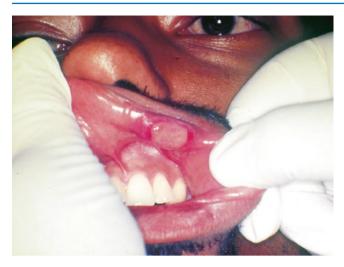


Fig. 2.28 Painless lesion located in the region between the red of the lip and the mucous membrane, with raised edges, well defined with an erythematous halo and a base covered in a whitish necrotic material. During examination the patient reported that the lesion had appeared 10 days previously after practicing oral sex with a prostitute. A sample was collected from the base of the lesion and the presence of spirochetes morphologically compatible with *Treponema pallidum* were identified, characterizing a primary syphilis lesion. The patient returned just 3 weeks later and the lesion had practically disappeared. However, VDRL presented a titer value of 1:128. During the first consultation, the patient was medicated with penicillin G benzathine



Fig. 2.29 HIV positive homosexual patient with leprosy who practiced oral sex, with an extremely painful ulcerative crater-shaped lesion full of intense inflammatory infiltrate with a necrotic base in the oropharyngeal transition area. The retroauricular and submandibular lymph nodes on the same side as the lesion were palpable, painful and movable. The probable clinical diagnosis was hard chancre, however, collection of material identified the presence of Fusobacterium necrophorum and Prevotella intermedia, as well as Bororrelia vincent, Porphyromonas forsynthesis, gingivalis. Tannerella Treponema denticola. Staphylococcus aureus and non hemolytic specimens of Streptococcus. Blood testing presented anemia and significant leukocytosis. The lesion had a fetid odor and was diagnosed as cancrum oris, serving as a differential diagnosis for syphilitic hard chancre



Fig. 2.30 Male bisexual patient who practiced oral sex, with an extremely painful crateriform ulcer with raised edges and a clean base located in the region of the lingual belly and extending to the left edge of the tongue. This had appeared 2 weeks previously and there were no other lesions in the mouth. Left submandibular lymph nodes were palpable and painful. Hard chancre was one of the considered diagnoses; however, collection of material for microbial analysis was negative, leading to a diagnosis of major aphthous ulceration. Medication with corticosteroids started the healing process. Investigations to seek any immunological origins for the lesion were then initiated



Fig. 2.31 Male patient of 54 years who reported practicing oral sex and using inhaled drugs, and who upon examination presented an ulcerative lesion with hardened and raised edges. Considering the patient's anamnesis and the clinical characteristics of the lesion, one of the considered diagnoses was hard chancre. After detailed observation of the ulcer, which had a base speckled with erythematous spots and a moriform appearance, diagnosis was confirmed using exfoliative cytology and biopsy. The fungus *Paracoccidioides brasiliensis* was found on histological sections impregnated with Grocott-Gomori methenamine silver stain. The patient was referred for systemic investigations, and among the most important findings were pulmonary lesions caused by paracoccidioidomycosis and HIV positive serology



Fig. 2.32 Male patient of 42 years, street seller and smoker who frequently practiced oral sex, presenting an irregular ulcer with elevated and hardened edges and a clean base fixed to underlying structures, located on the lower lip and extending from to the labial mucosa. The patient reported that the lesion had been present for 6 months. Since hard chancre on the lip mimics the clinical characteristics presented, we could include this as a probable differential diagnosis. Contrary to diagnosis of hard chancre were the time that the lesion had been present and risk factors for epidermoid carcinoma that included the patients profession, exposing him to UV radiation, and smoking. This diagnosis was confirmed after biopsy and histopathological examination



Fig. 2.33 Patient exhibiting a linear and irregular "snail track" erythematous lesion on the upper lip, which has been classically described by Alfred Fournier as one of the clinical signs of secondary syphilis. It should be observed that it is the patient lifting their own upper lip, as professionals must use gloves during physical examination to avoid possible contamination

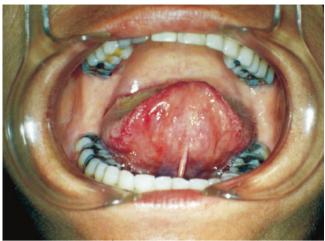


Fig. 2.34 Previously described patient presenting linear and irregular erythematous areas bilaterally covering the lingual belly during the secondary phase of syphilis



Fig. 2.35 Patient lifting her upper lip to reveal a labial mucosa with opal-white coloration and irregular erythematous serpiginous lines, a clinical sign of secondary syphilis



Fig. 2.36 View of the soft palate and oropharynx of the previously described patient, revealing opal-white plates with edges marked with irregular lines, a sign of secondary syphilis in the mouth

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Fig. 2.37 View of the anterior region of the buccal vestibule of the same patient, revealing the irregular erythematous area with the white necrotic plates associated with secondary syphilis



Fig. 2.38 Patient presenting irregular white plates on the lower lip surrounded by a erythematous halo, repeated in the region between the soft and hard palate in the second stage of syphilis



Fig. 2.39 White necrotic plates located bilaterally in the anterior region of the lingual belly, where erythematous areas can also be observed in the region between the lingual belly and the floor of the mouth, both clinical manifestations of secondary syphilis in the buccal cavity



Fig. 2.40 Female patient with an irregular white erythematous plate in the anterior region of the buccal mucosa, a clinical characteristic of secondary syphilis that was confirmed with serological exams (FTA-Abs and VDRL). The patient's partner presented hard chancre on the penis and on a finger



Fig. 2.41 The same patient presenting white erythematous areas in the anterior region of the buccal mucosa, identical to those observed on the other side, another sign of secondary syphilis



Fig. 2.43 The same patient presenting an irregular, elevated white necrotic plate with a wrinkled surface, located on the right side of the edge and the belly of the tongue

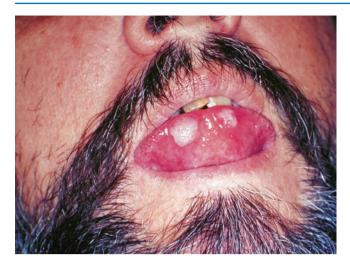


Fig. 2.42 Patient with secondary syphilis, presenting an elevated irregular white necrotic plate with a wrinkled surface located on the on the left side of the edge and belly of the tongue. This condition is known as flat condyloma or papular syphilide. At the top of the image an irregular red plate can be observed covering the hard palate close to the molar teeth



Fig. 2.44 Patient in the secondary phase of syphilis presenting irregular, elevated white necrotic plates, with a wrinkled surface and separated by erythematous areas, located on the right side of the tongue, characterizing syphilitic flat condyloma (condyloma latum)

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Fig. 2.45 The previous patient in the secondary phase of syphilis, viewed from the front, showing in detail the irregular and raised white necrotic plates, with wrinkled surfaces and separated by erythematous areas, characterizing flat condyloma



Fig. 2.46 Patient presenting an irregular white area (and other with necrotic) on the anterior and mid hard palate, permeated on its edges by erythematous areas. As well as these buccal lesions, the patient presented typical syphilitic roseola lesions spread across various cutaneous areas



Fig. 2.47 The patient described above, from a side view, presenting maculopapular cutaneous lesions typical of syphilitic roseola



Fig. 2.48 There is a well-known phrase by Ricord, who said: "Satellite adenopathy accompanies chancre like a shadow accompanies the body." Adenopathy is generally bilateral, mostly or totally painless, micropolyadenomegaly (olive stone) and not inflamed. It is obviously satellite to the inoculation chancre. If the chancre is in the mouth, adenitis will be cervical; if it on the finger it will be in the corresponding underarm. It may, as is shown in this figure, present one side more prominent than the other. The patient in question presented various syphilitic lesions on the vulva (Not hard chancre but papular syphilides) and cervicovaginitis caused by gonococcus and *Trichomonas vaginalis*



Fig. 2.49 Syphilitic adenitis may sometimes become inflamed, and may even drain spontaneously. This did not happen with this patient. She sought medical help for vaginal discharge, vulval lesions and a "lump" on her groin. She was prescribed with vaginal cream, oral acyclovir and doxicycline and incision and draining of the inguinal lump. She sought medical help the following day, complaining of arthralgia, headache, fever and red blotches covering her body. The result of VDRL was 1:256. This is clinically defined as a Jarisch-Herxheimer reaction. It is not recommend incision and draining of adenitis. Antibiotics will generally solve the problem. In these cases, healing can take a very long time



Fig. 2.50 Another case of syphilitic adenitis. We would include to the phrase that adenitis accompanies chancre that it also accompanies syphilids. This is the groin of the patient in Fig. 2.69



Fig. 2.51 Groin of another patient with papular syphilides on the penis. The *arrow* indicates the largest protrusion



Fig. 2.52 If the development of syphilitic lesions is observed, the progression of the disease can be seen. This figure shows a case of syphilitic roseola. These are red blotches on the skin, mainly on the trunk, characterizing the exanthematous stage. They are generally not itchy and tend to disappear in 30–40 days, even without treatment. The patient often presents with flue-type symptoms (low fever, asthenia, sweating, headache, arthralgia). This phase demonstrates the dissemination of *Treponema pallidum* throughout the whole body. The skin reflects what is happening, perhaps on a lower scale, to the spleen, liver and lungs



Fig. 2.53 This 74-year-old patient was prescribed with an antihistamine, as it was thought that he had eaten bad shrimp. In reality, he was having sexual relations with a woman who did not know she had syphilis. Not even her doctor knew this, as she had a discreet ulcerative lesion on the vulva, slight inguinal adenitis and was prescribed medication for recurrent herpes, because the patient in question had presented with a small similar lesion to that shown here 2 months previously. VDRL presented a positive result of 1:128 for her and 1:256 for him





Fig. 2.54 (a) Trunk of a patient with syphilitic roseola. In (b), areas of erythema with papular lesions, sometimes eroded and demarcated. The lesions presented at various stages



Fig. 2.55 As well as typical roseola lesions, erythematous plates can also be observed, with a superficial trauma appearing





Fig. 2.56 An adult, homosexual patient who had multiple partners without using condoms, presenting exanthema across all of his skin and buccal cavity, including palmoplantar rosellas. He is a patient at the STD clinic at UFF, where he was treated for early syphilis 5 years previously. Questioned about condom use, he claimed that oral sex with a condom made him vomit and that as he was homosexual he would

always be at risk. Serology was positive for syphilis and negative for HIV. When we advised him to refer his partners for treatment, his mother, who was with him during the consultation said: "There's going to be a huge line here, doctor". We responded that that wouldn't be a problem and that it would be better for everybody



Fig. 2.57 (a) This type of case of syphilis is not rare. (a) Satellite inguinal adenitis around lesions to the vulva; (b) palmar roseola; (c) papuloulcerative lesions to the vulva and perineum. (b) The *arrow* indicates a large inguinal protrusion, more notably to the left. In the genital

area, papuloulcerative lesions can be seen on the perineum. (c) A more detailed look at the perineal and perianal lesions. This case illustrates the need to observe the multiple lesions that early syphilis can present



Fig. 2.58 (**a–c**) A young adult patient presenting cutaneous lesions for 2 weeks, receiving oral antihistamine medication and performing potassium permanganate solution baths. The patient's history showed he had many partners but that he almost always used a condom, and that a little over month previously he noticed a small wound on his penis (glans), which he self-medicated with antibiotic cream. He also reported that at the time he had a "lump" on his groin, which was still present,

although much smaller. Serology was positive: VDRL 1:128. He also reported that before consulting us he had been to a health center, where he was prescribed penicillin benzathine. He refused the injection as the result of a painful experience he had when younger (for a dental abscess). We prescribed him with 1 g oral azithromycin per week for 3 weeks, which led to clinical and serological cure (a reduction of four titers in 6 months)



Fig. 2.59 Patients with accentuated syphilitic roseola. (\mathbf{a}, \mathbf{b}) are of the same patient. Note the ulcers that simulate genital herpes on the scrotum. (\mathbf{c}, \mathbf{d}) are taken of another patient, although the clinical presentation is almost identical to the patient in photos (\mathbf{a}, \mathbf{b}) . The two presented both syphilitic roseola and scabies. Both presented intense itching in

the genital area, causing a larger area of scarification. As well as being prescribed with specific medication for syphilis, the two patients received oral ivermectin (two 6 mg pills) for scabies, achieving clinical and serological cure for both



Fig. 2.59 (continued)





Fig. 2.60 (a–c) A young adult patient presenting intense erythematous papules across the whole tegument, characteristic of secondary syphilis. Paying closer attention, alterations to the tegument of the labia majora can be observed. Jarisch-Herxheimer reactions are much more commonly seen in patients with intense roseola, such as was seen in this case. When following cases like this, many physicians administer 4 mg/mL dexamethasone or an ampule of betamethasone 30 min before the first dose of treponemicidal (penicillin, erythromycin, doxycycline or azithromycin). This way, the symptoms of the reaction can be better controlled. However, one tablet of acetylsalicylic acid and an antiallergic, such as 10 mg of loratadine, are sufficient in order to control the situation. The patient must always be advised that a reaction can occur



Fig. 2.60 (continued)

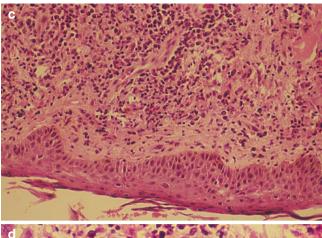


Fig. 2.61 Similar to the previous and following case: very intense syphilitic roseola





Fig. 2.62 (a, b) Another highly aggressive treponema in a patient with no indication of immunodeficiency. Serological testing for HIV was negative, although they presented high titers of antitreponemal antibodies. The patient initially had a differential diagnosis of other diseases, including leprosy, and had a cutaneous lesion biopsied. (c, d) Histopathology slides for a skin biopsy taken from a roseola. Note the preserved epidermis. There is an edema on the dermis with intense lymphocytic influx with vascular congestion. These are the alterations usually found in roseola. Where special techniques are available, spirochete bacteria can be observed



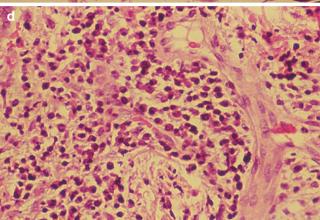


Fig. 2.62 (continued)



Fig. 2.63 The hands of a nurse assistant who worked in a private maternity ward in Rio de Janeiro in the 1970s. She reported using "medicinal" plant products, as she thought she had a problem with her liver. This is a classic case of a palmar syphilide at the exanthematous stage or secondary syphilis



Fig. 2.64 Syphilitic roseola on the forearm



Fig. 2.65 (a, b) Palmoplantar syphilides, a classic sign of early syphilis, at the exanthematous stage. Such roseola lesions to the trunk are a classic sign of early syphilis



b

Fig. 2.66 (a, b) Syphilitic roseola—also known as red skin blotches. These alterations undoubtedly are vascular, producing erythema. The blotches present as very red in white patients, but in darker-skinned patients they appear in a darker color due to their higher levels of melanin

Fig. 2.65 (continued)



Fig. 2.67 At first it would be easy to mistake this lesion for hard chancre. However, the patient presented other genital lesions as well as syphilitic roseola. Therefore, this is not hard chancre (initial lesion—inoculation chancre), but a more advanced stage of syphilis: exanthematous, particularly in the penile region, which can develop into an ulcer



Fig. 2.68 Male partner of a patient with a diagnosis of early syphilis who was treated at our clinic. He reported that 2 months previously he had a "wound" on his penis, which healed after 3 weeks of application of an antibiotic cream (cloramphenicol). Two weeks previously, he noticed some marks on his body. He sought help at a pharmacy and was recommended oral antihistamine medication. Examination showed that these were syphilitic roseola and that the genital lesions were also syphilitic and receding, as shown in the figure. The inguinal micropolyadenomegaly was bilateral, not inflamed and painless, as was the case for the cervical and axillary adenomegaly. The patient also presented scabies. Serology was positive for VDRL, 1:64, and negative for HIV



Fig. 2.69 This case is practically identical to the previous case, including in its serological testing. The difference was that this patient did not present scabies



Fig. 2.70 This patient presented some roseola to the trunk and also to the penis. VDRL was positive (1:64). Darkfield treponemal screening of a superficial shave biopsy of the lesion was negative. The sexual partner (fixed, not exclusive) was in the 32nd week of pregnancy and also presented positive serology. However, she did not have any mucocutaneous lesions. Penicillin G benzathine was prescribed, causing accentuated remission of the penile lesions 96 h after the first total dose of 2,400,000 IU (IM)



Fig. 2.71 Patient referred to the STD clinic at UFF presenting one ulcerative lesion to the penis (frenulum), accompanied by preputial edema. The base of the lesion was not hardened, as is typical of hard chancre. There was no syphilitic roseola to the tegument. Treponemal screening of a swab of the lesion was positive for some bacteria using darkfield silver impregnation (Fontana-Tribondeaux). Serology was positive: 1:64. The patient reported having multiple sexual partners and remembered that approximately 2 months previously he had a "wound" on his penis, which disappeared after he applied some wound healing powder that he had at home. As well as the penile lesion, the patient had a lump on his groin. This adenitis was present during our examination. Once again, the importance of taking a good patient history is evident



Fig. 2.72 Another case practically identical to the previous one, with the difference that this patient did not remember any previous genital lesions and was female. Note the discreet ulcerative lesion on the right labia majora and the large edema. We learned from the previous generation of our Brazilian colleagues that to facilitate finding T. pallidum in such lesions, you must pass a swab dipped in ether over the area for around 5 s. Wait 1 min and pass the swab dipped in saline solution. Wait another minute then carefully massage the base of the lesion without touching it directly, so as not to dirty the area with the talc on your gloves, bringing out the serous material. Collect it and perform treponemal screening. Perhaps the ether, by cooling down the lesion, facilitates the migration of treponema from the deeper layers of the lesion to the surface. It is known that T. pallidum is sensitive to heat and experiments have been conducted where lesions were produced more rapidly in rabbits when the skin was cooled using ice after being inoculated in the dermis. At first glance, adding a drop of sulfuric anther to the lesion seems to be cruel. It is not, however, as this is not very painful. The ether quickly reduces the temperature of the area, which practically eliminates all pain. In our experience we have never seen any irritation caused



Fig. 2.73 At first glance this looks like hard chancre or genital herpes. However, a doctor working at a STD clinic should never examine genital complaints alone. The penis in the image belongs to a patient referred to us because their partner presented vaginal discharge and lesions. Upon examination, the patient presented generalized adenomegaly and red blotches to the skin of the trunk. VDRL testing was positive (1:128)



Fig. 2.74 A patient in the second trimester of pregnancy referred for vulval lesions. Serology for syphilis had been requested and the results were still not available. Upon examination, ulcerative papules were easily visible on the vulva (a) and roseola on the skin of the buttocks and thighs (b). The *arrow* (c) shows the patient's advanced stage of pregnancy. The fast test for syphilis at the time of consultation was positive, as was treponemal screening of a superficial shave biopsy of the lesion on the labia majora



Fig. 2.75 A patient presenting areas of hyperemia across almost all of the vulva, from the start of the public region to the perineum. These were found more frequently in the folds and turned out to be early syphilitic lesions. Similar lesions were found on the skin of the trunk but were much smaller. Returning to Fig. 2.1 in this chapter: we need to think syphilitically. This way of thinking was positive. So was serological testing (VDRL 1:64). After an initial dose of 2,400,000 IU (IM) of penicillin, the condition involuted in 3 days



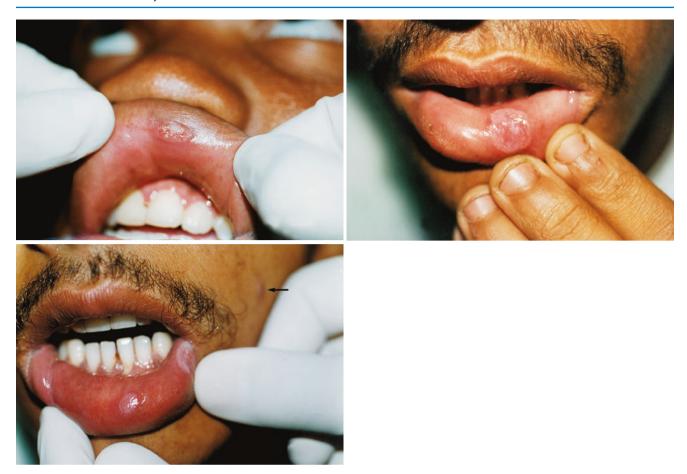
Fig. 2.76 In this case, syphilitic roseola was found on the skin of the vulva. A typical papular syphilide lesion can be observed on the bottom right of the photo



Fig. 2.77 In our experience, cases of syphilis can occur with a wide variety of appearances. Here a very strange lesion over a month old is presented, with edema to the labia majora and skin with the appearance of eczema. However, this patient did not complain of itching. If we take a closer look, there is an ulcerative lesion with an erythematous base on the vaginal fourchette. This was a case of early syphilis and not of an inoculation chancre



Fig. 2.78 Exanthematous stage of early syphilis (secondary phase) affecting the face. It is widely accepted that, although roseola may be infected with treponema, this does not have the power to infect. However, it should be noted that lesions on the buccal mucosa and gums do not have a corneal layer. Therefore, contamination may occur relatively easily during oral sex or kissing



Figs. 2.79-2.81 These images highlight the above. These are early syphilis exanthematous stage lesions in the mouth. Lesions of the labial commissures can be confused with canker sores and be medicated as

such. Syphilis is a systemic disease that normally starts on the genitals but that can simulate other pathologies. The *arrow* points to a roseola-like lesion on face skin

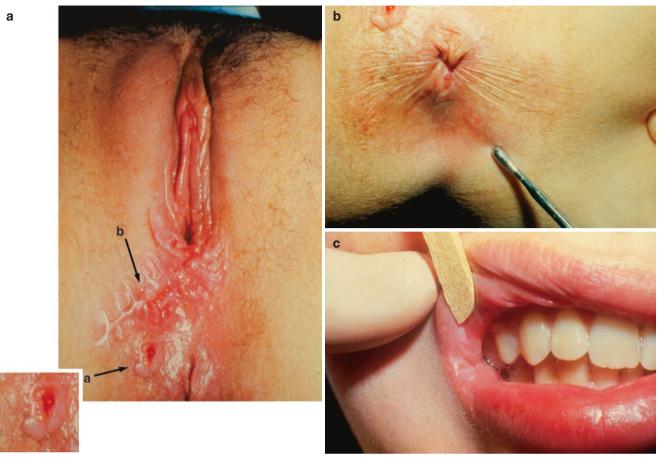


Fig. 2.82 (a) A patient from a high social class presenting an ulcerative papular lesion (a) just below the scar of a right mediolateral episiotomy (b) from a recent labor. These lesions were initially attributed to the wound not healing properly. In the close up we can observe the raised edges and a central erosion. (b) This patient also presented similar perianal lesions. (c) She was referred to a dentist experienced in STDs to treat the lesions on the labial commissure, and from the patients history of genital lesions and some red blotches on her body he correctly identified a possible diagnosis of syphilitic roseola. Serological testing for syphilis during the first prenatal consultation was negative. Her husband had sexual relations in a "sauna" during the second trimester of her pregnancy. Around 30 days later he discovered a single, hardened and painless ulcer accompanied by bilateral adenitis. He sought medical help and was prescribed penicillin benzathine, but he was not provided with any guidance, especially in relation to his partner. The husband did not mention anything to his wife or to her obstetrician. Since the latter had not been informed of any infidelity and saw them as a "high-level" couple, he did not carry out the usual routine

of requesting VDRL testing during the third trimester, but he reported that in the eighth month she presented intense vaginal discharge that improved with application of polyvalent cream. He did not carry out any microbiological tests on the secretions. This case illustrates a succession of errors very well: by the husband, the doctor that treated the penile ulcer, the gynecologist and even the neonatologist, who not having received recent tests from the mother must have gone through the normal routine. On the other hand, it demonstrates the wide knowledge of an orthodontist on systemic issues. In summary: the newborn was infected. The husband claimed that his behavior having relations with another partner and using condoms only when he was close to ejaculation was the result of a "childhood trauma". A sister of his had had two premature births because "she had a lot of sex during pregnancy". He claimed that he was very afraid that the same would happen to his wife, so he had avoided having sex with her during her pregnancy. With specialist medical help, the couple managed to get through this phase and stay together. Two years later, they had another child and maintained sexual relations during the pregnancy



Fig. 2.83 A patient who attended the STD clinic at UFF, referred by a professional on the Niterói Family Medical Program, presenting a typical case of exanthematous stage early syphilis, also known as secondary syphilis



Fig. 2.84 Palmar-plantar syphilis in a patient over 40 years old. He reported taking oral hypoallergenic medication to "treat" the lesions and applied hypoallergenic creams to the lesions



Fig. 2.85 A patient from a lower social class who came to the clinic complaining of vaginal discharge. Anamnesis and physical examination identified an inguinal adenomegaly, roseola and this lesion in the buccal cavity, also in the secondary stage of syphilis

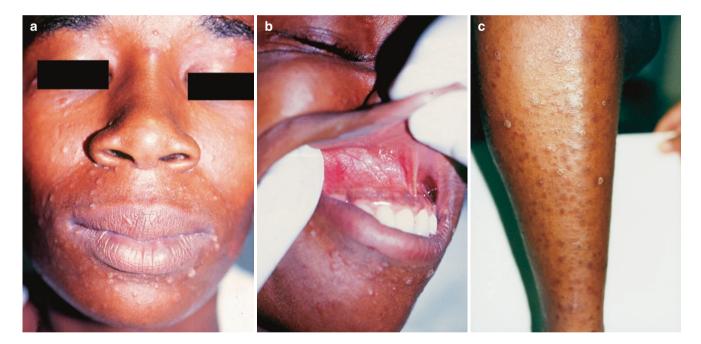


Fig. 2.86 (a–e) A patient who came to the clinic with a classic case of syphilis in the exanthematous stage, with lesions across practically all of the skin, including the mucosa of the buccal cavity. They had been prescribed an oral hypoallergenic and antiseptic soap. Screening for VDRL was positive and for HIV was negative. We emphasize that

investigations for syphilis should not be delayed in patients presenting these types of symptoms, especially when they have palmar and/or plantar lesions. Here is another patient lifting her upper lip to show a erythematous serpiginous snail track lesion, demonstrating secondary syphilis

Fig. 2.86 (continued)







Fig. 2.87 (a–c) Lesions of erosive papular syphilides on the labia majora and minor (right and left) of the vulva, as well as the lower lip of the mouth, representing alterations in the secondary phase of syphilis. If lesions are only found on the vulva and if the syndromic approach for STDs is used, in the case of genital ulcers it would be logical to also

prescribe medication for soft chancre. However, in our opinion the correct thing to do is to analyze the patient as a whole and perform a full physical exam. This way it will be much clearer if only syphilis is present. This benefits everybody, as unnecessary antibiotics will not be prescribed



Fig. 2.88 (a) A female patient with a white erythematous plate on the mucosa in the jugal region with an irregular periphery, clinical characteristics of a buccal lesion in the secondary stage of syphilis, confirmed by serological screening (VDRL and FTA-Abs). The partner presented



hard chancre on the penis and finger, the images of which can be observed in Fig. 2.89a and b. (b) The same patient in photo a; plates can also be observed on the lingual belly close to the edges





Fig. 2.89 (a) Image of the previous partner's penis of a patient, who presented an irregular ulcerative lesion on the balanopreputial groove, accompanied by inflammation of the inguinal lymph nodes. It was possible to collect material from the lesion and identify the presence of *Treponema pallidum* spirochetes, confirming a diagnosis of a primary syphilis hard chancre. (b) Image of the same patient's finger, on which an ulcerative lesion can be observed with hardened edges and inflam-

matory infiltrate. Material was collected from the ulcer and *Treponema* pallidum bacterial morphotypes were identified, confirming a diagnosis of hard chancre. It should be emphasized that the patient reported in his anamnesis the habit of inserting his finger into the anus of his partner during sex, who was now in the secondary phase of the disease. Therefore, the source of contamination was considered to be the woman, as he was only in the hard chancre phase

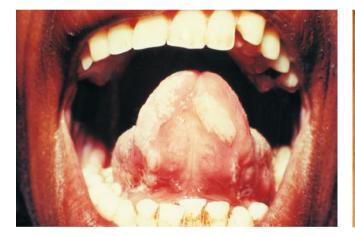


Fig. 2.90 Secondary syphilis mucosa plates in the lingual belly. These are papular-type syphilitic lesions



Fig. 2.92 Flat condyloma (papular syphilides) on the lower lip close to the labial commissure

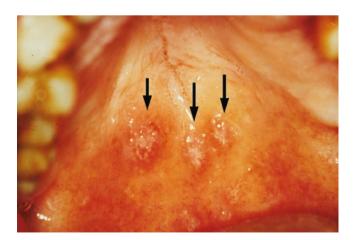


Fig. 2.91 Secondary syphilis lesions on the hard palate (see arrows)



Fig. 2.93 Exanthematous stage syphilitic lesion in the buccal cavity: ligual belly. On its own this lesion could easily be confused for herpes: this is a differential diagnosis. However, serology and roseola lesions on the skin help to confirm diagnosis in this case



Fig. 2.94 (a) This is a more typical case of papular syphilide—syphilitic flat condyloma—on the upper lip, labial commissure and a small part of the lower lip. (b) This is the same patient, but in this photo show-

ing lesions to the tongue. (c, d) The case was cured completely, and there was a decline in the titer value according to serology screening (from 1:128 to 1:4 in 6 months)



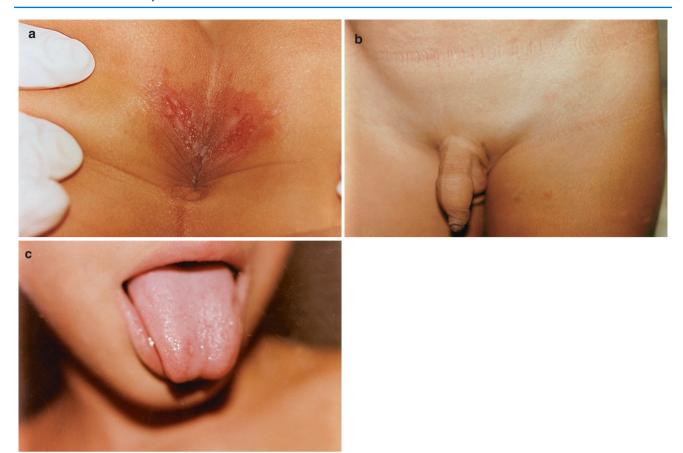
Fig. 2.95 Case of exanthematous stage syphilis in a 3 year old child, mainly effecting the genital area. According to the mother, she took the child to a health center twice, who was prescribed with local creams for rash. Although there were some lesions on the abdomen and thorax, these were not reported during the consultations. Not even the pediatrician completed the full examination of the child. Signs of sexual abuse were identified during our consultation. The patient was prescribed penicillin G benzathine. VDRL screening demonstrated levels of 1:64. This case was reported to the local Guardianship Council



Fig. 2.96 (a–e) Five-year-old child that was brought to us by her mother. Patient history: Around 1 week before the consultation she presented a lesion close to her vagina, with stinging and slight discharge. As the mother was a patient at the UFF STD clinic, she decided to take her daughter for a consultation. No medication had been used before the consultation. The mother reported completing prenatal screening, but there were no signs of VDRL when the child was born. Upon examination, the patient presented a macerated, moist and slightly painful lesion with undefined borders in the vulval region, typical of syphilitic flat condyloma. A bilateral inguinal adenomegaly was also present. The child's hymen was broken. VDRL screening was requested, which presented a titer value of 1:64. HIV screening was negative. Treatment with penicillin benzathine 1,200,000 IU (IM) was applied, repeated over two doses with an interval of 7 days. After treatment the patient showed clinical improvement and positive serological results, confirming cure. After an interview carried out at the clinic, the child reported having genital contact with a 15-year-old cousin, who according to her, had been going on "for a long time" and "close to the backyard". She was referred to the Child Neuropsychiatric Department at the Antonio Pedro University Hospital (HUAP) at UFF (Niterói) and to the São Gonçalo Guardianship Council. The probably abuser was "forgiven" by the family as long as he stayed away from the children of the house. (b, c) show the inguinal adenomegaly. (e) shows the rupture of the hymen



Fig. 2.96 (continued)



Figs. 2.97 and 2.98 (**a**, **b**, **c**) show the same patient: a male 6-year-old child taken to the STD clinic by his grandmother. The mother completed prenatal screening but did not present VDRL after birth. Patient history: Around 3 weeks before the consultation, the patient had a fever with a headache, which improved after taking a pediatric dipyrone suppository. (**a**) After approximately 3 days, a rash-like lesion to the perianal region appeared and then he was taken to a health center, where he was prescribed topical nystatin and advised to improve his hygiene in the genital and perianal area. (**b**) After 3 days of using the medication, blotches appeared all over his body along with adenomegaly in the inguinal region. Believing this to be an allergy, the grandmother contacted the emergency services, and an oral antihistamine was prescribed that did not lead to any improvement. As the boy had apparently suffered sexual abuse by a 19-year-old cousin, who presented similar lesions, an aunt recommended a visit to the STD clinic at UFF. Upon

examination, the boy presented oval erythematous macular lesions to the trunk, palms and oral cavity (c), including the tongue, characterizing syphilitic roseola. (a) In the perianal region there was a macerated, moist and painful lesion with undefined edges, typical of syphilitic flat condyloma. There was also a bilateral inguinal adenomegaly. VDRL screening was requested, which had a result of 1:64, and HIV screening was negative. Treatment of penicillin benzathine 1,200,000 IU (IM) was administered in two doses with an interval of 7 days. After treatment, the patient presented a clinical improvement and laboratory screening was positive, confirming cure. The boy was referred to the Child Neuropsychiatric Department at the Antonio Pedro University Hospital (HUAP) at UFF and to the São Gonçalo Guardianship Council. The patient's cousin was thrown out of the house by the family and moved to the middle of the state, where he was serving in the army at the time the patient returned

Fig. 2.99 Female 3-year-old child, born in Rio de Janeiro and resident in Itaboraí. She was brought in by her mother, referred by the proctology service. She had all the required vaccinations for her age and was born from a natural birth after prenatal screening without complication, and was allowed to leave the hospital within 48 h. VDRL screening after birth was negative. Previous patient history: The patient's mother did not report any previous illnesses. Updated patent history: The mother reported that 9 months before the consultation she visited the pediatrics department at a health center close to home, taking her daughter who complained of lesions to the vulva and perianal region. She was then referred by the pediatrician to the dermatology department. After consultation, a topical treatment with potassium permanganate baths were prescribed, using a cream containing ketoconazole and betamethasone dipropionate, and a urine exam was requested (abnormal elements and sediment analysis), which came back normal. The lesion was attributed to bad hygiene of the genital and perianal region. After around 15 days, returning to her doctor, the lesions on the vulva had disappeared but the perianal lesions remained, which was justified using reports of intestinal constipation by the patient. She was advised to continue taking the medicine and to increase the number of foods with laxative properties to her diet, such as papaya, prunes and orange with bagass. Since the problem worsened with the appearance of blood, the mother went to a gynecologist. She was recommended to keep administering the medication and tests were carried out with the following results. Urine: new abnormal elements and sediment analysis, without abnormalities. Blood: erythrocytes: 4:180.000 mm³; hemoglobin 12.1 g/dL; hematocrit 38%; global leukocytes: 7.450 mm³ with: myelocytes—0/metamyelocytes—0/band cells—4/segmented—41/ eosinophils—1/basophils—0/lymphocytes—50/monocytes—4; plate count—334.000 mm³. In summary, the exams were within normal limits for her age and gender. Homeopathic medication was prescribed, which corrected the constipation but did not heal the perianal lesion. After around 60 days of treatment, the constipation had not returned but the same initial complaint was present, so the mother went to a pediatrician again where a biopsy was taken of the condyloma acuminata, which was taken to another hospital. The mother went to a range of services and did not get seen, but in the end was seen by a proctologist. Treatment of topical podophyllin was prescribed, which did cause the lesion to heal after two cauterizations. She was then referred to the STD clinic at UFF. During clinical evaluation, a vegetative perianal lesion was observed, suggestive of syphilitic flat condyloma (photo). The child did not present adenomegalies or other symptoms or abnormalities. VDRL was requested, which presented titer levels of 1:128, and HIV screening was negative. Treatment was initiated with penicillin benzathine 600,000 IU (IM) and repeated after 1 week. Darkfield and silver impregnation analysis were negative. We believe that this was due to the manipulation of the lesion and the previous application of podophyllin, and to the fact that the mother had cleaned the child before bringing her to the consultation. When the second application of penicillin benzathine was administered, the patient already presented a significant improvement, and total cure was achieved after a month. New VDRL screening, carried out after 3 months, demonstrated a significant decline in titers, and was negative after 3 months. The child presented a history of sexual abuse by a neighbor, which was reported since the first consultation. The family were advised to go to the Children's Service in Itaboraí (there was no Guardianship Council in their neighborhood at the time of consultation) and the patient was referred to the Child Neuropsychiatric Department at the Antonio Pedro University Hospital (HUAP) at UFF. The supposed abuser appeared 6 months later as a result of a mandate issued by the Itaboraí police, not presenting symptoms upon clinical examination and with negative VDRL screening. He was head of the household where the patient lived and forced her to leave the house. These cases once again demonstrate the need to think of syphilis when examining any lesions/wounds on the genitals. Not doing this may delay the diagnosis of syphilis in many situations, especially in communities where there is a high incidence of the disease





Fig. 2.100 Three cases of early syphilis, papular syphilides and condyloma in children. (a) A 9-year-old male child, who 5 months before consultation at the Nossa Senhora da Glória Children's Hospital in Vitória, Espírito Santo, went to live with his father and 20-year-old cousin. It was not possible to prove that sexual abuse had taken place. The mother reported that she had been treated for syphilis during pregnancy. (b) A 5-year-old female, born by natural birth from a mother who had not carried out prenatal screening. Although not confirmed,

there was strong suspicion of sexual abuse. (c) Four-year-old child born by natural birth without prenatal testing. Vegetative papular lesions appeared 6 months before. Sexual abuse was not documented, although the alcoholic mother's sexual partner was physically aggressive. These cases demonstrate the difficulty in proving sexual abuse, as from the history of the disease and progression of the lesions, infection must have occurred a few months before the consultation and would not have been linked to the pregnancy or the absence of a prenatal consultation

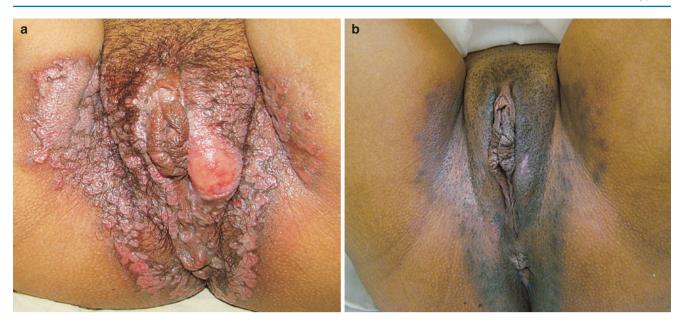


Fig. 2.101 Extensive papular syphilide lesions in a pregnant woman (a). In (b), 2 months after treatment with penicillin benzathine. These cases are often confused with condyloma acuminata (HPV)



Fig. 2.102 (a) A pregnant woman referred to our clinic for "problems in her intimate areas". Roseola can be observed on the buttocks and thighs. (b) As well as papular syphilides on the vulva, the patient also presented intense candida. However, the initial consultation was to

investigate a complaint of vaginal discharge with itching. Serological screening and examination of vaginal secretions confirmed a diagnosis of syphilis and candidal vulvovaginitis



Fig. 2.103 (a) A patient who complained of vaginal discharge. (b) However, during physical examination, it was observed that as well as leukorrhea (diagnosed as candida), she had syphilids on her vulva. These can often be confused with genital abrasions, due to the itching caused by mycotic infection. However, general analysis, inguinal ade-

nomegaly, and serological screening for syphilis lead to a more complete diagnosis. In such cases, the visualization of treponemes (by swabbing the lesions) is more complicated due to the intense infection of *Candida sp*.



Fig. 2.104 Papular syphilis in a multiparous woman in her fifties with a fixed and exclusive partner. The phrase "think syphilitically" must always be considered, mainly when faced with genital lesions and in populations with a high incidence of the disease



Fig. 2.105 (a) Papular syphilides in the genital area of a man. (b) These lesions often affect moist areas and folds. At this stage of syphilis, perianal lesions can often occur in individuals that do not report practicing anal sex



Fig. 2.106 (a) A man with a male partner presenting itchy ulcerative papular lesions on the anus and buttocks. He was using a polyvalent dermatological cream (antibiotic, antifungal, corticoid), which improved the lesions a little at first but which then worsened after a week. (b) Exposing the anus further, the papular syphilides can be

observed more easily. (c) As cited previously, sulphuric ether was applied with a swab to try to collect a high quantity of treponemes. This way, visualization can be much easier. This was a case of papular syphilis and scabies. HIV screening was positive and VDRL presented a titer value of 1:128



Fig. 2.107 Sometimes it is difficult to describe syphilitic lesions. These are syphilides on the glans, with a patient that presented a VDRL titer level of 1:64



Fig. 2.108 It is worth emphasizing: perianal lesions are not always caused by anal sex. This is a case of syphilitic flat condyloma in the initial stage. These lesions may have the highest levels of *Treponema pallidum*. These lesions are almost always moist and they always contain many spirochete bacteria



Fig. 2.109 Another case of perianal syphilitic flat condyloma. Roseola is not always simultaneously present in these cases. However, serological screening is usually positive. High titer levels are usually present. Such lesions are highly infectious. Therefore, the number of treponemes in these lesions is usually very high



Fig. 2.110 As well as erosive papular syphilids there was also vaginal discharge. The same presentation of syphilitic lesions is often found in the vagina, causing increased serosity. This causes vaginal discharge, which can be confused with vaginitis when the patient is not properly examined. Vaginal medications (creams, ointments, ovules and douches) cover the situation and also contribute to maceration of the vulvovaginal tissue. This causes further confusion doing clinical examination. The correct routine must be followed in order to obtain the correct diagnosis

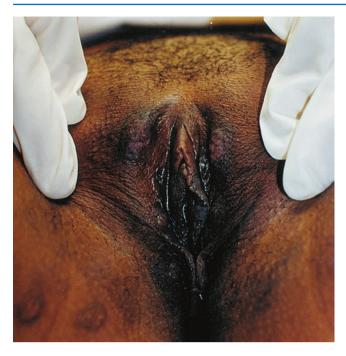


Fig. 2.111 Observe the erosive papular lesions on the upper labia majora and circinate lesions with hyperchromic edges on the buttocks and right thigh. These are early stage syphilids progressing into the latent phase



Fig. 2.112 Extensive erosive papular lesion starting bilaterally on the labia minora (close to the clitoris) and extending to the anus and part of the buttock. These are moist lesions with high levels of treponemes. This may be the most infectious phase of the disease. Observe the hyperemia—roseola on the skin of the buttocks



Fig. 2.113 Similar to the previous case. It may not appear so, but these are moist lesions: papular syphilides. Patients sometimes arrive for consultation after genital hygiene and using pads. This can make the lesion appear drier than it is



Fig. 2.114 Patient presenting vaginal discharge, identified as trichomoniasis + gonorrhea, intense acute bartholinite to the left and papular syphilides on the right labia majora and hemorrhoidal nipples. She self-medicated with mercurochrome solution. VDRL screening in 1981 presented a titer level of 1:64. In 1989, during a routine preventative visit, guidance on sexual health was given and samples were taken for new exams. VDRL screening presented a titer level of 1:2 and hepatitis B and HIV screening were positive



Fig. 2.115 As well as presenting yellow and bubbly vaginal discharge, ulcerative papular syphilides were present. Observe the elevated and shiny edges. At first this can be confused with initial stage syphilis



Fig. 2.116 Case of papular phase early syphilis (secondary for some). This photo taken 1 day after Bartholin gland marsupialization as a result of an abscess (on the right, observe the catgut sutures). The physician who performed this operation in the emergency room administered penicillin benzathine and referred them to our cynic for the appropriate follow up, including that of the sexual partner



Fig. 2.117 Early syphilis lesions in a highly infectious phase at various stages: papules and ulcers in the genital region of a woman who reported having a fixed exclusive partner, but with which she never used a condom



Fig. 2.118 Very similar to the previous case. A housewife over 50 years old with a case of vaginal trichomoniasis and genital syphilitic lesions. Observe in the close up the ulcerative papular lesion with a very red and raised center with a white surface in the pink-colored area—syphilitic flat condyloma. She reported having sexual relations without condoms with two partners. Both were consulted and both had penal lesions treated at health centers with penicillin benzathine. One was advised to advise his partners to go for check-ups. The other reported no other sexual activity with other partners in the previous 5 years. Neither presented active syphilitic lesions. Since she reported having sexual relations without a condom with two partners, we began conven-

tional treatment with both of them. Both presented a VDRL titer level of 1:8. One of them brought his other partner to the clinic. She only presented trichomoniasis, but VDRL screening presented a titer level of 1:32. She was then treated for both diseases. She referred another partner to the clinic. He did not have any lesions and serological testing was negative. He was advised to return in 30 days. The new exams were negative, as was screening for trichomonas in urinary sediment. We decided to simply follow the patient for syphilis. He reported always using a condom. All of the others received treatment for *Trichomonas vaginalis*



Fig. 2.119 Case of an early syphilis lesion on the foreskin. Palpation of the lesion demonstrated that is was hardened. It is possible to observe that there is edema. The patient also presented inguinal and cervical micropolyadenomegaly. He did not present roseola on the skin of the trunk. VDRL screening was positive with titer levels of 1:128. HIV screening was negative



Fig. 2.120 Early stage syphilis without hard chancre, with a very large syphilid on the shaft of the penis. By paying close attention, ulcerative lesions can be observed on the scrotum (see *arrows*)



Fig. 2.121 Another case of papular syphilide on the penis. Here it is possible to observe the inguinal adenitis with the help of the *arrow*



Fig. 2.122 Perianal papular lesion: intergluteal cleft of a female patient who attend the clinic for a routine preventative consultation. She reported that the previous month she had intense vaginal discharge and some "wounds" on her vulva. She sought medical help, and was treated with polyvalent vaginal cream and a single 500 mg dose of oral ciprofloxacin. There was a significant improvement, but she sought out our services to check. Observe that as well as the papular syphilide, she also presented a verrucous lesion nearby (see *arrow*). VDRL screening was positive with a titer level of 1:64, HIV screening was negative and histopathology of the verrucous lesion confirmed it was condyloma acuminata

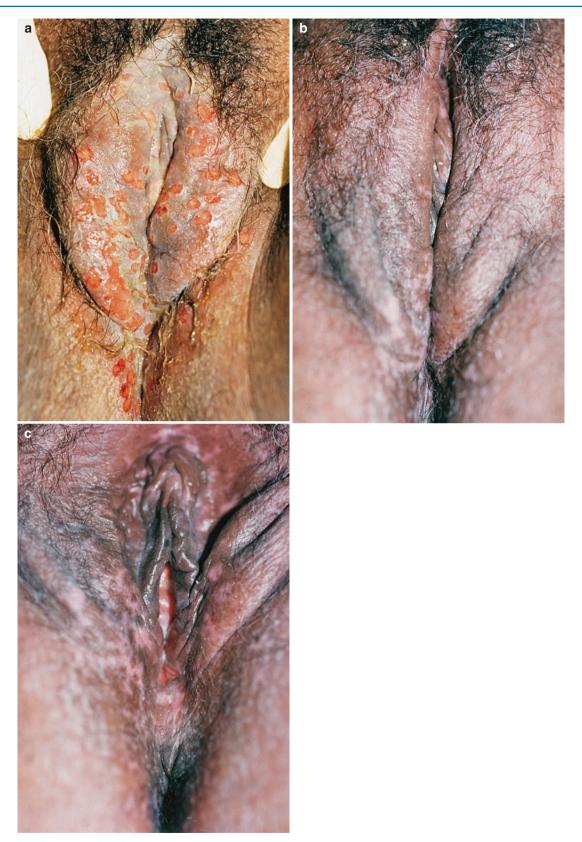


Fig. 2.123 (a) Diabetic patient in her sixties presenting these symptoms to her vulva. She reported having a fixed exclusive sexual partner (only one in the previous 20 years). She did not have itching or local pain. She presented bilateral inguinal micropolyadenomegaly that was not inflamed and with very little pain. Direct microscopy using the Gram staining technique on swabs of the lesions revealed a mixed microbiota. Direct examination and fungal cultures were negative.

Cytopathic effect screening for herpes was negative. Darkfield screening showed the lesion was rich in spirochete bacteria typical of *Treponema pallidum*. VDRL screening was positive presenting a titer level of 1:64. (**b**, **c**) Observe the complete remission of syphilitic symptoms after administration of penicillin G benzathine. The partner was examined and presented syphilitic lesions on the penis (flat condyloma)



Fig. 2.124 Adolescent with a history of sexual abuse presenting vegetative papular lesions, which could be confused with condyloma acuminata. It is important to remember that at this stage it is common for the patient to also present roseola. In this case the patient presented very discrete hyperpigmented roseola lesions in the palmoplantar region. *Treponema pallidum* screening using a darkfield microscope was positive, as was VDRL screening, which presented a titer level of 1:512

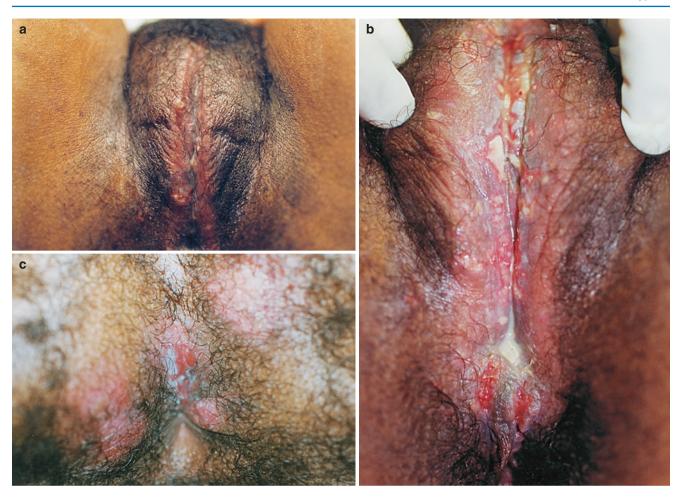


Fig. 2.125 (a) Patient over 40 years old referred to confirm diagnosis of genital lesions noticed 2 weeks previously. Without separating the labia majora and minora, these are not easy to see. (b) Exposing the vulva further, ulcerative papular lesions can be observed with macer-

ated areas and yellow-white secretions. Direct examination was positive for treponema and fungus. VDRL screening presented a titer level of 1:64. (c) The same lesions in the perianal region



Fig. 2.126 (a, b) Adolescent referred to the clinic presenting these symptoms that he had been experiencing for over 3 weeks. He was previously medicated with an analgesic/antipyretic and a single dose of quinolone. There was practically no improvement. Upon clinical examination, we noted a pungent odor (not fetid but rather disagreeable), found in some cases of papular syphilide and flat condyloma, and we

noticed very pronounced papules on the foreskin. As symptoms were very intense and advanced, we requested cytology of a swab of the lesion, biopsy of a discrete fragment and the usual bacteriological and serological screening. A positive diagnosis of syphilis was confirmed via direct examination and serology

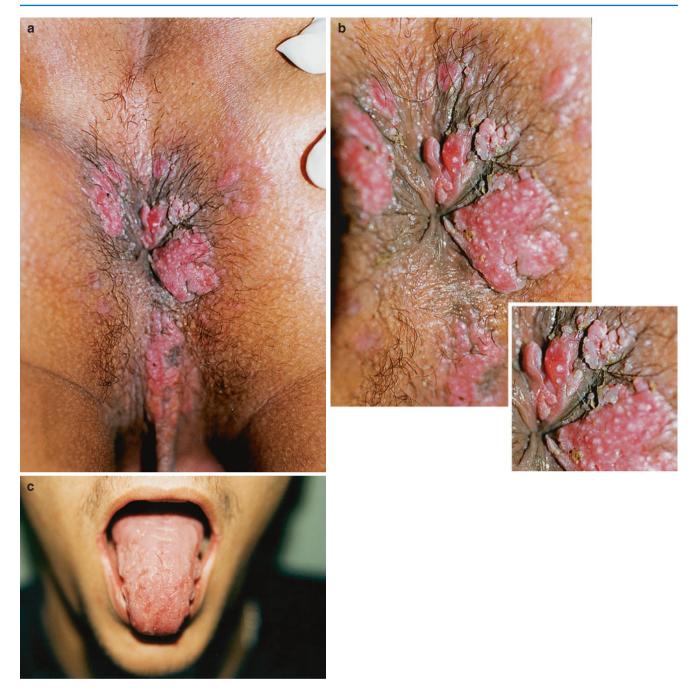


Fig. 2.127 (**a**, **b**) Homeless adolescent with multiple sexual partners and many experiences being raped by other "street kids", presenting syphilitic flat condyloma. Observe in the close up that some of the lesions have an eggshell-type appearance, which suggests infection with HPV (condyloma acuminata). However, there were just syphilids. We do not have a technical explanation, but many patients with syphi-

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litic flat condyloma stage lesions present a characteristically pungent odor, which is not fetid and is different to all the other odors that we know of. Once experienced, this smell is easily identified as characteristic of flat condyloma or condyloma latum. (c) As well as perianal and perineal symptoms, the patient presented exanthematous stage lesions on the tongue and roseola on the skin of the trunk





Fig. 2.128 (a, f) Pregnant adolescent in the second trimester, referred to our clinic for treatment of genital condyloma acuminata. Two rounds of VDRL screening were negative. Upon physical examination, the pungent odor was noticed, which we believe is typical of syphilitic infection: flat condyloma or condyloma latum. Both darkfield and silver impregnation (Fontana-Tribondeaux) direct microscopy showed a high quantity of treponemes. VDRL screening with pure serum (1:1) was negative. It was also negative with titers of 1:2 and 1:4. Only with a dilution of 1:8 was a positive result obtained, which went up to a titer value of 1:2.048. This pattern characterizes the prozone effect, which signifies an excess of antibodies in relation to antigens during the exam. If the serum is not diluted, test results will be negative. There is such a large amount of antibodies that the test will be negative when using pure serum. It is currently normal practice in laboratory analyses to use pure serum in VDRL screening together with dilutions of 1:4 or 1:8 in order to catch this phenomenon, which takes place in approximately 1-2% of cases. In our experience, the prozone effect occurs in cases of papular syphilides. It is important that laboratories follow routines and guidelines for every exam. It is also important that clinics report their diagnostic hypotheses in their exam requests. Observe that some lesions really do look like HPV lesions (Fig. 2.128c). However, the mucous plates, and mainly those of the labia minora, are typical of syphilids. (f) The patient was administered 1 g of oral azithromycin per week for 3

weeks. A rapid cure was confirmed clinically and via microbiological and serological screening. Our choice of azithromycin was due to lack of penicillin G benzathine at the time. During labor, VDRL screening of presented a titer value of 1:32 for the mother and 1:2 for the child. These two exams were carried out at the maternity unit. One month later, VDRL screening of the mother still presented a titer value of 1:32, and the result for the child was negative. At the time it was possible to carry out FTA-Abs IgM screening for the child, and the results of this were negative. No problems were found with the child during routine neonatal clinical examination up to at least 3 months after birth. However, the standard routine for such cases, which is treatment of the pregnant woman with a drug other than penicillin, was carried out with the newborn. There are many cases that appear to be condyloma acuminata (HPV) that are actually syphilitic flat condyloma. This is the same regarding the prozone phenomenon in serological screening. (g, g1) Case of a pregnant woman with flat condyloma who also presented the prozone phenomenon in serological screening. (h) This presents a case of syphilitic flat condyloma referred to an STD clinic (Fortaleza, Ceará) for treatment of extensive condylomatosis caused by HPV. This was a man with a male partner who presented lesions around 3 weeks previously. Direct darkfield microscopy was positive. The prozone effect was also present and VDRL screening presented a titer value of 1:512. HIV screening was negative



Fig. 2.128 (continued)



Fig. 2.128 (continued)

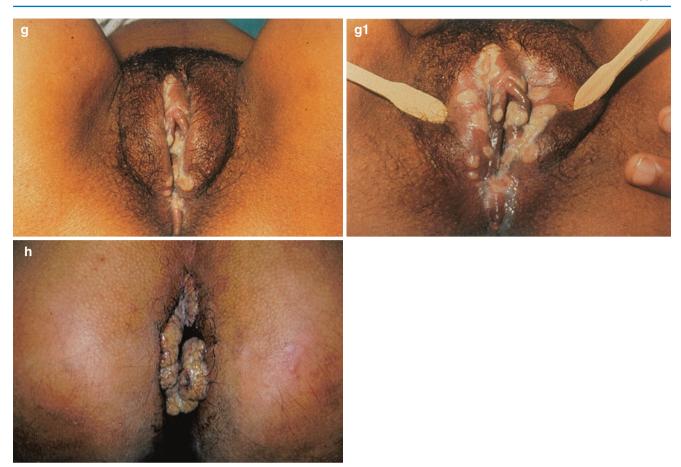


Fig. 2.128 (continued)



Fig. 2.129 (a) A patient who sought treatment for wounds on his penis. He presented various papules with elevated edges and a erythematous base. He also had edematous foreskin. (b) During general examination, we noticed vegetative papular lesions in his underarm and some roseola on his trunk. There was a lesion on the left side close to the underarm, but this looked like a gumma. (c, d) There was a moist papular lesion in the interdigital region of the left foot and on the right hal-

lux. Darkfield microscopy was positive for spirochetes typical of T. pallidum in all lesions (penis, underarm and toes). VDRL screening was positive with a titer value of 1:256. HIV screening was negative. (e) Atrophy of distal third of the eyebrow, Fournier's sign, which can occur at the end of clinical manifestations of early syphilis. Note the flat condyloma on the perineum and the scrotum (\mathbf{f} , \mathbf{g}). In (\mathbf{h}), we can see that complete cure was achieved after treatment



Fig. 2.129 (continued)



Fig. 2.130 Early syphilis lesions—papular stage in a patient who was referred to confirm a diagnosis of genital herpes



Fig. 2.131 Patient referred for peniscopy after his partner presented oncotic colpocytology typical of HPV, cervical intraepithelial neoplasia. Here we caught a case of papular syphilide. Initial VDRL screening (which the patient brought with him) was negative. This was another case of the prozone effect. New VDRL screening with a request for initial dilution revealed a positive result with a titer value of 1:1.024. There were no typical lesions or any suspicion of infection with HPV. His fixed but not exclusive parter was examined by us and did not present HPV. Colpocytology was repeated with a result of unspecific inflammation. Serological screening for syphilis was positive with a titer value of 1:32

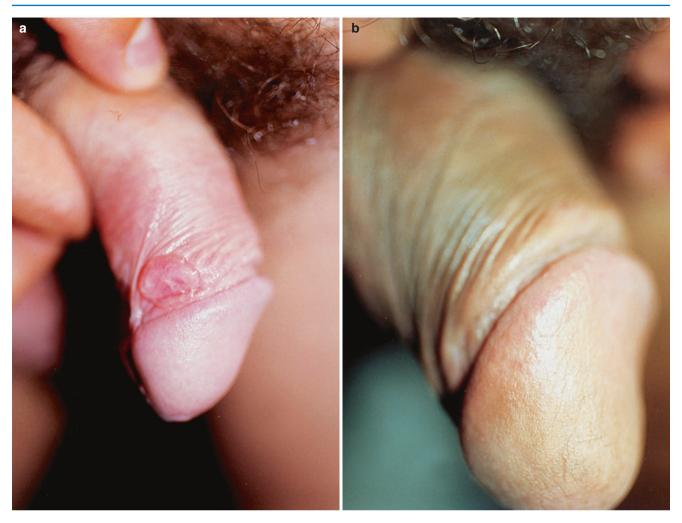


Fig. 2.132 (a) An adolescent with papular syphilide. In (b), cured after administration of oral azithromycin. The interesting thing about this case was that we performed clinical and serological examinations

on two friends of this patient who had sexual relations with the same two people in the previous 60 days, and these did not present any symptoms of syphilis





Fig. 2.133 (a, b) Pregnant woman attended in a private clinic (through her health insurance) with negative VDRL screening (which she brought to the consultation). She had a clinical history of hypersensitivity to penicillin. This is another example of the prozone effect. The patient was being treated by a colleague who did not think these lesions were syphilitic, mainly because it was a private clinic. In reality, these symptoms are much more frequently seen in the public health service; however, the phrase: "Any genital lesion has a chance of over 90% of being syphilis; we need to think syphilitically" must not just be used for lower class patients, especially in countries with high incidences of syphilis. We observe a lot of cases of the prozone effect, as we receive a lot of cases. Our experience is statistically "flawed", as we receive a lot of referrals. In general, these are rare cases. But it is important to remember that this occurs more at the papular syphilide stage



Fig. 2.134 (a, b) A patient with multiple papular roseola lesions to the external genitalia and adjacent skin that had been present for over a month. She had applied bandages to some of these, as can be seen with the white marks left by the bandages on the inner right thigh. Examination of the cervix using a speculum revealed vascular congestion in both lips with areas of leukoplakic plates. Treponemal screening was positive for the lesions on the vulva and the swab taken from the uterus. This was a case of papular stage early syphilis. In isolation, the lesion on the cervix could easily be diagnosed as HPV. However, as patients must be seen as a whole, together with the clinical history and examinations, a diagnosis of syphilis is clear. The lesions on the vulva could also be confused with soft chancre. Simple exams, such as microscopy using the Gram staining technique, darkfield screening and serology for syphilis should not be excluded from the normal routine for ulcerative, macerated and papular lesions to the genitals. There was a case of syphilis in a pregnant woman who had delayed diagnosis as initial VDRL screening was negative. The patient had a history of "allergy to penicillin" and said that she would not take this antibiotic. Neither then nor now do we have the means to find specialists to perform desensitization so that penicillin can be used (the best antibiotic for the treatment of syphilis). She was medicated with 1 g of azithromycin per week for 3 weeks, with cure being confirmed clinically and through serological screening. During labor, serology for the mother was 1:4 and negative for the newborn. After 1 month, both serological tests were repeated and the results were the same. Routine neonatal clinical examination did not detect any problems with the child up to 1 month after birth. Radiography exams were also normal. The child received regular treatment of penicillin immediately after birth. The sexual partner was not examined, as he had died a month before we consulted the patient



C

Fig. 2.134 (continued)

Fig. 2.135 (continued)







Fig. 2.136 A typical syphilitic flat condyloma. Some years ago, syndromic approach for STDs was very common in public health. This led to the fast treatment of many patients. However, it also led to many errors and the incorrect use of antibiotics. The common idea that syphilitic lesions are always ulcerative lesions should also be criticized. For a long time we have known that the lesions associated with syphilis are known for their multivariate character. In our opinion, syphilis is the great chameleon of medicine. Syphilitic ulcers should never be thought of as simply genital ulcers. Genital lesions come in many different forms. In our experience, we diagnose many more cases of syphilis that do not have the traditional label of genital ulcers. Health teams must be aware of the multiple clinical presentations that syphilis can take

Fig. 2.135 (a) A patient with a classic case of syphilitic flat condyloma. (b) During follow up of treatment with penicillin benzathine, we observed that between the syphilitic flat condyloma lesions there was a vegetative verrucous condyloma acuminata (HPV) lesion. (c) Here we can observe cure of both pathologies. Observe the image of the condyloma acuminata in the close up with the *arrows*



Fig. 2.137 Papular syphilide, syphilitic flat condyloma, in the vulva and perineal and perianal regions. Note the nodules on the labia majora and dermatomycosis around the perineal and anal lesions



Fig. 2.138 Papular syphilide (condyloma lata) in a 14-year-old patient. These symptoms could be easily confused with viral condyloma caused by HPV



Fig. 2.139 This seems to be a copy of the case in Fig. 2.134; early syphilitic ulcerative papular lesions



Fig. 2.140 Young patient presenting multiple papular lesions to the genitalia, some with the formation of plates. The lesions are located in the perianal region. It is important to remember that these are highly infectious lesions and easily confused with HPV



Fig. 2.141 Young patient presenting multiple lesions with superficial ulceration, located on the caudal part of the vulva, perineal region and intergluteal cleft. These lesions are commonly found in moist and folded regions. These are papular lesions, but they seem ulcerative as they are located in an area of friction. Sometimes, and as seen in many of the above cases, these can become macerated



Fig. 2.142 (a–k) A young HIV-positive patient who was not taking any antiviral medication, with a HIV-positive partner, presenting ulcerative papular lesions on his external genitalia, palmoplantar papular erythematous scaly lesions and Fournier's sign on his eyebrow. VDRL screening was positive with a titer value of 1:512. He reported a history of hypersensitivity to penicillin, and he was carrying a medical report relating edema of the glottis and eyelids and extensive erythematous plates on his skin after a skin test with dilute crystalline penicillin. He was given supervised therapy and 1 g oral azithromycin per week for 4

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weeks. Clinical cure was achieved very quickly. Serological screening was carried out at the normal time and a reduction of four titers was observed after 6 months. He was advised to have follow-up checks for retroviral infection as his partner also presented a high titer value. The patient also presented vaginal trichomoniasis, which was treated with metronidazole. This case, which we received in 1995, was our first experience using azithromycin for the treatment of syphilis when penicillin G benzathine could not be used



Fig. 2.142 (continued)



Fig. 2.142 (continued)





Fig. 2.143 (**a**, **b**) Pregnant patient presenting an extensive vulvar lesion in a bilateral papular plate, with ulceration on the caudal part of the labia majora and the perianal area. The ulcer was extensive, as shown in the image, with raised edges and base without purulent secretions. In this case, it wasn't possible to carry out darkfield microscopy. The Gram staining technique and biopsy were unspecific. VDRL screening was positive with a titer value of 1:16. As it was a confirmed case of syphilis, medication was administered. Cure was confirmed clinically and by serological screening in the usual time





Fig. 2.144 (a) A married patient of 28 years, referred from the Ceará Blood Bank (he went to donate blood and found out he had a disease) to the STD clinic at the Federal University of Ceará's University Hospital with VDRL results of 1:256 and a positive FTA-Abs exam. He had suffered from fever, myalgia and papular lesions all over his body for 3 weeks. He believed that the lesions could have been caught through sexual contact with a sex professional 3 months previously. His wife was invited to the clinic and her VDRL screening was positive with a titer value of 1:32, but she had no signs or symptoms of early syphilis. This was a case of latent early syphilis. Both were treated with penicillin G benzathine. We could not treat the other partner, although we did try. (b) A week after initial therapy, the dermatological lesions receded. However, the patient reported that around 4 h after the initial dose of penicillin he suffered from fever, headache and pain throughout his body, which subsided with 500 mg of oral dipyrone (Jarisch-Herxheimer reaction). This reaction is mainly observed in more symptomatic patients and/or those with elevated serological results, and generally occurs in the first 24 h after initiation of therapy for syphilis with any antibiotic that acts against treponema. This reaction does not occur with other uses of this medication. It is important to advise the patient in advance that this reaction may occur and to recommend therapy with analgesics/antipyretics so that the treatment with antibiotics is not completely abandoned. In many cases, the patient interrupts treatment thinking that they have an allergy. Unfortunately, some physicians think in a similar way

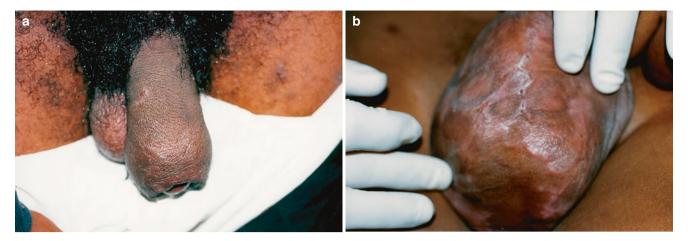


Fig. 2.145 (**a**, **b**) A patient without genital ulcers or papules, but with lesions on his penis and scrotum, surrounded by hyperchromic edges and a slightly hyperchromic center. He also presented some roseola-

type lesions on the skin of the abdomen and inner thigh, as shown in Fig. 2.145a. VDRL screening was positive with a titer value of 1:64



Fig. 2.146 (a–c) Similar to the previous case, but here the edges are more pink and the centers of the surrounding lesions are hyperpigmented (or the same color as the patient). He also presented ulcerative

papular lesions on the foreskin, which although relatively old, facilitate secondary infection. These are manifestations of secondary stage early syphilis



Fig. 2.147 Syphilitic alopecia in a 55-year-old woman, reporting not having had sexual relations for over 5 years. Examination of the external genitalia did not demonstrate any infection. VDRL screening presented a titer value of 1:16. This was treated as a case of syphilis over a year old (late syphilis), as we could not guess the period of development of the disease in this patient



Fig. 2.148 Patchy alopecia in a patient with syphilis. As mentioned above, we must always think syphilitically, especially in areas with a high incidence of the disease, and in young adults complaining of alopecia



Fig. 2.149 Syphilitic alopecia in a young adult who reported having a wound on his penis exactly 8 months previously, which was hardened and like "chewing gum", accompanied by "lumps" on his groin. He sought help from a pharmacist assistant, who recommended tetracycline. As he did not have money at the time, he took just four pills. As the lesion receded after 4 weeks, he thought he was cured. However, he remembered that the adenomegaly, although it was reduced, was still present. VDRL screening presented a titer value of 1:16. Despite this, we decided to treat him for syphilis of unknown duration



Fig. 2.150 An adolescent with patchy alopecia, characteristic of secondary stage early syphilis

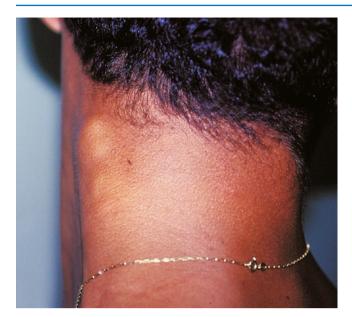


Fig. 2.151 Prominent cervical lymphadenopathy in a patient with secondary stage early syphilis. In rare cases this may be the only clinical expression of syphilis, and mainly in alcoholics. In our opinion, serological screening for syphilis should be routine and almost all initial consultations in sexually active or previously active patients. In such cases, it is common for serological results to be positive with low titers (up to 1:8)



Fig. 2.153 Annular syphilid: secondary stage early syphilis lesions found around natural orifices

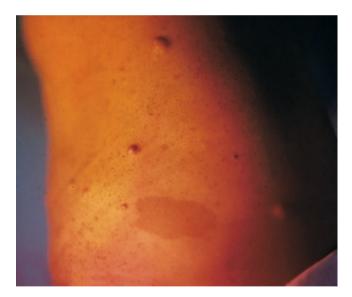


Fig. 2.152 Using the practice described in the previous case, it was possible to diagnose and treat these subcutaneous nodules as symptoms of the final stage of early syphilis. These clinical presentations can be very varied, from loosening of the nails to peripheral neuritis, covering the symptoms of hepatitis, nephritis and arthritis. It is important to remember that syphilis is the great chameleon of medicine



Fig. 2.154 Dermatological symptoms described as elegant syphilids or relapse syphilids. These are hyperchromic lesions surrounding the natural orifices of melanodermic individuals. Many specialists see these lesions as highly typical of syphilis

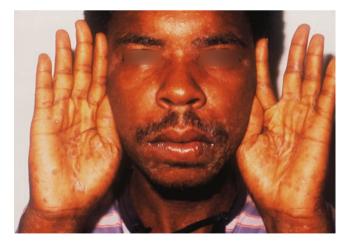


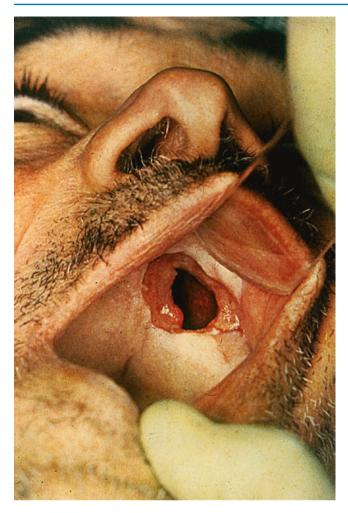
Fig. 2.155 This patient, as well as presenting lesions around his mouth, presented palmar syphilids



Fig. 2.156 Elegant syphilid (relapse) in the nostrils. Although described as highly-populated, the discovery of treponemes in these lesions is very difficult using darkfield or silver staining techniques, even using histological techniques. We do not have any experience with this, nor have we heard any reports from other specialists, but better results can be obtained if PCR techniques are used to find bacteria

HISTÓRIA NATURAL DA SÍFILIS	
ESTUDO DE OSLO DA SÍFILIS NÃO TRATADA	
BOECK-BRUUSGRAARD-GJESLAND (1891-1910-1929-1955)	
ESTUDO DE TUSKEGEE-ALABAMA U.S.A.	
ROCKWELL et al. (1932-1964)	
SÍFILIS TARDIA CUTÂNEA OU OUTRAS	15,8%
CARDIOVASCULAR	10,4%
NEUROSSÍFILIS	6,6%
ÓBITO POR SÍFILIS	10,8%
TOTAL	43,6%
SEM MANIFESTAÇÕES OU CURADOS	56,4%

Fig. 2.157 We have included this case to emphasize what can happen when a patient does not have their syphilis adequately treated. For a better understanding of this theme, we recommend the film "Miss Evers' Boys" on the US Public Health Service-sponsored "Tuskegee Syphilis Experiment", which describes the cases of black, male adults that have received syphilis diagnosis but have not received specific antibiotic medication, just a placebo. This and many other studies serve as a basis to discuss questions of ethics and research. However, as happens all over the world, we must pay attention to the period during which these events took place. Today we have clearly defined regulations that need to be adapted according to scientific and social progress. The film shows the standpoints of both those who wanted to continue with the study and those who wanted to interrupt it. During a ceremony at the White House in 1996, the president at the time, Bill Clinton, formally asked for forgiveness on behalf of the American people to nine survivors of the study. More recently, similar studies involving STDs were discovered and President Obama asked for forgiveness for these ethically unacceptable studies



 $\begin{tabular}{ll} \textbf{Fig. 2.158} & Late symbols lesion with a gumma perforating the hard palate \\ \end{tabular}$

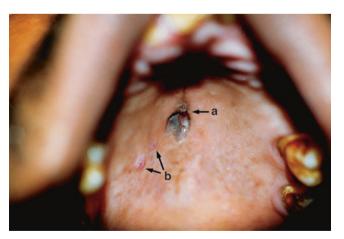


Fig. 2.159 Another late syphilis lesion perforating the hard palate (*a*). The *arrows* (*b*) indicate the lesion, which biopsy confirmed as another clinical hypothesis: condyloma acuminata associated with syphilis



Fig. 2.160 Perforation of the hard palate as a result of syphilitic gumma



Fig. 2.161 Male 53-year-old patient in the third stage of syphilis, presenting a destructive ulcerative lesion perforating the anterior region of the midline of the palate and provoking bucconasal communication as a consequence

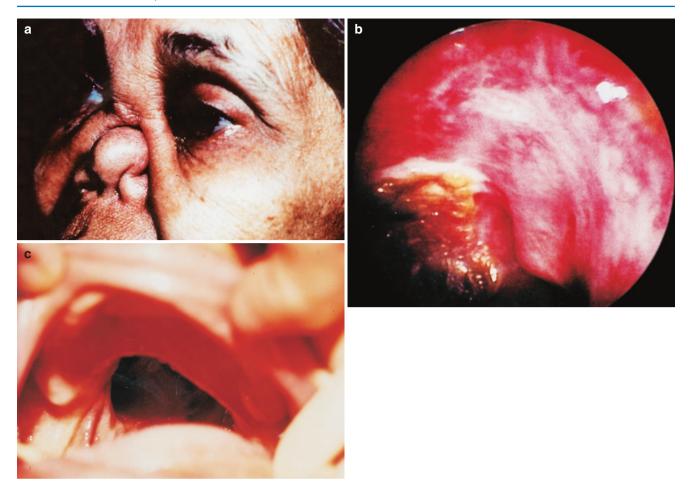


Fig. 2.162 (a) Clinical appearance of a patient presenting destruction of the turbinates and the bony septum and cartilage of the nose due to a tertiary-stage syphilitic gumma-type lesion. (b) Fiberoptic endoscopy image in which it is possible to observe the syphilitic gumma in the

oropharynx of the patient described in Fig. 2.162a. (c) Intraoral image of the area of tissue loss as a result of tertiary syphilis in the previous patient after treatment

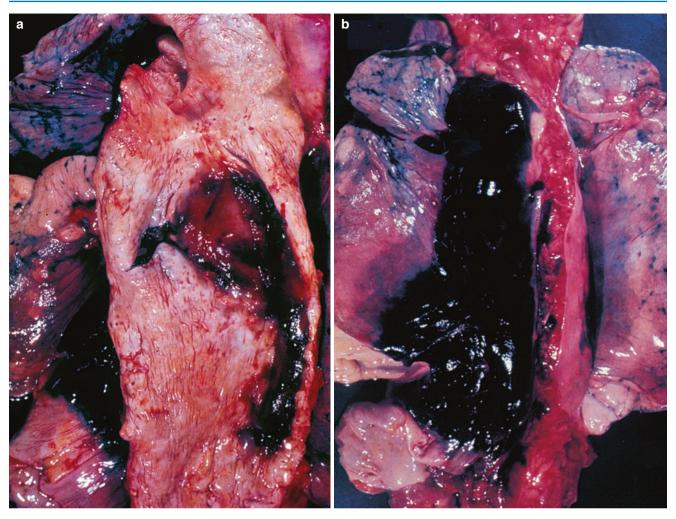


Fig. 2.163 (a, b) Pieces from the autopsy of a patient attended in an emergency clinic with symptoms of hemothorax caused by the rupture of a very large aortic aneurysm. From histopathological examination and the patient's clinical history, it was concluded that the basic cause

was a chronic syphilitic infection. As is the case for aortic aneurysm, cerebral aneurysm is reported in areas with a high incidence of syphilis, although mainly in young adults and of rare occurrence



Fig. 2.164 Macerated stillborn of a mother with exanthematous stage early syphilis, interned in a maternity ward in a city on the countryside of Rio de Janeiro State in 1978 as her unborn child had died in utero during the second trimester of her pregnancy. VDRL screening had not been carried out, even after two prenatal consultations. This was not even carried out when she was interned in the maternity ward. Even today in 2011 it is not rare to see this kind of situation

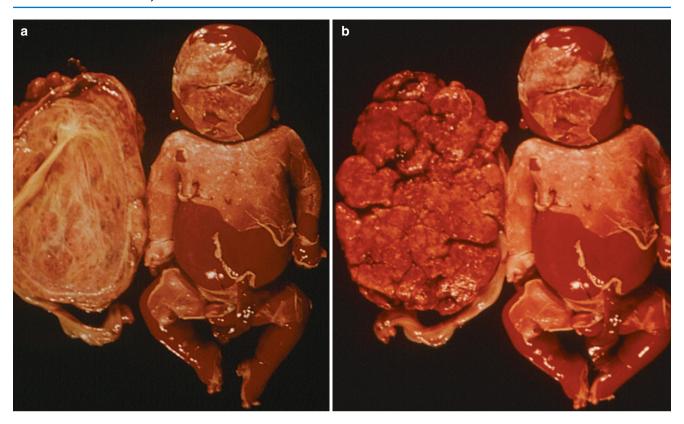


Fig. 2.165 (a) Placenta—fetal side: opalescence in the chronic vessels. Macerated fetus. Congenital syphilis. (b) Placenta—maternal side: increased volume and swollen. Macerated fetus. Congenital syphilis

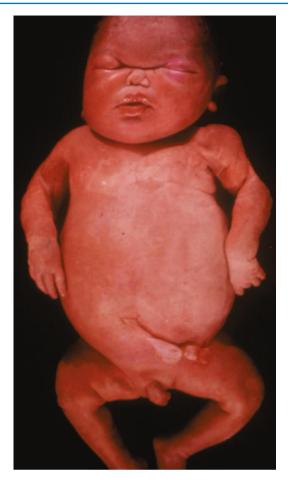


Fig. 2.166 Newborn presenting anasarca and abdominal distention. Congenital syphilis



Fig. 2.167 Newborn with congenital syphilis presenting pale skin and anasarca. Accentuated facial and scrotal edema

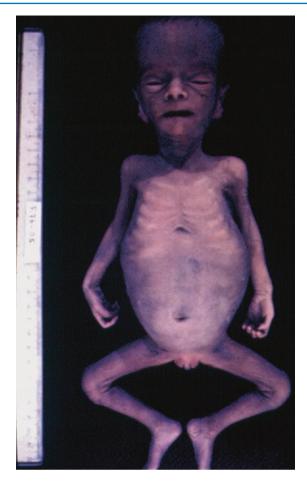


Fig. 2.168 Infant. Dystrophy—accentuated reduction in stature (congenital syphilis)



Fig. 2.169 Upper limb of a newborn. Ruptured blister in the palmar region (congenital syphilis). These lesions are generally infected with T. pallidum



Fig. 2.170 Hands—Ruptured and intact blisters on the back (congenital syphilis)



Fig. 2.171 Feet—Ruptured and intact blisters in the plantar region. These lesions are generally rich in treponemes (congenital syphilis)



Fig. 2.172 Lower limbs. Various blisters on the backs of the feet



Fig. 2.173 Newborn—back and gluteal region with hyperchromic erythematous lesions caused by congenital syphilis

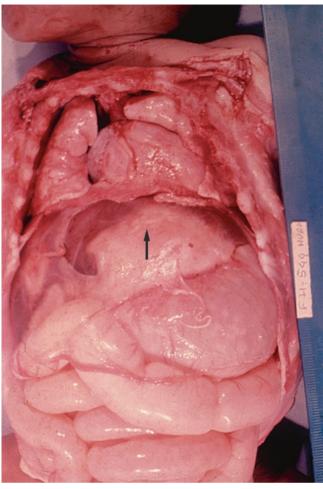


Fig. 2.174 Thoracoabdominal cavity—hepatomegaly in a child with congenital syphilis: liver presenting a highly defined white area (gumma), highlighted with the *arrow*



Fig. 2.175 The lung of a child with congenital syphilis—cut surface: whitish nodular area (gumma)



Fig. 2.176 Adolescent patient presenting saddle nose, one of the sequelae associated with late congenital syphilis. Patients generally present chronic syphilitic rhinitis, which destroys the nasal septum and causes the roof of the nose to collapse. This shape mimics the shape of a saddle, which is why it is referred to as saddle nose. It is important to

remember that in these cases, the newborns were born infected and were neither diagnosed or treated, causing the disease to progress. Another factor to highlight regards rhinitis itself: these lesions are populated with treponemes



Fig. 2.177 Sequela caused by late congenital syphilis: Hutchinson's teeth



Fig. 2.178 Another example of Hutchinson's teeth



Fig. 2.179 Upper and lower middle incisors shaped in the form of the head of a screwdriver, known as Hutchinson's teeth and characteristic of congenital syphilis



Fig. 2.180 First permanent molar in the shape of a mulberry, known as Fournier's molar. This hypoplasia is a result of congenital syphilis

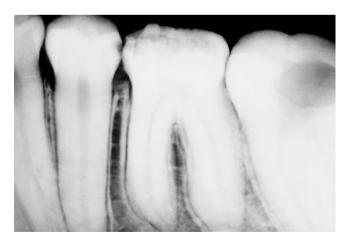


Fig. 2.181 Dental radiography showing its globular appearance, similar to a mulberry, observed on the occlusal side of a first molar. Caused by congenital syphilis



Fig. 2.182 Bone—femur: irregularity of the epiphyseal line, thickened periosteum and an area of necrosis (gumma) in the marrow



Fig. 2.183 Periapical dental radiography showing its globular appearance (see *arrows*) similar to a mulberry, observed on the occlusal side of a first permanent molar, characterizing dental hypoplasia as a result of congenital syphilis. Observe that the crown and the roots are smaller than the second molar, which characterizes a dental anomaly and is contrary to normal morphological dimensions



Fig. 2.184 Two specimens of first permanent molars demonstrating morphological alterations giving the occlusal area a globular appearance similar to a mulberry, characteristic of congenital syphilis



Fig. 2.185 Newborn. Saddle nose and olympian forehead



Fig. 2.186 Radiography of symptoms to the bone associated with congenital syphilis as a result of periositis and osteochondritis



Fig. 2.187 Congenital syphilis in a stillborn. Discharge must be very rare in these cases

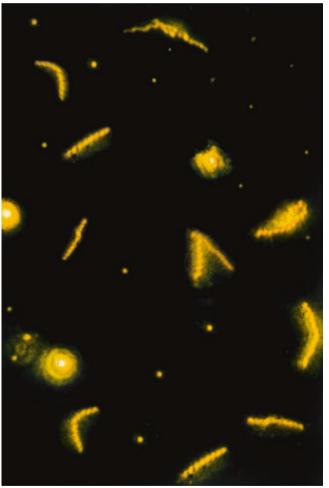


Fig. 2.188 Treponema pallidum visualized through a darkfield microscope on clinical material collected from a single clean ulcer with defined and raised edges (magnified 1.000×). As described in Fig. 2.24, after producing exudate and placing this on a slide with saline, mix, cover with a coverslip and immediately observe to avoid drying, and more importantly, as the bacteria is anaerobic and it can lose motility. This is the characteristic that allows the bacteria to be observed. This technique is good for direct examinations for the diagnosis of primary syphilis, however, it requires experience and good equipment. Other spirochetes (that do not cause syphilis) may exist in genital lesions. Courtesy of Roberto Maués

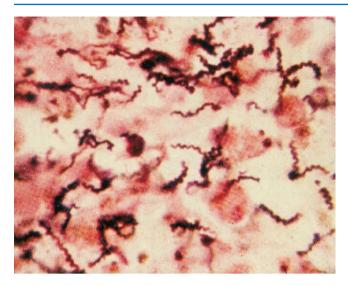


Fig. 2.189 *Treponema pallidum* from biopsy material from a case of congenital syphilis, visualized using the silver impregnation technique

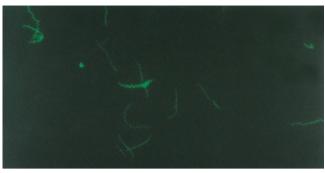


Fig. 2.190 Another direct examination technique is to use antitreponemal antibody material marked with fluorescein. Immunofluorescence microscopy should be used. The preparation of the slide is the same as that used for the Fontana-Tribondeaux technique and the reagents are those used in FTA-Abs serological screening

3.1 Synonyms

Febrile herpes.

3.2 Concept

Herpes is an infectious and contagious disease subject to recurrence. It may be transmitted through sexual relations or in the birth canal in infected mothers. In many cases the source of contamination is not defined.

3.3 Incubation Period

The incubation period is from 1 to 26 days (average of 7 days) after contact.

Contact with ulcerated or vesicular lesions is the most common form of transmission, but this may also occur in asymptomatic patients. In many cases, the incubation period can be longer and hard to define.

3.4 Etiologic Agent

Herpes simples is caused by two antigenic types of Herpes simplex virus: HSV-1 and HSV-2.

HSV-1 occurs more frequently in lesions of the lips, the face and areas exposed to sunlight. HSV-2 predominates in the genital region.

These are DNA viruses that are thermolabile and sensitive to ether, phenol and formaldehyde and are partially inactivated by ultraviolet radiation. They have a high resistance to cooling.

3.5 Clinical Presentation (Figs. 3.1–3.54)

- *Initial outbreak:* Preceded by subjective symptoms. The initial outbreak appears in about 24 h, including erythema, burning, itching and pain. Grouped vesicles appear on the erythematous base, which remain for 4–5 days and then recede. The whole process lasts from 2 to 3 weeks. The first symptoms to the genitalia may be accompanied by fever, headache, malaise and myalgia. Inguinal or femoral lymphadenopathy occurs in 75% of cases.
- Recurrent infection: As HSV remains latent in the myelin sheath of peripheral nerves, new outbreaks can be expected. These are less intense than the first occurrence. Lesions are generally larger and more painful in patients with AIDS or other immunosuppressive diseases.

3.6 Laboratory Diagnosis Tests:

Figs. 3.55-3.63

Samples collected by swabbing the lesions (preferably from the base of the vesicles) can be referred for the following tests:

- (a) Cytodiagnosis (Papanicolaou or Giemsa).
- (b) Cell culture.
- (c) Molecular biology (PCR).
- (d) Histopathological exams may be used in cases of extensive or chronic ulceration. During the active phase, serological screening reveals increased levels of IgG.
- (e) Serology.

Evaluation of laboratory methods

Exam	Sensitivity %	Specificity %
Tzanck Test	40-50	>99
Papanicolaou	30–40	>95
Direct IF	70-80	>95
Viral culture	25-90	>95
PCR	>95	>95

Should be used antibody based tests in G glycoprotein that is more specific type (100% sensitivity and specificities of 98% [HSV-1] and 96% [HSV-2])

Type specific serological tests may be requested when:

- 1. recurrent genital symptoms or atypical symptoms with negative cultures.
- 2. A clinical diagnosis of HSV without confirmation.
- 3. Partner (s) with genital HSV.
- 4. Consider yet for: people with STD, HIV and MSM with risk behavior.

3.7 Treatment

Table 3.1 Therapeutic regimens

	•	C			
Antiviral	Dosage	Frequency	Duration	Route of administration	
				administration	
Treatment of first infection					
Aciclovir	400 mg	8/8 h	7–10 days	Oral administration	
Aciclovir	200 mg	4/4 h (5×/day)	7–10 days	Oral administration	
Famciclovir	250 mg	8/8 h	7-10 days	Oral administration	
Famciclovir	1 g	12/12 h	7-10 days	Oral administration	
Treatment of recurrences					
Aciclovir	400 mg	8/8 h	5 days	Oral administration	
Aciclovir	200 mg	4/4 h (5×/day)	5 days	Oral administration	
Aciclovir	800 mg	12/12 h	5 days	Oral administration	
Aciclovir	800 mg	8/8 h	5 days	Oral administration	
Famciclovir	125 mg	12/12 h	5 days	Oral administration	
Famciclovir	1 g	12/12 h	1 day	Oral administration	
Famciclovir	500 mg single dose followed by 250 mg 12/12 h for 2 days			Oral administration	
Valaciclovir	500 mg	12/12 h	5 days	Oral administration	
Valaciclovir	1 g	1×/day	5 days	Oral administration	
Valaciclovir	500 mg	12/12 h	3 days	Oral administration	
Suppression treatment					
Aciclovir	400 mg	12/12 h	Up to 6 months	Oral administration	
Famciclovir	250 mg	12/12 h	Up to 1 year	Oral administration	
Valaciclovir	500 mg	1×/day	Up to 1 year	Oral administration	

Suppression treatment is recommended if there are six or more outbreaks during an interval of 12 months.

3.8 Other Medication

Some drugs such as trifluorothymidine, vidarabine and cidofovir may be used in specific cases.

Pritelivir, a HSV helicase-primase inhibitor, demonstrates anti-viral activity in vitro and in animal models infected with the herpes simplex virus (HSV). This drug has been tested, using a placebo as a comparison, to verify its efficacy and safety in healthy people with a HSV-2 genital infection. The study was randomized and included 156 HSV-2-positive individuals. The authors of the study concluded that pritelivir reduces levels of genital excretion of HSV and the number of days that lesions lasted, depending on the dose applied, in healthy men and women with genital herpes. We still do not know anything about this drug's commercial availability.

As a result of its properties (analgesic, anti-inflammatory and antiviral), the phytotherapeutic drug *Uncaria tomentosa* (Imunomax®) is indicated, in gel form containing 50 mg/g, to be applied topically to herpetic lesions three times a day until they improve or heal.

3.9 Complications

Infection of the central nervous system (meningitis/encephalitis) or disseminated disease.

Neonatal infection occurs frequently with visceral and central nervous system involvement. Around 70% of newborns infected with neonatal herpes are born of mothers that are asymptomatic at the time of labor.

In addition to congenital abnormalities such as hydranencephaly and chorioretinitis, fetal abnormalities can include miscarriage, premature birth and intrauterine growth restriction in cases of vertical transmission (mother-baby).

Factors that increase the chances of intrauterine transmission include: initial outbreak of the disease present in the mother, multiple herpetic lesions, premature rupture of membranes and introduction of electrodes for fetal monitoring in pregnant women with a history of recurrent genital herpes.

It has been observed that suppression therapy with 400 mg of acyclovir every 8 h from the 36th week of pregnancy and elective cesarian section significantly reduce the chances of infection of the baby in cases of mothers with recurrent herpes.

Recurrent herpes simplex is associated with the development of recurrent erythema multiform. HSV-1 is more commonly associated with hypersensitivity phenomenon.

3.10 Differential Diagnosis

Hard chancre, soft chancre, traumatic exfoliation, genital erythema multiforme and genital canker sores associated with AIDS.

3.11 Observations

- In many cases a clinical diagnosis can be made.
- In our experience, genital herpes is the most common diagnosis of an infectious disease when the presenting symptom is a genital sore, and that these even more common than syphilis lesions. However, this may vary according to region and community. An awareness of the prevailing epidemiologies of the surrounding area is therefore essential to good medical practice.

Fig. 3.1 Patient presenting the typical symptoms of genital herpes: grape-like grouped vesicles to the external genitalia (*arrow*)



Fig. 3.2 For etiological diagnosis of infection by herpes simplex, puncture the vesicle with a finely-gauged needle, taking care to open it laterally. This will avoid any bleeding, as the base of the lesion will not be punctured. Carefully lift up the skin of the vesicle exposing the base. Gently scrape it with a wooden spatula, then prepare a smear on a glass slide for posterior cytological analysis

- Wounds in anus should also be considered in the evaluation for HSV diagnosis. The same must be said for recurrent wounds (with vesicles or not) of the skin of buttocks, of thighs root.
- Cesarian birth is recommended in cases of genital lesions or if these have been present up to 1–2 weeks before the birth, especially if these were part of the initial outbreak of the disease. However, the availability of practical and safe conditions for the carrying out of this procedure should always be considered.



Fig. 3.3 This case had the same presenting symptoms as the case above. If diagnosis is performed using cytology, the Tzanck test can be used where the slide is left to air dry, using the Giemsa staining technique. If the Papanicolaou technique is chosen, the slide must be quickly introduced into the flask (the same used for PAP) containing a fixative (alcohol or an equal parts solution of alcohol and ether). Other fixatives (in liquid or spray form) may also be used, such as carbowax



Fig. 3.4 Male patient with a single vesicle lesion to the body of the penis. He claimed to have had similar symptoms on two previous occasions in the last 12 months. The ideal method for the collection of material from the base of the lesion is to break the vesicle and scrape the base with a wooden spatula, whether for staining cytology or for molec-

ular biology testing (PCR or hybrid capture). In this particular case, as the lesion was very small, we opted to collect a sample using the imprint technique, in which the vesicle is opened and a glass slide is applied in blotting movements



Fig. 3.5 A 14-year-old HIV-positive patient with severe symptoms of genital herpes and an intense secondary infection in the genital lesions (a) and the inguinal region (b). People with HIV or any other immuno-

suppressive disease often present more severe symptoms in terms of number, size and time before remission

Fig. 3.6 Female patient with symptoms of recurrent genital herpes (sic-according to information provided by the consultant), but who did not undergo any kind of testing to confirm this diagnosis. Observe the grouped vesicles on the left labia majora with signs of secondary infection. Some vesicles were already ruptured (a). A sample was collected from the lesion using the imprint method (b). Cytology was not specific, probably due to the stage of the disease, the secondary infection and because most of the material inside the vesicles degenerates when they are ruptured for over 24 h. However, we try to establish etiological diagnosis for all of the cases that we receive





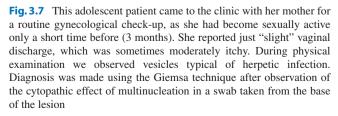




Fig. 3.8 A young patient with vesicular lesions on a hyperemic base on the skin of the left thigh (*arrows*), characterizing the initial stages of a herpetic lesion. During the initial phase, symptomatology includes hyperemia and itching followed by pain after the appearance of vesicles. With the rupture of the vesicles, painful ulcers are formed. Healing begins with the formation of scabs and takes a varying amount of time, depending on if it is the initial outbreak, a recurrent outbreak, if there are any associated infections or diseases, principally HIV, or any other chronic and/or immunosuppressive comorbidities



Fig. 3.9 Genital herpes in an area left unprotected by condoms. This is an initial outbreak with multiple coalescing vesicles in a young patient who reported that he routinely uses condoms. Many patients initially apply polyvalent creams and postpone consultation with a doctor. This makes diagnosis and proper management of these cases even more difficult



Fig. 3.10 Case involving vesicular and blistering lesions, given their size. Note that in this case there is no typical hyperemic base, which provides a differential diagnosis from blistering dermatitis. However, in initial-stage genital herpes, the hyperemic base may be visible only when the vesicles are broken



Fig. 3.11 In this case, hyperemia around the vesicular lesions is more evident



Fig. 3.12 These lesions were observed during a peniscopy and had the appearance of aceto-white macules in ulcerative regions on the base of the penis, suggesting post-phlyctenular herpetic infection (vesicles that precede the lesion). Clinical history can provide guidance in these cases. There is a high probability that all laboratory exams will be negative, even in cases of genital herpes



Fig. 3.13 Various phlyctenular lesions next to an exulceration, all of which caused by herpes and at different stages of the disease. This was a case of recurrent genital herpes with two consecutive outbreaks. Unfortunately, such patients are often medicated with antibiotics, following the syndromic approach for genital ulcers



Fig. 3.14 A patient that was referred to our STD clinic for treatment of lymphogranuloma venereum caused by inguinal adenitis (*arrow*). While taking the patient's medical history, we discovered that similar symptoms had appeared twice over a 2 month period. These receded within a week with the patient using just painkillers. This case is very similar to that shown in Fig. 3.6; however, the vesicular lesions are not very evident here. This was defined as a case of genital herpes. Two rounds of serological screening for syphilis, chlamydia and HIV were taken with an interval of 30 days and all tests were negative



Fig. 3.15 Herpetic ulcers on the hard palate of a patient who reported frequently having oral sex with a partner who had a clinical history and laboratory exams confirming herpes on his penis



Fig. 3.16 Male patient presenting multiple flat punctiform ulcers, some separate (see *arrow*) and others that coalesce and form larger irregular areas on the labial mucosa, characteristic of herpetiform aphthous ulcers, as they were not preceded by vesicles and were only present in non-keratinized areas of the mucosa such as the floor of the mouth, the lingual belly, the buccal mucosa, the soft palate and the labial mucosa, as opposed to herpetic lesions that are found in keratinized areas, such as the hard palate, the gums and dorsum of the tongue



Fig. 3.17 A case of genital herpes in a patient who reported that at no time during the many outbreaks that he had did he have vesicular lesions. However, he reported experiencing slight pruritus that made sex more pleasurable (increasing his libido) and led to faster ejaculation. However, after having sex for the first time he felt pain and "irritation" in the area, which prevented him from having sex again. Here we would like to highlight once more that in the absence of quality medical care, such patients may mistakenly be given antibiotics, following the syndromic approach, (penicillin, azithromycin, ciprofloxacin)



Fig. 3.18 Here some lesions in different phases during an outbreak of genital herpes can be observed: (a) intact vesicles, (b) broken vesicles and a (c) large area of hyperemic skin. Many patients, in the period before the appearance of genital lesions, experience light to moderate general illness involving a cold, headache and irritation, and palpable, slightly painful poly-lymphadenomegaly in the inguinal region



Fig. 3.19 A patient referred from another medical service after presenting with painful vulval ulcers that after 2 days of treatment with antibiotics for soft chancre did not improve. Physical examination revealed that genital herpes was a likely diagnosis. The patient reported that she sometimes felt discomfort and noticed small "wounds" on her external genitalia, and that she was usually medicated by her gynecologist with polyvalent genital creams. She also reported that she hadn't had sex for 6 months

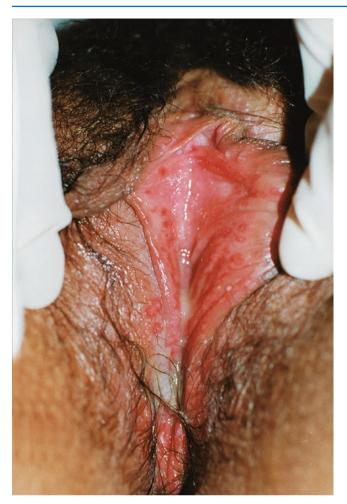


Fig. 3.20 A case very similar to the one presented above, however, here the patient had an active sex life with a fixed partner and also presented symptoms of bacterial vaginosis. It is not rare for this symptom to be a result of vulvovaginitis caused by *Trichomonas vaginalis*. Direct examination of vaginal samples is a routine part of our work



Fig. 3.21 Multiple ulcerative lesions that were painful upon contact with urine and during washing. This patient presented vulvovaginitis caused by *Candida sp.*, associated with genital herpes. Serological screening for syphilis was positive with titer levels of 1:64; screening for HIV antibodies was negative at the time of consultation. Five months later, the patient returned to the clinic especially for a pap smear and HIV screening. The pap smear revealed non-specific inflammation, but HIV screening was positive. According to the patient, she often didn't use a condom as her fiancé was her only partner. The fiancé was asked to visit the clinic and reported that he sometimes had sex with women at "massage parlors". He almost always used a condom. He described himself as a "very moderate" marihuana and cocaine user at "high society" parties. Serological screening for syphilis, HIV and hepatitis B was positive



Fig. 3.22 Genital herpes in a woman in her 40s with more than one child. This photograph shows lesions receding after an outbreak



Fig. 3.23 A 19-year-old patient who attended the emergency department of a private hospital at 11 pm presenting these symptoms, which had appeared 24 h previously and quickly become painful, mainly upon contact with urine or during washing. She reported that for the week preceding this initial outbreak of genital herpes she had lost her job, separated from her husband (her only sexual partner over the previous 4 years) and had to hospitalize her 3-year-old daughter who had been diagnosed with pneumonia. She reported that before the genital lesions appeared she experienced headache, fever and loss of appetite, as well as vulvovaginal discharge with slight itching. During examination we diagnosed genital herpes associated with candidiasis and urinary retention of 1 L. As the patient was under significant emotional stress, was anxious and did not have any family members accompanying her, we decided to admit her for observation and prescribe an anxiolytic, oral ketoconazole and oral acyclovir. We also prepared a sitz bath with camomile tea at room temperature, as camomile has demonstrated antiviral and anti-inflammatory effects in vitro. In our experience, this procedure significantly improves local discomfort in these situations. The inconvenience of this procedure is the difficulty to do it not at home. In cases such as this where the patient is in pain, we do not recommend the use of local anesthetics (such as Xylocaine gel); just oral painkillers and anti-inflammatories. Within 16 h the patient was much better and was discharged from hospital. We followed up her case for over 15 years and she did not experience any other outbreaks. The viral etiology diagnosis was achieved through cytology of a swab of the liquid and base of a vesicle (the lesion shown in the close-up is a blister) broken by us using a hypodermic needle. Her marriage and employment situation and the health of her daughter had already improved a month after her first consultation. Two rounds of serology testing for syphilis and HIV were not positive



Fig. 3.24 As cited above, in many cases of genital herpes it is not possible to observe vesicles. This was a case of just ulcerative lesions on hyperemic bases. It is worth noting that initial outbreaks can often be confused with other infections, mainly because using the syndromic approach for STDs it is possible to imagine that the administration of antibiotics cures the lesions, as they usually recede within a week



Fig. 3.25 Receding recurrent lesions will completely heal within a week in people with a normal immune system. Most of the time they do not leave behind any obvious scarring



Fig. 3.26 A case of genital herpes with some broken vesicles that are already contaminated with a secondary infection, which can easily complicate diagnosis. In the close-up, note the purulent discharge covering the ulcerative area. Even with a secondary bacterial infection in the lesions, we do not recommend the use of antibiotics (local or systemic). Maintaining personal hygiene and using regular (or antiseptic) soap is sufficient



Fig. 3.27 (a) A patient who came to our clinic complaining of edema, pain and lesions to the penis. In (b and c) multiple ulcerative lesions with hyperemic halos can be seen. Direct examination of the white discharge covering the glans and inside of the foreskin led to a diagnosis of *Candida* hyphae. The patient's fixed (but not exclusive) sexual part-

ner was examined and also presented a significant vulvovaginal infection caused by <code>Candida</code>. In (\mathbf{d}) , taken 15 days after the first consultation, the penis without hyperemic skin or edema is shown, which were very evident in (\mathbf{b}) and (\mathbf{c})



Fig. 3.28 According to the patient, these symptoms were preceded by four vesicles that were broken during washing. This led to their bases joining together, forming a single irregular ulcer (which did not harden upon palpation) and with a large erythemic halo. Before being seen by us in the afternoon, the patient received two IM penicillin benzathine injections at a public family health clinic in the morning. A pap smear of a swab from the lesion demonstrated presence of the cytopathic effect of multinucleation consistent with HSV infection



Fig. 3.29 Genital herpes lesions similar to those seen in the previous case that also coalesce around the frenulum and the inside of the underlying foreskin. It is also worth noting the edema and hyperemia in the affected areas. It was initially thought to be a syphilitic lesion, as according to the patient it was an initial outbreak. The bilateral inguinal micropolyadenomegaly were palpated, and fever (38 °C) and a slight cutaneous rash were identified. Examination of the sample collected from the lesion and serological screening for syphilis were both negative. Serology screening for syphilis and HIV were repeated twice and found to be negative on both occasions. As serology screening and PCR for herpes were not available at the time and the patient was easily brought under control, we opted to follow up this case twice a week and took measures against the local symptoms (bathing with camomile tea). The symptoms totally vanished within 8 days. New outbreaks occurred later (six in 1 year). In two of these outbreaks a pap smear of a swab of the lesion revealed herpes infection. We then prescribed suppression therapy with 400 mg acyclovir twice a day for 6 months



Fig. 3.30 This patient with recurrent genital herpes presented a herpetic outbreak consistent with symptoms of papulo-erosive syphilis and fungal balanitis (which can be seen more clearly in the close up). The lesion to the side of the frenulum was significantly hardened. This is different to all of the other cases. VDRL screening was positive with titer a value of 1:32. Darkfield bacteriology of a swab of the lesion was inconclusive. HIV screening was repeated twice with an interval of 60 days and was negative on both occasions. One sexual partner was also examined and tested positive for syphilis and for HIV



Fig. 3.31 This case is very similar to the previous one (Fig. 3.13), however these ulcerative lesions with erythemic halos were mainly found on the glans and in the balanopreputial groove



Fig. 3.32 Intense outbreak of recurrent genital herpes where coalescence of some of the ulcers can be observed. A striking characteristic in cases of genital herpes is the presence of hyperemic areas surrounding the lesions



Fig. 3.33 This case is practically the same as the previous one. This patient presented four consecutive outbreaks (one after the other) of genital herpes. Serology screening for syphilis and HIV was negative. We opted to prescribe acyclovir as suppression therapy



Fig. 3.34 A patient who was referred to the UFF STD clinic with symptoms that had started 8 days previously. He was prescribed with penicillin benzathine and ciprofloxacin on the second day of his outbreak, but no improvement was observed. He reported that around a year before he had a similar episode, which had healed more quickly. As the patient had not applied any medication to the area over the previous 2 days, we collected a sample for cytology, which tested positive for herpetic inclusions. The close up shows the erythemic borders of the ulcerative lesion with secondary bacterial inflammation



Fig. 3.35 (a) A patient that was referred to our sector with symptoms to her vulva that had been present for a week. She complained of intense pain in the area. She had been applying talcum powder in order to alleviate this. She presented polyadenomegaly, a slight cutaneous rash and reported that when her symptoms began she also experienced fever and headache. She was given an oral antibiotic (she doesn't remember which, but she remembers that it was a free sample given to her by a non-medical professional at public health clinic) which did not lead to

any improvement. In (b), after careful cleaning of the area with saline solution, the characteristics of the herpetic lesions can be observed. It is also worth noting the blisters on the skin around her vulva. As in the aforementioned case (Fig. 3.19), she also presented candidiasis. She reported this to be the initial outbreak, to have one fixed partner and to not use condoms. Her partner was examined and denied any previous herpes or other genital infection. Serology screening for syphilis and HIV were negative for both



Fig. 3.36 Similar case to the previous one, which also involved the presence of candidiasis. It is worth emphasizing that even when the patient complains of pain, we do not recommend that local anesthetic gel be applied. Treatment of candidiasis or any other associated infection is decisive in the rapid improvement of symptoms. We prefer to prescribe oral antifungal medication

Fig. 3.37 HIV-positive patient presenting an extensive recurrent outbreak of genital herpes that had been present for over 2 weeks. Note the secondary bacterial infection and local edema in the close up



Fig. 3.38 Female patient who was 35 weeks pregnant seen at the maternity ward at the Valença University of Medicine in Rio de Janeiro State, presenting symptoms of dysuria, itching and vulval pain that had been present for 3 days. She sought medical attention the previous day and was prescribed nystatin vaginal cream for the treatment of vulvovaginal candidiasis (sic). However, as there was no improvement to her symptoms, she returned the following day. She presented the typical symptoms of genital herpes. We opted to prescribe 400 mg oral acyclovir three times a day for 10 days. Total remission of the lesions was observed after a week





Fig. 3.39 A patient referred by a doctor working for a supplementary medical service complaining of a recently-formed genital lesion with intense stinging and pain. She reported that this was the first time she had had such symptoms and that the previous night when the lesion appeared, she felt generally unwell and experienced night sweats. (a) Note the ulcerative lesion in the region above the urethral meatus, with an erythematous base and hyperemic borders. A swab of the lesion was collected and investigated for herpetic cells, and multinucleation was verified (**b** and **c**). After collection of the sample, *Uncaria tomentosa* 50 mg/g gel was massaged into the lesion. While the serological exams were requested, medication (*Uncaria tomentosa* 50 mg/g gel three

times a day) and general instructions were provided, and the patient reported a significant improvement to the symptoms to her genitalia while still inside the consultation room. When the patient returned for a follow up appointment a week later, she reported that the lesion had disappeared in around 4 days (d), and that she had already resumed sexual activity using condoms. The pain and stinging to her genitalia stopped within 48 h. Serological screening for syphilis and HIV were both negative. As she couldn't remember having been vaccinated against hepatitis B and her anti-HBs and HBsAg exams were negative, we prescribed a course of hepatitis B vaccinations



Fig. 3.40 Another case of an initial outbreak of genital herpes in which *Uncaria tomentosa* 50 mg/g gel was massaged into the lesion three times a day. In (a) we show the lesion that the patient discovered and for which she sought medical attention. In (b) we show more lesions that were not

reported by the patient. The painful symptoms receded within 3 days, and the lesions disappeared. The patient was also prescribed a course of hepatitis B vaccinations, as she claimed not to have been vaccinated. VDRL, HIV, anti-HBs and HBsAg exams were negative



Fig. 3.41 An adolescent patient seen at a private clinic with slightly painful symptoms to her genitalia associated with vaginal discharge. Clinical examination revealed an ulcerating lesion to the vaginal fourchette (see *arrow*), as well as papular ulcerative lesions with central umbilication on the perineum and genitofemoral region (a). A swab of the ulcerative lesion on the vaginal fourchette was taken and sent for cytological testing, and one of the papular ulcerative lesions was excised. We prescribed 400 mg oral acyclovir three times a day and topical application of *Uncaria tomentosa* 50 mg/g gel, also three times a day. To our surprise, both exams were positive for the cytopathic effect (multinucleation), characterizing infection with the herpes simplex virus. We asked for the slides to be examined again, as these umbilicated lesions are characteristic of molluscum contagiosum; the results, however, did not change. All of the lesions receded completely within a week





Fig. 3.42 A patient who dropped in at the STD clinic with symptoms of intense stinging and genital pain. They reported that this was the first time that they had experienced these symptoms and also reported fever and feeling generally unwell the night before the lesions appeared (a), 72 h before seeking medical attention. The patient reported that the first signs appeared around 3 weeks previously and that they had already applied several topical creams. Physical examination revealed a small and slightly painful inguinal adenomegaly. Serological screening for

syphilis and HIV was negative. Darkfield bacteriology using the Gram technique was inconclusive. A pap smear revealed epithelial cells with multinucleation characteristic of genital herpes. The patient was prescribed *Uncaria tomentosa* 50 mg/g gel three times a day and the symptoms receded within 24 h, with total remission occurring within 3 days (b). A course of hepatitis B vaccinations was also prescribed, as the patient did not know if they had received these previously and anti-HBs and HBsAg exams were negative





Fig. 3.43 (a) A patient over 40 years old seen at the UFF STD clinic presenting 10-day ulcers and exulceration to the penis. He reported that he had been given oral azithromycin at another public health clinic, but with no improvement. He reported that this was the first time that he had experienced these symptoms. There was no inguinal adenomegaly and the lesions were neither hardened nor very painful, but the patient reported a sensation of stinging in the area. Samples were collected from the lesions for darkfield bacterioscopy using the Gram technique and a pap smear. Serological screening for syphilis and HIV was also requested. The Gram and darkfield examinations performed during the initial consultation and the pap smear were all inconclusive. The serological tests were negative. We recommended using a free sample of

Uncaria tomentosa gel three times a day for 5 days to relieve the symptoms. (b) One week after the initial consultation and after 4 days of using the topical cream recommended, the patient returned presenting a significant improvement, with the lesions already healing. Cytological testing was inconclusive for the cytopathic effect for HSV. This did not surprise us, as in cases such as this one there is a large margin of error in cytological testing of swabs. It is still not certain if the *Uncaria* gel healed the lesion or if the disease progressed naturally with this product having no effect. However, it is worth noting that the patient himself commented that on the first day of application of the cream, all the sensations of discomfort "quickly disappeared"



Fig. 3.44 After an initial outbreak of genital herpes, this patient retained a hypertrophic scar to the vulva (her reason for booking another appointment). This occurred approximately 2 weeks after specific treatment for herpes with oral acyclovir. Generally, these scars recede and have no connection to antiviral use



Fig. 3.45 An initial outbreak of genital herpes with coalescing ulcerative lesions across the whole of the vulva. The patient had significant difficulty urinating, as contact of these lesions with urine caused her a lot of pain. This situation may also cause urinary retention. It is also common to see achromatic or hypopigmented scarring, mainly in people with darker colored skin



Fig. 3.46 A 25-year-old male patient who dropped in at the clinic with an extremely painful perianal ulcer covered in a purulent discharge. He reported that in two other appointments at other clinics he had been given antibiotics, painkillers and anti-inflammatories. During none of these appointments were tests for syphilis and/or HIV discussed, nor were samples taken from the lesion for laboratory testing. He reported that he had had the lesion for around 3 weeks and that he had previously had some "small wounds" on his scrotum that had healed quicklyDuring our consultation, we advised him to undergo serological screening (VDRL and HIV). The final diagnosis was genital herpes (with severe lesions and secondary bacterial infection) in a patient with HIV



Fig. 3.47 This case is practically identical to the one above, differing only in the patient's medical history. The patient in question denied having had any previous episode of genital herpes. In this case, the symptoms associated with AIDS began with this aggressive outbreak of herpes. As previously cited, investigations into HIV, syphilis and hepatitis should never be delayed. This patient tested positive for all of the above. The syndromic approach towards genital ulcers was taken initially, but this did not help, and neither did treatment with oral acyclovir at the usual dose. In such cases, hospitalization for intravenous administration of acyclovir is more effective, above all in terms of the patient's quality of life





Fig. 3.48 (a) A patient who sought out our services after consulting various public health clinics about these symptoms that she had had for 3 months. She reported that she had already been given numerous types of local, oral and injectable medication and had experienced a slight and temporary improvement. During this time, no exams had been carried out. The patient was already demonstrating signs of cachexia, was complaining of "lumps" all over her body and vespertine fever. She was HIV positive and was experiencing an intense outbreak of genital herpes. In both (a) and (b) the aggressiveness of the lesions can be observed. (a) shows the vulval edema and (b) shows the very large ulcer on the left labia. In this case, a sitz bath in cold camomile tea can help to relieve symptoms. However, general supportive measures and physical, nutritional and psychological wellbeing together with intravenous antiviral medication (for herpes) and antiretroviral medication (for HIV) are all part of best practice in reducing symptoms



Fig. 3.49 (**a**, **b**) A HIV-positive female patient in her 26th week of pregnancy. She presented these symptoms, which had appeared suddenly. She reported this to be the initial outbreak. Treatment was started with 1800 mg acyclovir divided into three daily intravenous 600 mg doses. The symptoms healed within 2 weeks. Labor occurred at

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37 weeks, and the baby was born without any abnormalities. During both pregnancy and labor, a regime of AZT was maintained (according to Protocol 046). We currently have to follow the protocols approved and made available for each country



Fig. 3.50 (a) A 28-year-old HIV positive patient who had been aware of their condition for 2 years and was undergoing triple antiretroviral therapy. They had started to present a fall in CD4 cell count and resistance to their antiretroviral medication. At the same time, they pre-

sented these highly painful genital ulcers. The patient reported previous episodes of genital herpes, but never with this intensity. (b) The lesions healed after administration of high doses of intravenous acyclovir



Fig. 3.51 Serious case of genital herpes in a young male adult. Serological screening for syphilis and HIV should never be delayed in cases of genital lesions, as it is not unusual for these to be associated with HIV infection. In many cases, it is genital lesions that prompt the person to seek medical help and to discover that they have HIV



Fig. 3.52 A case of genital herpes in a male patient similar to the above case in terms of clinical severity. However, here the lesions do not have vesicles. VDRL, HIV, anti-HCV, anti-HBs and HBsAg exams should never be delayed



Fig. 3.53 An adolescent patient with genital herpes lesions. Observe that these are multiple, flat lesions with hyperemic borders and form a line along the balanopreputial groove

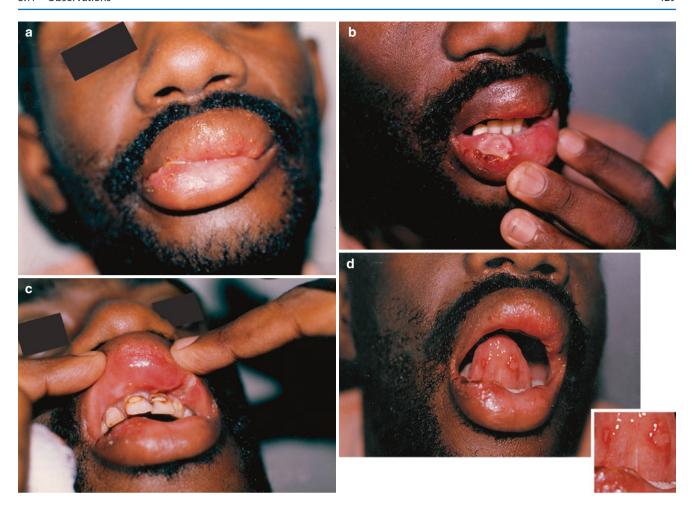


Fig. 3.54 (a–d) A patient referred to our clinic presenting these 2-month-old lesions to the mouth. Biopsies were performed but were inconclusive. During this time the patient was prescribed antibiotics, painkillers and anti-inflammatories but did not experience any significant improvement. He reported having had a fixed exclusive partner for the last 8 years. However, before that he had had a range of partners and during this time he didn't use condoms. HIV screening was positive,

and cytological examination of a swab taken from the lesions on his tongue revealed herpetic inclusions. His wife, a mother of two children, was seen and examined at our clinic and also proved to be HIV positive. She had a history of blood transfusions owing to a large hemorrhage during her second (natural) labor. She also reported that her partner was her only sexual partner and that they never used condoms

Fig. 3.55 In this photograph we can observe multinucleation and nuclear molding (one joined to the other), with the chromatin shifted to the nuclear periphery. It is said that the nucleus looks like matt, unpolished glass. Papanicolaou technique 100×

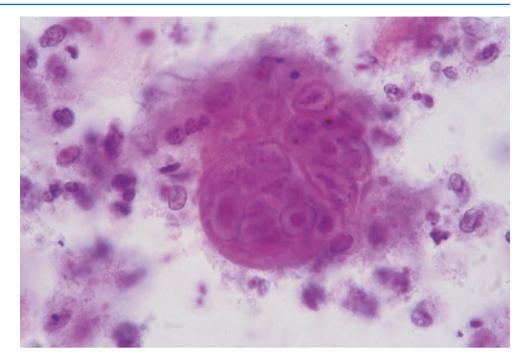
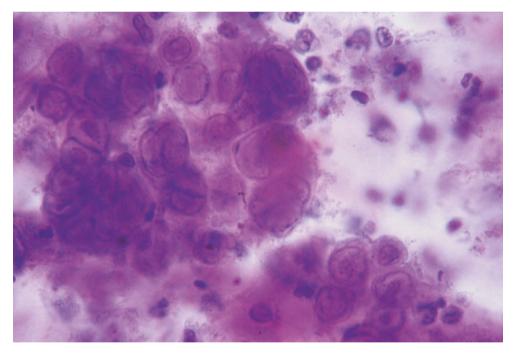


Fig. 3.56 In this photo, as for the other cytological exams of swabs taken from the vesicle base, it is possible to observe multiple viral inclusions next to multinucleations.

Papanicolaou technique 100×



3.11 Observations

Fig. 3.57 In this photo, nuclear molding, multinucleation and vital inclusions can be observed

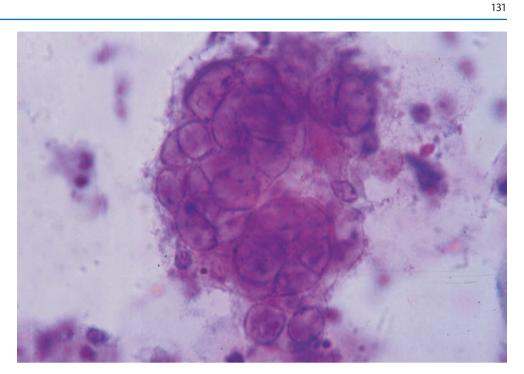


Fig. 3.58 It is typical to cite that the cytopathic effect of the herpes virus involves multinucleation, however, it is also possible to see cells that remains mononuclear, which can be observed in this photograph. On this slide, both multinucleation and mononuclear cells can be observed, both with inclusions caused by the herpes simplex virus. Papanicolaou technique 100×

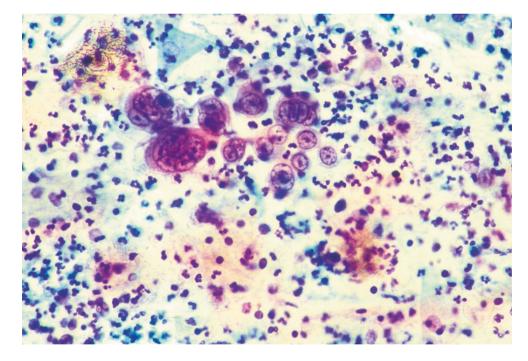
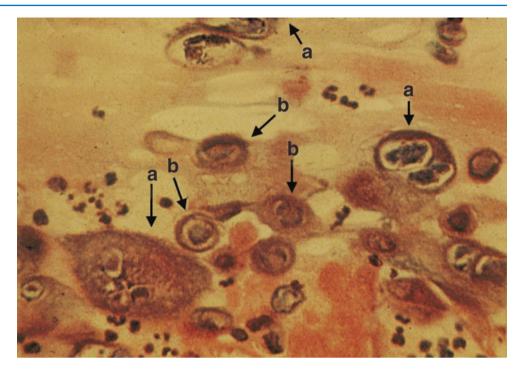


Fig. 3.59 (a) is cells with multinucleation. (b) is mononuclear cells can also be obsrved





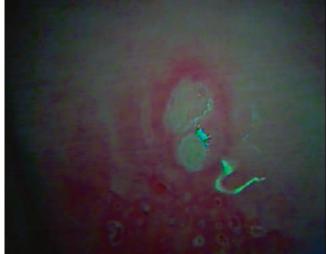


Fig. 3.60 Twenty seven years old woman, with a history of one delivery 5 years ago, with a claim of discharge with odor. In the specular exam was observed an aparent white lesion in anterior lip. On colposcopy was observed that the lesion was actually an ulcer. The figure shows a lower magnification of colposcopy, where there is a typical transformation zone, but with a lesion (*arrow*)

Fig. 3.61 Ulcers observed with higher magnification of colposcopy. Same case of Fig. 3.60

Fig. 3.62 Herpetic cells in liquid based cytology (SurePath) (400×). Same case of Fig. 3.60

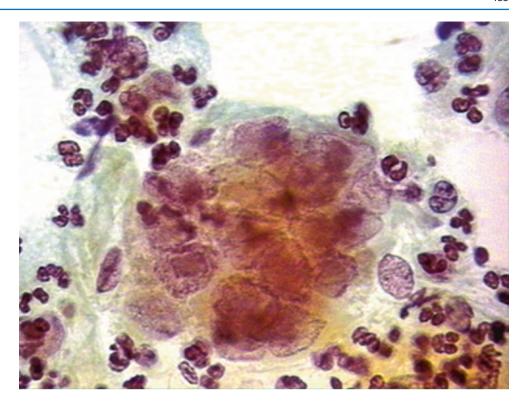
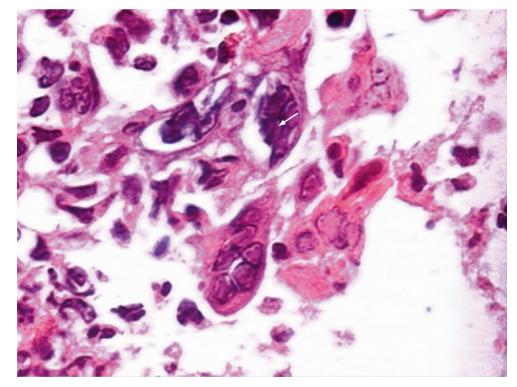


Fig. 3.63 Herpetic cells in a biopsy of the ulcer (*arrow*) (HE 400×). Same case of Fig. 3.60



Chancroid 4

4.1 Synonyms

Chancroid, simple chancre, ulcus molle, Ducreyi chancre, soft chancre.

4.2 Concept

Acute, localized, phagedenic and autoinoculable STD.

4.3 Incubation Period

From 2 to 5 days. Longer periods are rare.

4.4 Etiologic Agent

Haemophilus ducreyi: a Gram-negative coccobacillus, a facultative anaerobe that is grouped in pairs and difficult to cultivate in artificial media.

4.5 Clinical Presentation (Figs. 4.1–4.25)

Ulcerative lesions, generally multiple, with irregular borders and containing pus and a base with a soft consistency when long, phagedenic, painful and autoinoculable, generally accompanied by unilateral inguinal adenitis (buboes), which in 30–50% of cases develops to suppuration through a single orifice.

It occurs more frequently in **men** on the frenulum and the balanopreputial groove, and in **women** on the furcula and the inside of the small and large vulval lips.

It is predominant in men, with 40 cases for each case found in women.

4.6 Laboratory Diagnosis

- Direct examination of lesions: bacterioscopy of a swab taken from lesions using the Gram technique. It is recommended that excess pus must be removed before samples are collected from the borders of the lesion. Smear should be prepared by wiping in one direction so as not to alter the arrangement of the bacteria (Figs. 4.26–4.28).
- Culture: this should be prepared immediately after collection of the sample. The best results are obtained from samples taken from buboes, when these are present and are ruptured. This bacteria is difficult to isolate, and a Nairobi, Johannesburg or enriched chocolate agar medium should be used.
- Multiplex PCR (M-PCR): highly sensitive and specific method of diagnosis. This also allows simultaneous detection of *Treponema pallidum* and HSV-1 and -2.
- Other exams with varying specificity and sensitivity, still
 not commonly used in daily medical practice include:
 immunofluorescence (IF), research-based NAAT (nucleic
 acid amplification test), serological screening and spectrometry methods.

4.7 Evaluation of Laboratory Methods (Lewis, DA—modified)

Exam	Sensitivity%	Specificity%
Gram	5-63	51-99
Culture	35-91	>94
PCR	56-100	52-100
IF	89-100	63-81
Enzyme immunoessay serology— (various methods)	48–100	23–90

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4.8 Treatment and Control of Cure

Antibiotic	Dose	Frequency	Duration	Method of administration	Reference
Azithromycin	1 g	Single dose	_	Oral	CDC ^b ; EG ^c
Ceftriaxone	250 mg	Single dose	_	Intramuscular	CDC; EG
Erythromicin	500 mg	8/8 h	7 days	Oral	CDC
Ciprofloxacin ^a	500 mg	12/12 h	3 days	Oral	CDC

^aContraindicated during pregnancy, breastfeeding and in children

Longer-term treatment regimens are recommended in patients that are also infected with HIV.

Clinical studies using thiamphenical, spectinomycin and fleroxacin have demonstrated satisfactory results.

In cases of soft chancre, control of cure is prominently clinical.

4.9 Complications

Local deformities and sequelae resulting from the healing process.

4.10 Differential Diagnosis

Hard chancre, herpes simplex (principally in patients with immunosuppression), lymphogranuloma venereum, donovanosis, traumatic erosions and secondary infections.

4.11 Main Differences between Hard Chancre and Soft Chancre

Hard chancre (primary ulcer,	
chancre)	Soft chancre (Chancroid)
Incubation period—21 to 30 days	Incubation period—2 to 5 days
Generally a single lesion	Generally multiple lesions
Erosion or ulceration	Ulceration
Hard base (lymphocytic infiltration)	Soft base (purulent reaction)
Clean, erythematous, serous base	Dirty, purulent, irregular base
Flat borders	Undermined borders
Non-inflammatory, painless,	Inflammatory, painful and
multiple and nonfistulizing bilateral	single unilateral adenopathy,
adenopathy occurring in almost	fistulizing through a single
100% of cases	orifice, in 30–60% of cases

4.12 Observations

- This disease does not have a high incidence or prevalence and a general decline in recorded cases of chancroid has been observed, above all in developed countries.
- Soft chancre may be an important factor in the acquisition and transmission of HIV. As well as the facilitating role that genital ulcers play, *H. ducreyi* infection recruits CD4 lymphocytes and macrophages to the infected region, exposing HIV target cells to contamination.
- This diagnosis should be considered even when just one ulcerative lesion is present.
- This diagnosis is much more common in men than in women.
- Coinfection with hard chancre (syphilis) is reported in around 5% of cases and is known as Rollet's chancre. In these cases, soft chancre symptoms are observed at first followed by hard chancre symptoms.
- Patients who wash their genitals before their consultation may undermine the effectiveness of bacterioscopic diagnosis, especially if they use antiseptic products such as povidone-iodine or chlorhexidine.

^bCenters for Disease Control (CDC) (2010)

^cEuropean Guideline for the Management of Chancroid (EG) (2010)

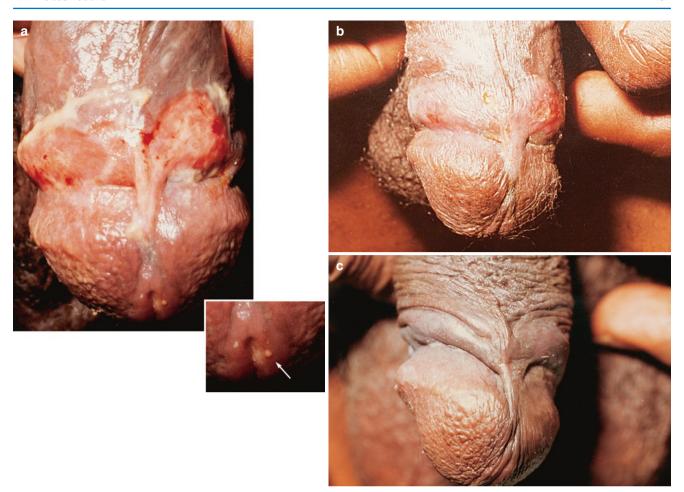


Fig. 4.1 (a) 58-year-old patient presenting an extensive ulcerative lesion containing a large quantity of purulent discharge and relatively serious painful symptoms. He reported having a fixed sexual partner, but that he occasionally liked to have sexual relations with prostitutes. The frequency of this turned out to be twice a week, or in other words it was routine behavior. He reported not using condoms, but simply washing his penis well after sex. According to the patient, these lesions

appeared 1 week after having sex with a neighbor (*arrow*). He said that this woman was married. In the close up, a small pustule can be observed close to the urethral meatus. (b) During the healing process: photograph taken a week after treatment (single-dose oral thiamphenicol 5 g). (c) The area healed completely after treatment. The patient did not report any side-affects. He mentioned noticing an improvement 24 h after taking the medication



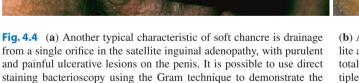
Fig. 4.2 Case of soft chancre involving multiple ulcers. Purulent discharge cannot be seen as the patient cleaned his penis with toilet paper, water and soap in the bathroom before the consultation. This makes direct or cultural bacteriological examination more difficult



Fig. 4.3 In this case, a noticeable characteristic of soft chancre can be observed: autoinoculability. In the past (until the 1970s) some doctors attempting to make a soft chancre diagnosis tried to demonstrate this characteristic in the following way: they removed the purulent discharge from the genital lesion and used a small needle to scarify the skin in the deltoid region, inoculating the secretion from the genital lesion in this area. They covered the skin with a watch-glass and after five days they looked for a typical soft chancre lesion. Some more rigorous doctors took a swab of the secretion using the Gram technique to look for coccobacillus grouped in chains, characteristic of infection by *H. ducreyi*. Perhaps these doctors were trying to identify the disease according to Koch's Postulates



presence of Gram-negative coccobacillus, consistent with H. ducreyi.





(b) A more detailed view of drainage from a hole in an inflamed satellite adenopathy, generally unilateral, of a soft chancre. This drainage is totally different to lymphogranuloma venereum, which occurs via multiple small holes, giving the appearance of a showerhead



Fig. 4.5 (a) Prominent unilateral inguinal mass associated with numerous ulcerative and purulent lesions on the penis. In cases of soft chancre, it is very common to observe the presence of significant inflammation caused by polymorphonuclear cells. (b) In this case, *H. ducreyi* infection (bacterioscopy using the Gram technique) and syphilis (bacterioscopy using darkfield microscopy and positive immunoflu-

orescence, VDRL 1:64) were diagnosed. This was not a case of Rollet's chancre, as the syphilis was at the papular syphilide stage and not in the initial stages of hard chancre (primary syphilis). This patient was also seropositive for HIV. (c) The *yellow arrow*, in the foreskin area, shows the papular syphilis lesion



Fig. 4.6 Soft chancre lesion containing a large amount of purulent discharge, which was leaking and is therefore easily confused with urethral discharge (see *arrow*). In these situations, the pus should be gently cleaned from the glans and the patient should be advised to try to empty their urethra from the lower part of the meatus. This will help to confirm a diagnosis of soft chancre with or without any simultaneous urethral discharge symptoms

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Fig. 4.7 Extensive phagedenic soft chancre lesions. (a) Posterior side of the penis. (b) Side of the penis. These lesions are often extremely painful, and in patients with HIV/AIDS, viral etiology for herpes simplex should be routinely investigated. Although we have never used it,

there is a molecular biology diagnosis kit for three causes of genital ulcers: *Herpes simplex*, *Treponema pallidum* and *H. ducreyi* (multiplex)



Fig. 4.8 Typical soft chancre symptoms: multiple painful purulent lesions, with rapid onset, in a patient with a history of not using condoms, having multiple partners and from a lower social class



Fig. 4.9 In this case, intracellular Gram-negative coccobacilli bacteria were found in the lesion, inside polymorphonuclear cells and/or grouped in chains, many of them resembling train tracks. Very close to the ulcer there was a papular lesion, which typically precedes the appearance of ulcers. A biopsy of this revealed cells with koilocytosis, characterizing infection by HPV. The HPV lesion is indicated by the *arrow* in the close up



Fig. 4.10 A patient who attended the Sexually Transmitted Disease unit at the Fluminense Federal University (DST-UFF), presenting lesions on his penis that had appeared five days previously. He reported pain in this area and in the left inguinal region. In (a), note the two lesions pointed out by the *arrows*. In (b) the lesion to the side of the frenulum is dirty. In (c) it has a clean appearance after swabbing for bacterioscopy using the Gram technique. With the lesion clean, we squeezed the base of the ulcer, which was soft, to take a sample swab to search for spirochetes. Another dirty lesion can be seen in (d), and we followed the same routine for the cleaned lesion in (e). While we were carrying out these procedures, we noticed a vegetative lesion with the appearance of a small cauliflower, *arrow* shown in (f). This was

removed, and histopathological screening revealed the presence of condyloma acuminata (HPV) in the urethral meatus. The results of bacterioscopic examination were totally consistent with soft chancre. Serological screening for syphilis and HIV gave a negative result, carried out on two occasions with an interval of 30 days. Although one of the patient's partners presented symptoms of vaginal and cervical discharge, she was not diagnosed with any STDs. Serological screening (syphilis and HIV) was also negative. Despite this, we decided to prescribe her the same medication as her partner: azithromycin. We weren't able to examine any other patients, as despite the fact that they were invited by the patient, they did not seek out our medical services.

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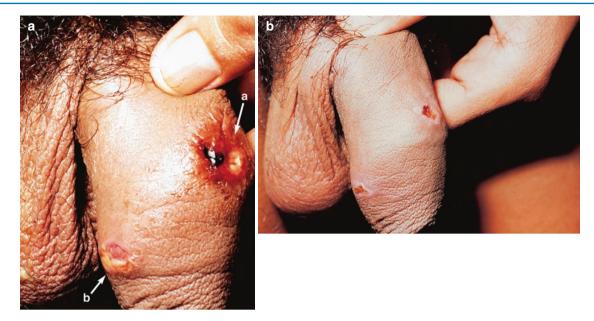


Fig. 4.11 (a) Patient presenting two very distinct lesions. The ulcer pointed out by the *arrow* in (a) was soft upon palpation and very hyperemic, with a small area of necrosis and purulent discharge. Direct examination revealed the presence of intracellular Gram-negative coccobacillus in polymorphonuclear (PMN) and in chains. The ulcer pointed out by the *arrow* in (b) had a base that was hard upon palpation, and direct bacterioscopy using the darkfield microscopy technique

revealed spirochete bacteria similar to *T. pallidum* and the absence of the bacterial forms typical of *H. ducreyi* (stained smear using the Gram technique). In our opinion this was not mixed chancre, as these were two distinct lesions and were easy to observe clinically. (b) During the healing process after a week of antibiotics (penicillin G benzathine and trimethoprim -sulfamethoxazole)

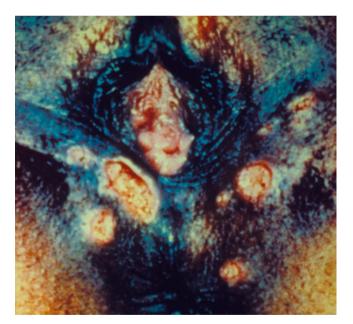


Fig. 4.12 Multiple ulcerative and purulent lesions on the vulva of an adult woman. The literature shows that cases are much more common in men than they are in women. Some sources have cited a ratio of 20 cases in men for every single case in a woman. There is no scientific explanation for this

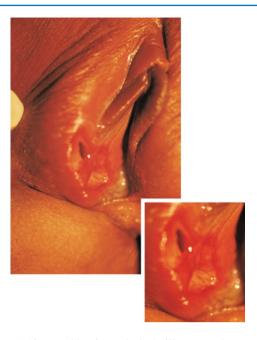


Fig. 4.13 A 13-year-old patient, who had still not started menstruating, who was homeless and had been working as a prostitute for a year. She was seen and prescribed medication according to the syndromic approach for ulcerative genital lesions without vesicles: early syphilis + soft chancre. Bacterioscopy of a stained smear using the Gram technique revealed a high quantity of polymorphonuclear cells with Gram-negative streptobacillus. Darkfield screening for Treponema and VDRL were negative. Serological screening for syphilis (VDRL) was repeated after a month and was still negative. HIV screening was positive. This situation demonstrates how serious child prostitution is, and in this case the child had not even started to menstruate, increasing the risk of HIV infection. We would like to take this opportunity to emphasize once more that there are very few medical services that have access to direct examination techniques during consultations (Gram technique, darkfield...). Therefore, the syndromic approach for genital ulcers (treat syphilis and soft chancre, provide guidance, offer serological screening for VDRL, HIV and hepatitis B and C, recommend that sexual partners attend the clinic, provide condoms and refer the case to the relevant surveillance service) can be effective. However, it is worth highlighting that the chances of overmedication (one antibiotic too many) are high



Fig. 4.14 Case of ulcerative lesions with a soft base that were developing quickly. Screening for syphilis was negative (bacterioscopy/serology). The adenomegaly was unilateral, moderately painful and inflamed. The patient reported that this was the first time they had experienced this kind of genital lesion. Bacterioscopy of a swab of the lesion revealed a typical clinical picture of soft chancre. Cytology of the swab using the Giemsa technique did not reveal any HSV viral infection. The patient was prescribed oral azithromycin 1 g and clinical cure was achieved within 1 week

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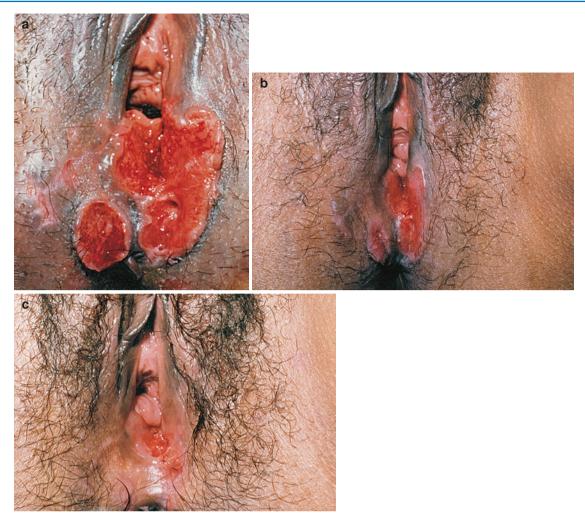


Fig. 4.15 (a) Extensive and painful genital ulcers in a young woman. Direct examination revealed a clinical picture consistent with soft chancre. Serology screening was carried out for syphilis (on three occasions), and all results were negative. This patient was seen at the beginning of the 80s, at a time when HIV screening was not available. She was given thiamphenicol and clinical cure was achieved very quickly. (b) Following on from the previous case. Photograph taken 1

week after treatment had begun. (C) Photograph taken after 2 weeks of treatment. Cases that are similar to this, wherever possible, should involve routine screening for *H. ducreyi* and *Treponema pallidum*, genital herpes, donovanosis and HIV infection, as well as serology screening and evaluation of the patient's vaccination history (hepatitis B, HPV...)

Fig. 4.16 Ulcerative lesions on the foreskin, with softened bases, accompanied by a large amount of purulent discharge. Serological screening (syphilis and HIV) was negative during the consultation. However, in order to avoid any surprises, serology testing should be repeated 30 after treatment. In this case, both tests were still negative. The partner was examined, and clinically examination revealed just bacterial vaginosis. Serology screening of the sexual partner was also negative. Under closer examination, multiple lesions can be seen on the scrotum. These were pruritic and the diagnosis was scabies. This was treated with two 6 mg pills of oral ivermeticin. Hygiene habits and certain types of underwear were recommended



Fig. 4.17 Extensive lesions covering the body of the penis and the scrotum. The patient also presented two other lesions to the foreskin. All of the lesions were soft and purulent. He also had moderately inflamed unilateral inguinal adenomegaly. He reported having a non-exclusive, fixed partner, and that he often practiced oral sex, during which his sexual partner would put his entire scrotum into her mouth and bite it "softly". She also did the same with his penis. He did not use a condom with this partner. He used a condom almost always with other occasional partners. Direct bacterioscopy of a swab from one of the lesions revealed the presence of Gram-negative coccobacillus in chains and inside polymorphonuclear cells and associated with Gram-positive cocci. Additional screening for donovanosis, syphilis and HIV was negative. As the patient had presented these lesions 3/4 weeks previously, we carried out a biopsy. Histopathological examination revealed just a highly purulent inflammation. The sexual partner was examined and was diagnosed with just bacterial vaginosis. Serological testing for syphilis and HIV was negative on two occasions. Interestingly, she reported having a dental abscess 1 month before her boyfriend developed his lesions







Fig. 4.18 (a) This case of soft chancre shows that, although rare, a single lesion can occur. However, the patient in question reported that at the start, a week before this photograph was taken, two small ulcers

appeared that in three days merged into just one. (b) The patient after full recovery. Photograph taken 5 weeks after treatment of a single dose of oral thiamphenicol 5 g

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Fig. 4.19 A case of soft chancre in an adolescent patient. Note that the lesions are deep and phagedenic



Fig. 4.20 Patient with penile ulcers diagnosed as soft chancre through stained bacterioscopy using the Gram technique. The patient reported a history of genital herpes. These symptoms had lasted for 2 weeks, even with application of topical and oral acyclovir. He mentioned that on the three occasions that he received a clinical diagnosis of genital herpes, the lesions had started off as "small bubbles". The lesions he presented with had started off as small sores. Bacterioscopy of a smear of the lesion suggested chancroid and also revealed hyphae consistent with *Candia* sp. infection. Cytology of the smear using the Giemsa technique did not reveal the cytopathic effect caused by HSV infection. The patient received 1 g oral azithromycin, clinical supervision at the center and guidance on hygiene. He later reported by telephone that he had fully recovered within a week. He never returned to the clinic. Serological screening for syphilis and HIV was negative



Fig. 4.21 In this case we can see an extensive ulcer with inguinal adenopathy. Although resistance to antibiotics is not very frequent (there are not many reports of this), it can happen. At first we considered this possibility, as the patient reported that they had already self-medicated with two types of antibiotic. However, after taking a detailed medical history, we discovered that on both occasions the patient did not take the antibiotics properly (in terms of dose or interval). After supervised medication at the clinic, a full recovery was achieved within a week

Fig. 4.22 In our experience, soft chancre is typically found in patients from low social classes. This case is an exception, as the patient had a high level of education and income. However, there were more peculiarities involved: this is a case of Rollet's chancre (soft chancre + hard chancre/syphilis). Clinically these lesions can be confused, as they have the characteristics of both diseases. It is most probable that in this case these had been contracted from different people. Three to four weeks before the lesions appeared, the syphilis was contracted, and 1 week before, soft chancre was contracted. The two diseases then manifested at the same time, presenting the characteristics of both. The patient reported having multiple sexual partners (more than 20 in the previous 6 months). This shows that it is only possible to obtain the correct diagnosis when genital ulcers are routinely investigated while considering the various possibilities. However, we emphasize that in around 25% of cases of genital ulcers, even where good clinical and laboratorial techniques are used, etiology cannot always be determined with much certainty. The arrow shows the area with the hardened lesion. Serological screening for syphilis and VDRL was positive (1:32). Screening for HIV on two occasions with an interval of 30 days was negative. Serological markers for hepatitis B and C were also negative. A course of vaccines for hepatitis B was prescribed. Note: during the revision of this edition we attended this patient who reported that his current wife had received a diagnosis of low grade squamous intraepithelial lesion (LSIL) from a Pap smear. Clinical examination of the patient did not reveal anything. However, serological screening for HIV was positive. The same result was obtained for his current sexual partner, who he reported to be exclusive







Fig. 4.23 (**a**, **b**) Rollet's chancre (soft and hard chancre). These cases present lesions that are clinically confusing (they appear to be both syphilis and soft chancre). Direct examination revealed the presence of spirochetes (darkfield microscopy) and Gram-negative coccobacillus in chains inside polymorphonuclear cells. These lesions were very phagedenic (destructive). The patient did not present any roseola. It is good that Rollet's chancre is extremely rare. Serology screening for

syphilis was positive (VDRL = 1:8 and FTA-Abs positive). Screening for HIV was carried out twice over 30 days and was negative on both occasions. Serological markers for hepatitis B and C did not react. A course of vaccinations for hepatitis B was prescribed. We emphasize that vaccination history for hepatitis B and markers for hepatitis B and C must be investigated for all patients, whether in STD clinics or other medical centers





Fig. 4.24 (a) Patient presenting a single, week-old uncreative lesion that was slightly painful, with a moderately softened base and containing a seropurulent discharge (not pus), which can be seen better in the close up. He also presented desquamation to the glands, which he also reported to be itchy. Adenitis was present, which was slightly painful, especially upon palpation, and which showed characteristics of micropolyadenomegaly. VDRL screening was positive with a titer

value of 1:8. Serological screening for HIV was negative. Direct bacterioscopy of a swab of the lesion (b) revealed this to be a case of soft chancre. Although darkfield bacterioscopy was non-specific, this case, with positive serological results for syphilis, could be another case of mixed chancre. We proceeded to provide treatment for both diseases: soft chancre and syphilis



Fig. 4.25 This patient presented extensive suppurating adenitis with an area of necrosis associated with a hyperemia on the skin of the inner thigh. These symptoms were associated with similar processes on the glands and the posterior side of the foreskin, and there was also a large edema on the penis. As a result of the patient's intense pain, it was not possible to properly visualize the penile lesions. However, a sample was collected with a thin swab for bacteriological examination. This provided a diagnosis of soft chancre. As a result of the severe symptoms, consistent with local secondary infection, we opted to prescribe antibiotics (ciprofloxacin) and an analgesic/anti-inflammatory (ibuprofen) for 10 days

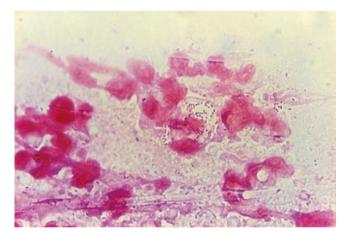


Fig. 4.26 Swab of purulent discharge stained using the Gram technique, taken from ulcers on the foreskin of this patient, demonstrated characteristics of intra and extracellular Gram-negative coccobacillus, suggesting *Haemophilus ducreyi* (×1000)

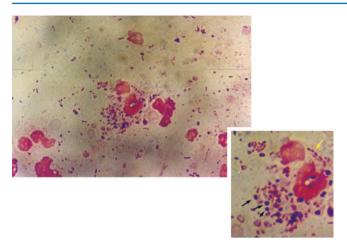


Fig. 4.27 Purulent discharge taken from an ulcerating lesion and stained using the Gram technique. Direct bacterioscopy revealed the presence of very small gram-negative rod cells, lined up and in chains and inside polymorphonuclear leukocytes, suggesting *Haemophilus ducreyi*. Another frequent situation can be observed: various grampositive cocci, probably of the genus *Staphylococcus*, that provide growth factor V (nicotinamide adenine dinucleotide)—a phenomenon known as satellitism. In the close up we show the lining up of gramnegative coccobacillus (*yellow arrow*) and gram-positive cocci (*black arrows*) (×1000).

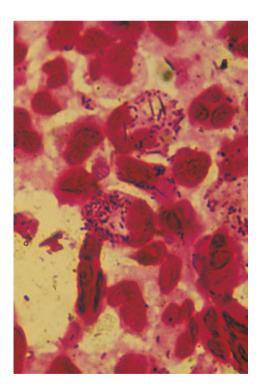


Fig. 4.28 Symptoms very similar to those shown in cases 24 and 25. Here the coccobacillus does not have its typical pink color and appears darker, however, as a result of problems with the coloring technique



Fig. 4.29 Photograph of a sample of a culture showing *H. ducreyi* grouped in chains, imitating train tracks (courtesy of Professor Kenneth A Borchardt)

5.1 Synonyms

Inguinal lymphogranuloma, Nicolas-Favre-Durand disease, climatic bubo, the fourth disease, benign suppurative periadenitis.

5.2 Concept

Sexually transmitted disease characterized by the presence of large inguinal buboes at an advanced stage.

5.3 Incubation Period

One to two weeks.

5.4 Etiological Agent

Chlamydia trachomatis, serovars L1, L2 and L3.

5.5 Clinical Manifestations (Figs. 5.1–5.12)

The main symptom is inflamed and painful inguinal adenitis (buboes). These may be due to advanced-stage genitoinguinal or chronic genitorectal lesions.

The advanced stage may develop into multifocal fistulation, which is recognized as a "watering can" type suppuration. During this phase, a feeling of general unwellness similar that associated with a cold may occur. The chronic phase may affect the pararectal lymph nodes, causing anal stenosis. The genital region may develop elephantiasis, fistulas and ulcers. On the vulva this is called esthiomene.

At the beginning of the outbreak, the patient often has a feeling of general unwellness, fever and loss of appetite, which can lead to weight loss.

5.6 Laboratory Diagnosis

Laboratory diagnosis to confirm LGV is still substandard in developing countries, demanding of health professionals a mixture of intuition and clinical acumen. Laboratory diagnosis can be carried out via: cytology through Giemsa or Papanicolaou staining with observation of inclusion bodies (Figs. 5.18, 5.19), detection of *C. trachomatis* by culture in cell media, serological screening (complement fixation test, immunofluorescence, microimmunofluorescence and dose of anti-*Chlamydia* IgA—anti-MOMP IgA), (molecular biology (PCR) of samples swabbed from lesions or buboes. Serological screening, complement fixation test) is important if titers are equal to or lower than 1:64.

Evaluation of Laboratory Methods (Lewis, DA—modified)

Exam	Sensitivity %	Specificity %
Giemsa	45	95
Papanicolaou	62	96
Elisa	70-80	>99
Immunofluorescence	80-92	>99
PCR	>95	>99
Serology	40-50	85

5.7 Treatment and Control

The therapeutic regimens recommended by the Centers for Disease Control and Prevention (CDC, 2010) and the UK National Guideline for the management of lymphogranuloma venereum (UK, 2013) are provided in the table below.

Antibiotic	Dose	Frequency	Duration	Route of administration
Doxicycline	100 mg	12/12 h	21 days	Oral
Doxicycline	200 mg	24/24 h	21 days	Oral
Erythromycin	500 mg	6/6 h	21 days	Oral
Azithromycin	1 g	1× week	3 weeks	Oral

Other therapeutic regimens using tetracycline, minocycline and moxifloxacin are described in the literature.

- Oral sulfametoxazol 800 mg + trimetoprim 160 mg, 12/12 h for 21 days.
- Oral tianfenicol 500 mg, 8/8 h for 21 days.

Laboratory control exams are not required if the recommended therapeutic regimen has been concluded.

5.8 Complications (Figs. **5.13**–**5.17**)

The difficulty of initial diagnosis of LGV or inadequate therapeutic approach may lead to complications, which include proctitis, proctocolitis sometimes imitating Crohn's disease, fistulas, stenoses and disfiguring fibroses, vulval ulceration, stenotic proctitis and elephantiasis of the vulva (esthiomene), penis, scrotum or perineum.

5.9 Differential Diagnosis

Soft chancre, syphilis, ganglionic or vulval tuberculosis, cat scratch disease (benign lymphoreticulosis) and Hodgkin's disease should be considered at first. Lapromatous leprosy and paracoccidiodomycosis (blastomycosis) with large inguinal masses may also be included in differential diagnosis.

5.10 Observations

- Antibiotics do not have a dramatic effect on the duration of inguinal lymphadenopathy, and the sequelae associated with the chronic phase do not recede. Advanced symptoms are quickly eradicated.
- Adequate therapy is associated with a decline in antibody titers detected through serological screening.
- In pregnant women, azithromycin may be the best option and doxycycline is contraindicated.
- Consider puncturing and draining buboes with a large calibre needle. Incision and surgical draining are formally contraindicated as they hinder the healing process or develop into fistulas.
- In the past decade, an increase in the number of cases of LGV has been observed in Europe, mainly affecting men that have sex with men (MSM) that are HIV positive and through serovar L2b of *C. trachomatis*. However, in our experience cases of LGV are rare.

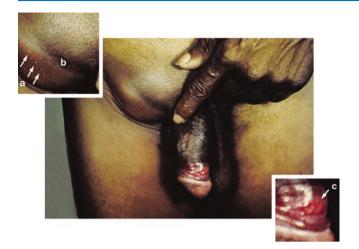


Fig. 5.1 Large and highly inflammatory inguinal mass that was painful and unilateral. These large adenitis are also known as buboes. In this rare case, the initial inoculation lesion can be observed in the balanopreputial groove. Observe the folding of the inguinal mass caused by it attaching to Poupart's ligament and forming a groove sign. In the close ups: (*a*) suppurating pores (with the appearance of a "watering can"); (*b*) attachment to Poupart's ligament; (*c*) inoculation lesion

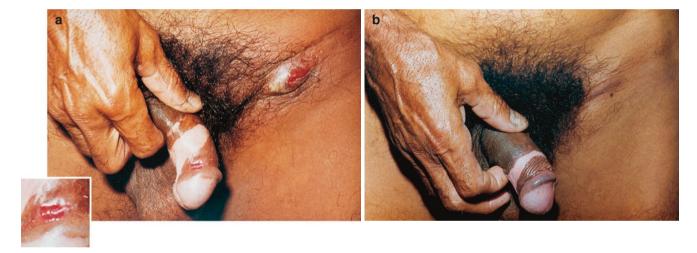


Fig. 5.2 (a) Very similar to the previous case. However, in this case the inguinal mass is smaller. The colorless area on the penis is vitiligo. In our experience, these cases of buboes together with the initial inoculation lesion (shown in the close up) are not common. We managed to

examine the regular sexual partner (the patient reported having multiple sexual partners), who did not present any genital infection. (b) Development with complete clinical cure



Fig. 5.3 Typical case of buboes caused by inguinal lymphogranuloma in acute-stage LVG. Although we show various cases of LGV here, we do not consider this disease to be a serious risk to public health. Observe the groove sign on the inguinal mass



Fig. 5.4 Identical to the previous case. One of the sexual partners was also examined and presented just vulvovaginitis caused by *Candida* sp. In all of the patients which we diagnosed with LGV, we did not find cases of lymphogranuloma venereum in sexual partner. In addition, in our experience this infection is found more frequently in men





Fig. 5.5 (**a**, **b**) Cases of LGV often present a lot of pain in the regions of the inflamed adenopathy. This represents acute-stage genitoinguinal syndrome. In these situations, puncturing the lesion with a large calibre needle can provide the patient with some comfort. Reducing the volume of the inguinal mass reduces the pain. Testing of this material for *Chlamydia* may be positive. Cytology of this type of material is a simple procedure, although it is not always possible to observe the inclusion bodies that suggest infection by *Chlamydia*. However, if the material taken from the buboes is grown in ordinary media, mainly pyogenic bacteria will grow





Fig. 5.6 (a, b) Same situation as described in the previous case. According to information provided by the patient, the sequel on his glans was from two previous episodes of soft chancre. To puncture the lesion, a small anesthetic button can be made using xylocaine and a fine needle (insulin needle) to reduce the pain of the insertion of the larger needle. However, some doctors prefer to insert the larger needle straight away as they believe that the local anesthetic does not significantly

reduce the pain of the main procedure (removal of thick purulent material). Both practices are valid in our opinion, as long as they are carried out carefully and slowly and that the patient's wellbeing is always kept in mind. Abrupt or "heavy handed" movements that may be used when only teaching or scientific interest are considered should be completely avoided. This patient was diagnosed as HIV positive during a follow up appointment 1 year after he was treated for LGV





Fig. 5.7 (a) Patient presenting an extensive inflamed inguinal lymphadenomegaly with areas that are already suppurating. Some of the holes also have periorificial necrosis. Patients with acute-stage LGV associated with painful buboes, which have a detrimental effect on mobility, often complain of a feeling of general unwellness similar to that associated with a cold, a low to moderate fever (38 °C), headache and loss of appetite. Diagnosis is essentially clinical in the vast majority of cases, through clinical exclusion and therapeutic evaluation. This is because

the tests that confirm LGV diagnosis are not carried out during consultation. When blood cell counts are taken they reveal slight leukocytosis and an elevated ESR (erythrocyte sedimentation rate). We usually recommend that patients remain absent from work for at least 3 days, mainly due to pain and difficulties in mobility. (b) During follow up, the patient's inguinal mass is clearly improving 1 week after antibiotics were administered



Fig. 5.8 Case of a 6-year-old child who was referred for incision and drainage of a large and painful inflamed inguinal mass at a general hospital. The child was initially diagnosed with a simple inguinal abscess requiring surgery. When we found out about the case we immediately suspended the procedure and started to investigate the possibility of sexual abuse. The mother informed us that an uncle who was very close to the family had presented very similar symptoms about a month previously. We decided to puncture the lesion with a large calibre needle to alleviate the pain of the bubo. We don't know the scientific explanation for this, but according to the testimony of our peers the healing of LGV buboes is very slow, and the improvement is rapid after administration of antibiotics together with anti-inflammatories/analgesics. Therefore, there is no justification for incision and drainage. Serological screening for chlamydia was highly positive. Many cases of suspected sexual abuse do not result in any conviction. This was one of those cases

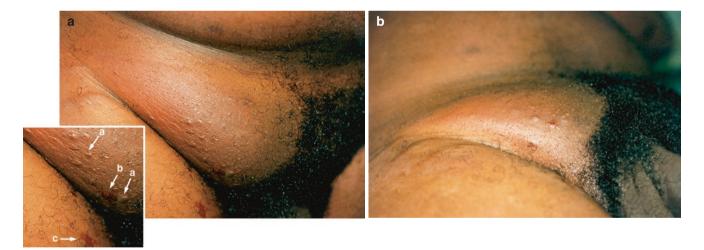


Fig. 5.9 (a) Patient with acute-stage LGV: genitoinguinal syndrome where the initial process that develops into fistulation into multiple orifices ("watering can" sign) can be observed. In this case in particular, complete fistulation did not take place as treatment was started. The classic treatment regimen includes tetracycline 500 mg 4× a day or doxycycline 100 mg 2× a day, always from 2 to 3 weeks. Currently, azithromycin can also be used, however not in a single dose. Remember

that for this disease therapy must include 2-3 weeks of antibiotics. If oral azithromycin 1 g is used, this should be repeated twice with an interval of 1 week. In the close up: (a) pores that are almost starting to suppurate; (b) a pore that is already drained; (c) secretion coming out of a suppurating pore. (b) A different view of the same patient showing the prominent inguinal mass

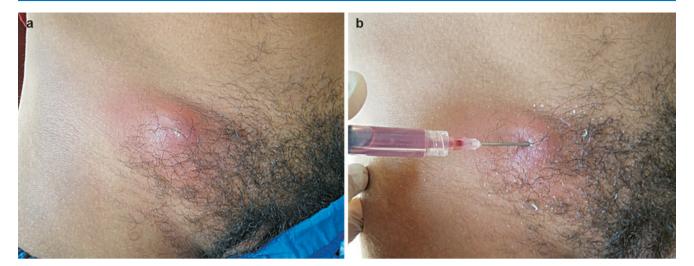


Fig. 5.10 (**a**, **b**) Adolescent of 19 years old presenting a tumor and heat and redness in the right inguinal region. He reported this appearing 2 weeks previously with a "wound" on his penis that disappeared shortly after, followed by discomfort in the groin area. He said that he sought treatment at a family health clinic in a rural area of Rio de Janeiro, where a nurse referred him to the STD clinic. First, we saw the patient outside of the health center. The following day at a medical center we emptied the bubo, requested exams and prescribed oral

azithromycin 1 g once a week for 3 weeks and oral piroxicam 10 mg once a day for 5 days. Since the patient reported not having been immunized against hepatitis, we prescribed a course of hepatitis B vaccinations. Serological screening for syphilis, hepatitis B, hepatitis C and HIV was negative. Serological screening (ELISA) for chlamydia was positive. A drop of pus taken from the bubo was smeared on a glass slide for cytological analysis. The results reveled a cytopathic effect suggestive of inclusions caused by *Chlamydia*

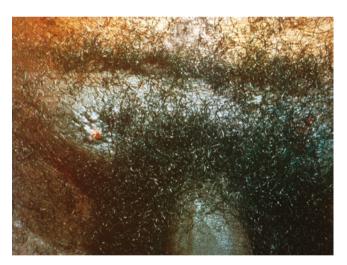


Fig. 5.11 Case of LGV in the healing phase with multiple fistulas in a patient whose treatment was started after fistulation occurred



Fig. 5.12 Although a classic observation in cases of LGV, "watering can" sign is extremely rare. Observe the multiple orifices with halos of inflamed hyperemia and suppuration. The "groove sign" can be seen in the middle of the bubo, meaning the lymph nodes underneath have attached to Poupart's ligament forming a groove



Fig. 5.13 Chronic-stage lymphogranuloma venereum with ulcerations in the scrotum and in the inguinal region. As well as ulcers, enlargement of the genitalia can also be observed. Differential diagnosis for soft chancre and donovanosis should be carried out in such cases



Fig. 5.14 Residual scarring from cured LGV in the right inguinal region. However, sequel with contractions caused by healing ulcers and fistulas cannot be removed very easily



Fig. 5.15 (a) Case of rarely occurring esthiomene, including vulvar edema (elephantiasis) and fistulas with pus and contractions, characterizing chronic-stage genitorectal syndrome. During this stage, fistulation of lymph nodes infected from the internal iliac chains to the rectum can also be observed, developing scarring, contractions and stenosis of the rectum. This alteration presents clinically as "stringy stools" as a result of rectal constriction. Surgical correction of stenosis may be recommended, however this is generally not successful due to chronic constriction. In most cases LGV diagnosis is clinical, other diseases and through therapeutic evaluation. Diseases such as vulvar tuberculosis,

paracoccidiodomycosis and Crohn's disease should not be forgotten as differential diagnosis. Serology for *Chlamydia trachomatis* may help, and if it cannot be done immediately, blood should be taken and the serum stored for future analysis as soon as possible. This should also be carried out for other materials, such as biopsy fragments (conserved in buffered formalin or kept in a dry, sealed flask in a freezer for future DNA analysis). (a) The *arrows* point out: (a) a fistula draining pus; (b) drained and healed fistulas with contractions; (c) rectal constriction with stenosis. (b) Observe the perineal fistula stretching to the vaginal furcula



Fig. 5.16 Genital elephantiasis in a male. This patient had a history of enlarged genitalia after an ulcerative STD contracted 15 years ago. He could not inform us exactly which STD he had or which medication he took. He reported that he had a painful and inflamed large mass in his groin. This was probably chronic-phase LGV with sequel



Fig. 5.17 Injury is uncommon to be observed even in MSM or women who practice anal sex, whose main manifestation is a hemorrhagic proctitis or proctocolitis with mucoid, bloody or mucopurulent secretion, with tenesmus, pain, anal pruritus, constipation or diarrhea

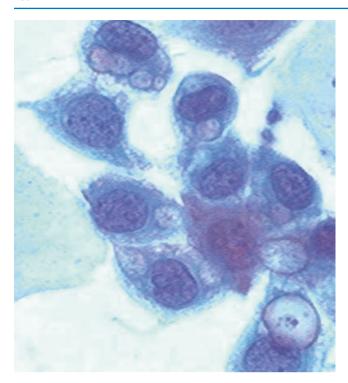


Fig. 5.18 Liquid-based cytology (SurePath®) suggestive of Chlamydia infection. Observe the cytoplasmatic inclusion bodies in vacuoles of thickened walls (1000×)

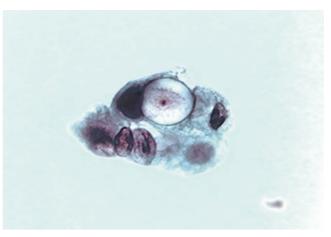


Fig. 5.19 Liquid-based cytology (SurePath®) suggestive of Chlamydia infection. The cytoplasmatic inclusion bodies are in vacuoles of thickened walls (1000×). The background is clean because of the technique that separates leucocytes

Donovanosis

6.1 Synonyms

Granuloma inguinale, granuloma venereum, granuloma inguinale tropicum, granuloma contagiosum, ulcerating granuloma, ulcerating sclerosing granuloma, chronic venereal ulcer, granuloma donovani.

6.2 Concept

Progressive disease characterized by ulcerating granulomatous lesions that are painless and self-inoculable. This disease mostly affects the skin and mucous membranes of the genital, perineal and inguinal regions.

6.3 Incubation Period

Widely variable, from 3 days to 6 months.

6.4 Etiological Agent

The etiological agent of donovanosis used to be known as *Donovania* and then came to be known as *Calymmatobacterium granulomatis*. In a well-founded study published in 1913, professors Aragão and Vianna [1], who were studying patients in the city of Rio de Janeiro, proposed the name *Calymmatobacterium granulomatis*. In 1999, Carter et al. [2] used molecular methods and phylogenetic similarities to propose the reclassification of the agent as *Klebsiella granulomatis comb. nov.* However, Kharsamy et al. [3], while studying 16S rRNA gene sequencing found a similarity of

approximately 95% for the Klebsiella and Enterobacter genera. Therefore, they concluded that *C. granulomatis* was a unique organism. This organism is a Gram-negative facultative aerobic bacteria, apparently an intestinal saprophyte and possibly opportunistic, which depending on individual susceptibility or bacteriophage action can penetrate the tegument and cause the disease.

6.5 Clinical Manifestations (Figs. 6.1–6.14)

The disease has a range of symptoms, including ulcerative lesions with a bright red granulomatous base that easily bleeds, with hypertrophic or flat borders, which may be ulcerovegetative or with elephantiasis and that may develop necrosis. A varying number of these ulcers can be observed and may sometimes be multiple, and they are chronic and usually **not** associated with regional lymphadenopathy. Extragential manifestations occur in 6% of cases and systemic dissemination via the blood causing damage to the bone and liver is rare.

6.6 Laboratory Diagnosis

Identification of *C. granulomatis* via Donovan bodies (Figs. 6.15–6.17) is most easily carried out using cytological smears and lesion biopsies stained by Wright, Papanicolaou, Giemsa or Leishman technique. These are found inside the cytoplasm of histiocytes and macrophages in the form of encapsulated cocobacilli, which are pleomorphic with rounded edges and become brightly stained with appearance of a safety pin. It is recommended that one swab be taken

from the center of the lesion and another from one of the recently developed borders. This procedure is also recommended for biopsies (using the Hematoxylin-Eosin staining technique), which must also contain healthy skin. To the Giemsa staining technique the slide should be air dried, and when using the Wright, Leishman or Papanicolaou techniques the slide should be fixed using alcohol or another cytological fixative agent. A specific kit should be used for analysis of swabs taken from lesions with liquid based cytology. It is true that liquid based cytology can make cellular characteristics easier to observe. However, we do not know of any comparative studies between conventional cytology and liquid based cytology. The culture for this type of bacteria is difficult in terms of its nutritional requirements. Genital lesions over 30 days old, particularly those that have not healed, require histopathological testing. Other diagnostic methods such as PCR and serological screening have still not been standardized or made commercially available.

6.7 Evaluation of Laboratory Methods

Exam	Sensitivity %	Specificity %
Swabs and biopsy	40-50	< 50

Cultures and PCR of swabs taken from lesions are unfortunately not available in routine medical practice, even in developed countries. However, in many cases it is possible to collect and store material for later molecular biology testing at a microbiological research laboratory

6.8 Treatment and Cure

The protocols set out by the Centers for Disease Control and the European guidelines for the management of donovanosis recommend the same medication. Treatment time is 3 weeks or until clinical cure has been achieved for all proposed regimens.

	CDC (2010)	EURO (2010)
Regimen	• Oral doxycycline 100 mg,12/12 h	• Oral azithromycin 1 g, once a week
	• Oral azithromycin 1 g, once a week	• Oral azithromycin 500 mg, once a day
	• Oral ciprofloxacin 750 mg, 12/12 h	• Oral Sulfamethoxazole/ trimethoprim (800 mg and 160 mg), 12/12 h
	• Oral erythromycin 500 mg, 6/6 h	• Oral doxycycline 100 mg, 12/12 h
	• Oral Sulfamethoxazole/ trimethoprim (800 mg	• Oral erythromycin 500 mg, 6/6 h
	and 160 mg), 12/12 h	• Gentamicin 1 mg/kg, IV, 8/8 h

	CDC (2010)	EURO (2010)
Pregnant women	• Oral erythromycin 500 mg, 6/6 h	• Oral erythromycin 500 mg, 6/6 h
	Consider adding a parenteral aminoglycoside (gentamicin, for example)	Oral azithromycin 1 g, once a week
Observations	Consider adding an aminoglycoside (for example, gentamicin 1 mg/kg, IV, 8/8 h) for any regimen if an improvement is not seen in the first days of treatment	Children: Azithromycin 20 mg/kg

Other therapeutic regimen have been used successfully, all of which for 3 weeks or until complete cure has been achieved:

- Oral ciprofloxacin 500 mg, 12/12 h (contraindicated for pregnant women, breastfeeding mothers and children);
- Oral thiamphenicol 500 mg, 12/12 h.

Control of cure is predominantly clinical.

6.9 Complications

Long-lasting lesions can suffer from secondary infections leading to deformations, mutilations and fistulas. In women this may lead to obstructive lymphatic obstructions that can develop into elephantiasis forms. Although rare, extragenital disease can occurr, generally resulting from a primary genital lesions and affecting the bones and other areas, especially in immunosuppressed patients. The development of squamous cell carcinoma in chronic ulcers is well documented, with a high incidence in patients with donovanosis.

6.10 Differential Diagnosis

Syphilis, soft chancre, cutaneous tuberculosis, ulcerative neoplasia, American tegumentary leishmaniasis and other ulcerative and granulomatous cutaneous disease.

6.11 Observations

 It is not common sexual partners have the disease, however any sexual partners from within the previous 60 days must be examined and offered treatment.

- This disease does not have a high occurrence/prevalence in areas with a high or very high Human Development Index (HDI).
- If it is not possible to perform exams during the consultation does not mean that material cannot be collected for a later examination.



Fig. 6.1 Patient presenting chronic ulcerative lesions (over 3 years old) with raised borders. She had on various occasions used a range of oral and parenteral antibiotics. This medication was used irregularly in terms of dose, interval and duration. Observe the marks left by plasters highlighted by the *arrows*. This was caused by bandages that the patient often had applied at health centers. For the duration of their "treatment" she never had any material collected for direct examination, cytology or biopsy (as reported by the patient). She remembered having been administered 10 ampoules of penicillin benzathine. She reported never having used a condom and having just two sexual partners that had no lesions on their penises. Material was collected for cytopathology (Giemsa and hematoxylin-eosin), and both tests were positive for Donovan bodies. This patient was seen in 1982

 In patients that come to the consultation having used topical products or cleaned the area we advise them to wash the area with regular soap (removing the product used) and return the following day without using any product. This way the lesion provides more data for diagnosis.



Fig. 6.2 This patient was seen at a public maternity ward (1978) in Niterói (Rio de Janeiro), during the expulsion stage of labor, presenting these vulvoperineal lesions that were over 2 years old. According to the patient, she attended over five prenatal consultations (within the public health system), but at no time was a gynecological examination recommended. As the lesions were not painful and she was ashamed of the problem, she didn't say anything to the obstetrician. She reported to have had over 10 sexual partners over the previous 10 years. Observe the large area of tissue necrosis. It should be emphasized that the best areas to collect material from-swabs for cytology (Giemsa, Papanicolaou, Warthin-Stary, Wright) or biopsies—are the borders with a more granular appearance, and the center of the lesion should also be considered for biopsy. In our routine we include at least three slides and/or three fragments from different areas of the lesions. This widens the chances of finding the cellular alterations that are typical of this etiological agent. Never collect necrotic material. Biopsies were carried out after the birth and removal of the placenta. The histopathological diagnosis was donovanosis

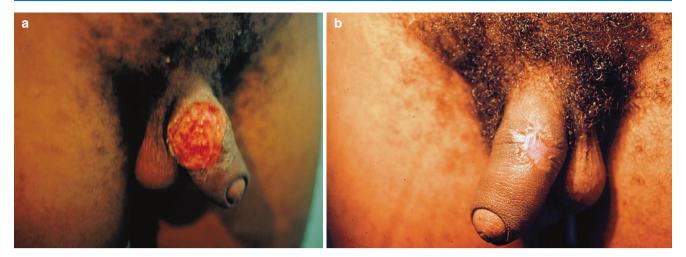


Fig. 6.3 This patient sought out our services presenting two large 4-week-old ulcers separated by an area of skin approximately 0.3 cm in size. He reported feeling slight pain. The lesions were covered with some seropurulent secretion. He also presented some non-inflamed unilateral adenitis. The patient reported not using condoms, having multiple partners and taking two ampoules of injectable penicillin 2 weeks previously, which lead to a slight improvement at first. However, after a week the lesions started to grow again. Our initial clinical diagnosis was soft chancre. However, we collected material for bacteriological examination, and under supervised treatment we administered 5.0 g

oral granulated thiamphenicol. (a) After 4 days the patient came back for follow up (when we took the photo shown in (a)), presenting this large ulcerative lesion to the body of the penis. The patient reported that the lesions merged after 2 days of taking thiamphenicol, but that he had already noticed a huge improvement in his genital and inguinal discomfort. The final diagnosis via histopathological examination was donovanosis. (b) Photograph taken 40 days after treatment was initiated, which began with 5.0 g granulated thiamphenicol and was followed by 2.5 g oral thiamphenicol every other day until five doses had been taken





Fig. 6.4 (a) Patient with a chronic donovanosis ulcer over 2 months old. (b) Patient completely cured, and similarly to the previous case, sequel and scarring are evident. This patient was treated with 500 mg oral thiamphenicol twice a day for 3 weeks. Serological screening for syphilis, HIV and hepatitis B was negative. We prescribed a course of

vaccinations against hepatitis B. Years later this patient returned to our center with fever and generalized adenopathy. Serological screening for syphilis and HIV was positive. He reported that he did not follow our advice to take the course of vaccinations against hepatitis B



Fig. 6.5 Donovanosis lesions almost always become chronic and phagedenic. This patient had already presented ulcers to the perineum that were treated (at another public health center) and healed. However, she then presented further ulcerations that were diagnosed as donovanosis





Fig. 6.6 (a) Diagnosing donovanosis lesions with a patient presenting the initial stages of the disease (less than 30 days) is very rare. This patient presented symptoms for just 2 weeks. Since wherever possible we include in our routine the collection of material for various exams, such as bacterioscopy using the Gram technique, darkfield bacterioscopy and/or the Fontana-Tribondeaux, Giemsa, Papanicolaou teh-

niques, direct examination and a reserve slide. We were able to identify this as a case of donovanosis. If lesions present 4 or more weeks, we include biopsies (center and new borders) with two or three fragments. Here the diagnosis was carried out via cytology of a swab of the lesion stained using the Papanicolaou technique. (b) Fifteen days after treatment with thiamphenicol

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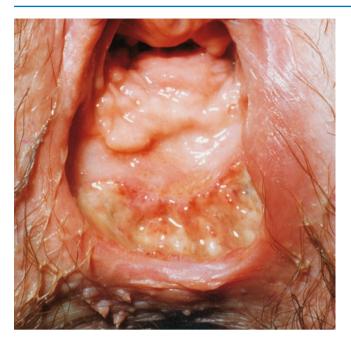


Fig. 6.7 Donovanosis on the vaginal furcula. This patient reported having a single partner who was examined by our team and did not present any genital alterations. All serological screening was negative. We also recommended vaccination against hepatitis B



Fig. 6.8 Clinically, donovanosis can present in various ways: ulcerative lesions with hypertrophic borders, vegetative lesions or extragenital lesions. It may even be systematic. Careful observation of this photograph shows a vegetative lesion in the perineum that could be easily diagnosed (clinically) as condyloma acuminata. Biopsy, however, revealed that it was donovanosis

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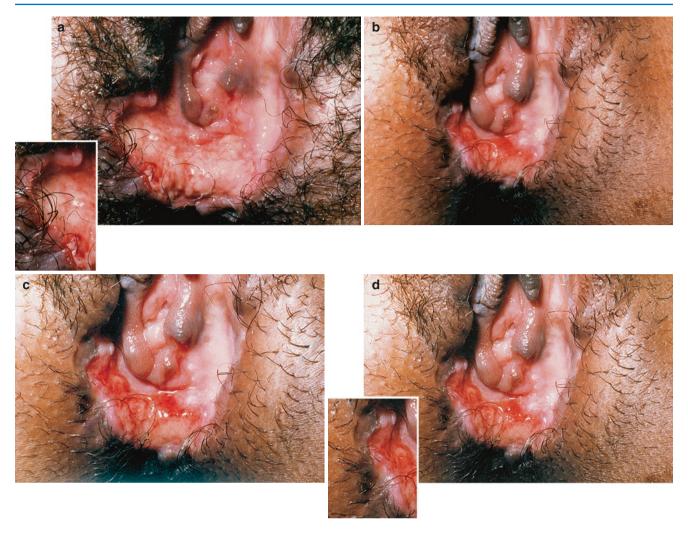


Fig. 6.9 (a) A case of donovanosis in the perineal region, with the hypertrophic borders shown in the close up. It is possible to observe the regression of the lesion (b–d). This patient's ulcer completely healed,

however, due to technical problems we don't have a photograph after it had fully healed. We examined the sexual partner and did not find anything abnormal on their genitals

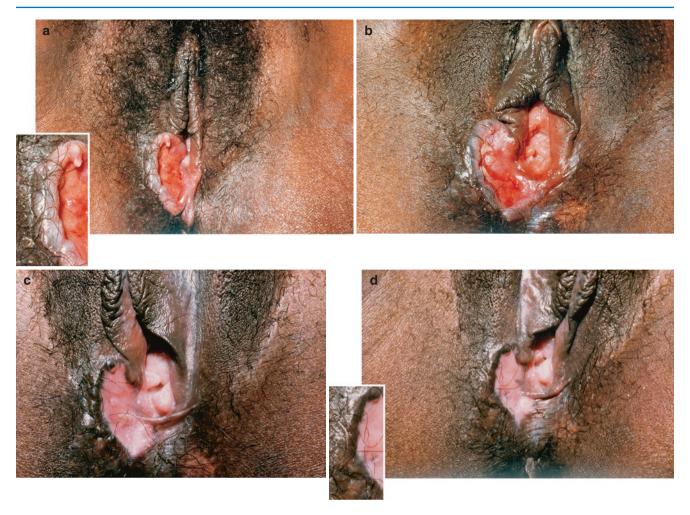


Fig. 6.10 (a) Very similar to the previous case. In the close up we show the hypertrophic border. This patient often had sexual relations with three different partners. We examined all of them and we did not find any case of donovanosis. She and her three partners tested negative for syphilis and HIV serological screening. However, one of them

tested positive for hepatitis B. This situation creates doubt about this disease to be a STD. In $(\mathbf{b-d})$ the regression of the ulcer until it has completely healed can be clearly seen. The sequel can also be seen on the skin of the vulva



Fig. 6.11 This 27-year-old male reported these lesions appearing 4 months previously. He reported that over the previous 2 years he had two sexual partners and that the lower lesion, which was the size of a pinhead, had appeared first and had gradually increased in size. He applied a range of local creams. And used sulfamethoxazole + trimethoprim for 1 week, with not much improvement. Then, he used oral tetracycline twice a day for just 5 days, as he could not get hold of the medication for any longer. Histopathological examination of a biopsy revealed donovanosis. At the time the public medical service in which we were working did not have a supply of oral antibiotics that we could provide to the patient. However, we did have a supply of streptomycin 1 g IM, which we administered once a day for 3 weeks. Complete cure was achieved by the end of this treatment. One partner was examined and presented just vaginitis caused by Trichomonas vaginalis. Serological screening for syphilis was negative for both patients. This was at the beginning of the 1980s. We would like to emphasize that we do not usually encourage the use of streptomycin in these situations



Fig. 6.12 This patient was in the second trimester of pregnancy when she sought the service of the STD clinic at the Alfredo da Matta Foundation in Manaus (Amazonas-Brazil) due to an extensive granulomatous lesion to her perineum and perianal region. This had appeared 3 months previously. Histopathological examination of a biopsy from the lesion, stained using the Warthin-Stary technique, identified the presence of Donovan bodies, confirming this as a case of donovanosis. She was treated with oral erythromycin (500 mg, 6/6 h) until clinical cure was achieved. She experienced a recurrence in her third trimester (also confirmed using histopathology). After the birth she was medicated with oral doxycycline (100 mg twice a day until clinical cure). It is worth noting that recurrences of donovanosis do not even respect previous scar tissue

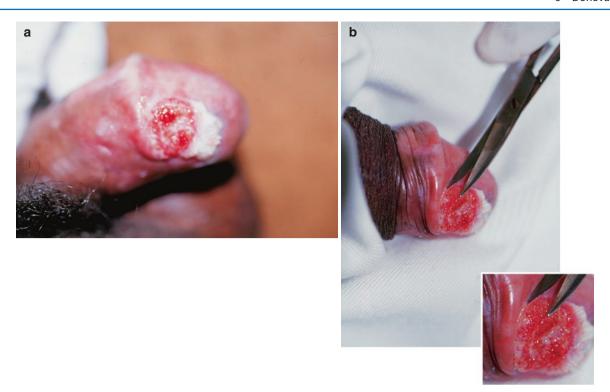


Fig. 6.13 (a) This 24-year-old patient presented an ulcerovegetative lesion with moderate purulent discharge. They reported it as being painless and there was no adenomegaly. They reported that it appeared 3 months previously with a small painless papule that developed gradually. They reported that they contracted syphilis 2 years previously and

had been treated with four injections of penicillin benzathine. VDRL was positive 1:2 and screening for HIV was negative. Biopsy and cytology using the Giemsa staining technique were positive for donovanosis. In (b) and in the close up the biopsy of a border using small curved scissors is shown

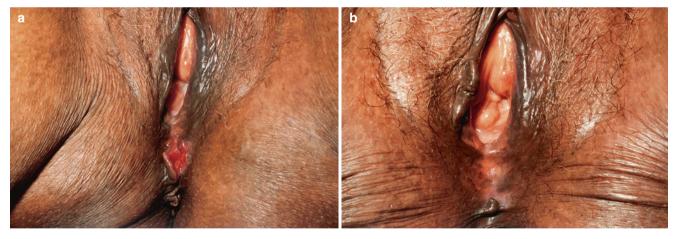


Fig. 6.14 (a) This 67-year-old patient reported not being sexually active for over 3 years. She had noticed a small lesion on her vaginal furcula 8 months previously, which grew despite her applying "antibiotic creams". She used oral pills and capsules of sulfa, ampicillin, erythromycin, tetracycline and fosfomycin irregularly and without finishing her courses of medication. All initial tests were negative. The patient was asked to refrain from using any type of local or systemic medication for 1 week. This was because in many situations these products can hinder or even prevent identify the etiological agent. The

patient returned 2 weeks later. Cytology using the Giemsa technique and biopsy provided a diagnosis of donovanosis. The public health clinic in which we were working did not have a supply of oral antibiotics that we could provide to the patient. However, we did have a supply of streptomycin 1 g IM, which was administered once a day for 3 weeks. This was in the beginning of the 1980s. (b) The lesion totally healed after administration of streptomycin 1 g IM/day. We would once again like to highlight that streptomycin should be avoided in cases of donovanosis and reserved for the treatment of infection by micobacteria

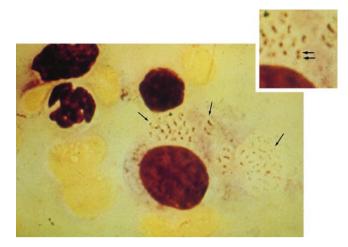


Fig. 6.15 Microphotograph of cytology using the Giemsa staining technique on a swab of a genital ulcer, showing the cytoplasmic vacuoles containing the bacteria that causes donovanosis—Donovan bodies (indicated by the *arrows*).



Fig. 6.16 Microphotograph of a swab of a donovanosis lesion showing Donovan bodies inside a mononuclear cell. The close up (*arrows*) shows bacteria in the form of dumbbells, well documented by two Brazilian researchers (Aragão and Viana) in 1912 in Rio de Janeiro. The observations of these professors were so good that the name *Calymmatobacterium granulomatis* (large capsule covering the bacteria and its granuloma inflammatory response) was given in recognition of their studies

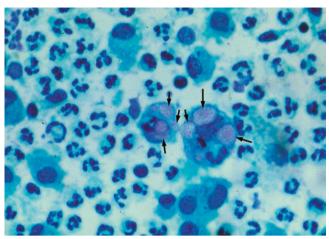


Fig. 6.17 This microphotograph of cytology using the Papanicolaou staining technique shows a smear with various polymorphonuclears, and the Donovan bodies in the middle of the field (indicated by the *arrows*). We emphasize that it is important to collect more than one slide, as finding the bodies containing the bacteria is not easy due to the low number of infected cells. In the same way, if the patient is using antiseptics or antibiotic creams, it can be even more difficult to find the etiological agent. Etiological diagnosis is not often viable

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References

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- Carter JS, et al. Phylogenetic evidence for reclassification of Calymmatobacterium granulomatis as Klebsiella granulomatis comb. nov. Int J Syst Bacteriol. 1999;49:1695–700.

3. Kharsamy AB, et al. Phylogenetic analysis of *Calymmatobacterium granulomatis* based on 16S r RNA gene sequences. J Med Microbiol. 1999;48:841–7.

7.1 Gonorrhea

7.1.1 Synonymy

Gonococcal disease, blennorrhea, clap, drip.

7.1.2 Concept

Infectious and contagious disease of the mucous membranes. Classic STD transmitted through intercourse in almost all cases; accidental or perinatal contamination is an exception.

More than a million STIs are acquired every day. In 2012, an estimated 357 million new cases of curable STIs (gonorrhoea, chlamydia, syphilis and trichomoniasis) occurred among 15–49 year-olds worldwide, including 78 million cases of gonorrhoea [1].

7.1.3 Incubation Period

Two to ten days after infecting contact. However, there are cases' reports of incubation period of 24 h and others which exceeds 20 days.

7.1.4 Etiological Agent

Neisseria gonorrhoeae. A diplococcus Gram-negative bacterium and polymorphonuclear intracellular. However, it may have its morphology and staining characteristics altered during chronic processes or after the use of antibiotics. This bacterium can be found extracellularly in the early stages of infection.

Sensitive to most antiseptics, dyes easily outside its habitat.

Often strains are detected with antimicrobial, plasmidial and chromosomal resistance.

7.1.5 Clinical Presentation (Figs. 7.1, 7.2, 7.4–7.26, 7.28–7.41, 7.44–7.51)

- Man: Sensation of formication or intraurethral itching with dysuria. Soon after, the urethral mucous arises and quickly becomes mucopurulent, with abundant and spontaneous elimination at the lightest pressure of the penis. The urethral meatus edges become swollen and erythematous.
- Woman: The gonococcal urethritis has no exuberance of symptoms as in men, and the clinical picture is composed of dysuria, urinary urgency and, less often, yellowish secretion. Cases are generally only explained by endocervicitis, which becomes a gonococcal infection suspicion when associated with the anamnesis data.
- It is assumed that half of the women infected with gonococcus is oligosymptomatic or even asymptomatic.
- Women with clinical sign of turbid or purulent cervical mucus complaining about pelvic pain or painful vaginal touch must be investigated into gonococcus and Chlamydia.
- Purulent vulvovaginitis due to gonococcus, although rare, is more frequent in rape victims and children, or during the first vaginal intercourse in pubescent women as they have the vaginal epithelium somewhat stratified.
- The pharynx and anus exposure of women and mainly of men who have sex with men is asymptomatic or oligosymptomatic in most patients.

7.1.6 Laboratory Diagnosis (Figs. 7.43, 7.52–7.60)

- Direct bacterioscopy: the Gram stain technique of urethral secretions shows the presence of Gram-negative diplococci inside polymorphonuclear.
- Culture: Thayer-Martin selective medium.
- Molecular biology technique (NAAT [nucleic acid amplification test]; hybrid capture)—high sensitivity and specificity

comparable to culture, which actually are increasingly obsolete. There are PCR kits that allow the diagnosis of multiple simultaneous infections including *Chlamydia trachomatis*, *Mycoplasma* sp., *Ureaplasma urealyticum*. Materials for these techniques can be collected by health professionals or by self-collecting. Specially, the first urine of the day.

- In cases of acute urethritis in men, the bacterioscopy is a good method. In woman, culture or molecular biology techniques of cervical canal is the best option.
- In women the simultaneous research in the urethra and endocervix is a good conduct, as the chances of positive results are increased.

Evaluation of Laboratory Methods

Exam	Sensitivity %	Specificity %
Gram		
Urethra	90-95	95–99
Endocervix	45-65	90-99
Vagina, anus	Not recommended	
Culture		
Urethra	94–98	>99
Endocervix	85-95	>99
Molecular biology		
PCR, hybrid capture	95–98	>99

7.1.7 Treatment and Control

Unrestricted access to antimicrobials combined with inadequate selection, overuse and subdoses of antibiotics, as well as the inherent genetic mutations of bacteria have contributed to the development of antibiotic resistance to *N. gonorrhoeae* throughout the world and is a constant concern of epidemiological control centers.

We have listed official protocols of cases of urethral, cervical and anorectal involvement with no complications of the Centers for Disease Control (CDC) 2015 [1], World Health Organization (WHO) Guideline, 2016 [2].

7.1.7.1 CDC 2015 [2]

Esquema recomendado: Ceftriaxona 250 mg, IM, dose única, **mais** Azitromicina1 g VO, dose única.

Esquema alternativo: Ceftizoxima 500 mg, IM, dose única; **ou** Cefoxitina 2 g, IM, com probenecida 1 g, VO, dose única; **ou** Cefotaxima 500 mg, IM, dose única.

7.1.7.2 WHO 2016 [1]

Treatment and Control of Gonococcal Infections

Genital and Anorectal Gonococcal Infections

The WHO STI guideline recommends that local resistance data should determine the choice of therapy (both for dual therapy and single therapy).

In settings where local resistance data are not available, the WHO STI guideline suggests dual therapy over single therapy for people with genital or anorectal gonorrhoea.

The WHO STI guideline suggests the following options: *Dual therapy* (one of the following)

- ceftriaxone 250 mg intramuscular (IM) as a single dose
 PLUS azithromycin 1 g orally as a single dose
- cefixime 400 mg orally as a single dose PLUS azithromycin 1 g orally as a single dose Single therapy (one of the following, based on recent local resistance data confirming susceptibility to the antimicrobial)
- ceftriaxone 250 mg IM as a single dose
- cefixime 400 mg orally as a single dose
- spectinomycin 2 g IM as a single dose.

Remarks: Because of the emerging resistance data for gonococcal infections and reduced effectiveness of some medicines, good practice dictates that the choice of treatment depends on reliable local data on antimicrobial susceptibility. Alternative single-medicine therapies, such as gentamicin or kanamycin, have not been suggested due to lack of surveillance data. Guidance for surveillance of antimicrobial resistance in N. gonorrhoeae is available from WHO [3]. This recommendation applies to pregnant women, who should be closely monitored for complications.

Oropharyngeal Gonococcal Infections

In adults and adolescents with gonococcal oropharyngeal infections, the WHO STI guideline suggests dual therapy over single therapy.

The WHO STI guideline suggests the following options: *Dual therapy* (one of the following)

- ceftriaxone 250 mg intramuscular (IM) as a single dose PLUS azithromycin 1 g orally as a single dose
- cefixime 400 mg orally as a single dose PLUS azithromycin 1 g orally as a single dose

Single therapy (based on recent local resistance data confirming susceptibility to the antimicrobial)

• ceftriaxone 250 mg IM as single dose.

Remarks: Treatment failures have been observed after single therapy for gonococcal oropharyngeal infections and therefore dual therapy is suggested over single therapy.

This recommendation applies to pregnant women, who should be closely monitored for complications.

Retreatment of Gonococcal Infections After Treatment Failure

In people with gonococcal infections who have failed treatment, the WHO STI guideline suggests the following options.

- If reinfection is suspected, re-treat with a WHOrecommended regimen, reinforce sexual abstinence or condom use, and provide partner treatment.
- If treatment failure occurred after treatment with a regimen not recommended by WHO, re-treat with a WHOrecommended regimen.
- If treatment failure occurred and resistance data are available, re-treat according to susceptibility.
- If treatment failure occurred after treatment with a WHOrecommended single therapy, re-treat with WHOrecommended dual therapy.
- If treatment failure occurred after a WHO-recommended dual therapy, re-treat with one of the following dual therapies:
 - ceftriaxone 500 mg IM as a single dose PLUS azithromycin 2 g orally as a single dose
 - cefixime 800 mg orally as a single dose PLUS azithromycin 2 g orally as a single dose
 - gentamicin 240 mg IM as a single dose PLUS azithromycin 2 g orally as a single dose
 - spectinomycin 2 g IM as a single dose (if not an oropharyngeal infection) PLUS azithromycin 2 g orally as a single dose.

Remarks: Before retreatment, reinfection should be distinguished from treatment failure, resistance data should be obtained when possible, and the WHO-recommended regimens should be used.

Gonococcal Ophthalmia Neonatorum

In neonates with gonococcal conjunctivitis, the WHO STI guideline suggests one of the following treatment options:

- ceftriaxone 50 mg/kg (maximum 150 mg) IM as a single dose
- kanamycin 25 mg/kg (maximum 75 mg) IM as a single dose
- spectinomycin 25 mg/kg (maximum 75 mg) IM as a single dose.

Remarks: Due to the large net benefit with treatment, good practice dictates that neonates should be treated for gonococcal conjunctivitis. The choice of treatment may depend on the cost and quality of the medicine in different settings and on equity considerations. Side-effects should be monitored in neonates.

For all neonates, the WHO STI guideline recommends topical ocular prophylaxis for the prevention of **gonococcal** and **chlamydial** ophthalmia neonatorum.

For ocular prophylaxis, the WHO STI guideline suggests one of the following options for topical application to both eyes immediately after birth:

- tetracycline hydrochloride 1% eye ointment
- erythromycin 0.5% eye ointment
- povidone iodine 2.5% solution (water-based)
- silver nitrate 1% solution
- · chloramphenicol 1% eye ointment.

Remarks: Recommendations 5 and 6 apply to the prevention of both chlamydial and gonococcal ophthalmia neonatorum. Cost and local resistance to erythromycin, tetracycline and chloramphenicol in gonococcal infection may determine the choice of medication. Caution should be taken to avoid touching eye tissue when applying the topical treatment and to provide a water-based solution of povidone iodine.

DO NOT USE ALCOHOL-BASED POVIDONE IODINE SOLUTION.

We point out that the single dose schemes should be restricted only to acute forms, not to complicated ones. In chronic, extragenital or disseminated infections, the therapy should not be less than 10 days. There are no alternative schemes for patients infected with HIV or with AIDS.

In male gonococcal urethritis the cure criterion is eminently clinical by the regression of signs and symptoms. Endocervix, anal canal and pharynx culture or methods of molecular biology should be carried out 7 days after treatment.

7.1.8 Complications

- Men: Balanoposthitis, littritis, cowperitis, prostatitis, epididymitis and stenosis of urethra.
- Women: Bartholinitis, salpingitis, pelvic inflammatory disease (PID), pelviperitonitis and perihepatitis.

The disseminated gonococcal infection is rare occurring in 0.3–3% of cases and affects mainly the skin (dermatitis), joints (arthritis) and, less frequently, the heart valves (endocarditis) and the meninges (meningitis).

7.1.9 Differential Diagnosis

- Men: Non-gonococcal urethritis (Chlamydia trachomatis, Mycoplasma sp., Ureaplasma urealyticum or Trichomonas vaginalis), chemical urethritis (by the introduction of irritant substances in the urethra with prophylactic or curative purposes); traumatic urethritis (habit of compression of the penis); testicular torsion or tumor in men in pain in this region.
- Women: Endocervicitis, bartholinitis and chlamydial salpingitis.

7.1.10 Observations

- Therapeutic failure can occur with any therapeutic scheme due to bacterial resistance.
- The transmission risk for men's partners with urethral gonorrhea is of 90–97%; in affected women partners there is a risk of 50–60%.
- In case of persistence of signs and symptoms after male gonococcal urethritis correct treatment, a chlamydial infection should be investigated. The permanence of the process should exclude trichomoniasis as there are coinfection reports of 5–10% of cases.
- Infectious arthritis processes in young adult have in gonococcus and in *Chlamydia* major etiological agents.

7.2 Infections with Chlamydia Trachomatis

7.2.1 Synonymy

Non-gonococcal urethritis, NGU, cervicitis, pelvic inflammatory disease, PID.

7.2.2 Concept

The STD that exposes itself in the way of urethritis, endocervicitis, subacute ophthalmia or PID.

7.2.3 Incubation Period

Two weeks, and may extend up to a month or more.

7.2.4 Etiological Agent

Chlamydia trachomatis strains D, E, F, G, I, J and K are obligatory intracellular parasites bacteria, mainly of cylindrical epithelial cells. They multiply within inclusions vacuoles leading to cell lysis in 72 h. Only develops in cell culture such as McCoy cells. Due to the small size and growth only in cell element, Chlamydiae were confused with viruses for a long time.

7.2.5 Clinical Manifestations (Figs. 7.3, 7.27)

- Men: Urethritis with clear and mucoid secretion, rarely purulent, accompanied by mild or moderate dysuria is the main symptom.
- Women: Endocervicitis with cervical mucus similar to the male urethritis, which, by the way, can also occur in females. Symptoms of ectropion and friability with cervical mucosa easy bleeding are not rare.
- However, more than half of men and women infected with Chlamydia is asymptomatic or oligosymptomatic.

7.2.6 Laboratory Diagnosis (Figs. 7.61–7.66)

Only those who think and search for *Chlamydia* will find the diagnosis. Material should be collected through swab from places under suspicion, mainly urethra and cervical canal, and packaged according to the laboratory kit standards. If PCR or hybrid capture were used, the first urine (male or female) and vaginal/endocervical secretion, in women, are the materials of choice. Materials for molecular biology techniques can be collected by health professionals or by self-collecting, especially the first urine of the day.

The serology is only indicated in cases of invasive or complicated diseases, as salpingitis, arthritis, pneumonia or lymphogranuloma venereum. Serologies will be considered positive when equal to or greater than 1:32 and only if Elisa-based synthetic peptides derived from MOMP show no cross-reactivity. Culture is currently restricted to scientific research centers.

The conventional or liquid medium colpocitology of endocervical canal material presenting change compatible with chlamydial infection, in our opinion should be appraised. This is very different from encouraging the research of *Chlamydia* infection using such methodology.

Evaluation of Laboratory Methods

Exam	Sensitivity %	Specificity %
Cytology, Giemsa	45	95
Cytology, Papanicolaou	62	96
Elisa assay	70-80	>99
Immunofluorescence	80-92	>99
PCR, Hybrid capture	85–95	>99
Serology	40-50	85

Treatment and Control

		CDC (2015) [2]	WHO (2016) [3]
Uncomplicated genital Recommended scheme chlamydia		- Azithromycin 1 g, orally, single dose; or	 Azithromycin 1 g, orally, single dose; or
	– Doxycycline 100 mg, orally, 12/12 h, for 7 days	 Doxycycline 100 mg, orally, 12/12 h, for 7 days 	
	Alternative scheme	- Erithromicin 500 mg, orally, 6/6 h, for 7 days; or	 Tetracycline 500 mg, orally 6/6 h, for 7 days; or
		 Erythromycin ethylsuccinate 800 mg, orally, 6/6 h, for 7 days; or 	 Erithromicin 500 mg, orally, 6/6 h, for 7 days; or
		 Levofloxacin 500 mg, orally, single dose for 7 days; or 	- Ofloxacin 200 mg, orally, 12/12 h or
		- Ofloxacin 300 mg, orally, 12/12 h, for 7 days	400 mg, orally, daily single dose, for 7 days
Anorectal chlamydial	Recommended scheme		Doxycicline 100 mg, orally, 12/12 h, for 7 days; or
infection			Azithtomycin 1 g, orally as a single dose
Genital chlamydial	Recommended scheme	Azithromycin 1 g orally in a single dose	Azithromycin 1 g orally as a single dose; or
infection in pregnant women			Amoxicillin 500 mg, orally, 8/8 h, for 7 days; or
			Erythromycin 500 mg, 6/6 h, for 7 days
	Alternative	Amoxicillin 500 mg orally 8/8 h for 7 days; or	
	scheme	Erythromycin base 500 mg orally 6/6 h for 7 days; or	
		Erythromycin base 250 mg orally 6/6 h for 14 days; or	
		Erythromycin ethylsuccinate 800 mg orally 6/6 h for 7 days; or	
		Erythromycin ethylsuccinate 400 mg orally 6/6 h for 14 days	
Ophthalmia neonatorum	Recommended scheme	Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days*	Azithromycin 20 mg/kg/day orally, one dose daily for 3 days, over erythromycin 50 mg/kg/day orally, in four divided doses daily for 14 days
	Alternative scheme	Azithromycin suspension, 20 mg/kg/day orally, 1 dose daily for 3 days*	
		*An association between oral erythromycin and azithromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS	

In the complicated or upper genital tract illness (endometritis, salpingitis, epididymitis, arthritis, etc.), the use of Doxycycline 100 mg, O, 12/12 h during 21 days is recommended.

New exams in the control of cure are not necessary, unless the symptoms do not regress or there is a great possibility of reinfection.

For all neonates, the WHO STI guideline recommends topical ocular prophylaxis for the prevention of **gonococcal** and **chlamydial** ophthalmia neonatorum.

For ocular prophylaxis, the WHO STI guideline suggests one of the following options for topical application to both eyes immediately after birth:

- tetracycline hydrochloride 1% eye ointment
- erythromycin 0.5% eye ointment
- povidone iodine 2.5% solution (water-based)
- silver nitrate 1% solution
- chloramphenicol 1% eye ointment.

Remarks: Recommendations 5 and 6 apply to the prevention of both chlamydial and gonococcal ophthalmia neonatorum. Cost and local resistance to erythromycin, tetracycline and chloramphenicol in gonococcal infection may determine the choice of medication. Caution should be taken to avoid touching eye tissue when applying the topical treatment and to provide a water-based solution of povidone iodine.

DO NOT USE ALCOHOL-BASED POVIDONE IODINE SOLUTION.

7.2.7 Complications

Mainly: epididymitis, orchitis, prostatitis, salpingitis, pelviperitonite, perihepatitis, infertility, sterility and arthritis.

7.2.8 Differential Diagnosis

Other urethritis, gonococcal urethritis particularly, as well as the ones caused by *Mycoplasma* sp., *Ureaplasma urealyticum*, *Trichomonas vaginalis* or chemical or traumatic urethritis. Men with testicular pain or increase may have tumor or testicular torsion.



Fig. 7.1 Typical symptom of acute gonococcal urethritis in young adult. There is an abundant purulent secretion that comes out spontaneously by the urethral meatus. Sometimes there is such a quantity of secretion that it drips on the floor; hence the popular synonymy with drip. Along with the picture of secretion, the patient usually complains about pain/burn on urination. It is not uncommon for the patient to use the expression: "Doctor, when I urinate, I guess everything is burning"

7.2.9 Observations

- The Chlamydia trachomatis infection has high incidence and prevalence worldwide. Women are the majority of cases. More than 90 million cases are identified in the world each year and most of them are asymptomatic. A third of women with this infection will have pelvic inflammatory disease.
- Routines employed in several developed countries to research *Chlamydia trachomatis* in sexually active teenagers reveal important rates of positivity. It provides diagnosis and early treatment and tends to prevent complications and sequelae in the upper genital tract.
- Quinolones and Tetracyclines are contraindicated for pregnant women, nursing mothers and children.
- In 2006, a new variant of Chlamydia trachomatis (swCT) was found in Sweden, but not identified by molecular biology tests commercially available. This happened because many patients with clinical processes compatible with Chlamydia had negative tests. We believe that over time this strain will spread all over the world, since cases were reported in Denmark, Norway and Ireland.



Fig. 7.2 Due to the quantity of secretion, this patient arrived at the medical service with his penis enfolded in a condom in order to avoid staining the underwear. Many men enfold the glans and even the penis shaft with toilet paper or handkerchief because the secretion flows in large quantity

Fig. 7.3 In general, one says that the urethral secretion by *Chlamydia trachomatis* is not so abundant; it is more watery and less purulent, causing minor discomfort on urination. It is often true. However, in our experience we should not blindly rely on symptomatology. Chronic processes allied to inadequate treatments can make a process of gonorrhea present characteristic signs and symptoms of *Chlamydia* infection. On the other hand, acute cases involving *Chlamydia* simulate the classical symptoms of infection with gonococcus. To disrupt the situation even more, the coinfection with the two agents is not uncommon. In our point of view, a good medical attention should involve research of those two most frequent urethritis agents









Fig. 7.4 Homosexual patient infected with HIV that maintains intercourse without condom, with regular partner also infected with HIV. Patient reported that the partner sought medical help in other medical service, complaining about anal burning and discomfort. Without being examined, he was medicated oral metronidazole. In our service at the STD Department of UFF we proceeded with the collection of urethral pus (a) for Gram stain

technique (b) and culture in Thayer-Martin medium. Bacterioscopy showed polymorphonuclear with intracellular Gram-negative diplococci. The client was oriented to attend to clinical control with the sexual partner. The patient received medication (c) at the time of consultation (supervised therapy). *Neisseria gonorrhoeae* has been identified through culture and biochemical identification. The sensitivity test showed sensitivity to ciprofloxacin



Fig. 7.5 Fifty-year-old patient examined at the STD Department of UFF complaining about urethral discharge and burning on urination. Patient reported intercourse with an acquainted partner 3 days before who complained about low abdominal pain. Reported use of condom during the first intercourse, but not in the second one, as there were no other condoms available. (a) Looking at the underwear with yellowish

stains it is possible to imagine the secretion being eliminated by the urethra. In (\mathbf{b}) urethral secretion can be observed, and although purulent, it is not too yellowish. In (\mathbf{c}) the vials with the solutions used in the Gram stain method. In (\mathbf{d}) polymorphonuclear with several intracellular Gram-negative diplococci (arrow)



Fig. 7.6 Patient attended at the STD Department of Fluminense Federal University (UFF) complaining about discharge, burning and urethral bleeding (**a**, **b**). Reported symptoms which started a few days ago, but 24 h before our attendance patient sought medical attention in a basic health unit of the municipality (BHU) but did not succeed to be examined. Next morning, the patient returned to the same BHU, and a doctor, without examination, led the patient to our public service. Bacteriological tests were carried out (**c**, **d**) and the diagnosis was gon-

orrhea. He was treated and counselled on sexual reproductive health education. Serologies were requested, and as the patient denied vaccination against hepatitis, an adequate vaccination schedule was prescribed. There are complaints that many people seek attendance at drugstores to get a treatment that should be prescribed by a physician. However, we should consider if people seeking medical care are welcomed and efficiently taken care of



Fig. 7.7 (a) Patient entered the clinic complaining about urethritis + burning on urination. During the anamnesis we were aware of arthralgia and a 38 °C fever. A typical purulent urethritis was noted, and after secretion collection and processing, *Neisseria gonorrhoeae* was identified. (b) During the genitalia examination we have noticed pustule in the penis skin (in detail), which also had its contents examined. Bacterioscopy showed Gram-negative diplococcus within polimorfonuclear. The culture identified *N. gonorrhoeae*. By the general symptomatology it was possible to suspect that the patient was starting a

process of gonococcal dissemination. Patient was treated with free sample of medication available at the clinic at that moment, lomefloxacin 400 mg, O, twice a day for 10 days, and a clinical and microbiological cure was obtained. The VDRL and HIV serologies were non-reactive twice. The markers for hepatitis B, HBsAg and Anti-HBs were also non-reactive. Hepatitis B vaccination schedule was prescribed. A sexual partner was examined and treated syndromically, since she was in use of ointment for "general-purpose vaginal discharge" at that moment



Fig. 7.8 Teenager with gonococcal balanoposthitis process. Patient have been presenting symptoms a week ago and believed it was not a STD because two other colleagues also maintained intercourse with the same partner and did not show any alterations. We have examined one of these two colleagues and they were completely asymptomatic. Despite this fact, we performed urethral swab tests (culture for gonococcus and Elisa-Vidas for *Chlamydia*). The results were negative for both bacteria



Fig. 7.9 Patient with acute urethritis symptom. The material collection for microbiological tests should despise the secretion that comes out spontaneously. Usually this material has many damaged cells for a good exam, and bacteria can also be deteriorated for growth in artificial medium. Therefore, removing this first drop of urethral milking enables the collection of a good material for examination. Introducing a 1–2 cm swab suitable for male into the urethra is even better

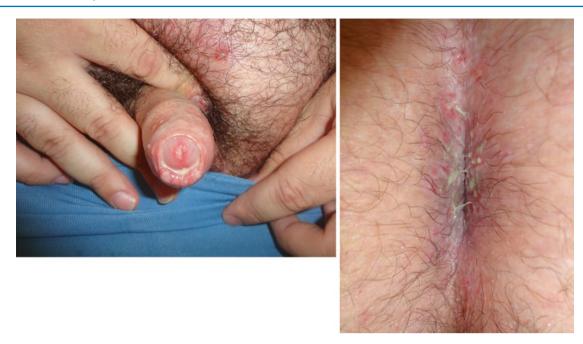


Fig. 7.10 In addition to urethritis, this patient had genital wart (*Condyloma acuminata*—HPV infection) on the edge of the urethral meatus. Associations of STDS are more common than many people

may assume. In the routine, serologic tests for syphilis, HIV, hepatitis B should be offered whenever possible



Fig. 7.11 Eleven year old boy with balanoposthitis and urethritis caused by gonococcus. He was brought to our service by his mother as she noticed "droppings" in his underwear. The mother did not talk about sexual activity of the minor. During the anamnesis, the boy told that had tried to keep sexual relationship with a boy from the neighborhood, but couldn't make the anal penetration. The partner then had oral sex with the boy. The symptoms began approximately a week after that relationship

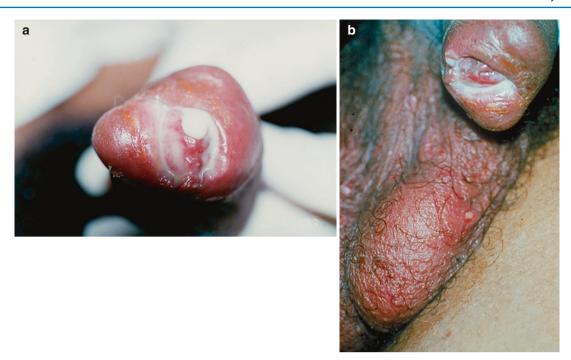


Fig. 7.12 (a) Patient referred for evaluation of "tumor on his penis". The examination found urethritis + gonococcal balanoposthitis + genital scabies + syphilis. The pus accumulated between the glans and the prepuce rear face caused this deformity. (b) Notice lesions in the scrotum caused by scabies. The serology for HIV and hepatitis B was non-

reactive, but the VDRL was positive, 1: 64. Even it is a case of acute gonorrhea in man, we think it was complicated due to the abundant accumulation of pus, and thus we opted for treatment in conventional doses and did not use medication in single dose. We also prescribed hepatitis B vaccination schedule



Fig. 7.13 (a) Patient sought public hospital emergency room complaining about increased and severe pain in the penis for more than a week. In triage, only by clinical history, he was taken to a general surgeon, who during examination found that it was not a case of surgery and immediately referred him to our opinion. It was about a gonococcal urethritis in which pus accumulated between glans and prepuce caused

an abundant volume. As the patient had long prepuce (phimosis), the secretion discharged by overflowing. (b) The accumulation of pus, pain and difficulty of hygiene made skin macerated, causing ulcers in the prepuce. The basic disease was gonococcal urethritis, which started 3 weeks ago, and according to the patient, he was taking some tetracycline pills given by pharmacy clerk





Fig. 7.14 (a) Patient over 50 years of age attended at the STD Department of UFF with severe process of gonococcal urethritis. From clinical history we emphasize that he didn't use condoms, had two fixed and other sexual partners. Patient was examined at our service 2 months ago with similar clinical symptom, and diagnosis by direct secretion bacterioscopy was gonorrhea. On that occasion he was medicated cip-

rofloxacin 500 mg, O, single dose. At current attendance the diagnosis was the same, however, we also collected material for culture and anti-biograme. He was medicated levofloxacin and not lomefloxacin, as by misconception was mentioned in the video attached. In (\mathbf{b}) , fully healed and with no relevant data on culture



Fig. 7.15 Patient referred to our service for clarification of genital ulcer symptom. Note that the secretion was intense. Due to pain caused by the manipulation of the area it has not been possible to show the urethral meatus. However, during a discreet milking from the distal urethra to proximal urethra, in the middle of the penis already, pus drained due to the excess of prepuce shown in picture. The cracks and even exulcerations and longitudinal ulcers are characteristic of maceration of the skin process by the secretion. It is obvious that it can also occur due to a fungal coinfection. The microbiological tests defined only *Gonococcus*. Although it is a picture of acute gonococcal urethritis in men, in cases like this we don't use single dose for treatment. On the other hand, it is worth remembering that it is of utmost importance to use laboratory resources at once. If it is syndromically assumed and treated as genital ulcers, the patient should receive other therapeutic schemes



Fig. 7.16 Symptoms are similar to the previous cases. However, here the ulcers are more evident, but continue longitudinal, and the urethral meatus is better observed, as well as the purulent secretion. At first, thinking about genital ulcer + urethral discharge syndrome may not be entirely wrong, as well as carrying out the therapeutic approach. However, for a professional with some experience, ulcerated lesions on the prepuce are signs of trauma by macerated mucosa by pus. The research for cancroid, syphilis and HIV were negative. The bacterioscopy of secretion was positive for gonococcus



Fig. 7.17 Seems to repeat the previous case; we shall add that anti-HIV test was positive for this patient



Fig. 7.19 Process very similar to previous ones, but this patient's lesions are papules and there are also syphilis lesions in the penis skin (*arrows*). It is a case of urethritis by *Gonococcus* and *Chlamydia* + recent syphilis (papular stage) + HIV positive. As they saying goes: those who have had a STD have a better chance of having another STD or others



Fig. 7.18 In this case the teenage patient was referred for evaluation because his wife had recurrent vulvovaginal candidiasis. In anamnesis, we were told that patient had other sexual partners, did not use condoms with constancy, and a week ago, besides the "itch" on penis, secretion, minor discomfort and burning on urination arose. The direct microbiological tests and culture defined process of *Neisseria gonorrhoeae* and *Candida albicans*



Fig. 7.20 Homosexual male patient presenting pain, edema and anal secretion. Process was microbiologically defined as gonococcal proctitis. The therapeutic option will never be the single dose. In fact, the patient had previously taken single doses of antimicrobials twice in 2 months, unsuccessfully. We'd like to remind that during material collection for direct bacterioscopy, material with faeces should be avoided. Techniques involving molecular biology are more efficient, both for *Gonococcus* and *Chlamydia*



Fig. 7.21 (a) Sixty-two year old patient, widower, retired, with genital ulcers that appeared 7 days after sexual intercourse with casual partner, without penetration, but "rubbing", as he was unable to maintain erection (according to customer information). The injuries began, concomitantly with papules that ulcerated quickly, with a slight pain and no secretion. Bacterioscopy was carried out through the Gram technique of shaving down the lesion, and numerous intracellular Gram-negative diplococci of polymorphonuclear were noted. The patient did not present discomfort or urethral secretion. As it was an extra-urethral

Gonococcus he was medicated ciprofloxacin, 500 mg, O, twice daily, for 7 days. (b) A week of initial therapy. This case stands out the need for classic complementary examinations for STDs. Indeed, we carried out the smear Gram stain of lesions thinking of cancroid diagnosis. But the result showed other etiologic agent. It is worth mentioning the patient's words: not penetrated, but rubbed a lot. Thus, the Gonococcus attacked the rubbed area and not the urethra, as conventionally. On the other hand, the client's hygiene habits substantially decreased the purulent process, common in gonococcal infections



Fig. 7.22 Gonococcal vulvovaginitis processes are rare. When they occur, they are more common in children, cases of rape, first intercourse, and partner with gonorrhea or infection of menopausal woman. This is due to the characteristics of local defense under these circumstances. This exuberant process of purulent secretion that overflows the vulva exists when there is acute massive infection with *Gonococcus*. In these situations the direct bacterioscopy by Gram stain technique often elucidates the issue



Fig. 7.23 Eight year old child with a vulvovaginitis process. In such situations one must think in sexual abuse and notify the municipal authority to childhood to better deal with the case. It's usually a difficult issue for clarification and even when sexual abuse is characterized the abuser rarely suffers criminal sanctions and psychological guidelines that the problem deserves. It is evident that when cases like this occur in regions where human population is developed, the chances of success in investigations increase considerably. This is the case of the child presented in Chap. 9 (HPV), Fig. 9.83; has been victim of sexual abuse by close relative 4 years before and presented important vulvar condylomatosis. In this context of gonorrhea it was not possible to establish causal relationship with sexual abuse. It is worth remembering that children living in an environment of low sanitary levels in homes with a single room with adults presenting purulent gonococcal infections can be possibly contaminated without direct sexual involvement



Fig. 7.24 Process of cloudy cervical mucus, ectropion, friability and congestion are propitious signs of the existence of *Gonococcus* infection, *Chlamydia*, *Mycoplasma*, *Ureaplasma*, among others. Defining the situation by clinical appearance is not safe, since it can show a positive test to one agent, two, three, or none. What we mean is: in order to define these processes, it is necessary to carry out good quality tests. Obviously in case of a suggestive epidemiologic history—especially a partner with current or recent urethritis symptoms—if the patient shows acute pelvic pain additionally to this process, the possibility of infection with *Chlamydia* or *Gonococcus* is very high



Fig. 7.25 In this case, the thick purulent secretion seems to "spring from" the endocervix. The bacterioscopy through Gram is reliable if it is positive for Gonococcus. But, if negative, the possibility of gonococcal infection should not be rejected. This type of examination serves well and also clarifies the case, but only when positive. We point out that whenever Chlamydia material is collected, caution should be taken to obtain the best material, such as epithelial cells, and not pus itself. Therefore, trying to remove pus with a brush or other tool (swab) can be an appropriate technique. The selective medium culture, such as Thayer-Martin, is recommended. Caution: collecting material in dry swab and asking patient to take it to the lab can be a waste of time, expectations and money. In case there is no suitable material (means of transportation) and speed (spending 2 h until material arrives at the laboratory), we believe it is better not to carry out this exam. However, if a specific kit for molecular biology techniques is used (for Gonococcus, Chlamydia, Mycoplasma, Trichomonas) all these problems disappear

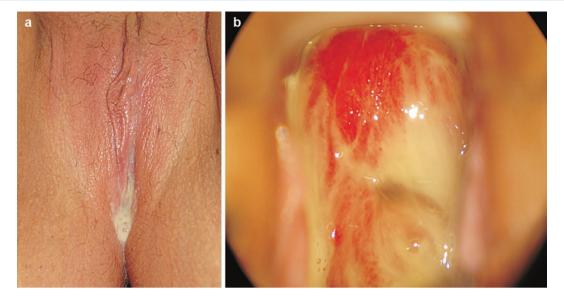


Fig. 7.26 (a) Adolescent patient complaining about vaginal discharge that overflows the vagina into the vulva. (b) The speculum exam showed a process of endocervicitis. Although the content is purulent,

the *Gonococcus* and *Chlamydia* research is mandatory, as well as the research for the main vulvovaginitis agents, as *Trichomonas vaginalis* and bacterial vaginosis



Fig. 7.27 Teenager with cloudy urethral discharge, but not apparently purulent, and discrete burning on urination reported use of condom during almost all intercourses. However, as he is "going steady" for 6 months with fixed and exclusive partner, he stopped using condoms for about a month. The research of Chlamydia was positive and the gonococcus research was negative through molecular biology (hybrid capture—hC). The sexual partner was consulted and reported dyspareunia. The speculum exam showed uterine cervix with red taint and cloudy mucus. The bimanual vaginal palpation was painful and the Chlamydia hC was positive. The test to Gonococcus was negative. The serology for syphilis, HIV and hepatitis was non-reactive in both patients. Were treated with doxycycline, and hepatitis B vaccination schedule was prescribed



Fig. 7.28 Teenager with gonococcal urethritis. Although it is a purulent discharge, the secretion color is milky white more than yellowish



Fig. 7.29 Patient attended at the STD Department of UFF reporting sexual intercourse without a condom a month ago, and a week after presented dysuria and urethral purulent secretion. Searched for care at a public health service, and was examined by a non-medical professional who only prescribed one pill of azithromycin based only in his clinical history. The patient reported a small improvement, but the "problem" continued. At the time of our examination a blurred urethral secretion was observed and patient informed discreet local discomfort, especially on urination. Material was collected for direct bacterioscopy through Gram stain technique (at the time of consultation) and the result was the presence of numerous polymorphonuclear with intracellular Gramnegative diplococci. Patient was medicated levofloxacin in the service by supervised therapy only for Gonococcus. The clinical evaluation after 2 weeks showed complete remission of symptoms. The serology for syphilis, HIV and hepatitis B were non-reactive. As the patient had no information about vaccination against hepatitis and markers were negative, we indicate vaccination schedule against hepatitis B. Even emphasizing the importance of examining the recent sexual partners, we weren't successful



Fig.7.30 Case of acute urethral syndrome in a 34 year old woman who also presented vaginitis caused by *Trichomonas vaginitis*, uretrocistocele and perineal rupture of second and third degrees. The etiologies for *Gonococcus* and *Chlamydia* cannot be forgotten, as well as the whole routine for investigation into vulvovaginitis



Fig. 7.31 It is true that acute or chronic bartholinite may be a complication of cervical/uretral infection with *Gonococcus/Chlamydia*. It is not true that this always occurs. In fact, in medicine, as in love, one should avoid saying *always* and *never*. It is good practice to investigate such possibilities before considering them a STD. The case presented here was a complication of gonorrhea, microbiologically defined. The patient also presented onychomycosis (highlighted in *arrow*)

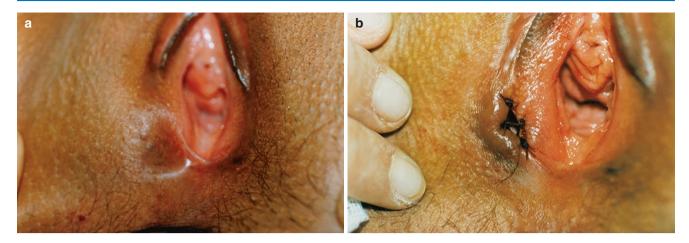


Fig. 7.32 (a) Young patient presenting acute episode (second time) of bartholinite. Since marsupialization and cleaning under general anaesthesia of short duration are not available at our service, patient was sent to the public health network hospital to carry out the procedure by another medical team. However, we have previously collected endocervical material for *Neisseria* and *Chlamydia* tests, vaginal content material for investigation on vaginitis, as well as blood for serology (VDRL,

hepatitis B, and HIV), after advice and general guidance, including the request for patient to return to our service. (b) In patient's return we notice that the procedure, although solved the abscess problem, was incised in the region where, originally, the glandular orifice is not located. However, the problem was solved. Of all tests, only the Gonococcus survey was positive by molecular biology (hybrid capture)



Fig. 7.33 Epididymitis, orchitis and infection of posterior urethra are possible complications of infection with *Gonococcus* and *Chlamydia*. Here we can observe increased scrotum process, where patient generally complains about pain. Clinical history of this case was of previous processes of urethritis (three episodes in the last 12 months). Each episode patient was treated (at other medical services) with IM benzathine penicillin amp (according to customer information)



Fig. 7.34 Another case of gonococcal urethritis complication, where a well-defined area with flush and tumor can be observed. Patient complains about heat and pain in right scrotal sac. In some cases, this symptom occurs after episode of urethritis not properly treated, in a period of time varying from 1 week to months. We believe that the opinion of an urologist is appropriate in order to avoid serious mistakes; for example, medicating as epididymitis or orchitis one case that, in fact, is a testicular torsion or other non-infectious situation. The hernia historic or sudden pain that worsens with no reported history of urethritis may help the diagnostic hypotheses, as well as trauma, especially in sports practice. As already mentioned, the treatment should not be a single dose scheme, but conventional doses for a period not less than 10 days



Fig. 7.35 Another case of epididymitis due to possible infectious urethritis complication. The patient in question reported over eight anterior episodes of urethritis, all medicated by pharmacy clerk, but in the last 3 months (within 6 months) used penicillin G benzathine. It' is still a "plague", at least in Brazil, a patient with urethritis be medicated benzathine penicillin. Many pharmacy clerks, as well as physicians, mistakenly indicate such a product. It should be said that rare cases benefit of this drug. Therefore, it should not be indicated to this purpose. We believe this situation also occurs in many countries around the world, including those with high human development



Fig. 7.36 Another case of orchiepididymitis due to urethritis complication. These patients usually have walking difficulty, general malaise, fever and loss of appetite in addition to local pain. Thinking of *Gonococcus* and *Chlamydia*, our conduct requires, in addition to antibiotic therapy, analgesic, antipyretic, bed rest for 48–72 h, and an interior adornment to prevent testicles distension. For our team, the patient has full indication to be kept away from his professional/student activities





Fig. 7.37 Man with 20 years of age with the following complaint: yellowish urethral discharge (**a**) noticed about 5 days ago, accompanied by dysuria. Was consulted, primarily, for presenting "red eye" in the last 24 h (*top*) (**b**) with copious purulent material ("secretion"). Ocular discharge material and the urethral discharge were collected for bacterioscopy by Gram stain technique at the time of attendance. Intra and extracellular Gram-negative diplococci were visualized through bacterioscopy. Diagnosis: gonococcal urethritis + gonococcal conjunctivitis



Fig. 7.38 Female patient, fellatio practicing, with edema and erythematous aspect of the uvula, pustular and erythematous areas in the posterior wall of the pharynx and irregular erosions of the dorsum of the tongue. The medical history revealed in anamnesis, as well as the material collected for laboratory swabs testing, were patents on identification of gonococci. Culture in Thayer-Martin confirmed gonorrhea diagnosis



Fig. 7.39 Homosexual male patient, oral sex practicing, seropositive for HIV, shows areas of intense inflammatory infiltrate that weakens the clinical and morphological aspects of the oropharynx resulting from gonorrhea

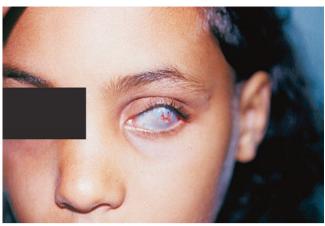


Fig. 7.40 Child with 5 years of age brought to our service by her mother to treat vulvar irritation. During the clinical examination, we found *Condyloma acuminata* lesion and could very quickly identify well-defined story of sexual abuse by close relative. About the change in the left eye, showed by photo, it was caused by neonatal ophthalmia not properly treated. The mother reported that the child was in use of eye drops for more than 2 weeks (couldn't remember the name) given by the public health service. The delivery was normal. The mother made prenatal of poor quality (just two appointments) without any gynecological examinations. During pregnancy her husband presented a "little infection in the penis", "handled" by a private pharmacy clerk. The wife made no concomitant treatment to the "treatment" of her husband. Our hypothesis is that the blindness sequel shown in this photo was caused by a neonatal gonococcal ophthalmia not treated in time

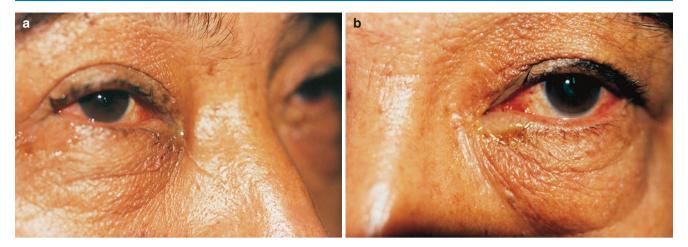


Fig. 7.41 (a) Man of more than 40 years of age presenting purulent ophthalmia in both eyes. (b) Notice hyperemia and purulent secretion. He claimed about itching, watery eyes, and local pain, and although improved with eye drops, it wouldn't go away completely. We advised patient to stay at least 1 day without any local antibiotic medication until material for microbiological research was collected. The patient

also reported urethritis by the same infectious agent (tests made in private medical care) back in the past (over 5 years) and in recent past (4 months). In complicated extragenital or chronic disease by *Gonococcus* or *Chlamydia*, the single dose is not indicated. In this case, the treatment was doxycycline 100 mg twice daily for 2 weeks

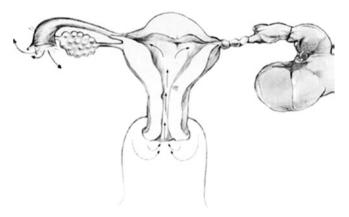


Fig. 7.42 This is a schematic of *Gonococcus* or *Chlamydia* dissemination at the bottom of vaginal sac and, especially, from the endocervical canal to the fallopian tubes. Microorganisms can come out by tubal pavilion and fall into the abdominal cavity or stay in tube, causing sequels of abscesses or obstructions. Patient generally has pain (lower abdomen, dyspareunia) and fever, the hemogram may show leukocytosis with batons, deviating to the left, an increased erythrocyte sedimentation rate, as well as an increased concentration of C-reactive protein in serum

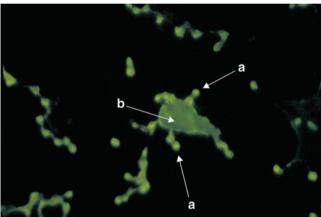


Fig. 7.43 Immunofluorescence showing diplococci bacteria (a) attached to the membrane of *Trichomonas vaginalis* (b). Maybe *Trichomonas vaginalis* and sperm function as vectors, carrying *Gonococcus* or other bacteria to the endometrial cavity and out to the uterine tubes, facilitating the dissemination way of the lower genital tract to the superior, mainly uterine tubes

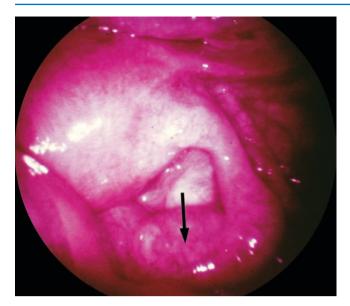


Fig. 7.44 Pelvic laparoscopy vision of woman who presented pelvic pain. Note edematous, hyperemic tube with distal obstruction (*arrow*). In these situations, the recovery of primary infectious agents in the uterine tubes is no easy task. *Gonococcus* or *Chlamydia* often climbs until the tubes and the problem begins. But the anaerobic bacteria are the ones that show up in the abscess and exacerbation phase. However, sometimes other bacteria (e.g. *Mycoplasma*), apart from *Gonococcus*/*Chlamydia*, are the primary causes of the so-called upper genital tract infection



Fig. 7.45 Note the great tubal abscess. Although it is nowadays technically viable to open this tube via videolaparoscopy for drainage and cleaning, most times the complete recovery of the tubal epithelium will not occur. Therefore, this can facilitate a tubal pregnancy, once estenosis, synechiae, and tubal motility changes may be forever present

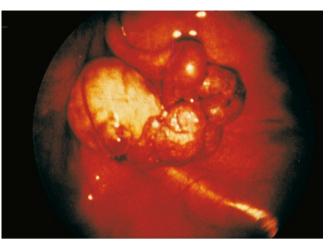


Fig. 7.46 Chronic salpingitis case, infection of the upper genital tract, where the tortuosity and hydrosalpingx are very evident. The search for etiological agents include abdominal fluid collection. The search for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* through molecular techniques (e.g., hybrid capture) is more reliable than the usual ones (culture, Elisa), hence should be utilized if possible



Fig. 7.47 Surgical piece (uterus and uterine tubes) showing severe process of bilateral hydrosalpinx in a patient with serious abdominal process, so laparotomy was necessary



Fig. 7.48 Less used today, but very used in 1970, histerosalpingography showing bilateral tubal obstruction and dilated, tortuous and irregular formations of the uterine tubes, with no contrast in the abdominal cavity



Fig. 7.49 Forty-eight year old patient, attended at emergency room, complaining about pain and swelling of left knee after trauma in football match. During the anamnesis, we were informed by the patient he had mild urethral secretion, almost without uncomfortable urination, evening fever of mild intensity, sometimes night sweats and that, in fact, had already mild pain in that knee before the match. The tests (bacterioscopy and culture in selective medium of synovial fluid obtained by lumbar puncture) showed gonococcal arthritis diagnosis. In these situations, the recovery by *Neisseria gonorrhoeae* culture does not occur in more than 60%. The liquid cytology, glucose, chloride and protein dosage should be included in the routine. *Gonococcus* and *Chlamydia* hybrid capture or PCR are much more effective, especially in every case of extragenital infection, where the amount of microorganisms is much smaller. To help the diagnosis composition of chlamydial arthritis, the serology for *Chlamydia* should be part of the laboratory tests



Fig. 7.50 Case of gonococcal dermatitis, where a pustule can be observed. This shows there is a systemic dissemination of gonococcal disease. The patient had history of recurrent urethritis processes with incomplete treatment with tetracycline tablets and benzathine penicillin injections



Fig. 7.51 Rare case of gonococcemia, which means massive hematogenous dissemination of *Gonococcus*, as indeed occurs more frequently in meningococcal disease. The complications of disseminated intravascular coagulation, adrenal gland shock and hemorrhage occur in a similar manner to meningococcemia. For the correct diagnosis, the blood culture with identification and classification of the etiologic agent must be included. Materials of dermatological lesions, which show large areas of necrosis, most of the time has negative results through bacterioscopy and culture. Laboratory methods involving molecular biology are generally more efficient



Fig. 7.52 When we think of recovering *Gonococcus* or *Chlamydia* in female genitalia, the search should be in the endocervix, mainly when culture or immunofluorescence is used

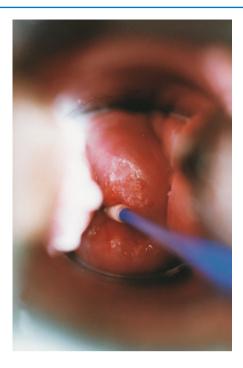


Fig. 7.53 Note that the cotton swab should penetrate in gentle rotational movements into the cervical canal in order to avoid bleeding and squeezing the endocervical crypts, and thus better collect material for *Gonococcus* and *Chlamydia* research. In some cases, kits are different, and two or more collections will be necessary. The first sample should be gonococcus if the collection is for culture. In this situation, the cotton must not touch the vaginal wall. If the molecular biology technique is used, only one collection is necessary. The endocervical pus is the best material for *Chlamydia* research if the search technique is direct immunofluorescence, because this technique needs more cylindrical epithelial cells

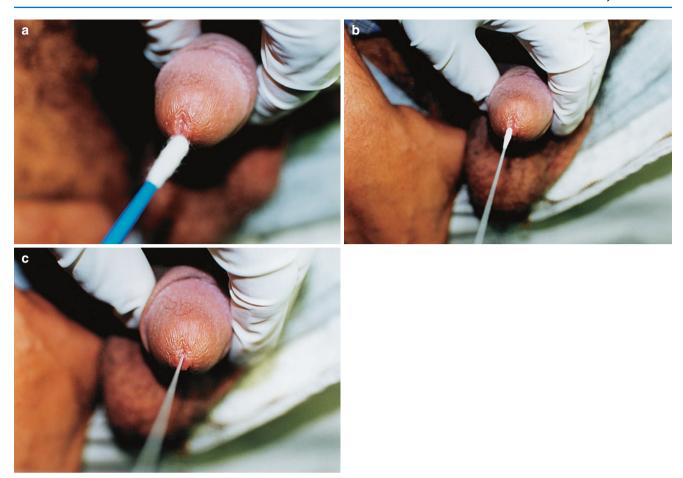


Fig. 7.54 (a) Care should be taken to use swabs proportional to the collection site. (b) In urethra (male or female), we recommend thinner material. (c) Note that the cotton disappears completely into the urethra. Insert 1–2 cm and make easy 180° rotational movements

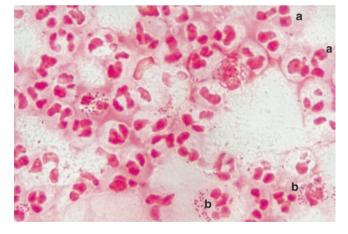
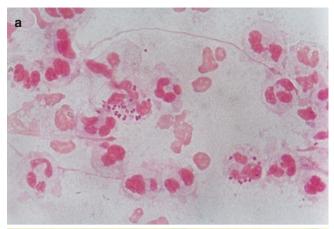
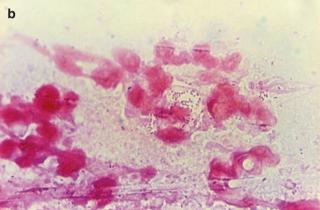
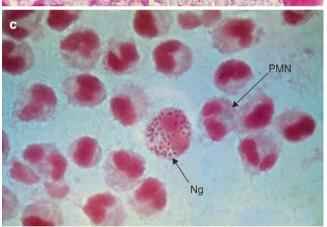


Fig. 7.55 Direct bacterioscopy by Gram technique: numerous polymorphonuclear (a) and Gram-negative diplococci inside PMN (b)







Figs. 7.56 (a, b, c) Presence of several Gram-negative bacteria, kidney-shaped, extra and intracellular, in some polymorphonuclear leukocytes (increase of 1000 times) (c) *PMN* (polymorphonuclear); *Ng* (Neisseria gonorrhoeae)



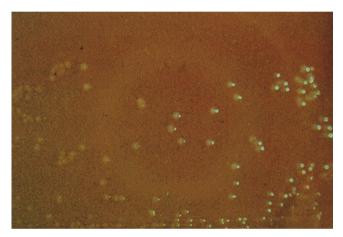


Fig. 7.58 Notice there are small, convex, mucoid colonies, and no production of pigments

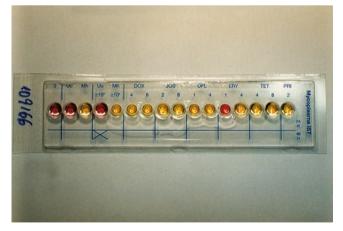


Fig. 7.59 There are several ways to identify *Neisseria*. Sugar fermentations tests are usually carried out. What is shown here is the API® bioMerieux kit, which arranges the multiple tests in a single card

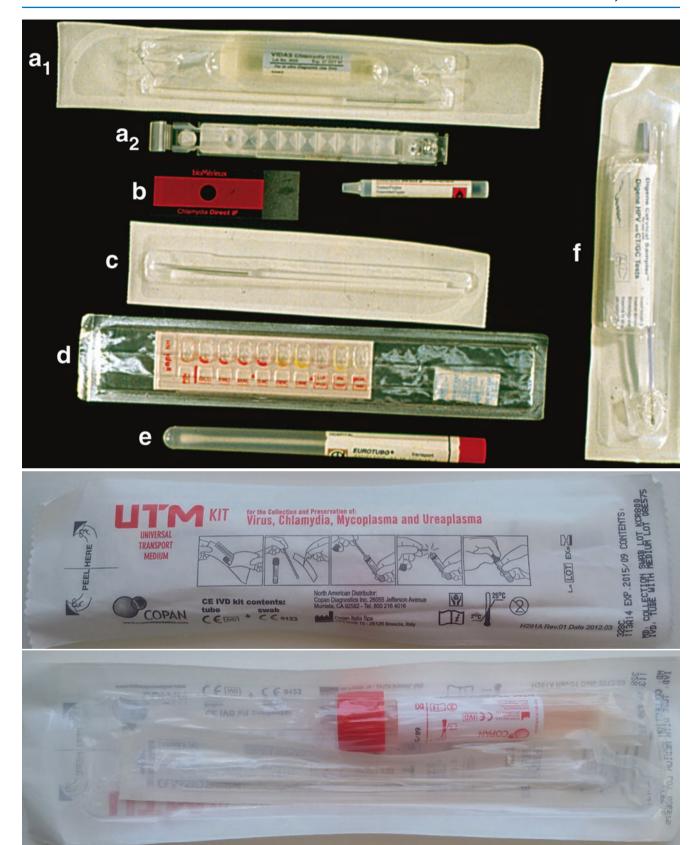


Fig. 7.60 As already mentioned, a suitable material for research of such bacteria is necessary a_1 and a_2 , collection and processing set of Elisa-vidas technique (Elisa with automated fluorescence reading); (b) blade slide for cytological smear by immunofluorescence technique; (c) delicate swab for the urethra or cervix with very small hole. (d) chart for

inoculation of culture sample for identification of *Neisseria*; (e) normal regular swab; (f) kit for analysis by hybrid capture technique. In fact, it's the same kit used for HPV research. *Gonococcus*, *Chlamydia* and HPV can be searched in the same sample, evidently in case of proper indication

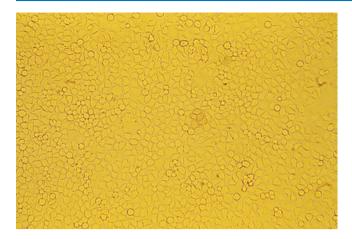


Fig. 7.61 Photo of intact McCoy cells monolayer ready to receive material for *in vitro* cultivation system for *Chlamydia trachomatis*. This technique has been widely used. Currently, due to the difficulties and cost of cell culture maintenance in laboratory of clinical analyses, and due to the improvement of other techniques of high sensitivity and specificity, molecular biology or not, it fell into disuse in medical practice

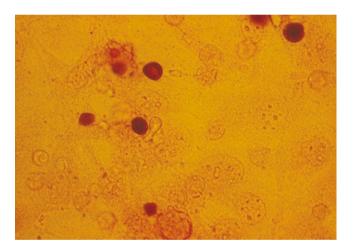


Fig. 7.62 Cytoplasmic inclusions of *C. trachomatis* in cell cultivation

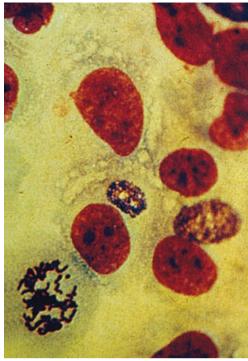




Fig. 7.63 Visualization of Gamma-Miyagawa corpuscles containing numerous reticular corpuscles, way of *Chlamydia* intracellular replication viewed by Giemsa cytological staining technique

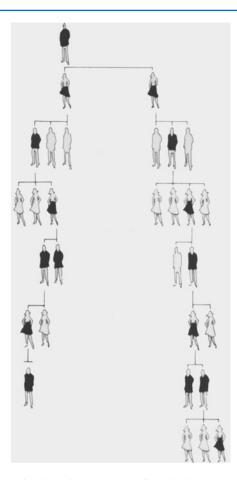


Fig. 7.64 This Figure is a gonorrhea dissemination schematic of an acute gonococcal urethritis in men. The ones wearing a black shirt or a black skirt are infected with gonococcus. Then, starting from a case, it is possible to identify 15 others making a dissemination chain. This diagram was introduced by the French physician Andre Siboulet, from the Institute Alfred Fournier of Paris. Through the diagram it can also be observed that the transmission is not 100% effective, as occurs in virtually all infectious and contagious diseases, from grippe to aids, passing by Ebola, cholera, tuberculosis, leprosy, hepatitis...

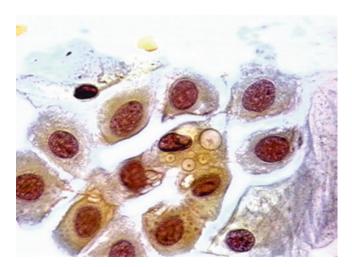


Fig. 7.65 Pap smear with metaplastic cells with cytoplasmic inclusions that could suggest *Chlamydia trachomatis* infection. It is not a good test to detect *Chlamydia* but sometimes is the opportunity to at least suspect (Pap 1000×)

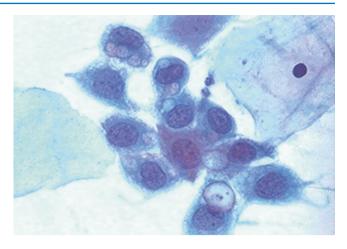


Fig. 7.66 In this picture is possible to observe in liquid-based cytology (Sure Path 1000×) with metaplastic cells with cytoplasmic inclusions that could suggest *Chlamydia trachomatis* infection

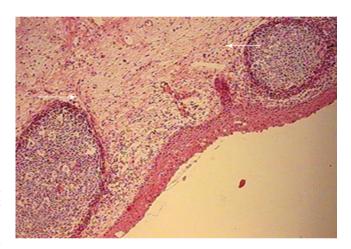


Fig. 7.67 This is a biopsy of follicular cervicitis, which can be associated with *Chlamydia trachomatis* infection (HE 100×). Observe the follicles in the stroma

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Vulvovaginitis

8.1 Bacterial Vaginosis

8.1.1 Synonyms

Vaginal discharge, bacterial vaginosis, BV.

8.1.2 Concept

BV is a syndrome that occurs due to an imbalance in the vaginal microbiome and is characterized by a reduction in lactobacilli, particularly those that are producers of hydrogen peroxide, resulting in a large increase in anaerobic bacteria.

8.1.3 Incubation Period

There is no determined incubation period.

8.1.4 Etiological Agent

Gardnerella vaginalis, Mobiluncus sp., Mycoplasma hominis, Bacteroides, Prevotella sp., Peptostreptococcus sp. and Atoponium vaginae, among others.

8.1.5 Clinical Manifestations (Figs. 8.37, 8.38)

This infection is symptomatic in 50% of cases and can produce a range of symptoms, including a grey, white or yellow-colored discharge, which is liquid and homogenous, and which is often described as having a disagreeable odor (of "rotting fish") that worsens after unprotected vaginal intercourse and during menstruation. Both semen and blood are

alkaline and increase the volatility of the substances produced by anaerobic bacteria, causing this characteristic smell. There is generally no vaginal inflammation, itching, dysuria or dyspareunia.

It has been reported that around 30% of cases of BV can vanish without any specific treatment. On the other hand, around 40% cases are recurring within 3 months of treatment.

8.1.6 Laboratory Diagnosis (Figs. 8.39–8.53, 8.69–8.71)

Direct examination of a sample taken from the vagina in saline solution: presence of guide cells, key cells, target cells or clue cells (epithelial vaginal cells with multiple superimposed bacteria in the cytoplasm). Where Mobiluncus is present, these pathogens may be identified via their characteristic shape and movement, as well as the formation of comma cells that have bacteria sticking to their surface in the same way as clue cells.

Bacterioscopy of vaginal swabs stained using the Gram technique show an absence of lactobacilli and polymorphonuclear cells with target cells and numerous cocobacilli or Gram-negative bacilli. The Nugent Score is considered to be the golden standard for the diagnosis of BV (Table 8.1).

Table 8.1 The Nugent Score

Score	Lactobacillus morphotypes	Gardnerela morphotypes	Mobiluncus morphotypes
0	>30	0	0
1	5-30	<1	1–5
2	1–4	1–4	>5
3	<1	5-30	
4	0	>30	

BV = score > 7; Intermediate = score 4–6; Normal = score 0–3

The pH of the vagina is above 4.5 and the amine test is generally positive (due to associations with other anaerobic bacteria).

A positive result for the KOH test (10%) represents the volatility of amines present in vaginal material that cause the strong smell of rotting fish or ammonia.

Colpocytology ("preventative") may reveal clue cells and an abnormal microbiota, however this procedure should not be routinely carried out for this purpose.

Enzymatic and biomolecular tests have recently been incorporated into clinical practice. These include BVblue® (BV blue® (Gryphus Diagnostics, Birmingham, AL, USA), an exam that evaluates the enzymatic activity of sialidase, an enzyme produced by enzymes such as Gardnerella vaginalis, Bacteroides spp., Prevotella spp. and Mobiluncus spp., which are all associated with BV, and Affirm VPIII® (BD Affirm VPIIITM, a molecular system to detect vaginitis caused by Candida, Gardnerella and Trichomonas. Processing just one sample, the test uses complementary DNA sequences that interlink with or hybridize just the nucleic acids from the target organism, generating a reaction that reveals a blue coloring in sphere shapes on the exam cards. Test results: the first card on the left gave a positive reaction for Gardnerella and Candida, the second gave a negative reaction and the third was positive for Candida).

The presence of polymorphonuclear cells in cases of BV diagnosed using Amsel criteria (Table 8.2) or the Nugent Score has still not been clarified, but some studies have demonstrated that this could be related to cases associated with *Candida* (mixed vaginitis).

Evaluation of Laboratory Methods

Exam	Sensitivity %	Specificity %
Direct examination	70–90	95-100
Gram technique	60-80	95-100
pH	75–80	60-70
Affirm VIII (BD)	70–98	98-100

Table 8.2 Amsel criteria for the diagnosis of BV

Criteria	
Homogenous discharge	
pH > 4.5	
Positive amine test (10% KOH)	
Supracytoplasmic bacilli	

8.1.7 Treatment and Control of Cure

- Oral metronidazole 500 g, 12/12 h for 7 days.
- Oral metronidazole, secnidazole or tinidazole 2 g, single dose.
- Metronidazole gel 0.75%, 5 g, applied to the vagina twice a day for 5 days.
- Oral clindamycin 300 mg, 12/12 h for 7 days.
- Clindamycin cream 2%, 5 g, applied to the vagina at night for 7 days.

Although treatment regimens involving a single dose are easier to follow, they are associated with a higher incidence of recurrence. Repeating the single dose a week later can increase their efficacy.

8.1.8 Complications

Increased risk of premature birth, chorioamnionitis, premature rupture of membranes, puerperal infection, infection (cellulitis) after abortion and intraepithelial neoplasia (this may be a co-factor for HPV). It is also an important risk factor for HIV.

8.1.9 Differential Diagnosis

Trichomoniasis, candidiasis, idiopathic vaginitis, aerobic vaginitis.

8.1.10 Observations

- The symptoms of trichomoniasis can be confused with those of BV, meaning that laboratory diagnosis is indispensable in these cases.
- The rate of recurrence within 3 months is generally 30%.
- It is not considered to be one of the classic STDs, and for this reason the sexual partner is not usually treated, except if they have symptoms and are carrying the agents associated with BV.
- Metronidazole may cause side effects, such as a metallic taste in the mouth, nausea and abdominal pain. Patients should be advised not to drink alcohol during their treatment due to the Antabuse effect.

 BV represents an important biological risk for other genital infections. Routine screening in pregnant women and patients infected with HIV is highly recommended, as the diagnosis method is very effective.

8.2 Candidiasis

8.2.1 Synonyms

Leukorrhea, moniliasis.

8.2.2 Concept

Infection caused by a fungus of the *Candida* genus in the female (mainly the vulva and vagina) and male genitourinary tract. Its presence in the oral cavity is related to immunodeficiency. Although some partners also present infection with *Candida* in the penis, it is not considered to be one of the classic STDs.

8.2.3 Incubation Period

Since *Candida* can be a normal part of the vaginal microbiome, imbalances in the vaginal ecology can lead to the growth of fungi and the onset of signs and symptoms. There is no defined incubation period for candidiasis.

8.2.4 Etiological Agent

Candida albicans is responsible for over 80% of cases of candidiasis. Other cases are caused by infection by other non-albicans Candida species. Candida is a commensal opportunistic fungus that lives in the mucous membrane of the digestive system and the vagina. It is a type of yeast that doesn't contain chlorophyll, is Gram-positive, develops better in more acidic environments (<4.0) and exists in two forms: vegetative growth (pseudohyphae/pseudomycelia) and reproducing (blastospore or blastoconidium).

8.2.5 Clinical Manifestations (Figs. 8.5–8.13)

• Uncomplicated candidiasis: light or moderate sporadic candidiasis caused by *C. albicans* and found in immunocompetent patients.

- Complicated candidiasis: recurring serious infections (3–4 attacks/year) caused by non- albicans Candida species or affecting patients with immunosuppression or uncontrolled diabetes.
- Women: vaginal discharge with the appearance of curdled milk, as well as itching, hyperemia and vulval edema (more intense in pregnant women). Complaints also include a stinging sensation during intercourse and painful and frequent urination.
- Men: balanoposthitis with light to severe erythema, edema and accumulation of a white secretion in the balanopreputial groove. Itching is also common.

8.2.6 Laboratory Diagnosis (Figs. 8.14–8.23, 8.53, 8.64–8.66, 8.69, 8.70)

- Direct examination (10% KOH) of vaginal swabs can reveal fungal pseudohyphae/pseudomycelia or blastospores.
 Bacterioscopy using the Gram technique may also be used.
- Vaginal pH < 4.0.
- · Cultures using a medium such as Sabouraud agar.
- Bacterioscopy using the Gram technique or colpocytology using the Papanicolaou technique can reveal both pseudohyphae/pseudomycelia and blastospores.
- Affirm VPIII®
- Since 10–15% of women affected are completely asymptomatic, Candida in the vagina does not necessarily mean there is a disease and that treatment is required. Clinical examinations should always be taken into account.

Evaluation of Laboratorial Methods

Exam	Sensitivity %	Specificity %
Direct examination (10% KOH)	40–60	>99
Culture	70–80	>99
Affirm VIII®	70–80	>98

8.2.7 Treatment and Control of Cure

Uncomplicated candiasis:

- Tioconazole, clotrimazole, isoconazole, miconazole, terconazole, nystatin cream, vaginal creams or pessaries, vaginal application at night in a single dose or over 10 days.
- Oral fluconazole 150 mg, single dose.
- Oral itraconazole 100 mg, two pills repeated after 12 h.
- Oral ketoconazole 200 mg, 12/12 h for 5 days.

Complicated candidiasis:

- Oral fluconazole 150 mg, three doses in intervals of 3 days.
- Boric acid 600 mg, in the form of a vaginal gel or pessary, applied to the vagina at night for 2 weeks (indicated for cases of non-albicans Candida).

8.2.8 Complications

Dissemination of the disease leads to endocarditis, meningitis and septicemia, which is often fatal. Dissemination is hematogenous. Candidiasis is the most commonly seen infection in patients with diabetes or immunosuppression, appearing at an early stage as soon as cellular immunity is compromised. As well as recurring vulvovaginal candidiasis, infections can be lead to oropharyngitis or in more advanced stages of immunosuppression can spread and cause esophagitis, lung abscesses and lesions to the digestive tract as far as the anus.

For patients with recurring vulvovaginal candidiasis, serological screening for HIV must be offered.

8.2.9 Differential Diagnosis

Other forms of vulvovaginitis, such as cytolytic vaginosis (Figs. 8.55–8.57), BV, trichomoniasis, hypotrophic vaginitis, inflammatory vaginitis, allergic processes, lichen and Paget's disease.

8.2.10 Observations

- Most women will experience at least one attack of candidiasis in their lives.
- The various treatment regimens available (local and/or oral) have similar efficacies that rarely exceed 90%.
- In recurring (over 3 episodes/year) or serious cases, screening for HIV and diabetes should be offered.
- Pregnant women should be given just vaginal medication for 12–14 days.
- · Not all vulvovaginal itching is caused by candidiasis.

8.3 Trichomoniasis

8.3.1 Synonyms

Trichomonas vaginitis, vaginal discharge.

8.3.2 Concept

Infection caused by the protozoan parasite *Trichomonas vaginalis* in the female and male genitourinary tract. Together with candidiasis and BV, this is one of the main types of vaginal infection. It is classified as a classic curable STD, alongside syphilis, gonorrhea and chlamydia.

It is estimated that there are over 276.4 million new cases of this infection in the world every year. In Brazil, this figure is estimated at over 4.3 million per year. Trichomoniasis is generally more prevalent in populations with lower socioeconomic development, and is even found in countries with a high human development index.

8.3.3 Incubation Period

T. vaginalis is a pathogen exclusive to humans. Therefore, there are hardly any detailed studies on its incubation. It is assumed that symptoms will appear within 1–2 weeks of after inoculation of *T. vaginalis* in the vagina. However, this depends on the quantity of inoculums, the virulence of the parasite and local immunity.

8.3.4 Etiological Agent

Trichomonas vaginalis: an oval protozoan parasite with high motility as a result of its four flagella. It is a little larger than a leukocyte and smaller than a vaginal epithelial cell.

It is easily killed by drying or prolonged exposure to sunlight. However, vaginal samples mixed with saline solution can keep the parasite active for over 5 h. Rare cases of non-sexual transmission by fomites have been reported, including in children.

8.3.5 Clinical Manifestations (Figs. 8.24–8.28)

Women are the main victims of this infection, although many (50%) are oligosymptomatic or asymptomatic. The main symptoms are a bullous yellow-green discharge with an unpleasant odor, a stinging sensation during intercourse and diffuse colpitis, also known as "tiger" (multifocal) colpitis. Many women with trichomoniasis present vulval itching. Most infected men are asymptomatic.

8.3.6 Laboratory Diagnosis (Figs. 8.29–8.36, 8.61)

Direct examination of vaginal swabs in saline solution reveals the protozoa actively moving between epithelial cells and leukocytes. The parasite can also be visualized via bacterioscopy using the Gram technique or colpocytology with staining.

Cultures in Diamond's medium provide excellent results, but recently this has been substituted with more up-to-date techniques, such as OSOM Trichomonas Rapid Test and Affirm VIII®, which are available on the market and offer good sensitivity and specificity.

Vaginal pH is >4.5 and the amine test generally produces positive results (as a result of association with other anaerobic bacteria).

Similarly to BV, in cases of trichomoniasis there is an extensive microbiota of anaerobic bacteria. Therefore, the amine test (10% KOH) on vaginal samples is often positive.

Evaluation of Laboratory Methods

Exam	Sensitivity %	Specificity %
Direct (saline) examination	50-70	>99
Culture	80-90	>99
DNA screening	>95	>99

8.3.7 Treatment and Control of Cure

- Oral metronidazole 2 g, 250 mg, 8/8 h for 7 days.
- Oral secnidazole 2 g, single dose.
- Oral tinidazole, 2 g, single dose.

Control of cure can be carried out with the same exams used for diagnosis 1–2 weeks after treatment. Even if sexual

partners are not experiencing any symptoms they should be called in for guidance, clinical examination, treatment and tests for other STDs, including HIV and hepatitis B.

Resistance to single doses of metronidazole has already been reported. In these rare cases, oral metronidazole 500 mg, 8/8 h, with vaginal metronidazole for 10 days is recommended.

Recurrences happen more as a result of lack of treatment of partners and/or non-completion of treatment in women.

Although regimens involving a single dose are easier to follow, they have a higher incidence of recurrence. Repeating the single dose a week later can increase their efficacy, but this increases the rate of side effects.

8.3.8 Complications

There is evidence that Trichomonas infection is associated with a higher risk of contracting HIV, a higher risk of complications during pregnancy and post-surgical infections.

- Men: Prostatitis and epididymitis, with oligospermia being an aggravating factor, sometimes leading to infertility.
- Women: Trichomonas vaginalis may be one of the microorganism vectors in pelvic inflammatory disease (PID).

8.3.9 Differential Diagnosis

Bacterial vaginosis, gonorrhea (Figs. 8.3, 8.4), candidiasis, hypotrophic vaginitis (also a symptom of multifocal colpitis) and inflammatory vaginitis (caused by Group B streptococcal infection) (Fig. 8.54), aerobic vaginitis.

8.3.10 Observations

- Vulvovaginitis, like all genital infections, promotes the transmission of other STDs, including HIV.
- After treatment for chlamydia and/or gonococcal urethritis in male patients, if discharge, stinging sensations and/or itching in the urethral meatus persists, screening and medication for trichomoniasis are recommended.
- It has been reported that 5–10% of men with gonorrhea also have trichomoniasis.

- We believe this to be a neglected epidemic. The number of new cases each year estimated by the WHO increased by 60% between 1999 and 2008
- Various international studies show that over 3% of cases of trichomoniasis are found during Papanicolaou screening, direct examination, selective culture media or molecular biology (PCR) of vaginal swabs taken from women attending gynecological clinics.

8.4 Self-Collection of Vaginal Swabs (Figs. 8.58–8.60)

We have developed a self-collection kit for vaginal swabs that has been tested in a range of situations, including private practice with female patients from a high social economic and cultural background, STD clinics and family health centers in the cities of Niterói and Piraí in Rio de Janeiro State (public health services).

This kit has been tested and compared to the gold standard. In other words, samples taken by doctors at their medical practices have been compared to samples taken by the patient themselves in their own home. The rates of satisfactory samples taken for microbiological analysis of vaginal swabs using the Gram technique were statistically similar for these two groups.

Therefore, we are confident that women can collect their own swabs at home and then take them for microbiological analysis using the Gram technique.

We are currently testing the idea of using the postal system to send swabs for analysis.

The most recent publication of this study can be found at Passos et al., 2008.

8.5 Procedures and Instruction for Self-Collection of Vaginal Swabs

Dear patient,

You will be taking a swab from your own vagina. Read the instructions carefully. In case of any doubt, consult the nursing professional who provided you with this kit.

IMPORTANT

Do not take any samples if you are experiencing vaginal bleeding, using any vaginal products or taking antibiotics. You should also not take any samples if you about to start your period.

You should not have vaginal intercourse or undergo any medical examinations for 3 days prior to sampling.

Wait until at least 3 days after your period to take samples.

Carefully follow this procedure

- Arrange all of the material provided in the kit so that you can access it easily.
- Remove your underwear and sit on the end of a bed, chair or toilet
- If you prefer, you can lie down on your back with your legs open and bent.
- Slowly insert the hollow tube as far as you can into your vagina.
- Place the small brush as far inside the tube as it will go until you can feel it touching the top of your vagina.
- Gently rotate the brush, collecting material from the top of your vagina.
- Remove the brush and gently rub it three times on the slide. First check that you have the right side of the slide by looking for the identification number.
- Immediately place the slide in the flask provided and close it.
- Place the brush and the tube into the plastic bag, close it with the tie and dispose.
- As soon as possible, take your self-collection kit to the health center indicated by your doctor. On this occasion a doctor will examine you and take further samples. YOU SHOULD DIRECT YOURSELF TO A HEALTH CENTER WITHIN TWO DAYS.
- Keep the proof of receipt you are given for your samples.
- Return to the health center 3 weeks later to collect your results and receive any medical advice.

YOUR PARTICIPATION IS IMPORTANT





Fig. 8.1 (a) Vulva with a normal appearance. It is very common to find discharge in the vaginal introitus but not observe any infection. On the other hand, it is common for ectoscopy of the vulva to reveal no clinical problems in a patient presenting an infection, mainly when this is in the vagina or the cervix. Observe the completely normal papillary formations on the internal face of the labia minora. (b) At the moment, many women remove hair from their vulva to excess. It is important that they

are advised that these hairs help to maintain the natural microbiome and protect the vulva. By maintaining the normal ecology of this area, it is more difficult for pathogenic microorganisms to cause an infection. The hair contains fatty acids that also offer protection. Another aggravating factor is that hot wax or razors can irritate the skin, making infection easier. Many women from all walks of life mistakenly believe that full or partial removal of hair from the genitals makes the area "cleaner"



Fig. 8.2 Here is a photograph of a vulva with a large quantity of bullous discharge. This suggests some kind of alteration to the area. This could be an STD (trichomoniasis) or an imbalance in the vaginal microbiome (BV). Both possibilities need to be investigated and treated



Fig. 8.3 Similar to the previous case in terms of the quantity of discharge; however, here it can be seen that the discharge is purulent, thick and yellow. These are quite different to the clinical symptoms associated with the main types of vulvovaginitis (BV, candidiasis and trichomoniasis). This case, which we have already discussed in Chap. 6, was a case of infection by gonorrhea



Fig. 8.5 Recurring case of serious vulvitis caused by *Candida* sp. where, as well as lumpy white discharge, with the consistency of a paste, wet talc or curdled milk, there is also vulval edema and hyperemia. Such cases should be classified as complicated candidiasis, and in these situations we do not recommend treatment with a single dose

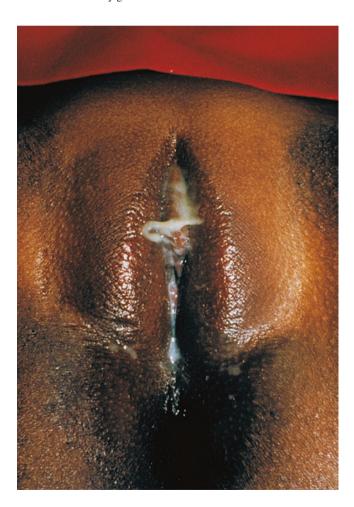


Fig. 8.4 This case was also discussed in the previous chapter: gonococcal vulvovaginitis in a child. Note that cases of gonococcal vulvovaginitis are rare, and when they occur they are more common in children, rape victims, menopausal women and adults whose first experience of vaginal intercourse was with somebody infected with gonococcus



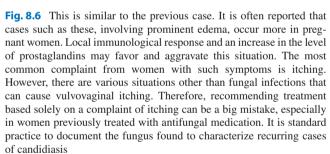




Fig. 8.7 White discharge sticking in plaques to the walls of the vagina. Clinically this is highly suggestive of candidiasis. However, this may also be associated with cytolytic vaginosis

Fig. 8.8 (a) Vulva with hyperemia and (b) lumpy vaginal discharge, with the appearance of curdled milk sticking to the vaginal walls and cervix. This is a very typical case of vulvovaginal candidiasis. However, this may also be associated with cytolytic vaginosis. Only laboratory exams can adequately confirm diagnosis in these cases







Fig. 8.9 We don't routinely recommend treatment for the partners of women with vulvovaginal candidiasis. However, we suggest they undergo clinical examination. If the partner has any specific symptoms and tests positive for *Candida* sp., we advise treatment for complicated candidiasis. This was the case for this patient presenting significant fungal balanoposthitis. The partner had had three episodes of candidiasis in the last 4 months. Serological screening for syphilis, HIV and hepatitis B was negative. We recommended a course of vaccinations against hepatitis B. Months after their first appointment both experienced a recurrence and serological screening for HIV was positive





Fig. 8.10 (a, b) The history of this patient is very similar to the previous case. The partner had recurring candidiasis. In this case there was an aggravating factor, as there was a history of multiple partners and he knew that he was HIV positive but he had still not told his current partner this, who he had been having a fixed, exclusive relationship with for the previous 6 months with irregular use of condoms. He took part in some interviews at out clinic and was given medical advice, and 1 month later his partner came in for a consultation. She also had genital candidiasis and screening for HIV was also positive. It is logical to sup-

pose that the hyperemia and fissures caused by mycotic infection had facilitated the transmission of HIV, assuming the partner was not HIV positive before starting a sexual relationship with the initial patient. Observe the fissures, hyperemia and white plaques that are characteristic of a large fungal infection of the penis. This case illustrates the importance of seeing both partners when one has genital infections, even in cases of non-classic STDs. It is wrong to "treat" infections without first performing an examination, providing medical advice and seeking to treat both partners



Fig. 8.11 Longitudinal fissures on the foreskin of this patient and his complaints of itching were important facts that lead to a suspected diagnosis of fungal balanoposthitis. The patient also had a partner with vulvovaginitis caused by *Candida* sp. It can be seen here that the lesions were dry. As a result of this, cultures of swabs provide better results



Fig. 8.12 Front view of a penis with a large area of erythema around the urethral meatus and on the posterior side of the foreskin. The sexual partner was seen afterwards and also presented clinical and microbiological symptoms of candidiasis



Fig. 8.13 This case, which was also discussed in the previous chapter, involves a young patient presenting balanoposthitis caused by *Candida albicans* and gonococcal urethritis



Fig. 8.15 Direct examination of a swab taken from the glans of a penis with pruritic balanoposthitis with 10% KOH. We carry out direct examination during the consultation at both our STD clinic and private practice. As the patient is getting dressed after clinical examination, we are usually already looking at the slides



Fig. 8.14 Direct examination of a vaginal smear placed with 10% KOH between a slide and a cover slip and left at room temperature for 10 min in a humid chamber. This process optimizes microscopic observation, as it makes the swab clearer and stimulates the refringence of the yeast structures, pseudohyphae and blastospores that are found in vaginal candidiasis ($400\times$)

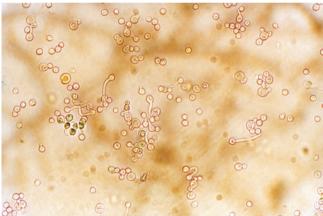


Fig. 8.16 The germinative tube test for *Candida albicans*. Homogenize one or two colonies of the isolate in 0.5 mL sheep or human serum. Incubate at 36 °C for up to 3 h. Observe the slide from the first hour. Results generally appear in the second hour. A 40× lens was used. The germinative tube can be defined as an appendage that is half the length and three to four times the size of the yeast structures, with a consistent shape and no constriction in the area where it is attached. This is a fast, easy and useful test to differentiate *Candida albicans* from other species of *Candida* that have an altered sensitivity to the drugs usually used for the treatment of vaginal candidiasis. It is important that *Candida dubliniensis* is recognized, especially in patients with AIDS, as this also produces germinative tubes

Fig. 8.17 Vaginal swab stained using the Gram technique revealing a microbiome rich in Grampositive rod-shaped bacteria. Pseudohyphae and blastospores—typical yeast structures that are always Gram-positive—can be observed in the foreground (1.000×)

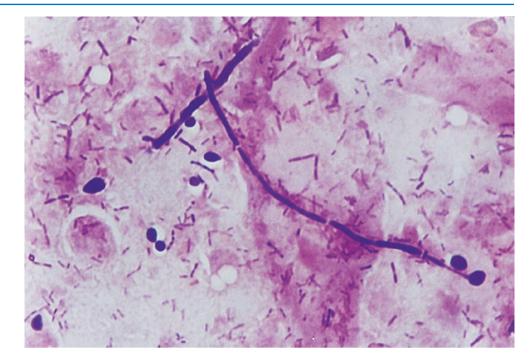


Fig. 8.18 Here, bacterial morphotypes around pseudohyphae are represented by short Gram-negative bacilli, some Gram-positive cocci and rare polymorphonuclear cells

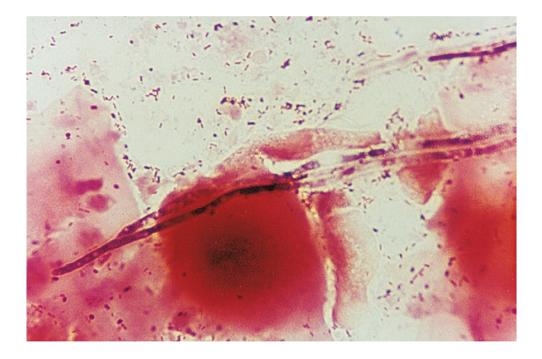


Fig. 8.19 Vaginal swab revealing epithelial cells and polymorphonuclear cells, lactobacilli morphotypes and *Candida* sp. spores (see *arrows*) stained in *dark blue*

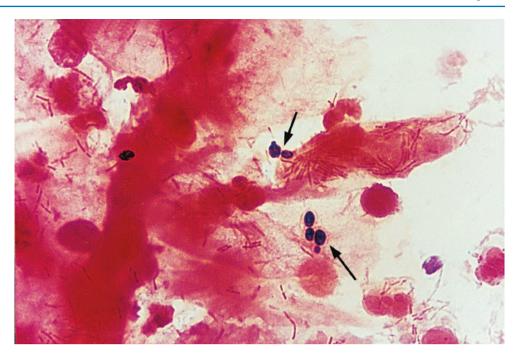




Fig. 8.20 As discussed previously, it is good practice to microbiologically identify Candida before assuming that female patients complaining of vaginal discharge and/or vulvovaginal itching have recurring candidiasis. Although it may be a myth that many women invent having a headache or other problem so that they don't have to have sex with their partners, we have already seen more than one case in which a patient was avoiding sex with her husband for 6 months, complaining of itching and stinging genitals. At first they just used vaginal creams prescribed by their gynecologist. Then, aware that this could cause further problems, at night they would apply a small amount of cream into the vaginal introitus, resulting in them being put on medication to control symptoms of discharge. The cream was affecting the vulval microbiota. We believe that this situation can worsen when doctors attending a female patient with candidiasis advise that they should "stop all sexual activity". We recommend that vaginal intercourse be avoided in situations with more serious clinical symptoms, and we would add that there are ways of being together without having penetrative sex. After all, the body, like the world, is very big

Fig. 8.21 Cervicovaginal swab stained using the Papanicolaou technique, where epithelial cells, polymorphonuclear cells (PMN) (arrows) and Candida pseudohyphae can be observed $(1.000\times)$. Oncological colpocytology (PAP) smears were developed to screen for cancer of the cervix. However, we believe that secondary findings from this important exam should also be taken into consideration, especially where this concerns information that may challenge any diagnoses of candidiasis, trichomoniasis or bacterial vaginosis

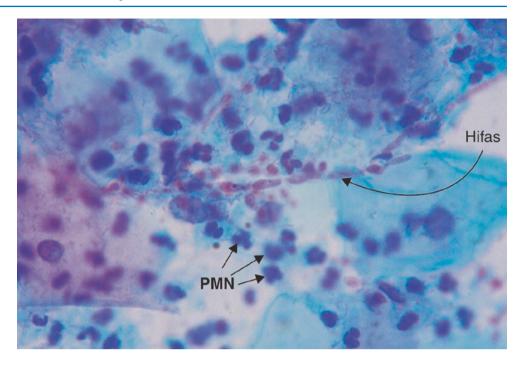
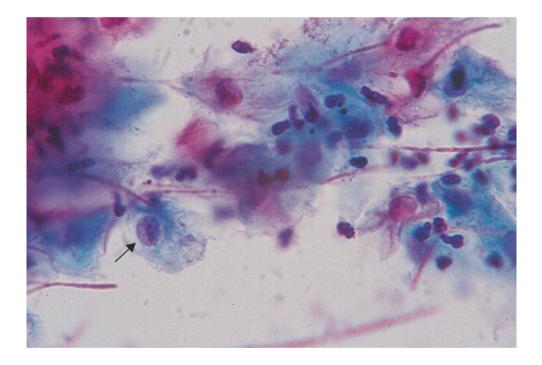


Fig. 8.22 In addition to the elements described in the previous photograph, perinuclear halos can also be observed (see *arrow*) in epithelial cells, which is a common effect seen in acute cervicovaginal inflammatory processes (1.000×)



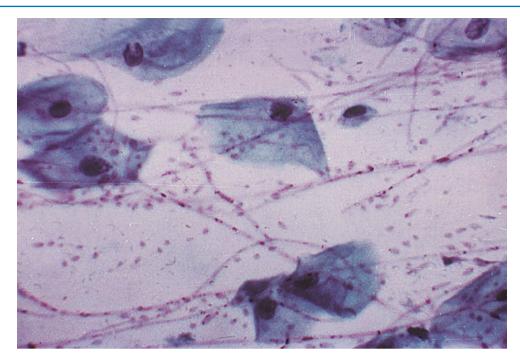


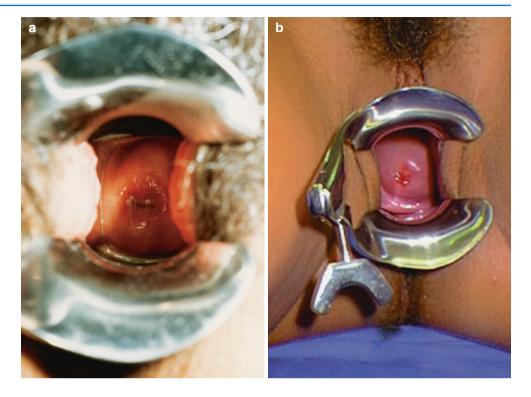
Fig. 8.23 The difference between this photo of a slide stained using the Papanicolaou technique (1.000×) and the previous photos is the scarcity of polymorphonuclear cells. Pseudohyphae, on the other hand, can be seen in larger quantities. Observe the increase in nuclear volume. Many medical colleagues often use colpocytology with staining (PAP)

to investigate and control cases of leukorrhea. It is common to see patients that have undergone two or more rounds of "preventive exams", with intervals of 1 year or more, for the diagnosis and treatment of vaginal discharge. In the vast majority of cases, direct examination during consultation can clarify diagnosis in such cases



Fig. 8.24 A case of colpitis with a large quantity of white-yellow discharge and numerous bubbles caused by bacteria associated with *Trichomonas vaginalis* infection

Fig. 8.25 (a) Colpitis with the cervix presenting a cloudy mucous and periorificial hyperemia, in which a range of etiologies should be screened for, including gonococcus and C. trachomatis. The only positive result was for Trichomonas vaginalis. (b) Another image of a cervix with signs of colpitis. The only positive result was for Trichomonas vaginalis. Examining and treating patients without conducting laboratorial exams generally leads to incorrect diagnosis



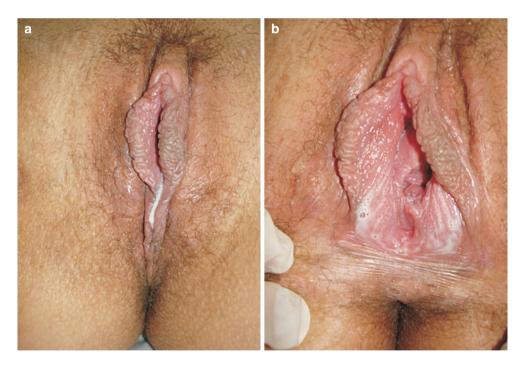


Fig. 8.26 (a, b) A young pregnant patient seen at the UFF STD clinic for a case of vaginal discharge. She reported experiencing slight itching and stinging to her genitals. Asked if she had experienced any disagreeable odor, she said she had not. She said that the doctor at the public health center where she carried out her pre-natal examinations had already prescribed nystatin cream on two occasions. She also reported not having been offered any local examinations to clarify the diagnosis,

and not even a cancer-prevention smear. We carried out direct examination of a vaginal swab and sampled material for oncological colpocytology. Both exams were positive for trichomoniasis. This emphasizes the need for laboratory exams to obtain the correct diagnosis for cases of vaginal discharge, the fact that not all cases of vulvovaginal itching are a result of candidiasis, and that having pre-natal exams does not necessarily guarantee that these exams will be of good quality

Fig. 8.27 Photo-colposcopy showing multifocal colpitis in a case of trichomoniasis. (a) Without any preparation and (b) after application of Lugol's solution. Differential diagnosis with cases of atrophic colpitis and colpitis caused by the herpes virus should not be forgotten

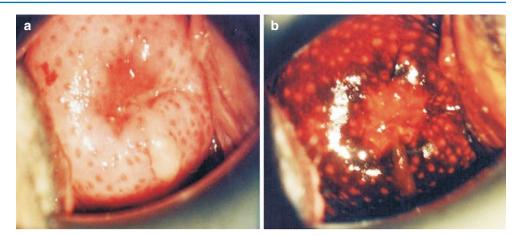


Fig. 8.28 Photos of colpitis caused by trichomoniasis similar to the previous cases. In (a) without preparation and (b) after application of Lugol's solution

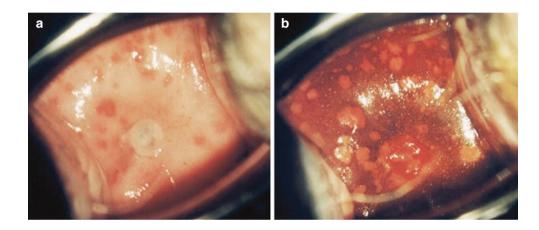


Fig. 8.29 Vaginal trichomoniasis. Direct examination with a common optical microscope, a low condenser and magnification of 400. Note that the protozoa (see *arrows*) loses its motility in a very short time and can be confused with pus cells present in the sample. An attentive and experienced observer can easily tell the difference between these

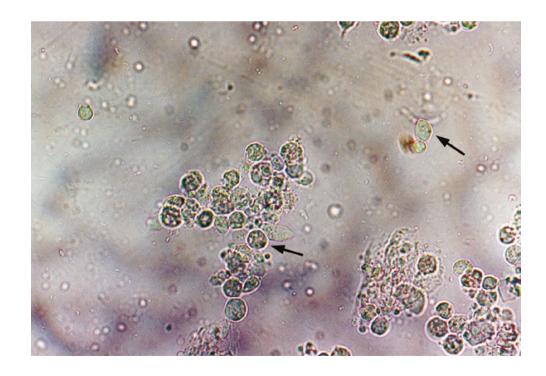


Fig. 8.30 Direct examination of a swab of discharge taken from the bottom of the posterior vaginal vault, with a bubbly appearance, pH above 4.5 and a fetid odor, containing Trichomonas vaginalis (arrow). Swabs can be taken with a zaragatoa swab, an Atre's spatula or a Pasteur pipette with a rubber end, placed on a slide with saline solution, mixed, covered with a cover slip and observed using a microscope with a low condenser and first magnified 10× to 20× and then 40×. A tip: all of the materials used must be clean. If the slide and/or cover slip are dirty and the view through the microscope (eyepiece and lenses) is dusty, this will make examination more difficult



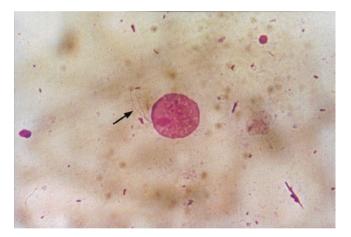


Fig. 8.31 *Trichomonas vaginalis* stained using the Gram technique using safranin as a counterstain. Using this, the protozoa appears in a characteristic apple-pink color and is rounded or pear-shaped. Note the subtlety of their flagella (see *arrow*) (magnified 1.000×)

Fig. 8.32 Colpocytopathology using the Papanicolaou staining technique showing a serious case of *T. vaginalis* infection (*a*) surrounding epithelial cells that appear with an enlarged nucleus (karyomegaly) (*b*) and polymorphonuclear cells (*c*)

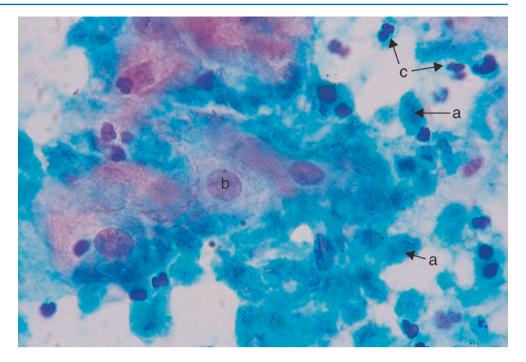
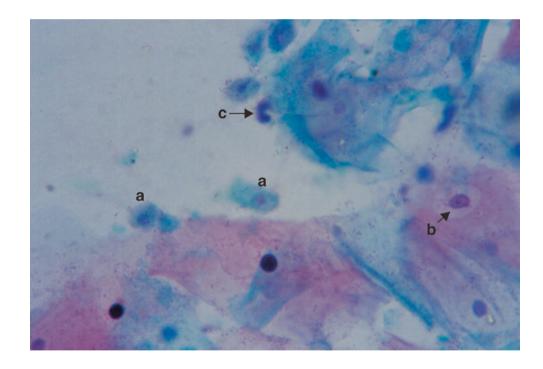


Fig. 8.33 As well as *T. vaginalis* (*a*) and polymorphonuclear cells (*c*), we highlight the perinuclear halos in epithelial cells that are common in these inflammatory processes, using oncological colpocytology (PAP) (*b*)



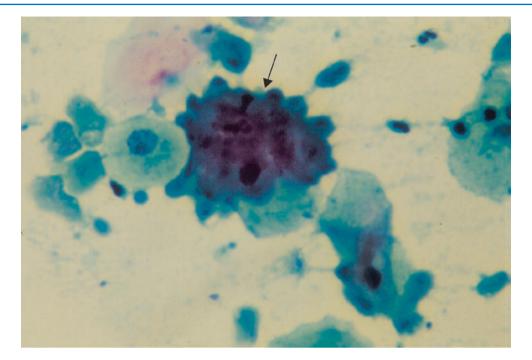


Fig. 8.34 This photograph of a vaginal swab stained using the Papanicolaou technique shows a typical inflammation caused by *Trichomonas vaginalis*: protozoa accumulating around epithelial cells (see *arrow*). It is worth emphasizing that trichomoniasis is a disease where according to classic medical guidelines, all treatment regimes should include the treatment of any sexual partners. However, we believe that this treatment should be administered after medical consul-

tation. We do not recommend prescribing drugs before seeing the partner indicated by the patient. As it is not common to be able to conduct diagnostic examinations such as cultures and PCR, we recommend clinical examinations and direct examination of vaginal swabs with saline solution during the consultation for control of cure. Although treatments involving single doses may be standard practice, in our area we prefer to prescribe metronidazole for 7–10 days, wherever possible

Fig. 8.35 Developed by Professor Ken Borchardt (San Francisco, USA), the In pouch TV is a kit including a growth medium for *T. vaginalis*, which in our experience provides excellent, practical results



Fig. 8.36 This slide reveals both the inflammatory process seen in *T. vaginalis* and atypical epithelial cells. When this occurs, and mainly in less severe cases, it is recommended that treatment for the protozoa be prescribed and colpocytology repeated after 6 months

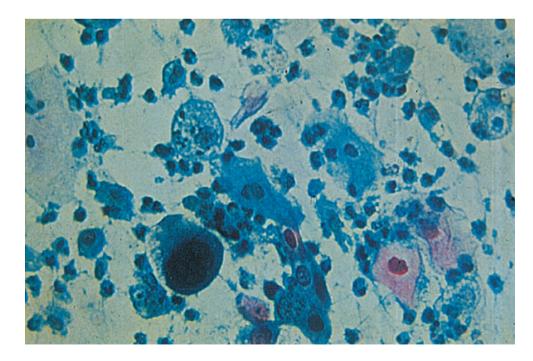


Fig. 8.37 A case of bacterial vaginosis diagnosed after bacterioscopy of a vaginal swab using the Gram technique. Note the hyperemia on the ectocervix, an uncommon symptom

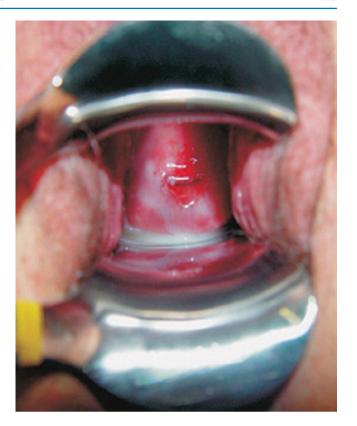


Fig. 8.38 (a) Vulva presenting white discharge in the vaginal introitus. Discharge can be white, grey or yellow. In cases of BV it is generally homogenous and the vulval and vaginal mucosa are not hyperemic. (b) In this case the vulva has a normal appearance and does not have any discharge or hyperemia. However, the vaginal discharge was characteristic of that found in BV. The patient's main complaint was of a very strong smell, especially after her partner had ejaculated (as reported by the patient). She reported not using condoms. (C) View of the cervix and the vaginal vault containing a large quantity of bullous whiteyellow discharge and with the vaginal epithelium not showing any signs of inflammation, typical of BV. The explanation for the worsening of genital odor after ejaculation in the vagina is that the pH of the semen makes the vagina more alkaline. This mimics the amine test









Fig. 8.39 In this photo we show a pH strip that has been placed on the vaginal wall of a woman presenting the symptoms of BV. Note that the scale shows an above-average pH value



Fig. 8.40 The same procedure as used in the previous figure, but with a different brand of pH strip. It is worth emphasizing that although this is a simple procedure that can provide more data in investigations into leukorrhea, in practice many medical services find this hard to handle. Good strips are not as cheap as may be expected. Heat, humidity and the direct handling of the strip can negatively affect the results of this exam



Fig. 8.41 Our normal procedure is to homogenize vaginal swabs with a drop of saline solution in a corner of the same slide and 10% KOH solution on another. The potassium hydroxide makes the culture alkaline and causes it to release amines (cadaverine, putrescine, trimethylamine), producing a strong smell of ammonia. These amines are products of the catabolism of the anaerobic bacteria (bacteroides, for example) that are associated with BV. Some women often report smelling a very disagreeable odor (like "rotten fish") after vaginal intercourse, when the partner doesn't use a condom and ejaculates in the vagina. As semen has an alkaline pH, it makes vaginal discharge alkaline, producing amines. It works in the same way as the Pheiffer test or the amine test

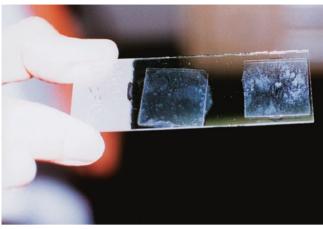


Fig. 8.42 After carrying out the procedure described above, we place a cover slip on top of the swab and analyze it using a common optical microscope. This is direct examination of vaginal discharge with saline solution and potassium hydroxide in a slide and a cover slip

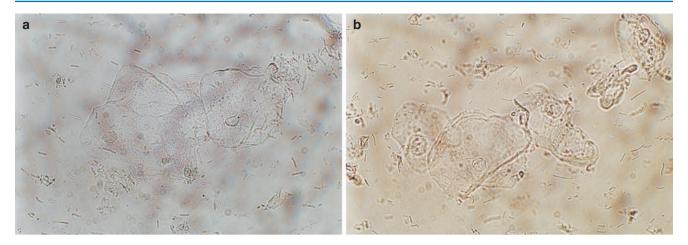


Fig. 8.43 (a, b) Direct examination of a vaginal swab sampled from a woman presenting normal and well-defined epithelial cells. This revealed a normal microbiome with a prevalence of *Lactobacillus* sp.

morphotypes. The swab was placed on a slide with saline solution and observed with $400 \times$ magnification

Fig. 8.44 Bacterioscopy of a normal vaginal swab using the Gram technique showing a microbiome of Gram-positive rod-shaped bacteria typical of *Lactobacillus* sp. (1.000×)

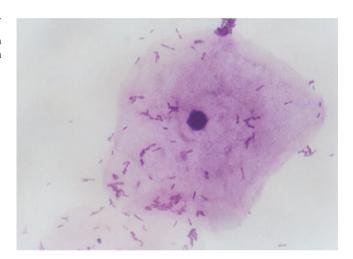
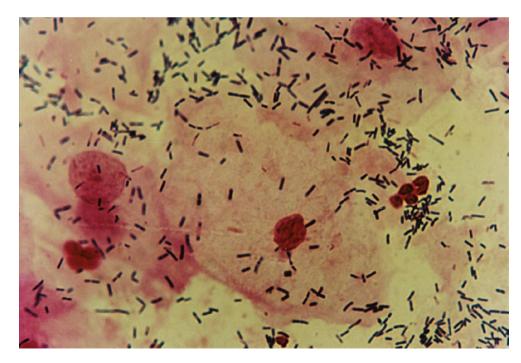
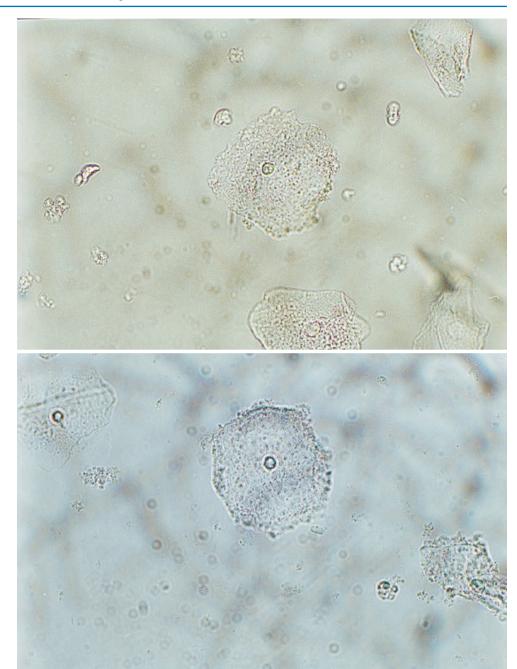


Fig. 8.45 Bacterioscopy of a normal vaginal swab using the Gram technique showing a microbiota with an elevated number of Gram-positive rod-shaped bacteria, possibly from a different species to *Lactobacillus* sp. (1.000×)



Figs. 8.46 and 8.47 Direct examination of a vaginal swab from a patient with a clinical diagnosis of BV showing clue cells. These are epithelial cells covered across their whole surface with coccobacilli bacteria, especially around the borders, leaving their contours badly defined and obliterated (400×)



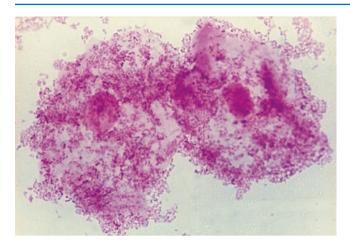


Fig. 8.48 Vaginal swab stained using the Gram technique, taken from a woman with a clinical diagnosis of BV. Many Gram-negative coccobacilli are stuck to the surface of the two cells, which are known as clue cells $(1000\times)$

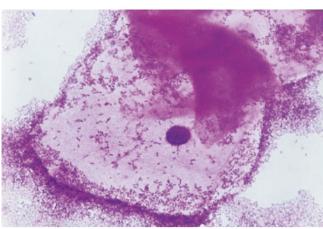


Fig. 8.49 Patient presenting grey, sticky and bullous homogenous vaginal discharge, pH > 4.5 and a positive result for the amine test with 10% KOH. Bacterioscopy using the Gram technique revealed an absence of *Lactobacillus* sp. morphotypes and no leukocytes were observed. This image (swab of vaginal discharge stained using the Gram technique) confirms the suspected diagnosis of BV, showing the characteristic bacterial colonization of the borders of epithelial cells, leaving them obscure: clue cell (magnified 1000×)

Fig. 8.50 Examination of vaginal swab of discharge characteristic of bacterial vaginosis, stained using the Gram technique, with epithelial cells completely covered in coccobacilli morphotypes, numerous curved rod-shaped bacteria indicating *Mobiluncus* sp. and also revealing some yeast-like structures (blastospores). Note the Gram-labile nature of these bacteria (magnified by 1000×)

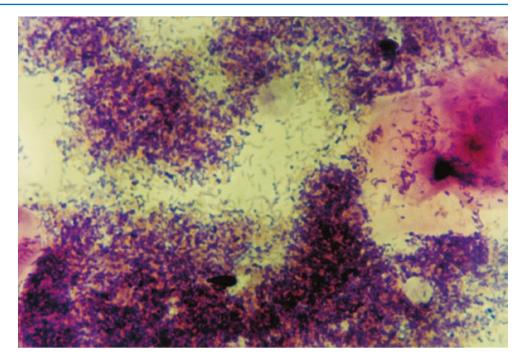
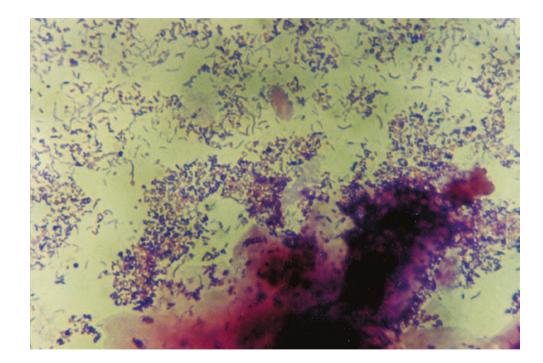


Fig. 8.51 Another vaginal swab revealing numerous curved Gram-labile rodshaped bacteria, with a prevalence of Gram-positive cells, suggesting *Mobiluncus* sp. (1000×). It is worth emphasizing again that these patients should immediately receive the full routine procedure for STD investigation, even though BV is not recognized as a classic STD



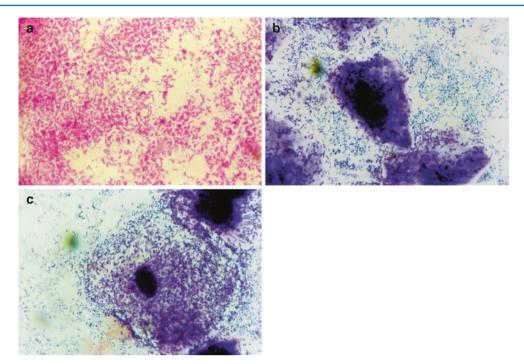


Fig. 8.52 (a) Vaginal swab stained using the Gram-technique modified by Kopeloff-Beerman, sampled from a woman with a clinical diagnosis of BV. There are numerous small Gram-negative rod-shaped bacteria (>10¹⁰ UFC/mL in an appropriate culture medium), characteristic of *Gardnerella* sp., *Prevotella* sp. and similar species. Note the absence of *Lactobacillus* sp. morphotypes (Gram-positive rod-shaped bacteria) and

the presence of *Mobiluncus* sp. morphotypes (curved Gram-negative rod-shaped bacteria) (×1000). (**b**, **c**) show other slides stained using the normal Gram technique (not Kopeloff). Although the morphology is the same, the colors are different. However, a careful observer will be able to carry out a good examination

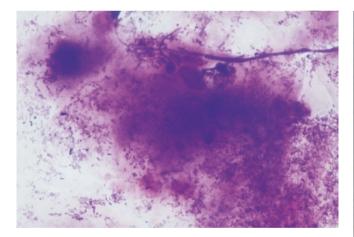


Fig. 8.53 This uncommon image of a vaginal swab shows bacterial morphotypes typical of BV, with a prevalence of curved Gram-negative rod-shaped bacteria suggestive of *Mobiluncus* sp. and associated with pseudohyphae and blastospores (magnified by 1.000×). However, recent studies have observed this association, somewhat paradoxically, in approximately 10% of vaginal swab examinations of female patients with a wide range of complaints. In a study recently published by our group using cytology in liquid media, we identify this association in 6.7% of women with vaginal discharge. In an ongoing study using molecular biology, we have observed a much larger rate of association (26%)

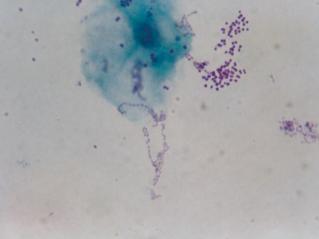


Fig. 8.54 This vaginal swab stained using the Gram technique shows a high presence of Gram-positive cocci in chains, typical of Streptococcus sp. In situations such as this, infection by S. agalactie (group B) must be considered, which in menopausal women and principally in pregnant patients (especially in cases of high risk pregnancies) can cause inflammatory vaginitis. This disease during pregnancy can develop into serious complications in the fetus and/or puerperal infection. Clinical symptoms in the vagina can include: yellow, itchy discharge causing hyperemia to the mucous membranes, a large presence of parabasal and polymorphonuclear cells, pH above 4.5 and a negative result using the amine test. Treatment is generally with oral amoxicillin or ampicillin in regular doses over 10 days. However, recolonization of bacteria in the vagina is common. Public health service guidelines do not recommend treatment for sexual partners. These symptoms (hyperemia + purulent discharge) sometimes lead medical professionals to confuse this with a classic STD (gonorrhea, chlamydia, trichomoniasis)

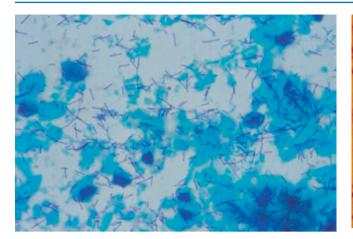


Fig. 8.55 Photograph of a slide from a case diagnosed as cytolytic vaginosis, although this was not accepted by everyone. In these cases there is a very large presence of lactobacilli morphotypes and numerous loose cell nuclei. For many, these are non-hydrogen peroxide producing lactobacilli that do not activate the protective response of the vaginal ecosystem and aggravate the vaginal mucosa, producing a white discharge, hyperemia and vaginal itching/stinging. These symptoms are very similar to those caused by *Candida* sp. Therefore, adequate microbiological examination of vaginal swabs must be carried out (PAP 1.000×)

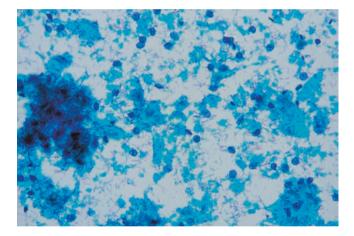


Fig. 8.56 Here the case described above can be observed with lower magnification (PAP $400\times$). Experience shows that many colleagues treat these cases using vaginal applications, such as bicarbonate water douches (10 g, two soup spoons for each 500 mL of clean water) once or twice a day for 1 week

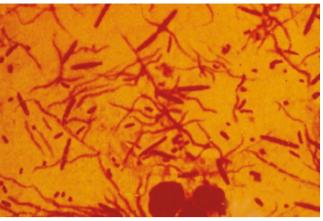


Fig. 8.57 This vaginal swab shows the unusual situation where a high prevalence of two bacteria can be observed (fusoespirilar) over lactobacilli and cocci in the vaginal microbiome. This patient complained of vaginal discharge and was prescribed local application of sulpha once a night for 1 week

Fig. 8.58 (a) Examples of positions for collecting vaginal samples. (b) Slide the cotton swab from position 1 to position 2. (c) Repeat the instructions from figure 2

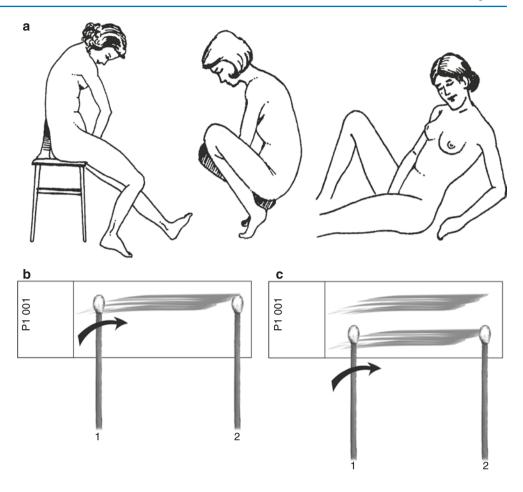


Fig. 8.59 Model of the material used in a previous study (Passos et al. 2007)

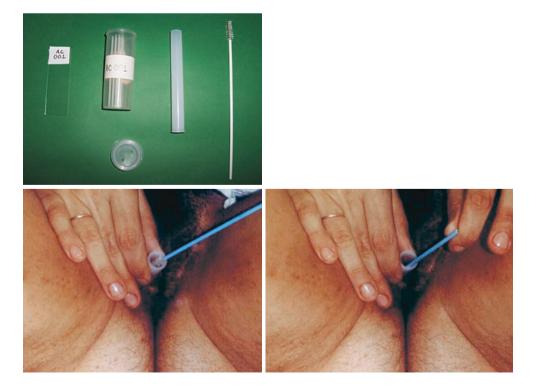
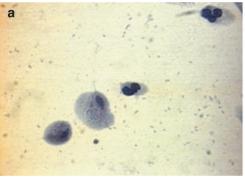


Fig. 8.60 (a, b) Model of the material being tested for postal delivery of the vaginal swab self-collection kit.

These will be sent for microbiological analysis using the Gram technique at the UFF STD clinic







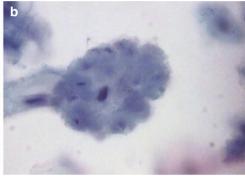
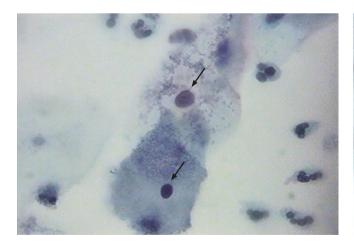
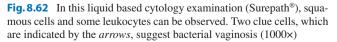


Fig. 8.61 Twenty-five-year-old patient without symptoms seen at a gynecology clinic for a routine smear test. She had a previous history of human papillomavirus (HPV) infection. Samples were taken for liquid-based oncological colpocytology (SurePath). The result of microbio-

logical screening was *Trichomonas vaginalis*. In (a), two *Trichomonas vaginalis* (1) can be observed next to polymorphonuclear cells (2) (1000×). In (b), *Trichomonas vaginalis* forming a rounded figure (1000×)





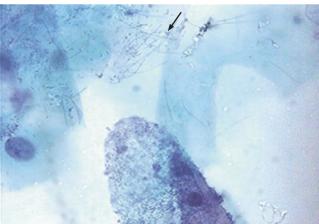


Fig. 8.63 In this liquid-based cytology examination (Surepath®), a clue cell suggestive of BV and a colony of long bacilli suggesting *Leptotrix* sp. (*arrow*) can be observed (1000×)

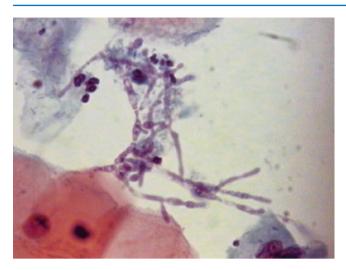


Fig. 8.64 Surepath cytology showing some squamous cells and Candida pseudomycelia ($400\times$)

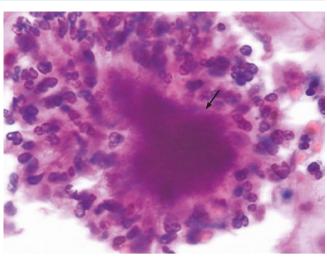


Fig. 8.67 Surepath cytology showing an *Actinomyces* sp. morphotype (*arrow*) surrounded by leukocytes (SurePath 1000×)

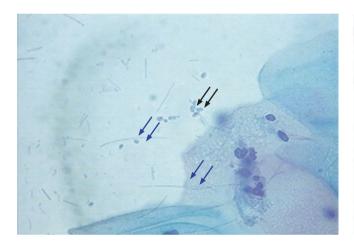


Fig. 8.65 In this liquid-based cytology examination (Surepath), squamous cells and small blastoconidia yeast cells (*black arrows*) can be observed. Some authors suggest that this morphotype is *Candida glabrata*. Long bacilli (*Leptotrix* sp.—*blue arrows*) can also be seen (1000×)



Fig. 8.68 In this liquid-based cytology examination (Surepath®), herpes infection could be suggested based on the multinucleated cell presenting nuclear inclusion (1000×)

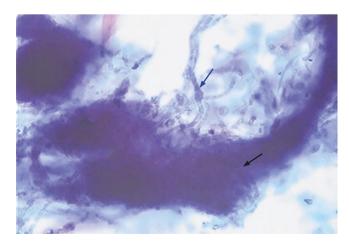


Fig. 8.66 In this liquid-based cytology examination (Surepath®), an uncommon association can be observed. The purple tuft-like structure suggests Actinomyces sp. $(black\ arrow)$ and Candida sp. pseudomycelia $(blue\ arrow)$ $(400\times)$

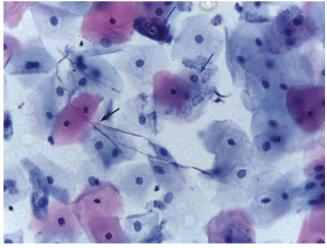


Fig. 8.69 A frequent association observed in liquid-based cytology (Surepath®) is between *Candida* sp. (pseudomycelia—*black arrow*) and *Gardnerella vaginalis* morphotypes (clue cell—*blue arrows*) (mixed vaginitis) (SurePath 400×)



Fig. 8.70 Candida sp. (pseudohyphae) (black arrow) and clue cell (blue arrows) suggesting Gardnerella vaginalis in Surepath® cytology (mixed vaginitis) (1000×)

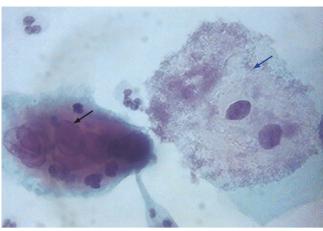


Fig. 8.71 Other associations between pathogens are possible. This is an example of *Gardnerella vaginalis* (clue cell—*blue arrow*) and herpes virus (multinucleated cell—*black arrow*) (SurePath 1000×)

Infection with Human Papillomavirus (HPV)

9.1 Synonymy

Condyloma acuminata, anogenital warts, cervical warts, thymus, ficus, cockscomb, HPV, intraepithelial neoplasia, intraepithelial lesion.

9.2 Concept

Caused by HPV (*Human papillomavirus*), it is the most common sexually transmitted virus. However, it is not always possible to determine the ways and time the contamination occurrs. It has similar incidence in both men and women and it is associated with genital and non-genital intraepithelial lesions. Its pathogenesis is based on the inducement of cellular multiplication (cellular hyperplasia) and interference in cellular cycle, depending on the host's immune response.

9.3 Incubation Period

It takes from 3 weeks to 8 months only for the genital warts process (an average of 3 months). This variability may be related to the immune capacity of the individual. However, incubation time can be indeterminate.

9.4 Etiologic Agent

HPVs are DNA-virus not cultivable *in vitro*. There are more than 200 types, around 45 anogenital and oropharingeal epithelium-specific. According to the increased risk of cervical carcinoma, the most frequent types are:

• Low-risk: HPV 6, 11, 40, 42, 43, 44, 54, 61, 72, 81, 89—are commonly not integrated into the host cellular genome. They are usually present in condylomatous lesions (warts).

 High-risk: have the ability to integrate into the host cellular genome. They are associated with low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL) and invasive carcinoma. Can be classified into:

High-risk possibly carcinogenic: HPV 53, 26, 66, 67, 70, 73, 82.

High-risk probably carcinogenic: HPV 68.

High-risk carcinogenic: HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59.

The high or low-grade lesions do not exclusively depend on the viral type, but rather on a complex and not yet fully deciphered aggression mechanisms and system defense. There are benign lesions caused by high-risk types, and malignant lesions caused by low-risk types, or both types. Squamous lesions of other genital and non genitals sites are also associated with HPV with similar characteristics. This resemblance has been observed meanly in intra-anal lesions, and in the vagina, vulva, penis, head and neck in small proportion.

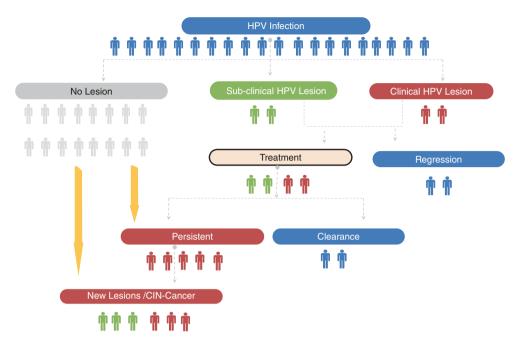
9.5 Clinical Presentation (Figs. 9.1–9.187)

Working with medicine by scientific evidence, ir can be currently asserted that HPV genetic studies have shown that these infections can follow three courses:

- Reveal transitory infections, in about 50% of the cases, with complete removal of the virus, if the organism is immunologically competent [1].
- Determine the appearance of lesions, which may regress spontaneously in 30–50% of cases [2].
- Develop into lesions that after treatment do not lead to the viral elimination, establishing persistent infections, resistant to conventional treatments and considered high-risk of cancer development.

The infection may be latent, i.e., without the lesions identification even through subclinical amplification where lesions will be diagnosed by cytology and/or colposcopy and, less often, show a clinical manifestation

(wart) seen with the naked eye. The lesions may be single or multiple, and may disappear spontaneously or evolve in number and size to form large vegetant masses of "cauliflower" aspect.



HPV infection Biology

Lesions associated with HPV affect genital and non genital sites.

9.6 Most Common Genital Sites

- Man: Glans, foreskin, frenulum, balanoprepucial sulcus, urethral meatus and scrotum.
- · Woman: Vulva, perineum, urethral meatus and cervix.

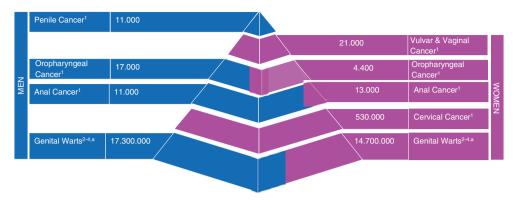
In both sexes there is frequent involvement of the anus, rectum and mouth.

To help visualization of subclinical lesions, acetic acid 3–5% is used, making whitish (acetowhite) the suspicious area. However, such aceto reaction is not pathognomonic of injury associated with HPV infection. Several reasons can attribute the white reaction to the acetic acid, without meaning a virus disease.

9.7 Some HPV Types and Their Manifestations

- **HPV 1a, b, c** \rightarrow Plantar warts.
- **HPV 2** \rightarrow Vulgar warts.
- HPV 3a, $b \rightarrow$ Flat juvenile warts, mild form of EV.
- HPV 6, 11 → Condyloma acuminata, cervical intraepithelial neoplasia, larynx papillomas, Buschke-Löwenstein tumor, penis cancer, cervix cancer.
- **HPV** 7 → Common warts of the hands (butchers).
- **HPV 13a, b** \rightarrow Focal epithelial hyperplasia in oral mucosa.
- HPV 16, 18 → Intraepithelial neoplasia (cervix, vagina, vulva, penis, anus), cancers, Condyloma acuminata, bowenoid papulosis.
- HPV 30 → Larinx squamous carcinoma.
- HPV $38 \rightarrow$ Malignant melanoma.
- HPV 57 → Intraepithelial neoplasia, skin warts, nasal inverted papilloma.

9.8 Impact of HPV in Men and Women in the World¹⁻⁵



Estimated global annual new cases of HPV-related disease in men and women¹⁻⁵. (1) Forman D, et al. Vaccine. 2012;30(Suppl 5):F12-23. (2) Executive summary: the state of world health, 1995. World Health Organization website. http://www.who.int/whr/1995/ media_centre/executive_summary1/en/index.html. Accessed March 12, 2013. (3) Greer CE, et al. J Clin Microbiol. 1995;33:2058-63. (4) Human papillomavirus and HPV vaccines: technical information for policy-makers and health professionals, 2007. World Health Organization website. http://whqlibdoc.who.int/hq/2007/WHO IVB_07.05_eng.pdf. Accessed March 12, 2013. (5) Health Protection Agency (HPA). Health Protect Rep. 2012;6:9-15. http://www.hpa. org.uk/HPR/archives/2012/hpr2212.pdf. Accessed March 12, 2013. (a) Estimated gender ratio of genital warts: 54% men, 46% women. Meta-analysis publication available in: http://www.plosone.org/ article/info%3Adoi%2F10.1371%2Fjournal.pone.0069238sobre The Aetiological Role of Human Papillomavirus in Oesophageal Squamous Cell Carcinoma os autores resumem: "Methods: Case-control studies investigating OSCC tissue for presence of HPV DNA were identified. 21 case-control studies analyzing a total of 1223 cases and 1415 con-

It is estimated that the incidence of recurring respiratory papillomatosis is of 4.3/100,000 children [3].

9.9 Laboratory Diagnosis (Figs. 9.188–9.205)

Cytology and histology can microscopically identify the most characteristic cytopathic effect: koilocytosis.

Electron microscopy and molecular biology techniques can be used to characterize the viral presence within the cells—hybrid capture or polymerase chain reaction (PCR), especially in real-time.

Colpocitology results suggestive of HPV should be regarded with caution and require combined analyses with clinical and colposcopic data. Currently the proposed Pap smear report system (Bethesda System) considers that cases suggestive of HPV cytopathy due to koilocytosis should be classified as low-grade squamous intraepithelial lesion (LSIL).

trols, met our inclusion criteria. HPV detection rates were tabulated for each study and all studies were assessed for quality. The random effects method was used to pool the odds ratios (OR). Results: From all OSCC specimens included in this meta-analysis, 35% (426/1223) were positive for HPV DNA. The pooled OR for an HPV-OSCC association was 3.04 (95% CI 2.20 to 4.20). Meta-regression analysis did not find a significant association between OR and any of the quality domains. Influence analysis was non-significant for the effect of individual studies on the pooled estimate. Studies conducted in countries with low to medium OSCC incidence showed a stronger relationship (OR 4.65, 95% CI 2.47 to 8.76) than regions of high OSCC incidence (OR 2.65, 95% CI 1.80 to 3.91). Conclusions: Uncertainty around the aetiological role of HPV in OSCC is due largely to the small number and scale of appropriately designed studies. Our meta-analysis of these studies suggests that HPV increases the risk of OSCC threefold. This study provides the strongest evidence to date of an HPV-OSCC association. The importance of these findings is that prophylactic vaccination could be of public health benefit in prevention of OSCC in countries with high OSCC incidence.

Lesions without koilocytosis but with nuclear atypical processes previously suggesting dyplasias are regarded as virtually associated with low-grade (LSIL) and high-grade (HSIL) viral action.

Biomarkers that detect and quantify the transcripts of viral oncogenes E6 and E7 are being considered for the assessment of oncogenic activity associated with viral progression of cervix infection/neoplasia. The use of protein p16ink4a, which identifies the high-grade intraepithelial lesions in cases of diagnostic doubt, is well established within the histopathological diagnostic routine. Some studies also demonstrate the usefulness of this marker associated with another one, Ki-67 (marker of tumoral proliferation) in immunocytochemistry for diagnosis of high-grade lesions. The identification of these oncoproteins activity may also be an element of prognostic evaluation in cases of squamous intraepithelial lesions of the uterine cervix.

9.10 Evaluation of Laboratory Methods

The routine use of the HPV test for molecular biology is increasingly indicated for diagnosis and prognosis of HPV infection and lesion cases. Some recent studies consider this test ideal for primary screening of squamous intraepithelial lesions of the uterine cervix. Another possibility of high-level evidence is the use with adjuvant in oncotic cytology in cases of atypical squamous cells of undetermined significance (ASC-US) for indication of colposcopy. Another indubitable indication is its HSIL post-treatment use in uterine cervix by cervical conization as a prognosis of the lesion persistence or recurrence. It is the degree of the cellular alteration and not the presence/absence of HPV what dictates the clinical conduct.

The viral persistence, which is considered a major risk factor for HSIL, is determined by two positive PCR tests for the same viral type at an interval of 1 year. It makes no sense, with the current knowledge, testing every 3 or 6 months.

Sensitivity and specificity of tests take into account the histopathological HSIL diagnosis (gold standard).

Exam	Specificity %	Sensitivity %
Oncology cytology	88-89	50-60
Colposcopy	90–99	40-70
Hybrid capture	90-95	95-98
Real-time PCR	94–96	97–99

9.11 Treatment and Control

Warts:

Application by patient:

Imiquimod (cream 5%): topical use. It is not indicated for internal use (vaginal/anal). Application must be in each lesion, three per week, for a period of 4–16 weeks. Side effect as local irritation/burning is not uncommon. It can be used alone or associated with physical removal method through surgical exeresis or electrocoagulation. The ideal practice is to make the application shortly before bedtime and wash the area with common soap and water 8 h after application. As a routine, client is informed to wash the area where imiquimod was applied 7 h later rather than 9 h later, which minimises the collateral effects.

Podophyllotoxin 0.5%: topical use. Used in cycles as follows: twice a day, for 3 days, with an interval of 4 days without application. More than four cycles should not be used. Local irritations are frequent, and patient should be oriented to suspend the use in such case. Not indicated for pregnant women.

Sinecatechins Oitment (Veregen®) 10% w/w in 15 g tubes (Canada). In the USA, this product is commercialized

with a concentration of 15%. Used only on skin, three times a day (morning, afternoon and evening). The treatment must be done until lesions disappear. But treatment should not exceed 16 weeks. The side effects are similar to those of imiquimod's. The application of sinecatechins oitment should be suspended in case of intense side effects.

Application by physician:

Podophyllin 10–25% (we prefer in tincture of benzoin. But it can be oily or alcoholic): topical use. The teratogenic origin is not indicated for the mucous membranes. The region must be washed 4 h after application. Care must be taken with excesses—application should be repeated every week.

Trichloroacetic acid—TCA (30–90%): topical use. Weekly serial applications until involution of lesions.

Surgical removal: perhaps the simplest and most effective method. There are many ways to carry out the lesion excision: with delicate surgical scissors and later soft cauterization of the bases through laser or electric scalpel (electrocoagulation).

Cryotherapy with liquid nitrogen: weekly serial applications until the lesions' regression.

Crvocauterization

Cryotherapy destroys warts by thermal-induced cytolysis. Healthcare professionals must be trained on the proper use of this therapy because over and undertreatment can result in complications or low efficacy. Pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, is common. Local anesthesia (topical or injected) might facilitate therapy if warts are present in many areas or if the area of warts is large.

Cryotherapy with liquid nitrogen or cryoprobe. Repeat applications every 1–2 weeks.

Fluorouracil (5-FU)

Fluorouracil (5-FU) is an antineoplastic agent, cytostatic, analogue of Uracil and therefore a pyrimidine antagonist, which inhibits the synthesis of viral DNA/RNA, and with immunostimulating action. The medication comes as a cream 5%. It is indicated for use in both skin and mucous membranes. It can produce side effects such as erythema, swelling, burning, itchiness, pain, ulceration and dysuria. Two treatment schemes are recommended: daily use for 5 days or weekly application for 10 weeks. Wash lesions 4 h after external applications. Vaginal and cervical lesions should use 3–5 mL of cream with applicator deeply at bedtime. Insert a vaginal tampon and protect the vulva with Vaseline or zinc oxide. The use in vulva produces vestibulitis, and in the vagina can cause chronic ulcerations and adenosis, reason why we do not recommend its routine use.

For some people, the combination of treatments can reduce recurrences. However, they may increase complications.

After 6 months without presenting clinical manifestation of the disease, patient must be discharged.

Podophyllotoxin and podophyllin should not be applied to pregnant women. Podophyllin and trichloroacetic acid should not be applied by patients at home.

Squamous intraepithelial lesions: can only be accompanied if they are low-grade lesions, especially among young women. Cases of low-grade intraepithelial lesions confirmed by biopsy, persistent and in women over 30 years of age may require destructive therapy or surgical excision. The high-grade lesions confirmed by biopsy should be submitted to excision by conization.

Prophylactic vaccine against HPV: immunogenic materials used are virus-like particles (VLP) HPV-specific types 6, 11, 16 and 18. These particles represent only the viral capsomers without any genetic content. This causes the immunogenetics to be maintained without the slightest possibility of causing infections. Such methodology is widely and safely used in other vaccines, such the hepatitis B. The first vaccine was approved in 2006 and has four VLPs (6, 11, 16 and 18). Thus, it protects against Condyloma acuminata (anogenital warts) and concomitantly intraepithelial neoplasias and cancer of the vulva, vagina, cervix and anus. The posology is three doses IM: 0 day, 60 days and 180 days. The second vaccine was approved for use in women and girls over 10 years of age and has proven effectiveness for the intraepithelial neoplasias and cervical cancer. This vaccine contains two VLPs (16 and 18). Must also be applied in three IM doses: 0, 30 and 180 days. In September 2009, the U.S. agency that regulates food and drugs administration (FDA) approved quadrivalent vaccine against HPV 6, 11, 16 and 18 in men from 9 to 26 years of age. In Europe, the similar committee, EMEA, also approved a very important decision: the extension of the use of the same vaccine for women over 45 years of age. Earlier, the World Health Organization awarded its seal to this product. The HPV 16 and 18 bivalent vaccine has also been approved by FDA. Nowadays, it is proved that the protecting effect of these prophilatic vaccines surpasses 9 years. In 2010, during the international event Eurogin Monte-Carlo, Joura EA et al. (Impact of Gardasil® in women who have undergone definite therapy, SS 4-3) have shown that there are benefits in using quadrivalent vaccine against HPV in women who have had cervix or vulvar diseases and were properly treated, once they have reported significantly lower rates of new diseases caused by HPV in the genital area. More recently, international study has shown good results with the quadrivalent vaccine in preventing penile and anal lesions in research involving only men. All this proves that these

vaccines bring great benefits for the human species, with low side effects. Some countries have already managed to vaccinate large portion of their teens. More recently, FDA has approved the nine valent HPV vaccine against types 6, 11, 16, 18, 31, 33, 45, 52 and 58. The nine valent vaccine was 97% effective in the prevention of cervical cancer in vulva and vagina caused by additional types 31, 33, 45, 52 and 58, as well as of diseases caused by the previous four types of HPV vaccine in clinical studies.

Therapeutic vaccine against HPV: there are studies about the therapeutic vaccines, which differ from the prophylactic vaccines due to the ability to act against infection and lesion manifestations established through the immunocellular via, assisting in the viral elimination. This process is mediated by T cells and not B cells as occurs in the prophylactic vaccines.

9.12 Complications

Complications are extremely related to the intraepithelial/cancer lesions of the uterine cervix, and with a variable frequency also with the vagina, vulva, anus, penis, oropharynx, and oesophagus.

Most cancers have multifactorial etiology. HPV seems to be insufficient to produce alone the malignant transformation. Several factors may be involved, mainly with coinfection with chlamydia and herpes virus. Smokers also have increased risk for malignant progression of HPV infection.

Large condylomatous masses may require large surgeries. Thus, deformities may occur.

Giant condyloma is an entity known as Buschke-Löwenstein tumor and means manifestation by strongly aggressive HPV 6/11, regarding the genital region damage. Histopathologically it is not malignant.

Complications for people who come across of the HPV three letters in emotional, sexual, social, marital, financial, and professional areas, in most cases, are difficult to identify and solve. However, the professionals who serve people suspicious of or confirmed HPV infection/disease diagnosis should be alert and available to minimize these complications.

9.13 Diferential Diagnosis

Condyloma latum (condyloma planum/papular syphilides—secondary syphilis), molluscum contagiosum, benign tumors and malignant neoplasias of non-viral origin.

9.14 Observations

Treatment of systemic and local secondary infections promotes the remission of lesions. The same happens in the post-delivery women with HPV lesions, especially genital warts. Numerous therapies are a sign that none of them is sufficient for an ideal control. All, without exception, have high rates of HPV recurrence (> 50%).

With the current knowledge, it is not true to say "once with HPV always with HPV".

Moast intraepithelial lesions, especially those of low-grade, also tend to evolve. However, the clinical, laboratory and emotional monitoring should not be neglected.

The cesarean delivery should be considered when there are lesions obstructing the birth canal, disabling any type of episiotomy, and also high-grade or vegetant cervical lesions, due to high risk of lacerations and bleeding.

Re-examining the patient 3 months after the disappearance of the lesions is a good behavior.

As we believe in sexual transmission and in the association with STD, we are favourable to classical medical examination of sexual partners. This is different from "peniscopy" only.

Emotional verbal untrue or exceeded concepts assaults may be worse than clinical lesions. In this particular topic we indicate the short-movie Lara's Show (https://www.youtube.com/watch?v=GgwlpwLyT-k).

Read the book "HPV, Que. Bicho É Esse?" (http://virushpv. wordpress.com)—Larah's program (in English) based on the novel "HPV, Que. Bicho É Esse?"

In 2010, an international study about histological samples from several countries was published, and showed the participation of isolated HPV 6 HPV (mainly) and HPV 11 in several penis cancer cases, although the most prevalent type is HPV 16. So far HPV has been detected in about 60% of cases of penile cancer. It has also been found, as the only present type, HPV 6 in pieces of histological cervical cancer.

The physician must not exaggerate the severity of the diagnosis or prognosis, nor complicate the treatment, exceeds the number of visits, examinations or any other medical procedures.

Primary screening for HPV-DNA to prevent cervical cancer. In the recent years there are some concern about the effectiveness of Pap smear as primary screening for cervical câncer, meanly in the development countries, where the incidence of cervical câncer is stable. An alternative defended by researchers is the use of DNA-HPV test, due to its high sensitivity to detect high-grade lesions and the possibility of auto-collect. Although rare, benign or malignant clinical manifestations are observed in very different areas from the usual ones, such as esophagus [4].



Fig. 9.1 Typical clinical manifestation of *Condyloma acuminata*: genital wart



Fig. 9.2 Although the lesions may be agglutinated, the multicentricity is remarkable. Notice the distance



Fig. 9.3 It is very difficult to ensure that the more keratinized, the lower the power of contamination. However, in our practice, we found several patients with clinical keratinized forms, dry, who have sexual partners, sometimes more than one examined, with no HPV lesions



Fig. 9.4 (a) Although isolated lesions occured, satellites (including in the urethral meatus and penis shaft), this case presents itself as a true mountain range, a collar that surrounds virtually the entire glans. (b) Whenever possible, we prefer to treat genital warts by exeresis.



However, in situations like this, a possible scar sequel can be disastrous. So, trying to decrease the number and size of lesions with trichloroacetic acid 60–90%, with imoquimod can be a good tactic

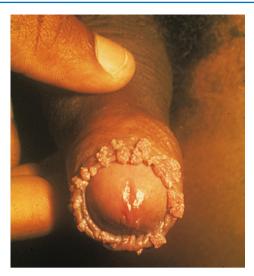


Fig. 9.5 The pathogenesis of HPV causes hyperplasia in the infected tissue, manifested as an excrescence as observed, once again, with this case, similar to the previous one, but smaller



Fig. 9.6 Patient with *Condyloma acuminata* in penile foreskin. Popularly, this disease is known in many regions as "cockscomb"



 $\textbf{Fig. 9.7} \quad \textbf{(a-c)} \ \textit{Condyloma acuminata} \ \text{in the urethral meatus.} \ \text{It is worth noting that the lesion is better visualized when the urethral meatus walls are separated}$

Fig. 9.8 (a) At first it seems that the condylomatous lesions are only around the urethral meatus. (b)
Observing more carefully, it may be noted that the bases of the *Condyloma* extend to the urethral mucosa







Fig. 9.9 Pregnant 15-year-old patient showing *Condyloma acuminata* lesions in vaginal introitus. Classical attention: do not use podophyllin, because this drug is highly toxic, causing serious problems on fetus, annexes and pregnant woman also. However, we often observe women doing podophyllin solution self-application, at home, prescribed by health professionals

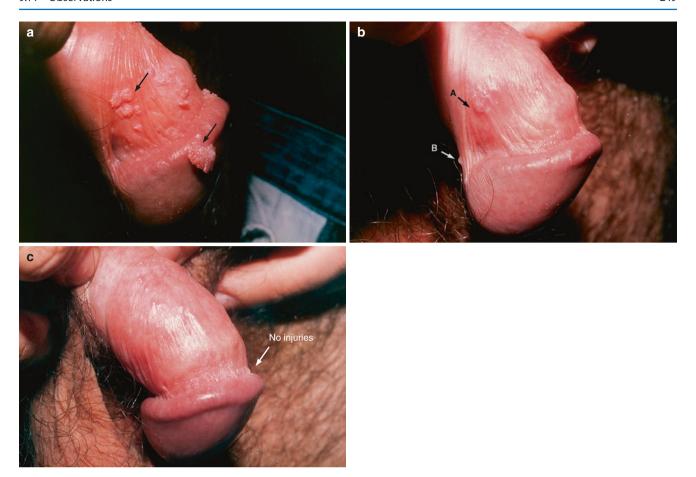


Fig. 9.10 (a) This case of *Condyloma acuminata* was part of a randomized, double-blind, multicenter study involving four groups: (1) surgical exeresis with electrocoagulation of the bases; (2) Interferon α 2b 2,500,000 UI in subcutaneous skin of the abdomen, on alternate days, in a total of eight applications; (3) Combination of procedures 1 and 2; (4) Placebo (interferon α 2b diluent liquid). (b) At the end of the treatment. (c) Two weeks after treatment with interferon only. The

result of this research, which involved 100 patients (25 in each group), was as follows: surgical exeresis: cure of 56%; Interferon: cure of 48%; exeresis + interferon: 72%; and placebo: 4%. The cure criterion used in the study was the absence of *Condyloma* lesions after colposcopy for a minimum period of 6 months after treatment. Details of the article are available on: http://www.dst.uff.br//revista16-2-2004/4.pdf



Fig. 9.11 After many failed attempts of caustic treatment in public health unit, this patient was referred to our service, also public, for final treatment. We have examined and re-examined, and decided to refer patient for evaluation of an urologist, then conducted patient to another service, due to a shortage of surgical conditions in our service (operating room and anesthesia). However, all STD cases routine procedures were conducted. At examination, the rapid tests for HIV and syphilis were non-reactive. Subsequently, feedback reported that the lesions were removed in a surgical environment





Fig. 9.12 (a) Another successful case of interferon α -2b protocol. (b) When it works, and in our experience only 48% does, the great advantage of interferon is the absence of residual scars. Disadvantages: high price, side effects (fever, headache, general malaise as the flu) and low cure rate. In very special cases, it may be a reasonable option therapeutic association

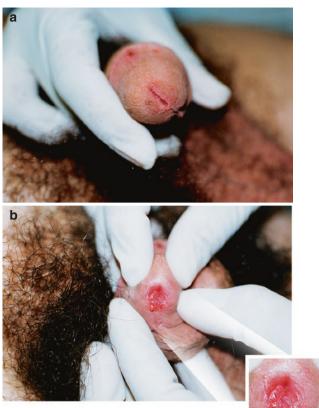


Fig. 9.13 (a) Young man, only partner of woman with vulvovaginal *Condyloma acuminata*, who was undergoing treatment with another professional, was referred to our service. While gathering medical history, we learned he was monogamous. His last sexual contact with another woman occurred more than 8 years ago. We were informed that he had already made two peniscopies in the last 2 months, with normal results. In photo (a), it is not possible to notice any suspicion of HPV. (b) However, when urethral meatus was opened, multiple *Condyloma* virus were seen. Thus, it is evident that the clinical examination must include the exhibition of both the urethral meatus and the navicular fossa





Fig. 9.14 (a) Patient presenting *Condyloma acuminata*, recurrent genital ulcer (genital herpes). (b) This photo shows the careful application of trichloroacetic acid in condilomatous lesion, and herpetic lesions with erythematous halos. It is worth mentioning that this patient spontaneously sought our service for treatment of genital ulcers. Patient

reported that the wart on the penis stem did not bother him, unlike the penile wounds. In the service routine the serology for syphilis, hepatitis B, hepatitis C, HIV, anti-HBS were non-reactive. Hepatitis B vaccination schedule was prescribed



Fig. 9.15 Patient referred to peniscopy, because his partner had HPV in uterine cervix. No HPV lesion was found in the penis or scrotum, however, condylomatous injuries were found in the anal margin. The patient denied homosexual relationship. He reported mutual oral sex with his partner, including in the affected area. In the service routine the serology for syphilis, hepatitis B, hepatitis C, HIV, anti-HBs were non-reactive. Vaccination schedule against hepatitis B was prescribed, as well as for the partner



Fig. 9.16 Child with extensive condylomatous lesion. The therapeutic option was the exeresis of injuries in surgical environment and under narcosis. We consider that the treatment in ambulatory environment is very painful and stressful for everyone: child, family and medical staff. Notice that in (a) the removal by dissection with cold scalpel was the option. The

base was wide and suture with categute was carried out. It was not possible to establish connection with sexual abuse, but we notified Child Protective Services. In the service routine the serology for syphilis, hepatitis B, hepatitis C, HIV were non-reactive. The vaccination card showed that the vaccines were updated, including the hepatitis B vaccine



Fig. 9.17 Female patient presenting *Condyloma* only in the anal area. She, however, had eventually anal sex, and lesions existed in inner mucosa after the anal sphincter. It is important to point out that, when examining a patient with suspected or presenting *Condyloma*, the physical examination must include the genitals, mouth and anus

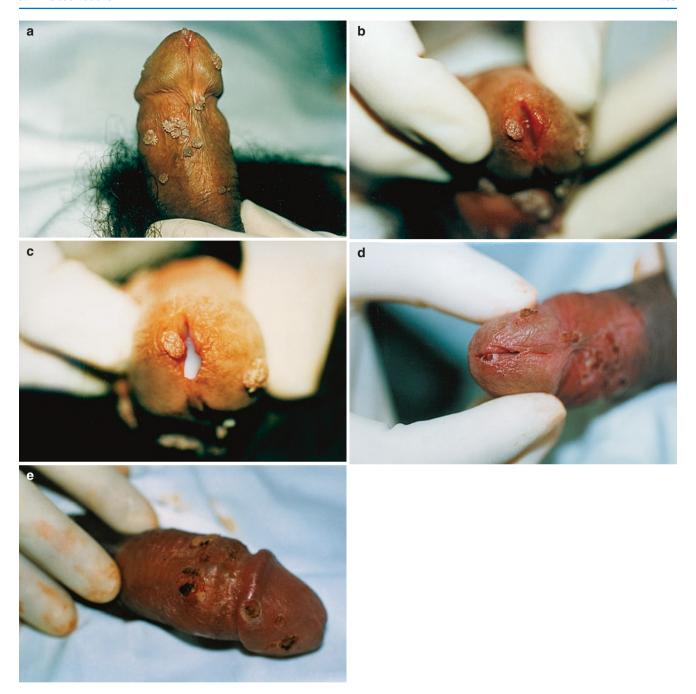


Fig. 9.18 (a) Teenager showing multiple lesions of *Condyloma acuminata*, complaining of burning and urethral secretion. (b) Vegetant lesion by HPV in urethral glans, not reaching the mucous membrane of the urethra itself. Notice that the urethral secretion is not evident, because patient urinated a few moments before the examination. (c) He was oriented to wait in the waiting room, without urinating so we could collect urethral material for tests. Direct bacterioscopy showed intracel-

lular Gram-negative diplococci in polymorphonuclear. Culture in Thayer-Martin medium and other biochemical tests identified *Neisseria gonorrhoeae*. (**d**, **e**) After surgical exeresis of the lesions, electrocauterization of the bases for complete hemostasis was carried out with delicate curve scissors. Procedure made in ambulatory under local anesthesia



Fig. 9.19 Teenage examined at the STD Department of UFF (Fluminense Federal University), Niterói-RJ, with extensive condylomatous lesions in penis. Notice condylomatous mass in penis shaft near the root, with a diameter of approximately 6 cm. Presents also smaller lesions of *Condyloma acuminata* spread throughout the genitals (**a-d**). It is possible to observe dermatomycosis in the pubic area too (*a*). The excessive time taken to solve the problem must be mentioned. The patient and his mother reported that have been looking for help for more than 7 months on the basic health system, but were not successful (*according to patient information*). Reported that the the lesion was small at first and that soon after that looked for medical help. Several solutions were applied, but it took many days, even weeks until next

sessions. Thus, the condylomatous mass kept growing. The unfortunate data are: the serologies for syphilis and HIV were requested only after 7 months of follow-up on the case. Although the mother had informed that teenager had received vaccinations against hepatitis, we have required serological tests, and anti-HBs marker was non-reactive. Hepatitis B vaccination schedule was prescribed. The serology for syphilis and HIV were non-reactive. Forty-eight hours after our first examination at Hospital Orêncio de Freitas, from the municipal health system, in Niterói, with surgical team led by urologist and anesthesiologst, exeresis of lesions was carried out in surgical center environment with narcosis complemented with local anesthesia (e-I)



Fig. 9.19 (continued)



Fig. 9.20 Similar case to the one shown in Fig. 9.13. However, this one shows that *Condyloma acuminata* lesions, besides the urethral mucosa, are also external

Fig. 9.21 (a, b) Middle-aged patient with verrucous lesions on the penis for more than 8 years. Lesions are extremely keratinized, characteristic of verruca vulgaris. Trying to treat such injuries with podophyllin solution or trichloroacetic acid solution is not successful most of the time. The cryocauterization (CO2, liquid nitrogen) can really help. Surgical removal can quickly remove the warts, but the scarring sequels cannot be forgotten





Fig. 9.22 As in the previous case, warts are very keratinized. In our practice, these lesions are not easily transmitted. They are very dry. On this case in particular we can assert that we have examined five sexual partners of this young woman and none of them showed suspicious or typical HPV lesions



Fig. 9.23 HPV lesions that although verricous, are more flattened: high relief rugose. As some lesions are at the root of penis, some of them might be outside the coverage of the male condom

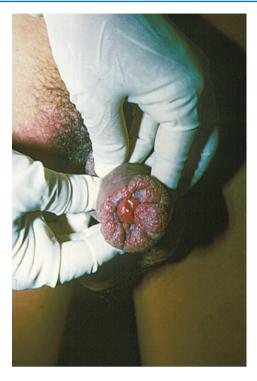


Fig. 9.24 In many cases the *Condyloma* lesions are resistant to various therapeutic methods, and become recurrent. This can lead to such distress that the patient himself uses formulas indicated by friends. In this case the patient "pulled" the lesions with nail plier. Notice associated dermatomycosis at hypogastric region skin also



Fig. 9.25 Condyloma acuminata in the urethral meatus. In many cases, it takes some time until patient be aware of the lesion. Frequently, the problem is noticed during medical examination and peniscopy, because sexual partner presents genital changes by HPV



Fig. 9.26 Patient with aids using HAART irregularly, examined at the STD Department of UFF with extensive HPV condylomatous lesion resistant to numerous treatments



Fig. 9.27 (a) Twenty-four-year-old patient referred to treatment of reddish plaques lesions in penis treated with antifungals. (b) Also presented high relief rugose lesions. Biopsy was carried out in two distinct points (reddish and high relief rugous lesions). In both biopsies the

result was positive for cellular cytopathic effect compatible with HPV infection conclusive of flattened *Condyloma*. Patient was medicated with imiquimod three times a week. (c) The lesions disappeared in a few weeks

Fig. 9.28 Extensive perianal condylomatous lesion in a 15-year-old pregnant patient. In cases like this, we must remember that the topical use of podophyllin is formally contraindicated. Numerous lesions cover the anus when we try to expose the anal orifice. We believe that a proctologist must carry out the surgical procedure for these lesions removal. After all, there are often also intra-anal lesions







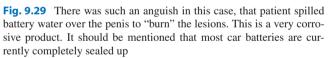




Fig. 9.30 The lesions often become macerated due to the humidity of the area. That's what happened with these lesions of *Condyloma acuminata* in the foreskin. One should always seek differential diagnosis or co-infection with syphilitic flat *Condyloma*. In this case, all serologies were non-reactive and the final diagnosis was *Condyloma acuminata*



Fig. 9.31 In patients with so voluminous condylomatous lesions, the first step is to treat the secondary infections to improve local immunology. Often, treating associated gonorrhea, chlamydia, trichomoniasis, and vaginitis, the number and volume of the lesions can be decreased. The same procedure must be adopted for syphilis and HIV. On the other hand, assaulting these lesions directly, concomitantly with other infections is not the best conduct, because the dead tissue facilitates the dissemination of the infection. Obviously a good professional wants to treat people with this process immediately. However, we must control our anxiety. Acting impulsively can cause a disastrous result for the client



Fig. 9.32 In the therapeutic process, close attention must be given to the sequelae of the lesion adjacent areas, mainly the clitoris and the urethra

Fig. 9.33 (a) Condylomatous lesions and pregnancy. This patient showed signs of good involution after childbirth. (b) After pregnancy, as "magic", the lesions often begin to recede spontaneously. Treating *Condyloma acuminata* in pregnancy is usually a big challenge. However, full attention must be given to diagnosis of associated infections as cervicitis, vaginitis, syphilis, HIV







Fig. 9.34 (a) This is one of the patients who have benefited from the use of interferon $\alpha 2b$ for *Condyloma acuminata*. (b) Complete remission after treatment. Although it works in some cases (48%), we believe

that the cost-benefit relation is not always useful. Nowadays, the drugs applied by the patient, at home, such as imiquimod, podophyllotoxin, sinecatechins, can bring good results



Fig. 9.35 Vegetant lesions of HPV infection Note, however, that the lesions are hyperchromic and with plane surface



Fig. 9.36 Although similar, this is another case of vegetant, verrucous and keratinized HPV lesions. Notice the good separation between the lesions





Fig. 9.37 (a, b) Patient had these warts for more than 7 years. Thus, as in the two previous cases, various topical solutions applications were used, all without any success. According to the patient, he has been at approximately 10 different hospital ambulatories/clinics (public), more than 50 times, looking for treatment. Here at the STD Department of UFF, we did not spend more than 20 min to surgically remove all visible lesions. The patient was observed for more than 1 year and showed no recurrence. The fixed sex partner was examined and did not present clinical and colpocytologic manifestations of HPV infection. The anti-HIV, anti-HCV, anti-HBs and HBsAg serologies were non-reactive. Patient received prescription for vaccination schedule against hepatitis B

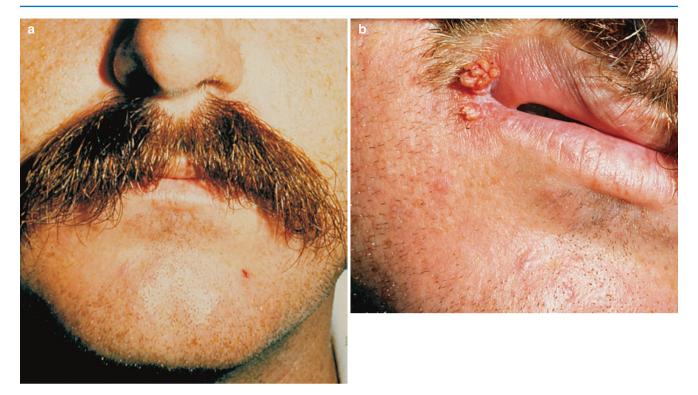


Fig. 9.38 (a) Patient was referred to us for a peniscopy procedure, because its only partner showed *Condyloma* in the genital (*according to patient information*). Colposcopy was negative. However, when we mentioned that the mouth should also be examined, patient reported

that he let a mustache grow, as he was ashamed of a wart on the "corner of the mouth". (b) During the examination, the patient reported that as an average (no math), every 10 times he had intercourse with his partner in 10 used the penis and in 1 had oral sex (he in her)

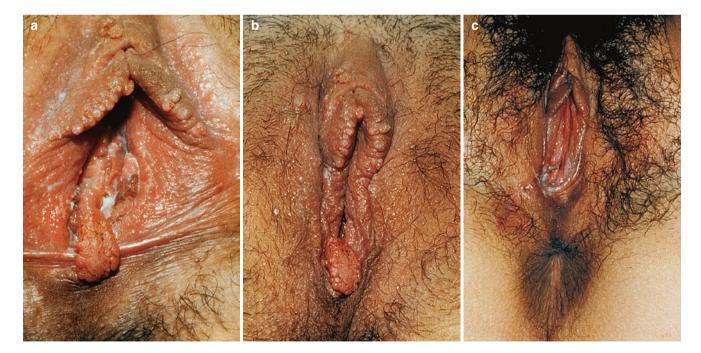


Fig. 9.39 (a) Vulva with *Condyloma acuminata* and vulvovaginitis by candida. This is the patient's partner of previous case. (b) Process receding. (c) Case totally cured of HPV condylomatous vegetant

lesions. Podophyllin 25% solution was used in tincture of benzoin. The anti-HIV, anti-HCV, anti-HBs and HBsAg serologies were non-reactive. Vaccine scheme against hepatitis B was prescribed



Fig. 9.40 *Condyloma acuminata* in mouth. Exophytic and rounded lesions, of irregular surface, arranged linearly on jugal mucous, and another identical lesion in the lateral border of the tongue in a patient practitioner of fellatio, whose partner had identical lesions on the penis

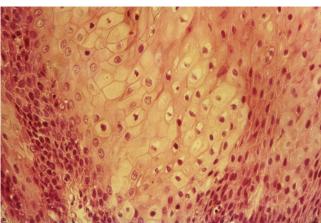


Fig. 9.42 Condyloma acuminata. Histological aspect of lesion removed from tongue, observed in optical microscopy, showing epithelial cells with intense intracellular edema, present in germinal extract, showing koilocytes often present in epithelial growth induced by HPV



Fig. 9.41 *Condyloma acuminata* in mouth. Multiple verrucous aspect lesions located in the jugal mucosa of a patient with aids



Fig. 9.43 HIV-positive patient with HPV infection in labial commisure. Patient denied having warts in any area of the body throughout life. The genitoscopy was negative for HPV and showed only mild fungal balanitis



Fig. 9.44 *Condyloma acuminata* in tongue. No genital injury. However, had medical history of sexual partners diagnosed with genital warts. Patient reports oral sex often



Fig. 9.45 HIV patient infected with extensive condylomatous lesions (HPV) in the oral cavity



Fig. 9.46 Patient examined at the STD Department of UFF with leukoplastic lesion (*arrow*) in hard palate evolving for more than a year. Has been forwarded to a colleague of the oral pathology ambulatory, Faculty of Dentistry at UFF, where the lesion resection was carried out and histopathological diagnosis of *Condyloma acuminate* was found. The research for PCR revealed HPV 11



Fig. 9.47 Six-year-old boy, with great oral unique vegetant lesion, suggestive of HPV infection. His sister and brother-in-law were patients of the STD Department of UFF and a suspicion of sexual abuse was raised. A complete physical examination was carried out to look for other signs of violence, as well as investigation through interview with psychologist and social worker, without any evidence of abuse. The discovery of the source of contact occurred when the child took an applicator of gynecological cream lying on the office's table and began to rub it on the affected gingiva. At that very moment his mother said "he always does that with his sister's tubes"



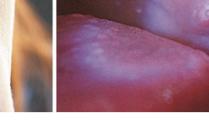
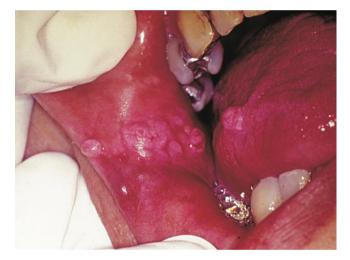


Fig. 9.48 Eight-year-old indigenous with multiple HPV lesions in the oral cavity. Some small, on lips, and other larger (see photo) on the buccal mucosa. This is a case of focal epithelial hyperplasia, also known as

Heck's disease. This is a benign disease and more commonly found in indigenous populations, among the natives of the State of Roraima, Brazil. It is correlated with human Papillomavirus types 13 and 32



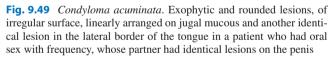




Fig. 9.50 Homosexual male patient, practicing fellatio (penis in mouth), seropositive for HIV, showing multiple sessile lesions of verrucous aspect, located on jugal mucous, bleeding when touched with instrument, whose removal and histopathological examination revealed *Condyloma acuminata*



Fig. 9.51 Right superior gingiva image of the patient of the previous photo, showinag multiple growths involving and weakening the gingival papillae, which bleed when touched, configuring *Condyloma acuminata* lesions



Fig. 9.53 Male patient, cunnilingus practitioner (mouth in the vulva), drug user, showing exophytic sessile lesion located in the median portion of the dorsum of tongue, with irregular reddish surface that was removed by excisional type biopsy and identified through histopathological examination as *Condyloma acuminata*



Fig. 9.52 Left superior gingiva image of the patient of the previous, photo showing multiple growths involving and weakening the gingival papillae, configuring *Condyloma acuminata* lesions. Multiple growths involving and weakening the gingival papillae are observed, configuring *Condyloma acuminate*



Fig. 9.54 HPV in larynx. During examination of digestive endoscopy for investigation of "gastritis", verrucous lesion (*arrow*) in the larynx was found. Histopathology of biopsy of the lesion revealed *Condyloma acuminata*. The HIV serology was positive, CD4 = 180 cells and viral load of 150,000 copies



Fig. 9.55 Male patient, bisexual behavior, fellatio practicer (penis in mouth), cunnilinguism (mouth in the vulva) and anulinguism (mouth in anus), carrier of HIV virus, showing numerous condylomatous lesions scattered on the back of the tongue, with different sizes and shapes, *whitish*, with red areas of rough surface partially interspersing the lesions. Other areas such as the jugal mucosa and the labial mucosa also showed identical lesions



Fig. 9.56 Male patient, 26 years old, oral sex practicer, during routine dental examination dentist observed a volume increase in gingival papilla between the upper left maxillary central incisor and the lateral incisor (*arrows*), and also in the lower region between the lateral incisor and the canine on the right side (*arrows*). The surface of the lesions had rough and granular aspect. The lesions were removed and the histopathological examination recognized *Condyloma acuminata* characteristics

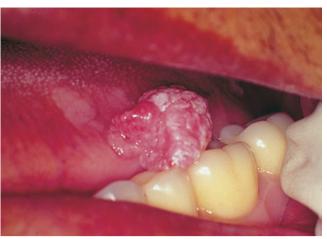


Fig. 9.57 Male patient, showing sessile base exophytic mass lesion of irregular surface in the lateral edge of the tongue interposing *rosy* and *whitish* areas, that were surgically removed by excisional biopsy. The histopathological examination recognized *Condyloma acuminata* characteristics



Fig. 9.58 Multiple rounded exophytic lesions, grouped in clusters, on the surface of the mucous of alveolar edge in child with 7 years of age. The histopathological examination confirmed *Condyloma acuminata*

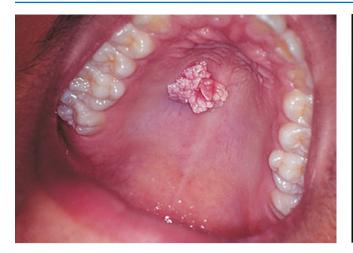


Fig. 9.59 Male patient, 32 years of age, showing irregular surface pedunculated papilliferum exophytic lesion, resembling a "cauliflower", *whitish*, on the right side of the hard palate in its median portion. The lesion was removed and the histopathological examination identified a squamous Papilloma. Unfortunately, it has not been possible to perform research of HPV-DNA



Fig. 9.60 Female patient, showing exophytic lesion of irregular papilliferum superficial aspect, pedunculated, *whitish*, located in the soft palate. It was surgically removed and the laboratory examination showed a scaly epithelial proliferation with multiple papillary projections showing islands of connective tissue, characterizing the diagnosis of squamous Papilloma. Unfortunately, it has not been possible to perform research on HPV-DNA



Fig. 9.61 Female patient, 9-years-old, showing multiple exophytic sessile lesions, separated, arranged linearly, located on the skin adjacent to the lower lip, with *whitish* coloration and irregular surface aspect. The child presented two identical lesions in the right hand thumb and indicator fingers. One of the lesions was surgically removed and taken to histopathological examination, revealing numerous papillary projections covered by stratified hyperkeratinized squamous epithelium with elongated epithelial peaks located on the edge of the lesion and converging toward the center, typical of verruca vulgaris. The other peribuccal and annular lesions were chemically cauterised with podophyllin resinous solution 20%



Fig. 9.62 Female patient, 68 years of age, smoker, with multiple thickened verrucous rough surface lesions involving the right side of jugal mucosa. An identical lesion was observed in gingival area of upper molar teeth on the right side. Three incision biopsies were made in different areas. Histopathological aspects showed sharp papillary surface projections, keratin variable thickness and large and enlarged, wide and blunted epithelial peaks. Therefore, these findings are compatible with the diagnosis of proliferative verrucous leukoplasia that somehow resemble condylomatous growths; however, it must be clinically controlled, because most of them evolve into carcinomatous lesions



Fig. 9.63 Vegetant lesions of *Condyloma acuminatum* on eyelids. It is very difficult to establish the source of infection in a case like this



Fig. 9.64 *Condyloma acuminata* in auricular pavillion of woman over 60 years of age. Once again, it is very difficult, in a case like this, to establish the source of infection





Fig. 9.65 (a) Professional sex worker patient, with verrucous lesions in the vulva for more than 3 years. (b) Showed *Condyloma acuminata* lesion in anterior lip. This woman received so many caustic treatments on the vulva that ceased to be a prostitute. According to her words, "took an aversion to sex" due to traumas in the genital region caused by local treatments. She was treated at our service in some sections of cauterization. The first intervention was the largest, and the procedure took place in surgical environment and under narcosis. She was conducted to psychological assistance. After a year, according to the patient's report, she returned to sexual activity. She got married, started to have monogamous behavior, had a daughter and continued working in the same "house", but as a cook

Fig. 9.66 (a) Pregnant patient, 6th month of pregnancy, showing process of more flattened than vegetant Condyloma. (b) During the investigation, serology was positive for syphilis and HIV. Examination of vaginal content revealed infection with Candida sp. and Trichomonas vaginalis. Using trichloroacetic acid 60%, once or twice a week, can be a good conduct to prevent the increase of lesions. However, the secondary infections treatment before the local application is a basic condition

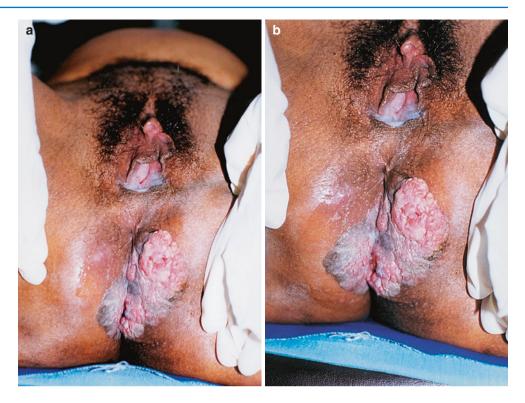




Fig. 9.67 In this case, the lesions of *Condyloma acuminata* has coalesced into a large perianal mass. Patient was referred as giant *Condyloma*. It is actually just a large *Condyloma*. Giant *Condyloma* is a nosological entity known as Buschke and Löewenstein tumor. Note that there is also difficulty of irrigation of the tumor due to necrosis areas



Fig. 9.68 This also formed a large mass. However, it was a cluster of *Condyloma*, with only a thin pedicle in the perineum. Both the patient of earlier photo and the current patient were rejected for treatment by various medical clinics (public services). They said (according to information of the patient) that cases like this are very difficult to be treated



Fig. 9.69 Exactly the same situation of the previous case. These patients had *Condyloma* for several months. The patients were quickly treated; the pedicle was cut, hemostasis was made, as well as some surgical points with categut to approximate skin. All these patients were operated at ambulatory environment under local anesthesia



Fig. 9.71 Notice in this patient, 16 years of age, the condylomatous pediculated lesion in the skin of the left groin. The condylomatous mass was so voluminous that it shifted the corresponding scrotum testicle to the right side. Once again we say that the most efficient treatment in situations like this is surgical removal





Fig. 9.70 Fifty-two-year-old patient, housekeeper, had a single sexual partner, sought STD service of the Federal University of Ceará hospital with vulvar verrucous lesion 8 months ago (a). The lesion was pediculated, with implantation in vulvar furcule in left labia majora (b). Was referred to surgical removal, and histopathology of lesion was *Condyloma acuminata* without findings of neoplasia. In this case, the lesion implantation base was very wide. In fact, it had multiple implantations



Fig. 9.72 Patients with minor vegetant lesions, digit shaped type, with distinctly keratinized aspect in the perianal region and vaginal furcula. In our experience, such lesions are highly resistant to treatments with topical creams and solutions. We chose surgical excision routine



Fig. 9.73 Patient with HPV lesions, like a mountain range, in the dorsal region near the balanoprepucial sulcus. In our practice, we use as a routine the case documentation with biopsy, in order to establish more clearly the diagnosis



Fig. 9.74 This is a very similar case to the previous one. Nevertheless, (a) there were other isolated lesions besides those like a mountain range. This patient also presented history of "little wound" on the penis, around 2 months ago, which healed with antibiotic ointment used for 3 weeks. Along with the wound on penis, patient noticed "lump" in the groin, shown in this photo as adenitis (b). The VDRL was reactive with title 1:64. It is worth the thought and the practice: those who have more STDs are the ones who already have one STD





Fig. 9.75 (a) At first, seem different cases, but they're not. Teenage patient with condylomatous lesions for more than 10 months. During the anamnesis reported was a victim of sexual abuse by close relative in childhood. She mentioned only one partner, who also had Condyloma acuminata in genital. The last period occurred in the same month of the first consultation. (b) After several sections of treatment (trichloroacetic acid, electrocauterization), lesions have not diminished. On the contrary, they increased. During this period, about 2 months ago, nothing was asked about last menstruation nor commented by patient. As there was no improvement, in a review of the case we questioned about the date of her last period. She could not remember, but said it was missing. The pregnancy test was positive. As the process kept increasing, in the course of the 6th/7th month we decided to perform surgical exeresis in hospital conditions and with locoregional anesthesia. (c) Final moment of the procedure. We must emphasize that all attention should be given to the patient in order to avoid or rapidly intercede in case of preterm

labor. The physical, psychic and uterine rest must receive all care, as well as secondary infection and local pain. We kept patient hospitalized for 48 h after the intervention to better control the items already mentioned. (d) More than 400 g of *Condyloma* were removed. The limit between removing a large quantity of tissue, leaving *Condyloma* and having little sequeal is very delicate. (e) The last photo of the case, taken 4 years after the intervention and two normal births with right mediolateral episiotomy. As a complication of the case, we should say that there were recurrences of three minor lesions, but they were cauterised with trichloroacetic acid solution 70%. The husband also had minor injuries, removed surgically. Patient no longer presented *Condyloma acuminata*. However, about 10 years ago showed highgrade intraepithelial lesion and cervical cancer. She was treated with conization of the cervix. Continuous oncological colposcopy and colpocitology dit not register recurrences

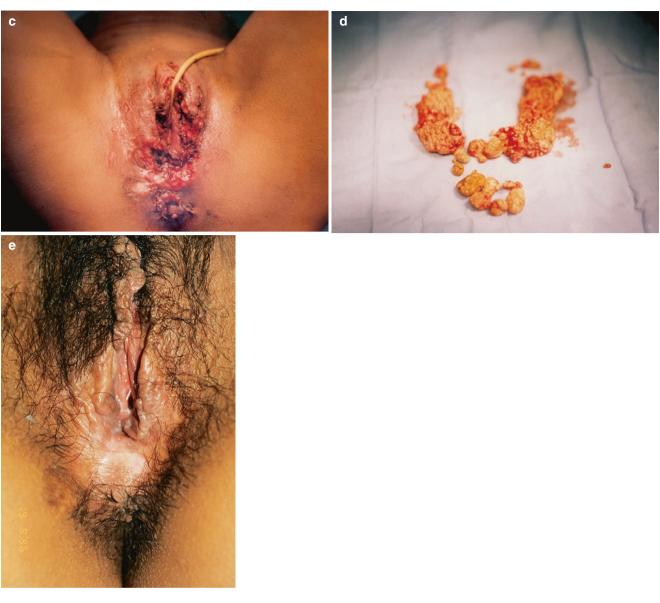


Fig. 9.75 (continued)

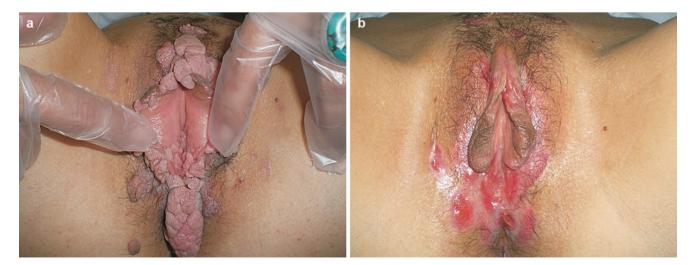


Fig. 9.76 (a) Patient with extensive recidivous condylomatous lesions. (b) Treated with topical application of imiquimod and surgical exeresis. Complete description of this case can be read in the Brazilian



Fig. 9.77 Patient with 107 years of age, resident in nursing home in Maceió, capital of Alagoas State, wheelchair user, rebellious, aggressive, was referred to Posto de Assistência Médica Salgadinho (public health service) by the home's medical care. Histopathological diagnosis: *Condyloma acuminata*. For us, the pathology is essential to make differential diagnosis with other diseases, including malignant

Fig. 9.78 (a) Case similar to the one of Fig. 9.75. (b) Photo immediately after surgery. The photo can't show, but there were several injuries at vaginal introitus involving urethra and clitoris

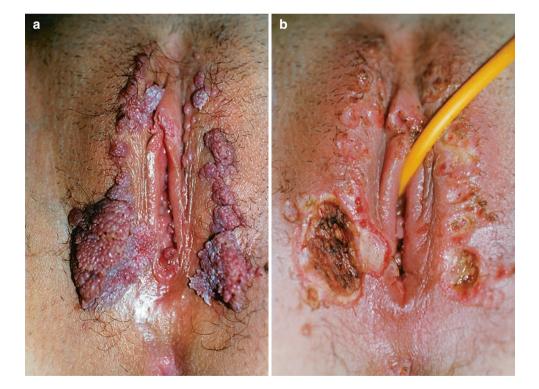




Fig. 9.79 Considering the area, maybe this is the largest *Condyloma* case ever observed by us. The patient claimed that had this process for more than 2 years. Due to difficulties in hospitalization at the time of examination, the patient was referred to another institution, with the purpose of carrying out surgery. Unfortunately, we didn't have feedback from patient



Fig. 9.80 This is a genital photo of the patient's previous partner. Reported sexual activity in the last 4 years, but never had any typical lesion of HPV infection. Actually, patient had no sexual activity with this partner for 3 months



Fig. 9.81 Patient had for months countless papular, hypochromic lesions, with velvety surface, which we define as rugose high relief lesions. Treating such HPV lesions can be traumatic, since lesions must be attacked individually. We treat this patient with 5-fluorouracil, twice a week for 4 weeks. Care must be taken with dermal aggression of the product. In case of great irritation, suspending the application for a week is a good conduct



Fig. 9.82 HPV lesion. In detail, aspect of common wart in teenager middle finger. Notice similar beginning process on the ring finger



Fig. 9.83 Four-year-old child, sexually abused by close relative, has been showing process of *Condyloma acuminata* for several months. Patient returned to our service about 4 years later with vulvitis by gonococcus. This infection was thoroughly investigated and we could not define it as a new sexual abuse. Shown in Chap. 6 (Fig. 6.23)



Fig. 9.84 Six months of age child with several *Condyloma acuminata* lesions. The grandmother reported that the mother also had lesions of same aspect during pregnancy. However, they only noticed the verrucous lesion in scrotum when child was 2 months old, when they sought medical help in the medical unit of the neighborhood. The physician examined the child and referred him to a dermatologist. As dermatologist was on vacation and due to other health problems in the child's family (mother and father), they only returned to that unit after 2 months. The treatment proposed by us was cauterization under narcosis in hospital environment. In this case, after some approaches to family members, suspected acts of sexual abuse were not identified. As in all cases, serologies for syphilis and HIV are required. In this case, were non-reactive



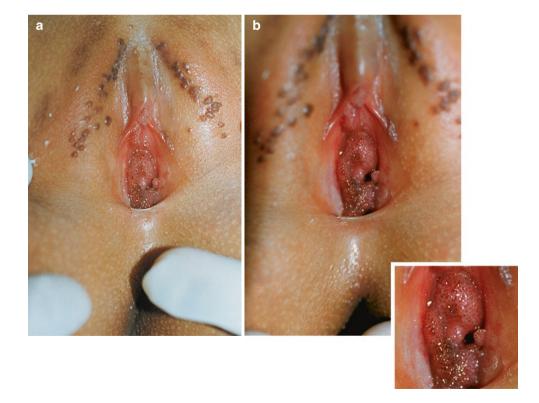


Fig. 9.85 (a) Ten years of age patient, who already had sporadically sexual activity, showing *Condyloma acuminata* in glans. (b) Fully healed of those wounds after electrocauterization. In the service routine serologies for syphilis, hepatitis B, hepatitis C, HIV, anti-HBs were non-reactive. Vaccination schedule against hepatitis B was prescribed. We couldn't examine sex partner

Fig. 9.86 Three-year-old child showing various papular lesions of smooth surface in vulva and perineum. HPV infection was identified after a biopsy. Note that only a perineal lesion near the anus had verrucous aspect. In this case, it was not also possible to establish any connection with sexual abuse



Fig. 9.87 (a) Child, 4 years of age, with great evidence (by clinical history) of sexual abuse, showing lesions on the lips of the vulva, in the upper portion, very similar to the previous case, HPV also. (b) However, in the vaginal furcula and in the internal face of vulvar minor lips there are classic Condyloma acuminata lesions. As usual in our environment, as well as in many countries in the world, although well investigated by Child Protective Services or corresponding institution for each country, the organ where all cases of suspected maltreatment or sexual abuse against child-teenager must be reported, the abuser was not formally punished



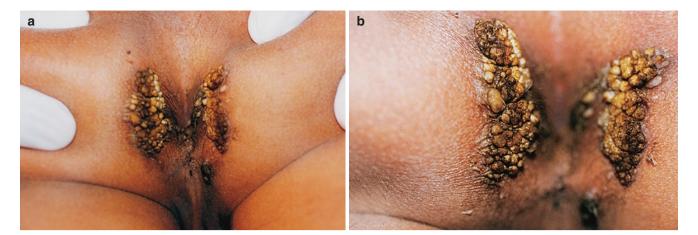


Fig. 9.88 (a, b) Two-year-old child, victim of sexual abuse by a relative, has been conducted to our service after numerous daily sessions of trichloroacetic acid application. Notice burns area of vegetant lesions. Unfortunately, these cases are difficult to monitor in ambulatory, as several applications in the affected area are necessary. Often the child reacts to the procedure, once the physical pain is intense. This is added to the emotional aggression because, once again, the genitalia are being attacked. The situation gets worse when the financial conditions of the family are not enough even to pay for transportation until the medical

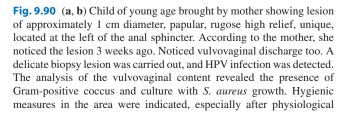
service. We believe that, in many cases like this, a good conduct is to keep the child hospitalized to treat the lesions at one time with sedation. Although, at first sight, such a procedure may seem far more distressing to the child, in our experience, the manipulation, twice a week, for several weeks, is much more exhausting for everyone, including for the health team that is observing the case. These kids have great chance of developing psychological problems related to the sexual area, especially in sexuality



Fig. 9.89 (a) Seven-year-old child, with no history of sexual abuse, showing *Condyloma acuminata* lesions. (b) Child used to scratch the affected area due to irritation and itching at the site. This probably led to HPV infection in the fingers of the hand. (c) Children use to suck their fingers.

Thus, we imagine that it has also infected the mouth, showing clinical manifestation of wart on lower lip. In the service routine, the serologies for syphilis, hepatitis B, hepatitis C, HIV were non-reactive. The vaccination showed that the vaccines were up to date, including hepatitis B vaccine







needs, and lesion was treated with trichloroacetic acid 70%, twice a week. It has not been possible to establish any causal relationship with sexual abuse in this case also. According to the mother, no close relative had reported genital injury. In situations like this, we apply a good amount of local anesthetic cream with lidocaine 25 mg and prilocaine 25 mg (Emla 5%) 60 min before the biopsy. This decreases the discomfort at the time of infiltration (with insulin needle) of the local anesthetic



Fig. 9.91 (a) Child, 4 years of age, with a well-defined story of sexual abuse by neighbor, showing numerous *Condyloma acuminata* lesions, noted by the mother several months ago. (b, c) Another views of the same lesion. We were asked to give an opinion about the case, and as the child was hospitalized in the Pediatric Clinic, we chose exeresis of the lesions, with electrocoagulation of the bases under narcosis and complementation with local anesthesia. (d) During the examination we found verrucous lesion in the external face of right leg, which according

to her mother, already existed before the *acuminata* lesions. (e) We proceeded with exeresis and the materials were sent for histopathological analysis, whose result was viral *Condyloma*. The research for HPV-DNA was positive for HPV 6Note that it is possible, if there is a delicate material, to remove the lesion without much aggression. (f) The wart of the leg was also removed by excision with reparation points. The material was also sent for viral typification by PCR technique, conclusive of indeterminate HPV



Fig. 9.92 Twenty months of age child, born by Cesarean delivery of mother with condylomatous HPV lesions during pregnancy and child-birth, with extensive condylomatous HPV lesions. The father reported lesions of *Condyloma acuminata* in penis treated with trichloroacetic

acid during pregnancy. In cases like this, topical treatments rarely succeed. We believe that surgical removal with specialized professional is a good conduct. We consider that patients should not be treated in pediatrics or STDs' ambulatories



Fig. 9.93 Perianal *Condyloma* in child of early age. The same final considerations of the previous case are used for this one



Fig. 9.94 Child, 5 years of age, referred to the STD Program ambulatory in the city of Maceió, State of Alagoas, by DCFS and mother. The child had history of sexual abuse by stepfather. *Condyloma acuminata* lesions were treated with imiquimod. The papule, in groin, disappeared spontaneously. The stepfather was examined and no typical or suggestive lesions of HPV infection were found. Serologies were non-reactive. The case had judicial forwarding

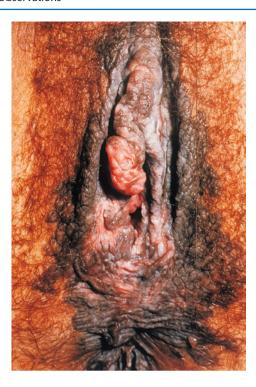


Fig. 9.95 Although it is basically possible to observe rugosities, this HPV patient shows hyperchromic and even *black* lesions, in plaques, occupying nearly the entire vulva



Fig. 9.96 Patient with multiple HPV vegetant lesions. In this patient, the use of interferon $\alpha 2b$ resulted in therapeutic failure



Fig. 9.97 Even though it is easy to observe typically cauliflower-like lesions areas, many of them has coalesced, becoming sometimes real plaques, affecting labia majora, labia minora, clitoris, vaginal furcula and perineum



Fig. 9.98 In addition to the process of vaginal discharge (bacterial vaginosis), the patient presented multiple lesions of *Condyloma acuminata*



Fig. 9.99 Patient over 50 years of age presenting HPV infection on external genitalia for more than 10 years, characterized by keratinized *white* and *rosy*, predominantly *black*, lesions. Such lesions reached the skin of the buttocks. Rarely, in cases like these, topical treatments can be successful. Maintaining topical applications, in general, only delays the lesions' healing process. We considered a good conduct surgical removal with specialized professional



Fig. 9.100 Teenage patient, a street girl, showing extensive verrucous lesion with a small *rosy* area. The lesion occupies the entire vulva, perianal, perineal region, even the intergluteal sulcus, hyperpigmented due to the large degree of keratinization. Hospitalization was scheduled for surgical exeresis of the lesion, but it was not performed since patient abandoned treatment



Fig. 9.101 Young patient, with large condylomatous mass occupying both labia majora (middle third/distal) and perineum. It is possible to notice some areas already getting *dark* due to keratinization by trauma in the area



Fig. 9.102 Elderly patient, with white nacreous rugose lesions, mainly periclitorial fistulas (*arrow*). The histopathology of the larger lesion revealed koilocytosis and dyskaryosis, typical of HPV



Fig. 9.103 Patient with history of chronic vulvar itching, also presenting verrucous lesions in the vulva (top of labia minora, interlabial sulcus and clitoris). Histopathology identified vulvar intraepithelial neoplasia (LEV II) + HPV



Fig. 9.104 Verrucous aspect lesions forming small isolated and spherical masses. Patient presented these injuries for more than 3 years and had already made several topical applications with several products in a very irregular way



Fig. 9.105 This patient, over 50 years of age, was the first case to call our attention in the 1980s due to the atypical clinical aspects of HPV infection. In the detail, we can observe that lesions were solid, not with a liquid content, as could be falsely thought, under a hyperemic skin, of an eczematous area. The biopsy revealed the presence of koilocytosis and dyskaryosis, histopathological aspects revealing HPV infection. We started treatment with 5-fluorouracil cream 5% (5FU). However, the patient never returned to medical care. We tried a home visit, but we could not find the informed address

Fig. 9.106 Very aggressive process of extensive condylomatous lesion, with central areas of necrosis, and we had no choice but to make a simple vulvectomy to remove the lesions



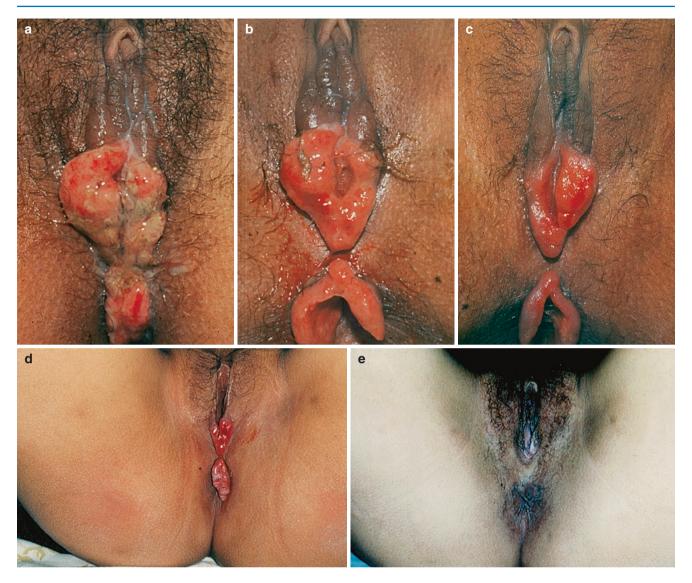


Fig. 9.107 (a) Teenager treated in another medical service, in late 1980s, with this lesion that didn't cede with the use of antibiotics (penicillin G benzathine + sulfamethoxazole + trimethoprim for 2 weeks, then lincomycin for 2 more weeks) was referred to our service. All direct tests did not clarify the case. The serology for syphilis was negative in three opportunities. There was no satellite adenitis or cutaneous rash. However, the biopsy revealed an intense amount of koilocytosis. A fragment was sent to a research institute in Europe, which identified positivity for HPV-DNA, however indeterminate type. (b) Note edema in labia minora. In this photo we are straining the perianal skin, as we also did in the previous photo. (c) On that occasion we administered interferon α 2b 2.500.00 UI in subcutaneous skin of the abdomen, on

alternate days, for 4 weeks. Note the involution of the process in the second week of treatment. (d) The lesions decreased very well with the systemic interferon $\alpha 2b$ procedure. The side effects, intense flu-like malaise, received support of analgesic, antipyretic, and decreasing antibiotic, as usual, during time of treatment. (e) Completely free of lesion and virtually no skin sequels. Once again, we emphasize that it is imperative to "watch" the patients with long-term illnesses regarding pregnancy. Despite all the information provided on this issue, the patient became pregnant in the course of treatment. Delivery was normal and according to routine tests at birth, the child did not show any abnormalities until about 1 year after. The sexual partner did not show genital HPV lesions, nor past history of Condyloma

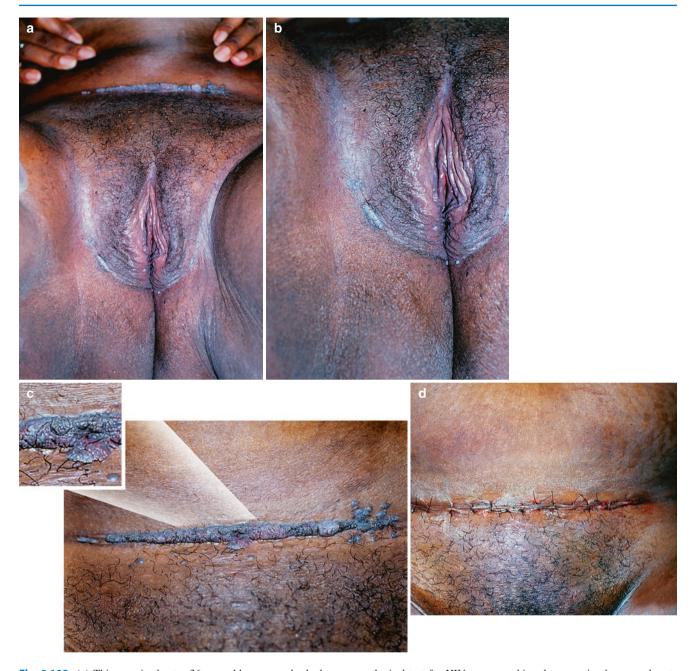


Fig. 9.108 (a) This case is about a 36-year-old woman who had ten pregnancies, five births and five abortions, and searched for our service complaining of warts on genitals and abdominal incision scar (abdominal total hysterectomy about a year ago). Reported intercourse with the same partner for 2 years, and partner had warts in the vulva, which disappeared spontaneously (according to information of the patient). In early history reported diabetes, chronic hypertension, cardiac problems and sexual abuse by her stepfather in childhood. (b) During the examination we found these lesions in the vulva and some of them nearly affecting the skin of the buttocks. On colposcopy, we noted inconspicuous area of acetowhite epithelium and diffuse colpite signals. (c) In all Pfannenstiel scar it is possible to observe Condyloma acuminata measuring 12 cm in lenght x 1 cm height. (d) Exeresis of lesions was indicated. The main results of tests performed were as follows: VDRL non-reactive; 246 mgdL glycemia; oncology colpocytology: CIN I + HPV + Trichomonas vaginalis; histopathology: Condyloma acuminatum (abdomen and vulva); HPV typification (PCR), both pieces: HPV 6. Even after numerous interventions, neiher the patient carried out the

serological test for HIV, nor we achieved to examine her sexual partner. The patient was referred to treatment with internist. After a month patient made new exams: 96 mgdL glycemia. Patient was medicated for trichomoniasis with metronidazole and after 2 months the examination of vaginal content was of normality. It is very difficult to precisely establish the way Condyloma is installed in surgical scar, but it's possible to imagine an autoinoculation, with HPV coming out of own vulva, or by tribadism (intercourse vulva with vulva), HPV has left the partner to deploy on the vulva and scar. The truth is that the patient initially presented small lesions in the vulva (about 2 months before the abdominal surgery). During this period, ensures that her partner had "little warts in the vagina". Reported that after laparotomy her partner still had minor lesions, "almost disappearing", and sexual activity involved fondling and direct friction of both vulvar and pubic regions. We think that the associated chronical pathological conditions may have facilitated the implementation of HPV in recent surgical wound. Both ways, sexual and autoinoculation, may have also contributed. We will never know for sure, mainly because we don't have any exams of the sexual partner

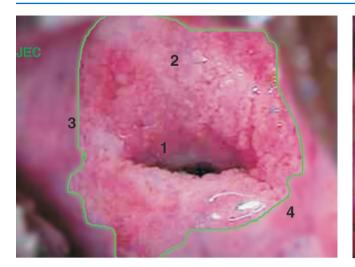


Fig. 9.109 Colpophotograph showing an extensive transformation zone. (1) Cervical canal. (2) The stage of squamous metaplasia with the merger of the original squamous epithelium villi. (3) The squamocolumnar junction (SCJ). (4) The original squamous epithelium. This condition is called ectopy. The transformation zone is type 1. Such a process should not be confonded with infections, mainly with HPV



Fig. 9.110 Colpophotography evidencing thin mosaic after acetic acid 5% application (*I*). The biopsy histopathology revealed low-grade intraepithelial neoplasia (LSIL)

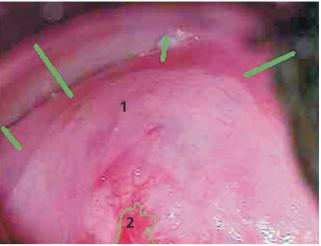


Fig. 9.111 Colpophotography after acetic acid 5% application showed extensive area of plain acetowhite epithelium (I) and SCJ (2). The biopsy histopathological examination proved to be compatible with low-grade intraepithelial neoplasia (LSIL)



Fig. 9.112 Colpophotography after application of acetic acid 5% showed dense acetowhite epithelium (I) and (2) gross punctate. The biopsy histopathological result revealed high-grade intraepithelial neoplasia (HSIL)



Fig. 9.113 (a) Male adult with HPV wart in scar of abdominal emergency surgery. Patient reported exclusive partner for a year. (b) During the physical examination, we did not find any other HPV verricous lesion or suspicion in any part of the body, including the patient's genital. The history of the sexual partner informed a past of vegetant lesions in the vulva, treated at another medical service with an acid (TCA?). However, both remember that shortly after the surgery, had sexual intercourse using condom, while she was still undergoing treatment for the "warts" on the vulva. Both confirmed that due to surgery "it was quickie and not too often: once a week. Sometimes not even that." Informed that since they got to know about her lesions, they reduced the fre-

quency of intercourse and began to use condoms most of the time. Words from both of them: "In 99% of the time only with condom." The partner was clinically examined by us and showed only important process of bacterial vaginosis. She was treated and 2 months later she was re-examined, with results of oncological colpocytology and genitoscopy (vulva, vagina, cervix, anus) with no evidence of disease/infection with HPV. The patient remained for 6 months with genitoscopy without changes. We imagine that the stress at the time of surgery somehow facilitated the installation only in the area surgically assaulted, since they did not use condom every sexual intercourse



Fig. 9.114 Young patient showing papular lesions with smooth surface (detail), looking like small "pellets", as he called it. This case is similar to the Fig. 9.105's, but without hyperemia. Clinically, one might think in bowenoide papulosis, however, histopathology confirmed typical HPV koilocytosis. The research of HPV-DNA confirmed HPV 6/11



Fig. 9.115 Patient showing a regular surface papular lesion (see detail). Whenever possible, our conduct consists of surgical exeresis, and sending the piece to histopathology, so that the etiology can be documented. After all, the classic medical routine says that all surgical material must be submitted to histopathological examination. Many patients present changes of skin, plica type (which means only a fold of skin, of saccular shape, smooth surface, without any changes, less viral by HPV), who are labeled as HPV infecting people. Several of these individuals receive local caustic treatment, many times without any need. For aesthetic reasons, exeresis may be indicated, particularly when there are several plicas in the pubic area, scrotal or perineal sac. In this case, histopathology indicated HPV infection, caused by classic koilocytosis pattern



Fig. 9.116 This case differs from the previous one only in the amount of spicular lesions (*arrows*). One must be careful with the differential diagnosis with prominent sebaceous glands, which occur in the proximal third of the penis. However, the glands can occur throughout the penis. This case was histopathologically definined as HPV infection



Fig. 9.117 Patient with rugose lesions in the scrotum sac. As our conduct includes biopsy for documentation, this case was also defined as HPV



Fig. 9.118 Case of lesions in the distal foreskin dorsum. The biopsy revealed koilocytosis. This patient was referred to peniscopy as his sexual partner has *Condyloma acuminata* in external genitalia



Fig. 9.119 Patient showing solution of continuity in the dorsal region of the preputial sulcus. Histology documented moderate penile intraepithelial neoplasia (PIN 2). Patient was treated with 5-fluorouracil cream, thin layer applied with cotton swab, twice a week for 3 months and maintenance once a week, every 15 days, for 3 months. It is appropriate to protect subjacent areas, especially where the penis lies when the patient is laid down. A sheet of plastic covering the scrotum sac can be used, or zinc oxide ointment can be applied in this area, to prevent cytostatic cream to reach the skin of the scrotum



Fig. 9.120 Hypochromic papulous lesions. The biopsy revealed koilocytosis only, not neoplasia

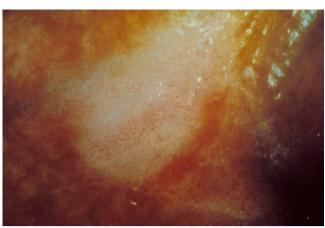


Fig. 9.122 Penis showing thin dotted areas and acetowhite lesion. Histopathology was pure koilocytosis. HPV infection

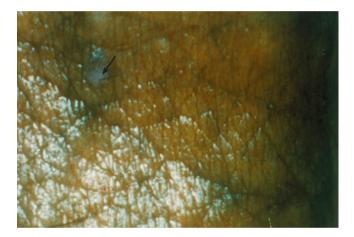


Fig. 9.121 Flat PIN hypochromic injuries I (low-grade lesion). The treatment was also 5-fluorouracil

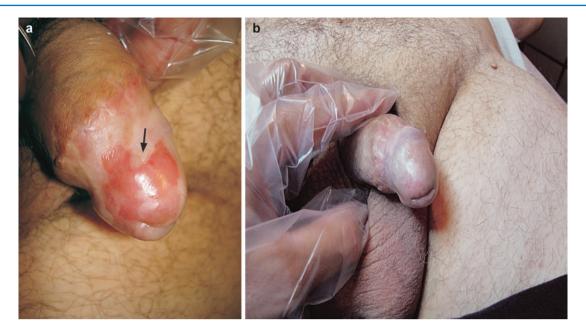


Fig. 9.123 (a) Seventy-year-old patient with histopathologic diagnosis of papulous bowenoide in recurrent lesions. Blade revision was requested because the area marked with the arrow was leucoplasic and of rugose high relief. The diagnosis was high-grade penile intraepithelial neoplasia (PIN III). Patient was instructed to apply imiquimod three times a week on the affected area and stop application in case of ulcerations. The treatment was generally well tolerated, but every four appli-

cations, approximately, after the second week, the patient stopped treatment for 7 days due to light local side effects. (b) By the 30th application the lesions disappeared. We continued accompanying the patient for more than 10 months and he remained without recurrence. However, a few years later he returned to our service with clinical and laboratory symptoms (histopathology) of *Molluscum contagiosum* in genital

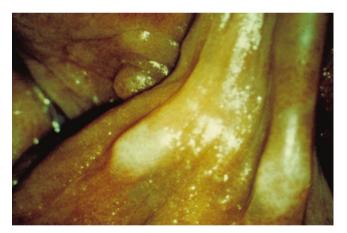


Fig. 9.124 Lesion also aceto-reactive in penile frenulum: case of PIN I (low-grade penile intraepithelial neoplasia)



Fig. 9.125 Patient, 35 years of age, partner of carrier of vulvar infection with HPV, referred to peniscopy. Only subclinical lesions were observed after application of acetic acid 5% on the penis and scrotum. The penis lesions biopsy revealed cell changes, consistent with HPV infection



Fig. 9.126 *Condyloma acuminata* and acetowhite macules in penis ventral region (peniscopy ×6)



Fig. 9.129 Acetowhite epithelium biopsied area with gross punctate in larger expansion (peniscopy ×10). The final diagnosis was HPV infection

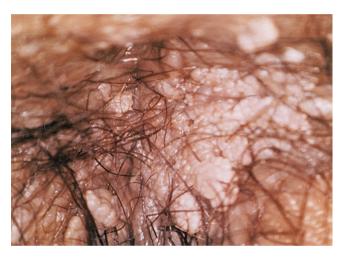


Fig. 9.127 Extensive Condyloma in anal and perianal regions (peniscopy $\times 10$)



Fig. 9.130 Patient with 38 years of age, referred to HPV infection research as he is a partner of patient with vulvar condilomatous lesions. The examination confirmed sub-clinical lesions of penis, scrotum and anal region which biopsy identified as cellular alterations compatible with HPV infection. Acetowhite epithelium in the right side of the penile body (biopsy), corresponding to HPV infection (peniscopy ×10)



Fig. 9.128 Vegetant lesions (*arrows*) in male perianal region. The differential diagnosis with other diseases should be made by biopsy (peniscopy ×6)



Fig. 9.131 Twenty-seven-year-old patient underwent a peniscopy as he was a partner of HPV infection carrier. Only sub-clinical lesions were observed in penis and scrotum, and biopsy showed cellular changes compatible with HPV infection



Fig. 9.132 Acetowhite macules on the anterior of the scrotum sac (peniscopy ×10). Biopsy revealed the presence of several koilocytosis



Fig. 9.133 Man of 37 years of age, referred to peniscopy for HPV lesions research, as he was a partner of CIN II carrier. Only sub-clinical lesions were observed. Some biopsies confirmed HPV infection. Acetowhite macules in the balanopreputial sulcus, ventral region (biopsy), corresponding to HPV infection (peniscopy ×10)



Fig. 9.134 Vegetant lesions after application of acetic acid in the prepuce (peniscopy $\times 10$). The histopathological exam revealed *Condyloma acuminata*



Fig. 9.135 Young 19-year-old patient referred to differential diagnosis of urethral injury. Condylomatous lesions were observed in urethral meatus and other sites during examination, in addition to sub-clinical lesions suggestive of HPV infection



Fig. 9.136 Vegetant lesion (*Condyloma acuminata*) in the balanopreputial sulcus, dorsal region (peniscopy ×10)



Fig. 9.137 Patient, 39 years of age, carrier of vegetant lesions in penis, referred to diagnosis. Condilomatous lesion was observed in the balanopreputial sulcus, dorsal region, commonly called "cockscomb"



Fig. 9.138 Macules and acetowhite epithelium areas on the inner surface of the prepuce in the right side (biopsy) of man referred to peniscopy (×10)



Fig. 9.139 Twenty-five years of age patient referred to peniscopy as he was a partner of patient with cervix indeterminate grade intraepithelial neoplasia. During examination, we observed various macules and acetowhite epithelium. The aspect is easily confounded with superficial mycosis, and in case of doubt it is recommended a specific diagnosis/ treatment for a possible mycosis; repeat the peniscopy. A posterior examination, after topical treatment with antifungal medication, maintained same aspects. Biopsy revealed HPV infection



Fig. 9.140 Twenty-five years of age patient conducted by the Urology service for HPV treatment. Patient reported several topical treatments with trichloroacetic acid, podophyllotoxin, and imiquimod, and sometimes lesions were "burned" with electric scalpel. However, in the first week lesions reduced and then started to grow again. As the diagnosis was only clinical and the process was recurrent, we chose to remove three injuries (including the largest) to try to identify their etiology. The histopathological report described numerous koilocytotic cells compatible with HPV infection. We carried out the removal of all lesions with cauterization of the bases, since the various previous therapeutic tactics have failed



Fig. 9.141 Twenty-five years of age patient referred to peniscopy for HPV lesion research. Sexual partner was HPV carrier. *Condyloma* in the glans and balanopreputial sulcus was observed



Fig. 9.143 Thirty-seven years of age patient referred to peniscopy for HPV lesions research, as he was a partner of woman with this infection. Condilomatous lesions were observed, acetowhite epithelium. Biopsy found cell alterations compatible with HPV infection. *Condyloma acuminata* in prepuce and dorsal region (×10)



Fig. 9.142 Forty years of age man referred to peniscopy for HPV lesions research, as sexual partner presents alterations of squamous cells of indeterminate significance (AUSCUS). Hyperchromic vegetant lesions were observed and biopsy revealed cellular changes compatible with HPV infection



Fig. 9.144 Observe aceto-reactive epithelium (after the application of acetic acid 5%) on the inner surface of prepuce, left side region. Biopsy revealed HPV infection (×10)



Fig. 9.145 Condyloma acuminata and acetowhite macules in glans $(\times 10)$

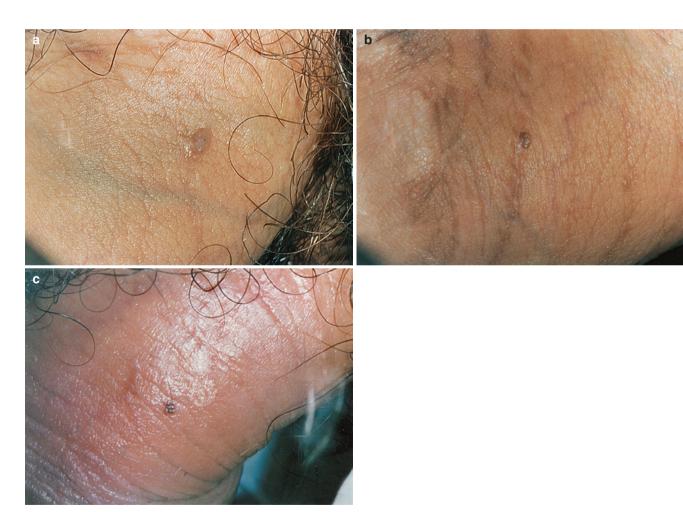


Fig. 9.146 (a) Twenty-six-year-old patient referred to peniscopy as his partner is HPV carrier. Vegetant hyperchromic lesions observed (*Condyloma acuminata*). One of them was biopsied and showed cellu-

lar changes compatible with HPV infection. (b) Vegetant hyperchromic lesion also in the side of the penile body, more distal (×10). (c) Another hyperchromic papule (biopsy) on the ventral region of the penis (×10)



Fig. 9.147 Acetowhite papule (after application of acetic acid 5%). Biopsy was performed on the left side of the penile body and the result was HPV infection (×10)





Fig. 9.148 (a) Man, 35 years of age, referred to peniscopy for HPV research. During examination, extensive areas of acetowhite epithelium were observed, previously imperceptible, that biopsy revealed HPV infection. One of the areas of aceto-reactive epithelium had extended to

the anterior of the scrotum sac. (b) Another area of acetowhite epithelium in the ventral region of the penile body, next to the base, extending to the scrotum sac $(\times 10)$



Fig. 9.149 Twenty-three-year-old patient referred to peniscopy to search for sub-clinical lesions caused by HPV. His sexual partner presented oncologic colpocytology suggestive of HPV infection. During the examination tiny *Condyloma acuminata* (arrows) were observed (arrows) after application of acetic acid 5%. A biopsy of a group of these lesions confirmed the clinical hypothesis of *Condyloma acuminata*

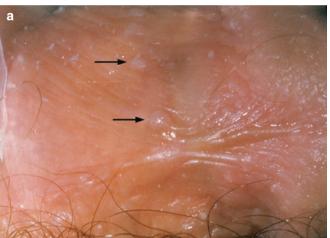




Fig. 9.150 (a) Twenty-six-year-old man referred to peniscopy for being partner of woman diagnosed with high-grade cervical intraepithelial neoplasia (CIN II). During examination, in addition to subclinical (*arrows*) lesions, numerous *Condyloma* were observed, histologically confirmed, that patient believed to be "signs of birth."

Small vegetant lesion close to frenulum ($\times 10$). Note that there was no similar contralateral lesion, which would make us think of hypertrophy of the papilla. (b) Several hyperchromic vegetant lesions ($Condyloma\ acuminata$) in the dorsal region of the penile body ($\times 10$)



Fig. 9.151 Hyperpigmented and keratinized *Condyloma acuminata* in the left perianal region. The diagnosis was made by the anatomopathological study of the lesion exeresis (×10)



Fig. 9.153 Vegetant lesions and acetowhite papule on the prepuce, dorsal region of penis $(\times 10)$

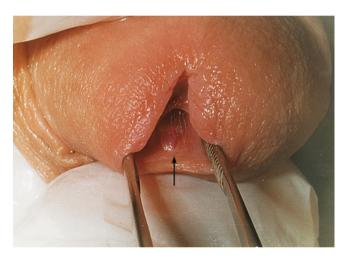


Fig. 9.152 Twenty-seven-year-old man referred to peniscopy, partner of woman with HPV infection. During examination sub-clinical lesions suggestive of HPV infection and urethral *Condyloma (arrow)* were observed. This photo shows the importance of a careful clinical genital examination, which involves the visualization of at least 1 cm of the proximal urethra. Note that this attitude avoids sophisticated devices



Fig. 9.154 Vegetant lesion in the ventral region of the penile body of patient who was referred to peniscopy as partner has history of infection with HPV in the genital area (×10). It is easy to understand that many customers were referred to examination and medical consultation due to diagnosis of HPV infection of sexual partners. It reaffirms the importance of global attention, concomitantly, to sexual partners involved



Fig. 9.155 Vegetant lesion in left perianal region. Biopsy was carried out and revealed HPV infection. The patient was referred to peniscopy. However, a good clinical examination must include all anogenital area



Fig. 9.156 Several maculo-papular acetowhite lesions in the ventral region of the penis, reason for examination (×6). Although medically suggestive of HPV disease, we believe that a good conduct is the histopathological examination



Fig. 9.157 Young patient with rugose high relief, *rosy* color papular lesions on the glans, whose biopsy revealed papulous bowenoide, which is the involvement of HPV 16, leading to an anisonucleosis histological process, macronucleosis, dyskeratosis, para/or hyperkeratosis, nuclei increase and irregularity, increased mitotic pattern, koilocytosis, infiltration of lymphocytes and plasma cells in the dermis, and broadening and coalescence of epithelial projections at baseline. The treatment is similar to the *Condyloma's*, as they usually have a benign evolution, many of them regress spontaneously, several are recurrent and rare cases develop into invasive carcinoma



Fig. 9.158 Middle-aged patient showing rugose surface hypochromic lesion in right labia minora. The patient complained of chronic pruritus in vulvar region. Histopathology revealed koilocytosis, HPV infection. The patient had already reported the same complaints to two other medic colleagues. Who argued that it was vitiligo in vulva and that treatment was not necessary. However, the rugose aspect and the absence of other similar lesion in another area of the body lead us to ask for a biopsy of the lesion

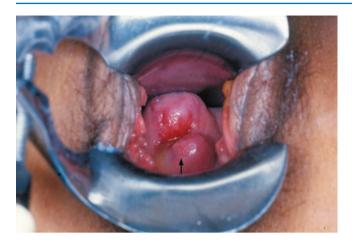


Fig. 9.159 Examination of the cervix with the naked eye. Even so, it is possible to observe rugose lesion in posterior labia (*arrow*). Also note darkish mucus aspect in the external orifice of cervix. The examination of this material showed the presence of *Neisseria gonorrhoeae*. The biopsy of cervix lesion revealed histopathological process of *Condyloma acuminata*



Fig. 9.161 Also a cervix examination with the naked eye, this photo shows a leukoplakia area of irregular shape and surface, configuring dyskeratosis, which is occurring in this area infected with HPV. Although it is common that acetowhite lesions in cervix are suggestive of HPV, the leukoplastic lesions are considered major aspects of complication of infection with HPV, HSIL

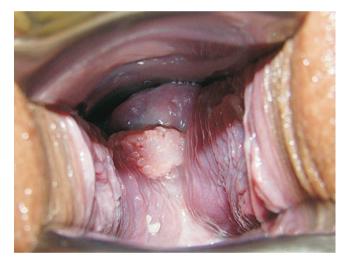


Fig. 9.160 Condyloma acuminata in cervix and vagina of pregnant woman. Not uncommonly these lesions reduce after delivery, even without treatment. However, the association of cases like this with recurrent respiratory papillomatosis has been reported, mainly in naturally born children



Fig. 9.162 Photo taken with colposcope showing multiple vegetant and verrucous lesions, also called HPV mature lesions, in uterine cervix, i.e., *Condyloma acuminata* in cervix

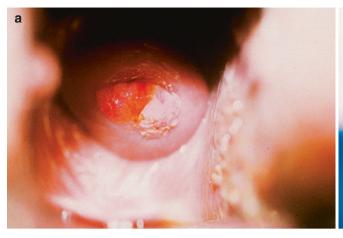


Fig. 9.163 (a) Similar aspect of the previous photo; however, there is a single mass in posterior labia of the uterine cervix. (b) Aspect immediately after exeresis through high-frequency surgery. The surgical



piece microscopic report was *Condyloma acuminata*. The HPV-DNA fragment research was positive for HPV 11

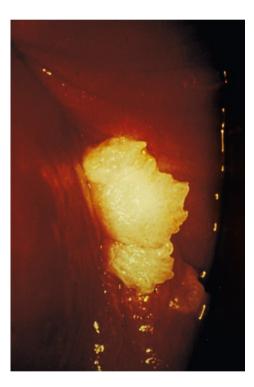


Fig. 9.164 Vision through colposcope of a typical *Condyloma acuminata* vegetant lesion in the side wall of the vagina. The colposcopic examination should be extended to regions of the vagina, urethra, vulva, perineum and anus whenever a HPV patient is investigated. The mouth is another area to be included in this clinical routine



Fig. 9.165 Photograph of a vegetant lesion in uterine cervix through colposcopy. Notice the prominences with the central irrigation vessels. This explains why such lesions bleed so much when traumatized



Fig. 9.166 Vision of cervical epithelium through colposcopy with more aggressive aspects, irregular mosaic, gross punctuate, leukoplakia of possible infection with HPV of high oncogenic potential (16/18/45)



Fig. 9.167 Patient examined in a STD ambulatory clinic of a public hospital in the city of Rio de Janeiro's metropolitan area, in 1983, showing these injuries. Patient was extremely affected and passed away 24 h after admission. According to report and copy of examination (biopsy) shown by family, it was Löewenstein and Buschke tumor and he had already undergone two surgeries some months before in another hospital of the region. Buschke and Löewenstein tumor (1925) refers to an HPV-6 related involvement which shows a benign histopathological result, but a malign clinical behavior. Since no remote metastases occur, its dissemination by contiguity is violently aggressive. The treatment is generally done with debridement of the affected necrotic areas, which often leads to important consequences and recurrences. The local and general immune competence is involved in these situations. Our assistante was restricted to trying to reestablish homeostasis to indicate specific therapeutics, which unfortunately was not achieved. Due to technical problems, we could neither keep the patient's serum stored for further analysis nor fragment of biopsy carried out at that time. We ask the families to review the histopathological exam result. However, no patient's relative returned to our medical service. We tried a new contact with the family, but we were not successful to investigate the case. Currently, it would be possible to store a fragment of biopsy in dry, sealed vial in freezer, to undergo analysis by molecular biology. Buschke and Löewenstein tumor is also known as giant Condyloma. Mistakenly, many call a great condilomatous lesion (volume and size) giant Condyloma. Giant Condyloma should be restricted to the denomination of the tumor of Buschke and Löewenstein. At that time, 1983, serology for HIV was not available. The serology for syphilis was non-reactive



Fig. 9.168 Young man, 19 years of age, noted these prominences for more than 6 months, which since then have not changed. The lesions were asymptomatic and did not present any changes after the application of acetic acid solution 5%. This is a typical diagnosis of corona hirsuta of the penis or hypertrophy of papillary glands or glands of Tyson. It is not uncommon to be confounded with *Condyloma acuminata*. The conduct must only be carried out with guidance on this anatomical appearance



Fig. 9.169 Young patient was referred to STD Department of Universidade Federal Fluminense, Niterói, after numerous attempts of "treatment" of this process of papillae hypertrophy. Although it is easy to recognize that these are prominent hypertrophy, such a situation is not an infectious process, neither caused by HPV. Many *black*, white, rich, poor, educated, illiterate men have some kind of papillae hyperplasia to a greater or lesser extent. But they certainly disappear in old age; the same situation also occurs in the vulva; they are the well-known vestibular papillomatosis. These anatomical formations (in men and women) are often severely attacked causing serious physical and

psychic consequences of difficult reversion. In (a, b), side view of same penis with hypertrophy, which is so big in this case that one might think of HPV lesions. On the other hand, it is necessary, before characterizing as normality, observe carefully if men with a history of *Condyloma acuminata* have a typical lesion of *Condiloma acuminata* in the middle of the papillae hypertrophy. However, we must not miss the opportunity to offer guidance on sexual and reproductive health education, offering serologies (syphilis, HIV, etc.) and orientation and verification of vaccination status (hepatitis B, HPV, etc.)



Fig. 9.170 Thirty-two-year-old patient with *Condyloma acuminata* in the genital region; by indication of a "friend", he threw boiling water on penis for "treatment" (according to information of the patient). In (a), the way found by the patient to better carry out the curative, using a

surgical pubian compress in area not affected by the hot water and in the affected area. Patient underwent multiple debridement and cleaning to treat the burns, and as shown in (\mathbf{b}, \mathbf{c}) the tissue is in the stage of granulation, where graft will be tried



Fig. 9.171 Patient referred to our service to try treatment with interferon α 2b, because, at that time (late 1980), we were studying such a product. This patient has not joined the protocol, but due to the availability of medicine, we began with 2,500,000 UI scheme in subcutaneous tissue of the skin of the abdomen, on alternate days, for 4 weeks. In (a), biopsy revealed vulvar intraepithelial neoplasia of light/moderate intensity and cytopathic effect, koilocytosis, dyskariosys and dyskeratosis, characteristic of HPV. *In situ* hybridization (Enzo Diagnostic) was positive for the types 6/11 and 16/18. The verrucous process in hands and other areas of the body, verruciformis epidermodysplasia,

will be presented in Chap. 10. In (b), vegetant verrucous lesions well keratinized are observed.(c) Lesions in plaques in the vulva (VIN I), along with the hands of the same patient. There was no improvement with the use of interferon $\alpha 2b$; in fact, during the use of the medication, it was noted that the lesion almost reduced. However, after the fourth week, we chose to discontinue the use of product, since the process had not changed. Due to several difficulties, among them the distance of patient's home (a city more than 100 km away), she abandoned our monitoring and, according to family member, returned to previous Dermatology service. We lost the contact with the customer



Fig. 9.172 Young patient showing *acuminata* lesions in intergluteal sulcus, toward the coccyx, sometimes hyperpigmented and sometimes *rosy* or *whitish*. The biopsy and analysis of viral DNA did not reveal intraepithelial neoplasia, but infection with HPV 6/11



Fig. 9.173 Fifty-one-year-old patient with vulvar intraepithelial neoplasia III. Reported HPV when she was 35-years-old and that the problem reappeared



Fig. 9.174 Forty-nine-year-old patient with vulvar itching process in area of rugose aspect leukoplakia. She reported numerous applications of podophyllin solution and trichloroacetic acid to treat warts in the vulva. Also reported that, throughout her life, had no more than three sexual partners. In none of them noticed any vegetant lesions, only the first husband, with whom she lived for 15 years, "had a few small wounds on the head of the penis". Vulvar lesion biopsy revealed accentuated vulvar intraepithelial neoplasia (VIN III). The current husband was examined and the genitoscopy was negative



Fig. 9.175 Fifty-three-year-old patient showing this vulvar process for 8 months. She was medicated with polyvalent dermatological creams (antibiotic, antihistamine, corticosteroid and antifungal medication) multiple times. She was examined in two services, and none of them proposed a biopsy. She made use of thuya solution on the affected area for 2 months. Reported that at first noted some improvement, but process has evolved after that. The biopsy, held by us, revealed VIN III + HPV result. Research for molecular biology (PCR) identified HPV 6/11



Fig. 9.176 (a) HPV disease, vulvar intraepithelial neoplasia (VIN III) in 45-year-old patient, showing multiple lesions, some *black*, other *whitish*, *grey* and *rose*, located in labia minora and clitoral prepuce. There are other dark lesions, distributed in a satellite way. (b) Therapeutic option was surgical exeresis with clitoris conservation + cauterization of the satellite lesions



Fig. 9.177 HPV disease, vulvar intraepithelial neoplasia (VIN III) resistant to various clinical treatments. Elderly patient showing lesion only in caudal portion of the right labia majora, with dark edges and hyperemic centre. In elderly women, the tendency of such injuries is to be unique. The proposed treatment was surgical excision of the lesion

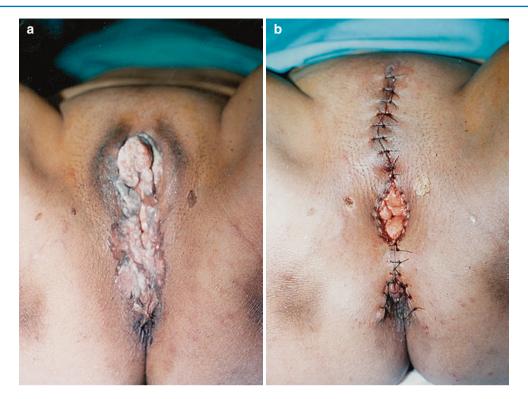


Fig. 9.178 HPV disease, vulvar intraepithelial neoplasia (VIN III).(a) Extensive lesion occupying clitoris, labia minora and perineal region. Observe the multiplicity of aspects with *rose*, *gray* and *black* areas, accompanied by two other hyperpigmented satellite lesions. Although from the clinical point of view such aspects are linked to HPV 16, only by molecular biology it can be defined. These are injuries of difficult

therapeutic approach, mainly because of the extension and the involvement of the clitoris. (b) We opted for simple vulvectomy, after prior consent of the patient, because this was an extensive lesion; several previous treatments with caustic solutions had already been employed by other medical services



Fig. 9.179 Fifty-five-year-old woman with leukoeythroplasic lesion in unique papular plate. Histopathology: VIN undifferentiated. It is worth saying again that people showing lesions with evolution of months have to be submitted to surgical removal. Thus, we have the opportunity to check the histopathological appearance



Fig. 9.180 Woman, 53 years of age, with leukoerythroplasic lesion in extensive papular plaque affecting the vulva and perianal region. The result of biopsy histopathology was undifferentiated VIN



Fig. 9.181 Fifty-six years of age woman with extensive erythroplasic lesion in unique plaque. Biopsy histopathology of lesion revealed differenciated VIN



Fig. 9.182 Sixty years of age patient with extensive leukoerythroplasic lesion of eczematoid aspect. Histopathological diagnosis evidenced VIN undifferentiated



Fig. 9.183 Seventy-year-old patient with erosive lesion on advanced lichen sclerosus. Histopathology identified VIN differentiated



Fig. 9.184 Fifty-year-old patient with a single lesion in polychromic and extensive papular plaque. Biopsy histopathological diagnosis was VIN undifferentiated

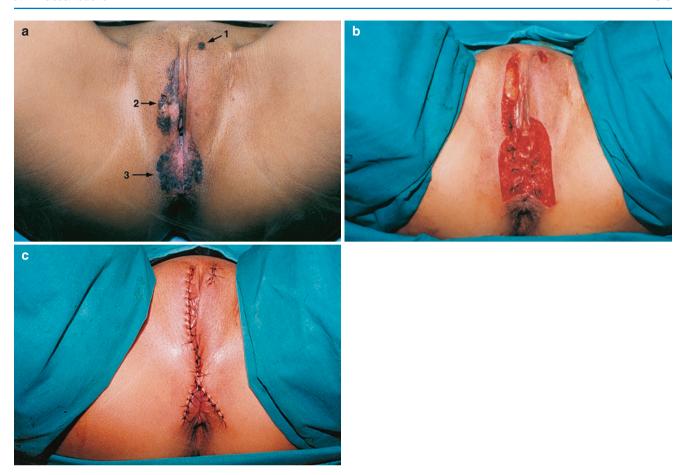


Fig. 9.185 (a) HPV infection, vulvar intraepithelial neoplasia: (*I*) satellite hyperpigmented lesion in left labia majora; (*2*) extensive papular lesion, hyperpigmented, with *rosy* central area reaching part of the right labia majora and interlabial sulcus; (*3*) lesion with same aspect of previous one, reaching labia majora caudal portion and perineal region. (**b**) Treatment: surgical excision of superficial lesions. (**c**) Appearance at the end of the surgical procedure. It is worth saying again, that when

people have lesions evolving for months/years, with several unsuccessful treatments, we try to surgically remove them. Thus, we have the opportunity to check the histopathological appearance. In addition, we have a better chance of curing the patient. However, we are not totally free of recurrences, but, in general, the new lesions are smaller and more easily treated

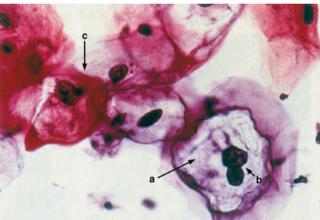


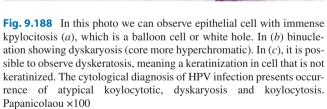
Fig. 9.186 (a1, a2) 32-year-old patient with recidivous VIN III lesions (a). Patient reports that has been submitted to several treatments, including surgery, but without total success. Note area of surgical sequel due to suture dehiscence, and healing occurred in the second intention in vulvar area (b). Patient was medicated with topical applica-

tion of imiquimod, occurring only reduction of lesions. (b) Resection of lesions. (c) After suture with maintenance of vulvar anatomy. (d) Ten days after surgery, with removal of some points. (e) Patient cured. View of vulva 7 months after surgery

Fig. 9.187 Multiple recidivous lesions of vulvar *Condyloma acuminata* treated with topical application of imiquimod







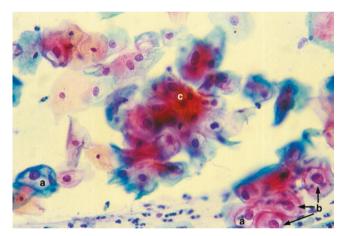


Fig. 9.189 This photo shows koylocytosis (a); dyskaryosis (b) and dyskeratosis (c). Papanicolaou $\times 40$

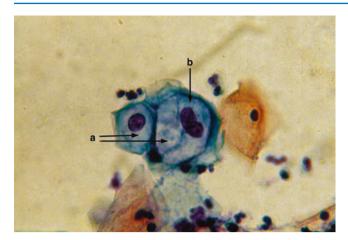


Fig. 9.190 This photo shows dyskeratosis; however, in (a) classical koylocitosis, and (b) binucleation with dyskaryosis. Papanicolaou $\times 100$

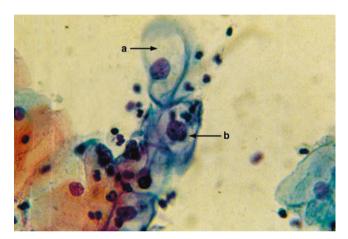


Fig. 9.191 Typical case of cytological commitment with HPV: koylocytosis (*a*) and dyskaryosis (*b*). Papanicolaou ×100

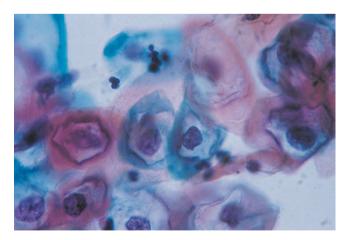


Fig. 9.192 This HPV case: koylocitosis + dyskaryosis (Papanicolaou ×100)

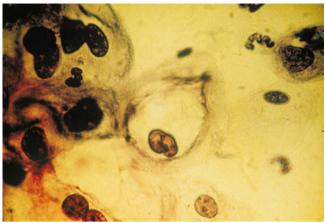


Fig. 9.193 In the center of this photo, exuberant koylocitosis, binucleation and important dyskaryosis are observed. In our view, many reports of koylocitosis "outlines" can be perinuclear halos of other etiologies, especially when dyskeratosis and dyskaryosis are not described. These blades should be revised or remade with new materials. We should also remind that dyskeratosis occurs frequently in areas that have been traumatized, especially in prolapses

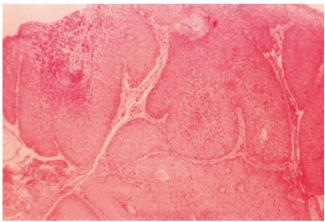


Fig. 9.194 The condilomatous disease is characterized by papillomatosis: epithelial hyperplasia. This is what shows this genital tissue histopathology with $Condyloma\ acuminata\ (HE \times 20)$

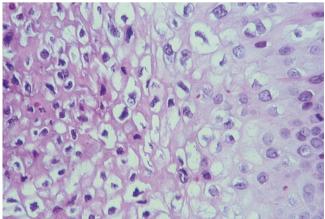


Fig. 9.195 This histopathology shows koylocytosis and dyskaryosis. HPV 16/18 (HE ×40) was identified in this material

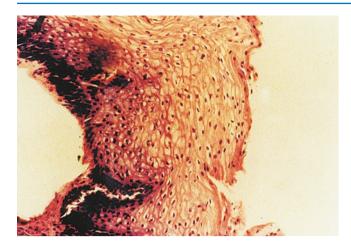


Fig. 9.196 A cervix biopsy showing koylocytosis. Through molecular biology technique, this material was positive for HPV 31, 33 and 51 ($\rm HE \times 20$)

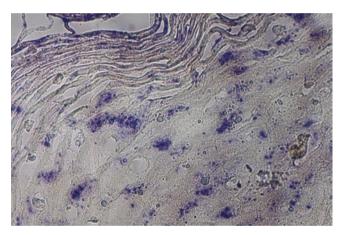


Fig. 9.197 *In situ* hybridization using biotin markers of biopsy material of perianal lesion of HIV-positive patient with HPV 6 infection (×400)



Fig. 9.198 Immunohistochemistry demonstrating changes in p 53 protein expression (tumor suppressor protein, associated with the development of human cancer). Biopsy of uterine cervix invasive carcinoma (×400)

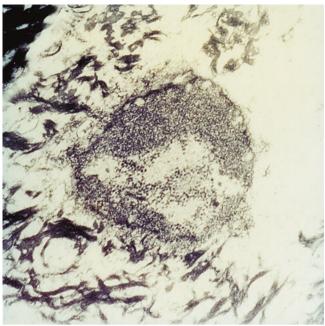


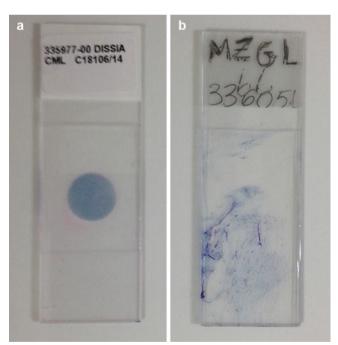
Fig. 9.199 Observation through electron microscope of HPV particles in the epithelial cell nucleus of genital tissue with *Condyloma acuminata*



Fig. 9.200 HPV 16/18 cytopathic effect on epithelial cell nucleus. (*a*) Chromosomes breaks are observed in the infected epithelial cell nucleus. Electron microscope

Fig. 9.201 Surepath® brushes and vial. *1*. Rovers® Orcellex® Brush RT for oral collection. 2. Rovers® Anex®Brush RT for anal collection. 3. Rovers® Cervex-Brush. *4*. Vial with CYTORICH RED PRESERVATIVE FLUID





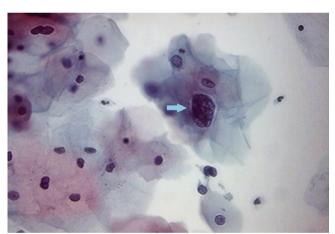


Fig. 9.203 Low-grade squamous intraepithelial lesion (LSIL *arrow*) in liquid-based cytology (Surepath® 1000×)

Fig. 9.202 Comparison of Surepath smear (a) and conventional (b)

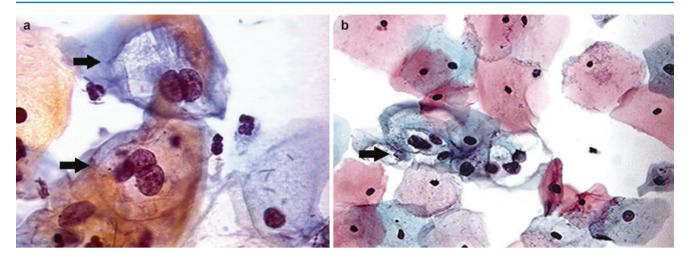


Fig. 9.204 Low-grade squamous intraepithelial lesion (LSIL *arrow*). Aspect in conventional cytology (Pap 1000×) (a) and liquid-based cytology (SurePath® 400×) (b) showing koilocytes (*arrow*)

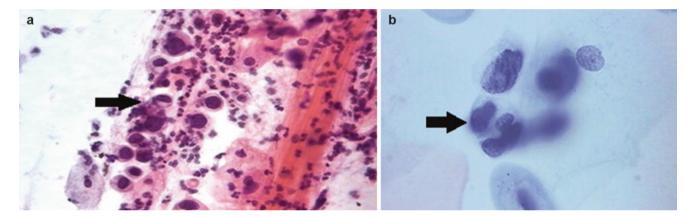


Fig. 9.205 High-grade squamous intraepithelial lesion (HSIL *arrow*). Aspect in conventional cytology (Pap 400×) (a) and liquid-based cytology (SurePath® 1000×) (b) showing atypical cells with high nucleocytoplasmic relation (*arrow*)

References

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When cases of AIDS began to be reported in the early 1980s, in the most of the time cutaneous mucous manifestations presented profuse clinical forms, occurring typically in the immunocompetent individual. In fact, these more aggressive forms are most visible in immunosuppressed patients not only by HIV, but also by other causes (neoplasia, transplanted, frequent users of steroids, antineoplastic...).

On the other hand, we should not ignore that infectious diseases are usually dependent on the following factors, among others: number of infectious germs, virulence of these germs and host resistance. Thus, the clinical manifestations can be very aggressive in an immunosuppressed individual if the infecting load is too large and/or the infecting virulence of the etiological agent is also very high.

Nowadays, especially in Brazil, where almost all HIV people registered in STD/AIDS programs receive antiretroviral last generation drugs, some manifestations, once common, have become much less frequent. There is a same concerning about the vertical transmission, as well as the deaths caused by HIV/AIDS. It usually happens due to the decrease of the blood viral load and the increase in the CD4 cells number which considerably reduce the manifestation of opportunistic infections. However, the use of antiretroviral drugs, here and around the world, may cause several side effects.

Our message is addressed to all professionals working with STD, mainly the health team actuating in regions where there is a prevalence of STD/HIV. As with STD, we should not postpone the opportunity of an early approach on sexuality topics, STD/HIV and reproductive health, including counseling on a possible syphilis, HIV and hepatitis B testing. Oncotic colpocitology for women should be included.

10.1 Synonymy

AIDS, Acquired Immune Deficiency Syndrome.

10.2 Concept

Represents an advanced immunosuppression state caused by HIV virus. The main viral action is to induce the decrease of T CD4+ (CD4) lymphocyte count to levels below 20% of the normal value (i.e., <200 cells/mm³).

10.3 Incubation Period

For aids: 5–10 years without antiretroviral treatment.

10.4 Etiological Agent

HIV vírus belongs to the *Retroviridae* family, which is composed of four virus: HTLV I, II, III and IV. HTLV III corresponds to HIV. Later on, two types of HIV (1 and 2) were discovered with distinct geographical predominance, and each one of them with subtypes A, B, C, D and E. They consist of RNA genome with protein capsid and lipoprotein cover inside the capsid. Enzymes such as the reverse transcriptase, protease, and others responsible for the viral multiplication are found in viral RNA, over which the current antiretroviral therapy is based. The envelope contains two glycoproteins, Gp120 and Gp41, which guarantees the binding of the virus to the host cell. HIV has tropism to T *helper* lymphocytes, macrophages and dendritic cells.

10.5 Clinical Manifestations

(Figs. 10.1–10.115)

 Acute Infection: acute infection is defined as the first few weeks of HIV infection until the emergence of anti-HIV antibodies (seroconversion), which usually occurs around the fourth week after the contagion. Currently it is known

that 50-90% of individuals infected have a set of clinical manifestations, called Acute Retroviral Syndrome (ARS), formerly called Seroconversion Syndrome, which usually occurs between the first and third week after infection, limited to 3-4 weeks. It has a very varied range of clinical pictures, from oligosymptomatic forms to lagging manifestations with rarer complications, such as aseptic meningitis and Guillain-Barré syndrome. In a third of cases ARS can manifest itself as a Mononucleosis-like syndrome (symptoms of an acute viral syndrome: fever, adenopathy, axillary and cervical occipital, erythematous, cutaneous mucous rash pharyngitis, myalgia, arthralgia, diarrhea, headache, nausea, vomiting and hepatosplenomegaly). Cutaneous mucous lesions are small aphthous ulcers that can be observed in the mouth, anus and genitals. Along with the viremia there is an abrupt fall of CD4 lymphocyte. A transient leukopenia with lymphopenia and later CD4/CD8 inversion can occur. Then, due to the biological response of the organism, CD4 rises up and the viral multiplication falls, remaining at stable levels. The level of viral multiplication will dictate the progression (fast or slow) for what we call aids.

- Asymptomatic or Latent Phase: 3–12 weeks from the beginning of the infection, most patients seroconverts (serology). Anti-HIV humoral immunity partially stops viral replication, causing the decrease of viremia and the increase of CD4 levels, however, never to previous normal levels. This phase can last from 2 to 20 years (an average of 10 years) and generally the CD4 count is higher than 350 cells/mm³.
- Symptomatic Phase: emerges with the continuity of the viral replication increasing the viremia and making the CD4 drop to values below 350 cells/mm³. It is characterized by mild to moderate immune compromised with increased frequency of manifestations of some diseases such as bacterial, fungal and common protozoan infections in the community and even neoplasia. With no treatment, a progressive CD4 drop to less than 200 cells/mm³ happens, determining a strong immunosuppression and emergence of severe opportunistic diseases, defining the acquired immunodeficiency syndrome (AIDS), which can lead to death of patient. This phase has a varied duration, but an average of 2–3 years.
- The list of diseases defining AIDS, main opportunistic diseases, therapeutic consensus and pregnancy procedures can be found in www.aids.gov.br/aids.

10.6 Laboratory Diagnosis [1, 2]

Diagnosis can be made of two ways, combined or not, as follows: directly, the detection of the virus or its components (proteins and other antigens, genetic material, culture isolation, etc.), or indirectly, by detection of the immune response to the virus. The antibodies through serum tests are the methods traditionally carried out. The serologic positivity usually occurs between 3 and 12 weeks from contamination. Almost all infected patients present positive serology up to 6 months of contagion. In the immunological window period, ranging from HIV infection until the laboratory detection, patient can transmit the virus, but the serology is still negative. The technology advance has allowed a diagnosis with a smaller immunological window, currently 4–6 weeks.

Tests types are as follows:

- (a) Serologic classification tests:
 - Immunoassays (IE), as the immunoenzymatic type tests ELISA (Enzyme-Linked Immunosorbent Assay).
 The latest, of fourth-generation, combine detection of antigens, besides the traditional antibodies.
 - 2. Rapid tests (RT): simple immunoassays that can take 30 min. There are several formats of RT, and the most frequently used are: devices (or strips) of immunochromatography of lateral flow, dual migration immunochromatography (DPP), immunoconcentration devices and the solid phase.
- (b) Complementary tests: false-positive results may occur in classification tests. For this reason, additional tests are necessary for the diagnosis definition. Additional tests use different formats and principles. Are included in this category:
 - Serological: Western Blot (WB), Immunoblot (IB) or line immunoassays (LIA—Line Immuno Assay), including Rapid Immunoblot (RIB) and Indirect Immunofluorescence (IIF), HIV-1/HIV-2 antibody differentiation assay [MultispotTM], the latter a rapid test of ultimate generation.
 - Molecular tests: detect pro-viral DNA or RNA, is the second most used, called the "viral load", and commonly made by the quantitative polymerase chain reaction method.

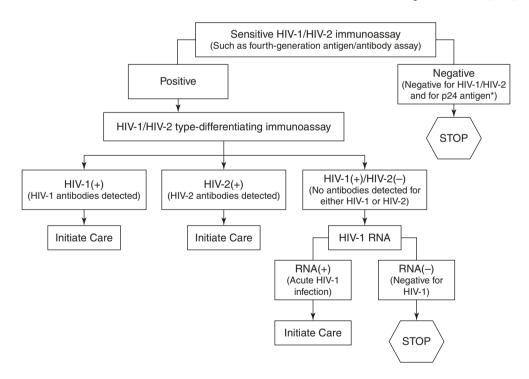
10.7 WHO Case Definition for HIV Infection

- 1. Adults and children aged 18 months or older. HIV infection diagnosis based on:
 - positive HIV antibody test (rapid or laboratory-based enzyme immunoassay). It is usually confirmed by a second HIV antibody test (rapid or laboratory-based enzymeimmunoassay) relying on different antigens or of different operating characteristics.
 and/or;
 - positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination.
- 2. Children younger than 18 months. HIV infection diagnosis based on:
 - a positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination taken more than 4 weeks after birth. Positive antibody testing is not recommended for definitive or confirmatory diagnosis of HIV infection in children until 18 months of age.

10.8 Evaluation of Diagnosis Methods

Since the beginning of HIV epidemic, the infection serologic diagnosis is made with at least two tests, one for the classification and the second, more specific and different from the first one, to confirm. The most widely utilized combination, usually called the gold standard, was accomplished through a selection immunoassay, such as ELISA, followed by Western Blot (WB) as a confirmation test. The World Health Organization (WHO) accepts, for example, that two different rapid tests in series are sufficient to conclude the diagnosis in locations with few resources and high prevalence. Modern tests allow the using of flowcharts for the diagnosis, according to the local prevalence of the disease and the availability of resources in each scenario, so it should be observed the protocols defined for each country to confirm the disease. It is important to point out that all newly diagnosed individuals should test their viral load, which in fact constitutes a third test to ratify the presence of infection. If there is any doubt about the diagnosis it is recommended to repeat the tests in intervals of at least 30 days.

Some web sites contain the algorithms of laboratory diagnosis of the main regions and the 2014 Algorithm of the U.S.A CDC recommended for areas of low prevalence of HIV, such as U.S.A., Europe and Brazil [1–2].



10.9 Treatment and Cure Control

An incurable, but tractable disease.

The antiretroviral treatment is mandatory as soon as possible of all individuals presenting aids defining illnesses, as well as of pregnant women and of those with less than 500 CD4 cells/mm³. There is an increasingly world tendency towards an early start, even in asymptomatic individuals with good immunity. This tendency was adopted in Brazil since 2014 to reduce HIV sexual transmission. The precocity of the treatment also postpones the breakdown of the immune system, and reduces the inflammatory process induced by HIV, the supporter element of thromboembolic phenomena, thus preventing cerebrovascular and cardiovascular diseases, and premature aging of the organism. To treat HIV it is necessary at least three antiretroviral combination drugs, two of them belonging to different classes. Treatment is complex and needs medical supervision to assess adaptations of the organism to the treatment, their side effects and possible difficulties in following correctly the medical recommendations, that is, to adhere to treatment. A good multidisciplinary monitoring can keep the disease under control for many years. So, with no viral resistance (a growing problem) or uncontrollable intercurrences. It is obvious that the patient, their family members and sexual partners must actively participate in this monitoring.

According to its capabilities and delivery model for medications, each country has therapeutic protocols concerning the initial scheme, drugs used with co-infections such as tuberculosis and viral hepatitis, rescue schemes for patients with resistant virus. The treatment usually begins with two nucleoside reverse transcriptase inhibitors and non-nucleoside inhibitor or a protease inhibitor potentiated with ritonavir. In Brazil, for example, there is the universal recommendation to start the treatment by combining tenofovir, lamivudine and efavirenz. As there is a large number of researches on AIDS, data arise every year often modifying the procedures. We recommend the regular consultation of the some guidelines [3–5].

10.10 Antiretroviral Drugs Classes [3–5]

Reverse Transcriptase Nucleoside Inhibitor: act on the enzyme reverse transcriptase, incorporating to the DNA strand created by the virus. Make this chain imperfect, preventing the virus reproduction. They are the following: Abacavir, Didanosine, Stavudine, Lamivudine and Zidovudine.

Reverse Transcriptase Non-nucleoside Inhibitors: block directly the enzyme action and the virus multiplication. They are the following: Efavirenz, Nevirapine, Rilpivirine and Etravirine.

Nucleotides Inhibitors: Tenofovir.

Protease inhibitors: act on the protease enzyme, blocking its action and preventing the production of new copies of cells infected with HIV. They are the following: Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Nelfinavir, Ritonavir, Saquinavir and Tipranavir.

Fusion inhibitors: prevent that virus enter into the cell, thus it cannot reproduce itself. Example: Enfuvirtide.

CCR5 receptor antagonist: Maraviroc.

Integrase inhibitors: block the activity of the enzyme integrase, which is responsible for the integration of HIV DNA into the human DNA (genetic code of the cell). Thus, inhibits the replication of the virus and its ability to infect new cells. Examples: Raltegravir, Dolutegravir, Elvitegravir/ Cobicistat.

10.11 Complications

Result from the immunosuppression caused by viral infection (opportunistic infections, neoplasm, consumptive syndrome) and by adverse reactions to therapy with antiretroviral drugs (hepatotoxicity, neuropathies, pancreatitis...).

10.12 Differential Diagnosis

Differential diagnosis should be made with all diseases capable of manifesting as a mononucleosis syndrome: cytomegalovirus, rubella, toxoplasmosis, hepatitis, syphilis (especially in the roseola's fase).

10.12.1 Notes

- Transmission can occur through blood transfusion, accident with perforating and cutting material, sharing of syringes and needles, sexual and perinatal contact (transplacental, during delivery and during breastfeeding).
- The mother-to-child transmission can be drastically reduced if antiretroviral therapy is carried out during pregnancy, especially at time of birth. Today the elective caesarean is a great choice of delivery route, reducing the possibility of HIV transmission to the fetus. However, patients with a viral load of less than 1000 copies/mL may not benefit from the c-section. In such cases, the indication of c-section can be by obstetric criteria. However, we should be aware that the emergency caesarean section increases the possibility of vertical transmission. Clamping the cord as soon as possible is imperative, as well as avoiding invasive measures in the fetus.
- Breastfeeding is formally contraindicated.

- Recurrent vulvovaginal candidiasis may be the first clinical manifestation of HIV infection.
- HIV infected patients with PID manifestation or invasive cervical cancer have disease classification changed.

10.12.2 Vaccines in People Living with HIV

Vaccination recommendations for HIV carriers, adults or children, usually follow the same principles of the rest of the population, with some exceptions/special care.

First, the immunogenicity in this group of people is smaller, mainly those with CD4 counts less than 200–350, and more doses or higher doses are needed. Special care must be taken with vaccines made with live attenuated agents. None can be used if the CD4 cell count is less than 200 cells/microL (or percentage less than 15% in children up to 5 years of age) or clinical signs of immunosuppression.

All the attenuated vaccines (rotavirus, varicella zoster, yellow fever, MMR) should be administered individually with an interval of at least 1 month. Exceptions: do not use attenuated vaccines against polio or influenza, even in those with good immunity. Choose the vaccines with inactive antigens.

The BCG vaccine is controversial: contraindicated by the American CDC, independent of the immune status. The Ministry of Health of Brazil recommends vaccination of children with HIV with good immunity in a single dose, without reinforcement.

10.12.3 Zoster/Varicella

The zoster and varicella vaccine, despite using the varicellazoster attenuated virus, has different presentations, indications, and dosages.

Immunization against varicella: recommended for children and adults with CD4 count equal or greater than 200 cells/microL (or percentage greater than or equal to 15% in children up to 5 years of age), without clinical signs of immunosuppression, and do not have vaccine history (2 doses) or varicella. The anti-varicella IgG serum dosage can solve doubts.

Dosage: Example: VarivaxTM, two 0.5 mL SC doses with at least 4–8 weeks interval.

Immunization against zoster: promising evidence recommend vaccination of HIV carriers with more than 60 years of age with CD4 count equal or greater than 200 cells/microL, without clinical signs of immunodsuppression, and preferably in use of antiretroviral drugs with suppressed viral load. Check the recommendations according to indication of local health authorities.

Example: ZostavaxTM 19,400 UI/0.65 mL dose. Dose: single SC dose in deltoid. Discontinue use of anti-herpetic medications 24 h before the dose and do not use them for at least 14 days.

10.13 HPV

People living with HIV should receive HPV vaccination scheme. In countries where the Gardasil 9 ValentTM vaccine (6, 11, 16, 18, 31, 33, 45, 52, 58) is already available, this should be the first indication. Otherwise, our specification is vaccination with Gardasil 4 ValentTM (6, 11, 16, 18). The vaccination schedule should be three doses: 0 day, 60 days and 180 days in boys/girls more than 9 years old, men/women

Other vaccines are in research.

10.14 Hairy Leukoplakia

A particular form of leukoplakia described in 1981 for the first time as a white lesion of epithelial hyperplasia and hyperkeratosis, which is not removed during the scraping with wooden spatula, for example. Its presentation varies from white vertical strokes to leukoplastic thick and wrinkled areas. Represents an opportunistic infection related to the presence of the Epstein-Barr virus (EBV), almost exclusively in patients infected with human immunodeficiency virus (HIV). Although rare, there are cases reported in patients receiving organ transplants and even in immunocompetent individuals.

It is a well-defined white lesion, which varies from flat to a plaque with vertical roughened striations. Frequently it occurs along the side edges of the tongue, with occasional extension to the dorsal or ventral surface, being common the bilateral presentation, however, it occasionally occurs unilaterally and can rarely get in the jugal mucosa.

Clinical differential diagnosis of hairy leukoplakia includes idiopathic frictional hyperkeratosis, leukoplakia (biting tongue), tobacco and candidiasis associated leukoplakia.

The treatment of hairy leukoplakia is not usually specific or necessary.

10.15 Noma

Condition also known as *Cancrum oris*, noma stomatitis or necrotizing stomatitis. It is an opportunistic infection with rapid progression caused by normal components of the oral microbiota that becomes pathogenic during periods of commitment of the immunity state. The most common predis-

posing factors are the following: malnutrition, dehydration, poor oral hygiene, recent diseases, malignant neoplasm, immunodeficiency (including aids).

The process often begins as a painful ulceration in the gingiva extending quickly and causing necrosis as in acute necrotizing ulcerative gingivitis. The areas of necrosis may develop in the soft tissue without continuity with the gingiva or extend deeply into tissues and develop pale zones originating areas of yellow necrosis. The process can spread to the underlying bone, with large areas of possible osteomyelitis. The typical characteristics are: fetid odor, significant pain, fever, general malaise and regional lymphadenopathy.

Treatment consists of controlling the predisposing factors, as well as the infection itself. Nutrition must be restored, as well as hydration and electrolyte balance, along with the administration of antibiotics. Conservative debridement should be performed in large areas of necrosis.

10.16 Kaposi's Sarcoma

Kaposi's sarcoma, first described in 1872 by the Hungarian physician living in Austria Moritz Kaposi, is an uncommon vascular neoplasm originated in the proliferation of endothelial cells, although the dermal dendrocytes and submucosa, macrophages, lymphocytes and mastocytes may play a role in the genesis of the lesions.

The possible etiologic factors are: genetic predisposition, infection (especially viral), environmental influences and immune aberrations.

However, in all forms of Kaposi's sarcoma lesions, a new herpesvirus (HHV-8 or KSHV) was identified.

Three different types of Kaposi's sarcoma were described. The first is a classic form, which is a rare skin lesion prevalent in older men, inhabitants of the Mediterranean basin and manifests itself as multifocal reddish-brown nodules mainly in the skin of lower extremities. Oral lesions in these cases are rare with indolent course and good prognosis. The second type is the endemic, identified in Africa. The most commonly affected organ is the skin. Oral lesions are rare, their clinical course is prolonged and the prognosis is good.

The third type was observed in immunodeficient patients, especially by AIDS and transplanted. Thus, the skin lesions are not limited only to the extremities and may be multifocal. The patients belong to a younger age group. The oral lesions can be the initial site of the development or the single location, ranging from a flat lesion to a node and can be single or multifocal. The gingiva and the hard palate are the places of greater involvement by the tumor. The color usually ranges between red and blue. The differential diagnosis of oral lesions should be made with the hemangioma, erythroplakia, and especially with pyogenic granuloma, a common injury in the mouth.

10.17 Major Aphthous Ulcers or Sutton's

It was formerly called recurrent necrotic mucosa periadenitis or Sutton's disease. Currently it is considered the most serious manifestation of aphtous stomatitis. The aphthous ulcers have an increased size (0.5 cm), are more painful and last longer than smaller aphthas. The ulcerations are deeper, giving a crater form, taking from 2 to 6 weeks to heal, and can cause scarring. The number of lesions varies and any oral surface area may be affected, but the predilection for the oral mucosa is typical, and the labial mucosa, lingual belly, soft palate and tonsillar crypts the most commonly affected sites. In patients presenting a course without remission, with significant pain and discomfort, health can be compromised because of the difficulty in eating and psychological stress.

Immunosuppressed patients, especially by HIV virus, may show long-term and repeated episodes of major aphthous ulcers. There is no specific treatment for the condition, and the use of steroids, both local and systemic, has been the drug of choice. Other medications have been used in an attempt to solve the disease, such as chemical cauterization acid, topic aminosalicylic-5 acid, vitamins, hydrogen peroxide, chlorhexidine, tetracycline, dapsone, levamisole, and some studies have shown the use of thalidomide, especially for immunosuppressed patients, saving the necessary precautions.



Fig. 10.1 Pseudomembranous candidiasis. White detachable plates by scraping, located in oropharynx, characterizing pseudomembranous Candidiasis in a patient with AIDS. It is possible to observe a brown pigmented area in the back of the tongue due to smoking. In this region, the tongue papillaes are hypertrophied due to *Candida* infection, giving the clinical aspect of the so-called *black hairy tongue*



Fig. 10.2 This image shows white plates easily deployable and intensely erythematous erosions in the jugal mucous and dorsum of the tongue due to pseudomembranous Candidiasis, which constitutes one of the most common clinical findings in HIV positive patients



Fig. 10.3 Candidiasis represented by an eroded irregular erythematous area well demarcated with disappearance of the filiform papillae on the dorsal surface of the tongue of a patient with AIDS



Fig. 10.4 Candidiasis in patient with AIDS. Clinical manifestation less intense than those presented previously. It is classic in medical practice the involvement of oral, pharyngeal and esophageal mucosa by *Candida* sp. infection in immunodeficiencies, and it should be pointed out that it involves not only HIV

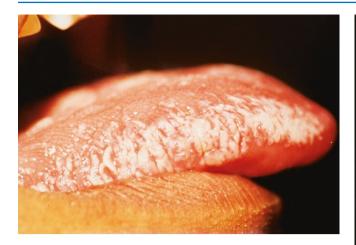


Fig. 10.5 Hairy leukoplakia in patients with AIDS. White plaque extending around the lateral border of the tongue, roughened in its surface and showing vertical striations

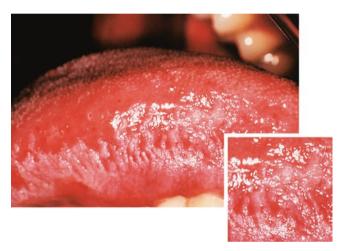


Fig. 10.6 Hairy leukoplakia in patients with AIDS. In the zoomed image its striated and wrinkled appearance can be observed



Fig. 10.7 Oral hairy leukoplakia in patients with AIDS. The Figure shows the presence of bilateral leukoplakia, as well as lesions extending into the ventral surface of the tongue, which are common aspects of the condition. It is important to point out that this lesion is suggestive of aids and its causal agent is the Epstein-Barr virus (EBV-HHV-4)



Fig. 10.8 Same patient of previous Figure, in which it is observed in detail the wrinkled and ridged appearance of whitish plaque characterizing oral hairy leukoplakia on the left side of the lateral border and lingual belly



Fig. 10.9 The image of the lateral border of the tongue on the *right* side of the same patient of previous Figures reveals the presence of a corrugated and grooved white plaque, characterizing bilateral oral hairy leukoplakia



Fig. 10.10 White plaque located on the lateral edge of the tongue of irregular surface and rough aspect in HIV-positive patient. The lesion involves the entire length of the lateral border of the tongue. The biopsy of material revealed hyperkeratosis and balloon cells in the *upper* layers of the stratum spinosum. In addition, nucleus of epithelial cells showing an aspect of "pearl necklace" was observed. Such microscopic findings are compatible with the diagnosis of oral hairy leukoplakia



Fig. 10.11 Patient in the secondary stage of syphilis, being possible to observe the presence of high *whitish* color plaques with rough surfaces and irregular forms located in the ventral lateral edge and the left side of the tongue. This condition is known as plane condyloma or papular syphilide. It should be noted that this is a necrotic lesion and that it can be removed by scraping, as opposed to hairy leukoplakia. An eroded irregular erythematous area on the palate can be observed



Fig. 10.12 Histological section showing irregular and thick parakeratosis and keratinization on the surface of the epithelium, which is hyperplastic and shows a stained band of balloon cells, little *rosy* on the *upper* portion of the spinous layer. This epithelial picture is not exclusive of hairy leukoplakia, however, when combined with practice, it is strongly suggestive of the diagnosis. Viral DNA detection of Epstein-Barr virus should complement the recognition of the lesion



Fig. 10.13 Necrotizing periodontitis showing ulceration of the gingival tissue associated with gingival papillary necrosis in patients with



Fig. 10.14 Noma in patient with AIDS. Extensive yellowish necrosis area with rapid progression, which began in gingiva and extended to the jugal mucosa, promoting severe tissue destruction resulting from anaerobe microorganisms, fusiform bacilli (*Fusobacterium fusiform*) and a spirochete (*Borrelia vicent*)



Fig. 10.15 Noma in patient with AIDS. Exteriorization of cutaneous lesion as a result of intrabuccal tissue destruction observed in Fig. 10.14

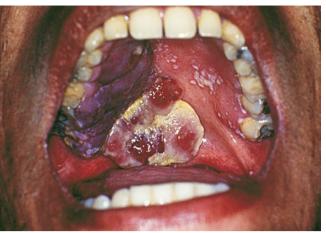


Fig. 10.16 HIV positive patient showing two tumor masses in the oropharynx. One lesion extends from the hard palate on the *right* side to the *middle line* of *purple-blue* staining and the other *reddish* lesion covered partially by necrotic *whitish* material, occupying area of hard palate and soft palate. Constitute lesions of Kaposi's sarcoma. Small *whitish* areas of candidiasis can also be observed on the left side of hard palate. In addition to the oral lesions, the patient presented nodules and cutaneous macules, and visceral involvement by the tumor



Fig. 10.17 *Reddish-purple* spots scattered by the hard palate and a posterior small papular elevation. The two clinical forms are relative to Kaposi's sarcoma in patients with aids. We should pointed out that in the oral cavity these clinical presentations tend to evolve to form tumor masses and do not tend to be extinguished when submitted to diascopy by vitropression



Fig. 10.18 Kaposi's sarcoma in female patient with AIDS



Fig. 10.19 (a) Kaposi's sarcoma in female patient with AIDS. (b) Kaposi's Sarcoma at the apex of the tongue in male patient with AIDS



Fig. 10.20 Male patient, HIV positive, showing *purple* color tumor mass on the edge and *right* side border of the tongue



Fig. 10.21 *Purple* tumor mass located in the previous superior alveolar edge in the *inner* side, invading the bone and causing tooth mobility compatible with Kaposi's sarcoma in patient with AIDS. This neoplasia is caused by the Human Herpes Virus type 8 (HHV-8)



Fig. 10.22 Presence of Kaposi's sarcoma located in the oropharynx of HIV positive patient, involving mainly the uvula, which shows a great volume increase with *reddish-purple* color

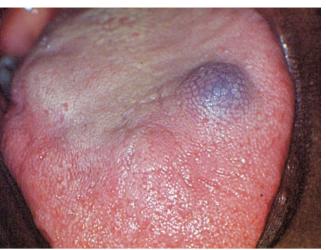


Fig. 10.25 Presence of three nodular elevations, located on the back of the tongue, being the *bluish* the most evident located near the lateral border of the tongue on the *right* side of the image. This lesion concerns a venous malformation with diffuse growth



Fig. 10.23 Presence of two Kaposi's sarcoma lesions located at the *bottom* of the anterior *upper* vestibule with a *reddish-purple* color in a patient with HIV



Fig. 10.26 Bluish tumor mass located in jugal mucosa regarding a venous vascular malformation present since patient's childhood



Fig. 10.24 Same patient of previous Figure showing tumor mass of Kaposi's sarcoma located in the anterior region in the hard palate *midline*



Fig. 10.27 This image shows the process of diascopy by vitropression held in the lesion of the same patient of previous Figure. It should be emphasized that Kaposi's sarcoma is not "deleted" by vitropression, despite being a vascular injury



Fig. 10.29 Tumor mass of blackened coloration located on the anterior region, *red* at the rear, measuring, approximately, 6 cm in greatest diameter. The lesion is located on the gingiva of molars and it is also pedunculated. Its clinical development has a hyperplastic reaction character, bringing out a pyogenic granuloma



Fig. 10.28 Venous malformation located in the *right* of the *midline*, in the anterior third of the hard palate, with *purple* color, that should be considered in the differential diagnosis of Kaposi's sarcoma



Fig. 10.30 Tumor mass of rounded shape with smooth surface, *brownish* color, slow growing, located on the surface of the *upper* incisive teeth that were removed. The histopathological examination revealed it was a reactive hyperplastic growth, with giant cell involvement and infiltrated hemorrhagic with dispersion of hemosiderin, which gives the peculiar coloring of the lesion. The diagnosis conclusion is peripheral giant cell granuloma



Fig. 10.31 Slow-growing exophytic tumor mass, involving gingival tissue in the posterior area of the mandibular region, which dislocated dental elements, being fully removed and whose diagnosis by histopathology was peripheral giant cell granuloma



Fig. 10.32 Major aphthous ulcers located in the lateral border of the tongue and the retromolar region in patient with AIDS

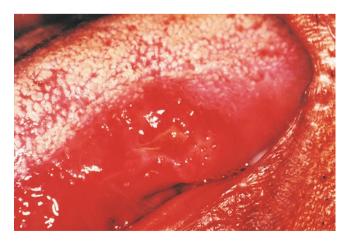


Fig. 10.33 Crater form painful ulcerated lesion on the lateral border of the tongue meaning major aphthous ulcer. The patient, seropositive for HIV, reported episodes of repetition and presence of other concomitant lesions located in the transition region of the oropharynx





Fig. 10.34 (a) Patient showing vesicular lesions in the nasal region, with ulcerated areas covered by crusts extremely painful, compatible with herpetic infection. HIV serology was requested, confirming the patient's seropositivity. (b) Same patient with areas of shallow ulcerations revealing oral manifestation of herpetic infection, and other *whitish* areas as the result of necrotic material related to pseudomembranous candidiasis



Fig. 10.35 Tongue dorsum covered by necrotic material resulting from pseudomembranous candidiasis in HIV positive patient. It is important to point out that oral candidiasis manifestations, even during highly active antiretroviral therapy (HAART—Highly Active Antiretroviral Therapy) are an important clinical finding

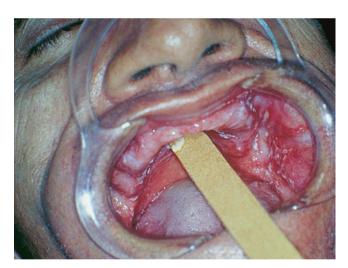


Fig. 10.36 Pseudomembranous candidiasis necrotic material in the oral cavity being removed by a wooden spatula. Such a procedure is really important for the differential diagnosis of other white-keratotic lesions of the oral cavity as leukoplakia, a precancerous lesion in some circumstances



Fig. 10.37 Atrophic candidiasis showing eroded erythematous areas involving tongue interspersed with *white* necrotic plaques and ulcerated areas in labial commissures characterizing angular cheilitis in HIV-seropositive patient



Fig. 10.38 Female patient with AIDS showing onychomycosis and necrotic white plaque due to *Candida* infection in the oral cavity



Fig. 10.39 Clinical procedure of scraping a lesion by *Candida sp.* in the floor of the mouth of the same patient of previous Figure, which usually causes a bleeding area



Fig. 10.40 Image shows lingual venter *whitish* plaque that cannot be removed by scraping, characterizing its keratotic structure and establishing the clinical diagnosis of leukoplakia. This type of lesion should be biopsied and sent for histopathological examination, because it is possible to detect histological malignancy features in some of them. In general, patients who develop this type of lesion are smokers and alcohol users



Fig. 10.42 Male patient, 48 years old, inveterate smoker, unapologetic user of distilled beverages showing white lesions of irregular shape, corrugated surface, located in the transition of hard palate to soft palate, non-detachable by scraping. The lesion was removed by excisional biopsy, and histopathological examination showed signs of squamous cell carcinoma



Fig. 10.41 Patient showing keratinized *white* area in the lingual venter whose biopsy detected atypical cells compatible with the diagnosis of squamous cell carcinoma. The patient denied smoking and alcohol intake, however, reported practice of oral sex, and probably such lesion is related to HPV infection. Methods more accurate to identify the virus were not available at this occasion

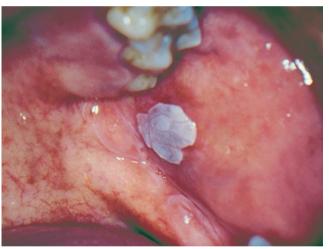


Fig. 10.43 Female patient with well-marked white plaque of irregular contours located in the jugal mucosa that cannot be removed by scraping. Incisional biopsy was made. The histopathological examination showed only hyperkeratosis without findings suggestive of malignancy



Fig. 10.44 HIV positive patient showing irregularly recurrent ulceration in oropharyngeal region for more than 1 month, extremely painful. The bottom of the lesion is covered by necrotic material, and its periphery is erythematous due to inflammatory infiltrate. The clinical diagnosis was major aphthous ulcer. The lesion did not respond to treatment with corticosteroids, then the option was thalidomide, successfully

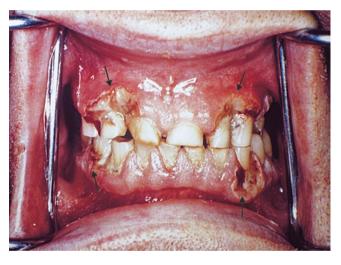


Fig. 10.45 Male patient, 36 years old, homosexual, injection drug user, HIV positive, showing ulcero-destructive lesions involving several areas (*arrows*) gingival bleeding and painful, friable, fetid smelling, with presence of *white yellow* pseudomembrane at the *bottom* of the ulceration. The diagnosis is necrotizing ulcerative gingivitis



Fig. 10.46 Male patient, 24 years old, HIV positive, bisexual behavior, showing ulcer-destructive lesion involving the vestibular gingiva in molar areas, which were crispy, bleeding at touch and with fetid odor. The diagnosis is necrotizing ulcerative gingivitis



Fig. 10.47 The same patient seen in the Figure above, with necrotizing ulcerative gingivitis, showing atypical shape regarding the location, as it involved the gingival palatine region



Fig. 10.48 Male patient, 21 years old, HIV positive, showing linear erythematosus involvement in marginal gingiva region that didn't respond to conventional measures of microbial control by dental brushing and flossing, and who presented, however, remission of clinical case after prescription of systemic fluconazole



Fig. 10.49 Male patient, 47 years old, trucker, heterosexual behavior, HIV seropositive, who reported intense pain in dermatome corresponding to the path of the mandibular nerve. Four days after the painful episode, occurred the emergence of vesicles involving the facial region, lips, jugal mucous structures, floor of mouth, labial mucosa and back of the tongue of the affected side. The vesicles broke up making eroded and ulcerated areas in the face with *yellow* crusts. Aspects described correspond to the clinical manifestation of herpes zoster as a result of reactivation of the varicella-zoster virus, causative agent of chickenpox



Fig. 10.50 Detail of the oral cavity of previous patient showing erosive and bleeding areas involving the gingiva and vestibule, with necrotic whitish material between the teeth



Fig. 10.51 Intraoral view of the same patient, a herpes zoster carrier, showing erosive areas on the back of the tongue, right dimidium partly covered by a *whitish* necrotic material of pseudomembranous candidiasis



Fig. 10.52 Intraoral vision of the patient with herpes zoster where we can observe an intensely erythematous jugal mucosa with small erosions of irregular contours covered with necrotic whitish material



Fig. 10.53 Male patient, 25 years old, homosexual, with irregular ulceration involving regions surrounding the *upper* and *lower* lips on the *right* side with crust formation. Inside the mouth, crater shape irregular ulcers with back of moriform aspect were present. The lesion was biopsied and tissue examination with staining by impregnation of silver methenamine (Grocott-Gomori method) it was possible to identify large yeasts with the production of multinucleated giant cells inside the cytoplasm, giving the aspect of "Mickey Mouse ears" or "sailor's helm", characterizing the diagnosis of Paracoccidioidomycosis. The patient was admitted to hospital and during routine tests the seropositivity for HIV was identified



Fig. 10.54 Female patient, 37 years old, housewife, monogamous heterosexual behavior, presented lesions in high irregular plaques, granular surface, with an erythematous halo around the left jugal mucosa. The lesion was biopsied and the histopathology revealed the presence of numerous yeasts encompassed by multinucleated giant cells, characteristic of Paracoccidioidomycosis. Patient was referred to hospital for treatment. Routine admission exams identified lesion involving the lung hilum and it was detected seropositivity for HIV



Fig. 10.55 Male patient, 35 years old, HIV positive, showing tumor mass on the right side of the hard palate, recent onset and rapid growth, showing soft consistency on palpation, *purplish-red* colour, with eroded areas covered with necrotic material. During incisional biopsy, it was observed that the tissue showed consistency similar to "fish sticks". The histopathology and immunohistochemistry diagnosed non-Hodgkin's lymphoma caused by type B lymphocytes



Fig. 10.56 Male patient, 60 years old, already diagnosed as HIV carrier, showing tumor lesion of purple color, soft and elastic consistency on palpation, located in the region of the hard palate, near the incisal papilla. The lesion was biopsied and the tissue examination showed diffuse infiltration of the connective tissue underlying the tumor mass, composed by intense population of little differentiated cells with cytoplasm reduced lymphocytic series. The patient was transferred to a cancer hospital where lab tests confirmed cytogenetic and immunohistochemical diagnosis of high-grade large B cells diffuse lymphoma



Fig. 10.57 Female patient, 32 years old, showing extensive tumor mass already covering some teeth, rapid growth and recent emergence, occupying the hard palate and the vestibule on the left side of the maxilla, with irregular surface aspect and mixing *red-purplish* and *whitish* areas of necrotic material. The lesion invaded the underlying bone, causing destruction and intense pain. The HIV seropositivity was confirmed by additional tests during the process of this tumor diagnosis. The histopathological exam enlightened the diagnosis of high-grade B cells non-Hodgkin's lymphoma, which consists of 60% of non-Hodgkin's lymphomas in oral cavity

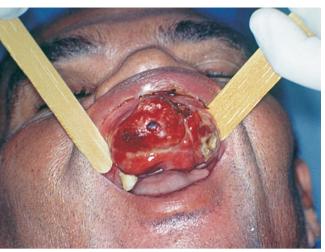


Fig. 10.58 Male patient, bisexual, HIV positive, showing exophytic tumor mass in anterior region of maxilla that projected out of the mouth, of *red* color, irregular shape, soft consistency, bleeding, painless and sessile. In addition to this lesion, the patient had pseudomembranous candidiasis involving the mouth and oropharynx. The lesion was biopsied and the laboratory tests diagnosed B-cell non-Hodgkin's lymphoma. We should emphasize that in AIDS patients non-Hodgkin's lymphomas in conjunction with Kaposi's sarcoma are the malignant neoplasms prevalent in the mouth



Fig. 10.59 Fast-growing tissue mass, with soft consistency and painless that occurred after extraction of a tooth. Despite the rapid process development is upsetting, the diagnostic procedure should contemplate the radiological tests in the region to identify the possible presence of dental remains or bone fragments that could have been left within the dental alveolus during the dental extraction. The diagnosis for this condition is granulomatous epulis. Such a name is used to describe excessive growths of granulation tissue in the face of a foreign body



Fig. 10.60 Periapical radiographic image of the previous patient, revealing the presence of dental remains after extraction, the stimulator factor of the reaction hyperplastic granulomatous growth called granulomatous epulis (*arrow*)



Fig. 10.61 Male patient, 34 years old, drug user, seropositive for HIV, showing ulcerated lesion on the lateral border of the tongue, crater form, with *whitish* periphery and diffuse infiltrate. Clinical and laboratory investigations diagnosed histoplasmosis, disseminated and pulmonary damage. It should be pointed out that histoplasmosis is indicative of AIDS



Fig. 10.62 Female patient, housewife, 61 years old, monogamous, HIV positive, showing irregular and ulcerated, hardened, *whitish* lesion with a crater form and high edges located in the anterior lingual belly. The lesion was biopsied and the histopathological examination, using special colors like the PAS stain method and Grocott-Gomori silver methenamine showed *Histoplasma capsulatum* yeasts features. It is important to emphasize that the patient was a breeder of pigeons and other birds, which are a source of histoplasmosis contamination



Fig. 10.63 The same patient seen in previous Figure, showing a large crater form irregular ulcer with granular surface, *white-red* color, located on the *left* side of the jugal mucosa, whose appearance simulates the squamous cell carcinoma



Fig. 10.64 Male patient, 42 years old, HIV positive, smoker, showing extensive high edges and hardened crater form ulcer, fixed to the underlying structures and painful. The submandibular and submental lymph nodes were increased, with inflammatory pain and mobility features. The clinical aspect of the injury is quite significant for the diagnosis of squamous cell carcinoma. However, histopathological results from biopsy demonstrated the formation of granulomas with limited collections of epithelioid histiocytes, lymphocytes, and multinucleated giant cells with central caseous necrosis. The special Ziehl-Neelsen staining facilitated the identification of *Mycobacterium tuberculosis hominis*. Sputum culture confirmed tuberculosis



Fig. 10.65 Front view of the patient described previously, showing in lymph nodes volume increase and submandibular and submental chain (*arrows*)



Fig. 10.66 Male patient, 57 years old, HIV carrier for 12 years, smoker, showing ulcerated lesion of high edges, permeated by leukoplastic areas in the periphery, showing *bottom* with necrotic material, painless and attached to underlying structures. Biopsy was made and the histopathological examination showed an intense inflammatory infiltrate; however, in the opposite region epithelium changes were observed with atypical dysplastic figures with nuclear and cytoplasmic aberrant changes, loss of epithelium relationship with connective tissue and tissue invasion areas. In the conjunctive, intense proliferation of vessels characterized the process of angiogenesis. The diagnosis of squamous cell carcinoma was conclusive. It should be pointed out that HIV infection does not constitute a direct cause of squamous cell carcinoma, however, immunodeficiency seems to facilitate the main carcinogenic factor represented by the tobacco



Fig. 10.67 Traumatic lesion forming petechiae on the junction of the hard palate with the soft palate, resulting from fellatio practice. In this case, the differential diagnosis must be made of infectious mononucleosis and *Streptococus* bacterial infection. Regarding this lesion, we should pointed out that the examiner should still consider the possibility of mechanical trauma by sharp aliments or episodes of persistent and intense cough capable of rupturing terminal capillaries



Fig. 10.68 Ulceration in the oral floor caused by the practice of cunnilinguism. Irregular and sharp edges of anterior teeth are observed. The differential diagnosis of mouth ulcers causing diseases such as syphilis or herpes should be established. It should be emphasized that the immediate cicatrization of mouth ulcers are important, because they allow the transmission of various infections, including, among the most important, the viral hepatitis and the HIV itself, when the mouth is used as an organ of sexual practices



Fig. 10.69 Severe infectious process, purulent, bacterial in HIV-positive patient, whose diagnosis was made recently. The patient was not yet in use of antiretroviral therapy



Fig. 10.70 Fourteen-year-old patient, first pregnancy, in the 26th week of pregnancy, showing, in addition to HIV seropositivity, (a) Scabies, (b) genital herpes, (c) gonorrhea and VDRL-positive





Fig. 10.71 (a) Patient assisted at the STD Sector of Fluminense Federal University—UFF with manifestation of painful and itchy genital lesions for several months. Reported to be HIV infected with irregular use of HAART, without viral load tests and lymphocyte count. Material for smear cytology and biopsy in areas (*a, b*) of the lesion was collected.(b) Photo and video on 01/24/2011 showing discreet recovery of the lesions. Patient reported sensitive improvement of local symptoms like pain.(c) Photo and video on 02/11/2011 showing the aggravation of genitals lesions. The result of the cytology and histopathology was squamous carcinoma. We are convinced that this case could have been diagnosed and treated early. The delay in warning postponed the convenient service. The patient was transferred to a specialized cancer service (Instituto Nacional de Câncer-INCA, Rio de Janeiro)



Fig. 10.71 (continued)



Fig. 10.72 Patient assisted in the STD Sector of UFF with this genital manifestation. Genital herpes was an interrogation, especially because there were reports of recurrent sores on genitals, which healed in a week. Patient had even received oral acyclovir by medical prescription. The serology for syphilis and HIV were not reactive. The patient returned 2 weeks later complaining of general malaise, evening fever and myalgias. Generalized lymphadenopathy was identified. New tests were requested and the HIV serology proved positive this time. These symptoms of cutaneous mucous rush happen in all diseases related to viremia. Concerning HIV, it is known as the first viremia. Therefore, it is evident that a second serology must be requested when the first one is non-reactive in cases of genital lesions



Fig. 10.73 Erythema nodosum in seropositive HIV patient



Fig. 10.74 Seropositive HIV patient with extensive symptoms of pityriasis versicolor



Fig. 10.75 (a) Patient with AIDS showing extensive manifestation of scabies. In such cases, the CD4 count is hardly above 400. (b) Note the extensive commitment by lesions of scabies in humid folds area, such as the backside



Fig. 10.76 Patient with AIDS showing important involvement of onychomycosis on every finger



Fig. 10.77 Ulcerated lesion in the dorsal region, as first manifestation of Paracoccidioidomycosis in a patient with AIDS



Fig. 10.78 (**a, b**) Female patient, 24 years old, HIV-positive for 18 months, without use of antiretroviral drugs, showing papule bullous lesions on the face and on the oral mucosa, besides gummous lesions in

the skin of the arm. The VDRL result was 1:64. This symptom is called malignant syphilis, whose cutaneous lesions are intensely populated by treponemas, therefore quite infectious

Fig. 10.79 (a) Perianal lesions of genital ulcerating herpes, with purulent secondary infection in HIV-positive patient. We emphasize once again the need to investigate immunosuppression in persons with a symptom like this one. (b) Similar to the previous manifestation, only sex change. Both patients had sought previous medical aid, but only antibiotic was prescribed, without improvement



Fig. 10.80 Fourteen-yearold patient with severe herpes simplex symptom accompanied by secondary bacterial infection in genital (a) and inguinal region lesions (b)



Fig. 10.81 Thirty-year-old patient, HIV positive, referred for treatment of condilomatous lesions in the vulvar region. Physical examination revealed papular lesions of varied sizes with central umbilication distributed in the large lips, pubic area, perianal, inguinal folds and gluteal region (a). Clinical diagnosis was of Molluscum contagiosum. Lesion was biopsied and the histopathological report revealed infection compatible with Molluscum contagiosum $(HE \times 40)$ (**b**). Topical treatment started with imiquimode, 3 times a week, and an important decrease in the number of lesions was observed (c) one month after the beginning of the treatment



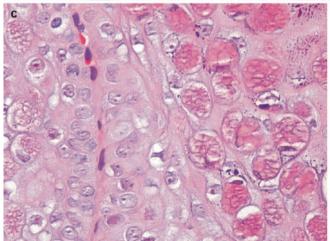






Fig. 10.82 (**a, b**) Twenty-five-year-old patient, reporting history of several episodes of genital herpes. Five years ago noticed the first manifestation of vesicles. Made numerous topical treatments with thuya and acyclovir. Three months ago noted minor warty lesions in penis that quickly increased in number and size. Also informed that about 20 days ulceration in the penis emerged and that, unlike the previous times, there was a lot of pain. Penicillin benzathine and sulfa were prescribed. to use for just 1 week, due to little improvement. He sought new medi-

cal care, and tetracycline was prescribed. Not feeling better in 4 days, he was transferred to a specialist service in STD. During anamnesis reported that at no time was asked about partners, condom use or serologic testing for syphilis and/or HIV. Tests proved positive for syphilis (VDRL 1:128), genital herpes, *Condyloma acuminata*, hepatitis B and HIV. One partner was examined and only syphilis was diagnosed (papular lesions in the vulva and VDRL 1:64)



Fig. 10.83 Patient with AIDS showing white superficial onychomycosis. Dermatophytosis in wrist can also be observed

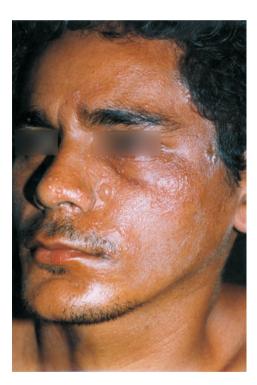


Fig. 10.84 Patient showing initial symptom of herpes zoster, which can be confused with contact eczema. If not treated properly, could evolve into permanent and unaesthetic scars



Fig. 10.85 Kaposi's sarcoma lesions in a patient with AIDS at an advanced stage



Fig. 10.87 Hyperpigmentation of nails due to prolonged use of AZT

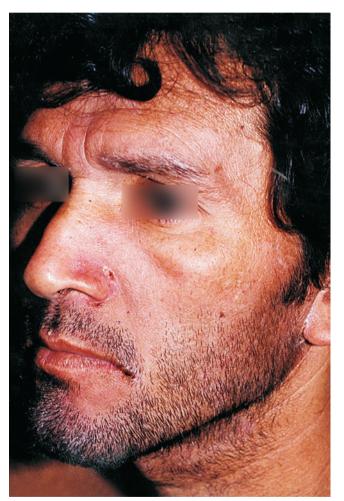


Fig. 10.86 HIV-positive patient with chronic diarrhea and weight loss. Showing cheilitis, pyodermitis and seborrhoeic dermatitis



Fig. 10.88 Gonococcal urethritis in a patient with AIDS. It should be noted that HIV-positive patients with urethritis have a higher viral load of HIV in semen compared to those who do not have such intercurrence



Fig. 10.89 Patient with AIDS in use of HAART irregularly assisted in the STD Department of UFF with extensive HPV condyloma resistant to numerous treatments

Fig. 10.90 Patient of 22 years of age with AIDS, undergoing treatment with antiretroviral drugs and viral load above 70,000 copies. Patient shows this extensive condylomatosis for more than 6 months, with no results for conventional treatments





Fig. 10.91 Patient of 28 years of age with AIDS, showing lesions of Condyloma acuminatum resistant to various treatments



Fig. 10.92 HIV positive patient showing hyperchromic papules with well-defined borders located in the body of the penis. The biopsy was suggestive of HPV infection



Fig. 10.93 (a) HIV positive patient, sex worker, with <200 CD4 cells and viral load of 560,000 copies/mL. Despite the diagnosis of infection for more than 6 months, was not in use of antiretrovirals, had sex daily and never wore a condom. Reported recent treatment (8 months) for

tuberculosis ganglia. Presented lesions of *Molluscum contagiosum* and *Condyloma acuminata*. (b) Another AIDS patient with lesions of difficult treatment due to HPV infection



Fig. 10.94 (**a, b**) Patient showing cutaneous lesion with 3 months of evolution besides weight loss and diarrhea. The border with gelatinous aspect is clinically suggestive of cryptococcosis. The diagnosis is by direct examination, imprint and histopathology with Grocott stain and Alcian blue

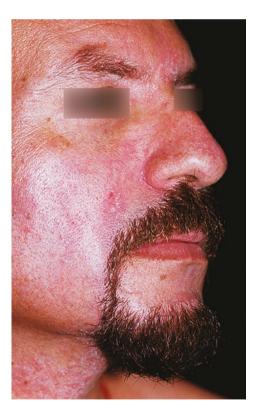


Fig. 10.96 Classic manifestation of oral candidiasis in AIDS patient

Fig. 10.95 Profuse symptom of seborrhoeic dermatitis in HIV positive individual



Fig. 10.97 Extensive symptom of disseminated herpes zoster in immunosuppressed patient by HIV



Fig. 10.98 Patient with AIDS showing Kaposi's sarcoma simulating melanoma in the plant of the heel region





Fig. 10.99 Thirty-three-year-old woman, housewife, was admitted to the hospital complaining of fever, weakness, prostration, chest pain, non-productive coughing, dysuria and significant weight loss. Reported that about approximately 6 months ago noticed vaginal discharge and genital ulcers. In the last 3 months has evolved into evening fever and other charges described above. The quick test for HIV was positive and the serological non-treponemal reactor test (1:8). The VDRL of liquor was non-reactor. Clinically showed candidiasis in oral cavity, papular lesions with central umbilication in pubic area (a), vulvar ulcers (b) and nodular lesion in region of great right lip of the vulva (c). The research of *Treponema pallidum* in vulvar ulcers was positive. Pubic lesion biopsy revealed *Molluscum contagiosum*. However, the biopsy of the nodular lesion suggested Kaposi's sarcoma. Medicated with penicillin G benzathine 7,200,000 IU IM and antiretroviral scheme (lamivudine, stavudine and efavirenz) patient evolved with improvement of clinical condition



Fig. 10.99 (continued)



Fig. 10.100 HIV positive patient showing, as in the case of Fig. 10.93, lesions of persistent *Condyloma acuminata*. Recurrence of HPV lesions after treatment is common, particularly when the patient has aids

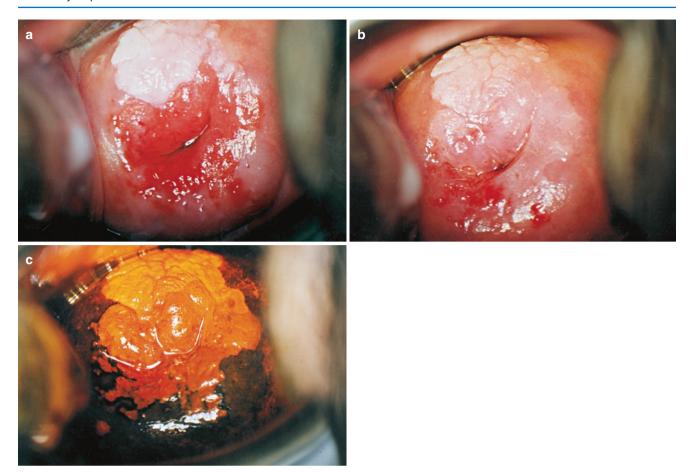


Fig. 10.101 (a–c) HIV positive patient, still without antiretroviral medication, was referred for routine gynecological evaluation. It is possible to observe an important area of leukoplakia in the cervical anterior lip and thick acetowhite epithelium mainly in the posterior lip. In (c),

the negative iodine appearance in the lugol's test. The histopathological examination revealed high-grade squamous intraepithelial lesion (HSIL)



Fig. 10.102 HIV positive patient, forwarded to gynecological routine examination. Although the initial Pap smear was just an inflammatory process, biopsy was performed on the commissure of the left lip due to major colposcopy changes, where it is evident the irregular mosaic condition and thick acetowhite epithelium. The histopathological diagnosis was of high-grade squamous intraepithelial lesion (HSIL)

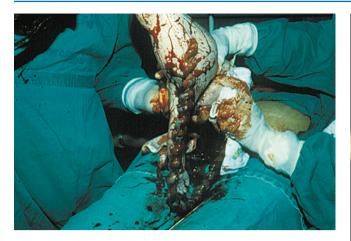


Fig. 10.103 This photograph shows a c-section with a lot of blood during the procedure. There must be the utmost care with the hemostasis in a surgery like this, because in addition to the biosecurity of the surgical team, it is possible to occur greater contamination to the fetus. We have heard from obstetricians that the faster the surgery is finished, the better for the team, because it solves the problem. This is a serious mistake, because if the hemostasis is not associated with fast movements, it is easier for accidents to occur. For the fetus, the great contact with the maternal blood would also facilitate the transmission. Antivirals, mainly AZT in childbirth, should not be forgotten

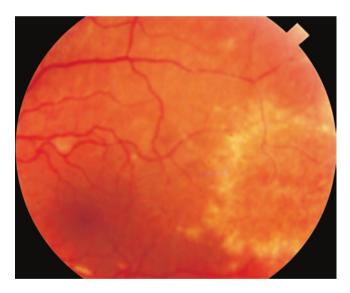


Fig. 10.104 Cytomegalovirus retinitis, granular type, in AIDS patient

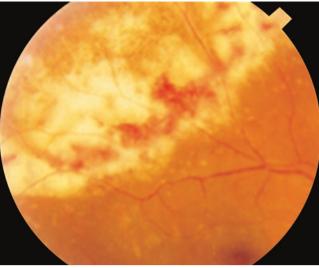


Fig. 10.105 Cytomegalovirus retinitis, hemorrhagic edematous type, in AIDS patient

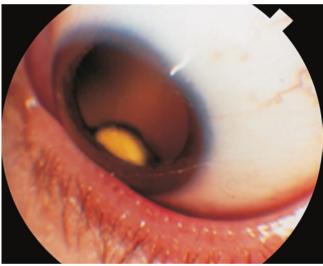


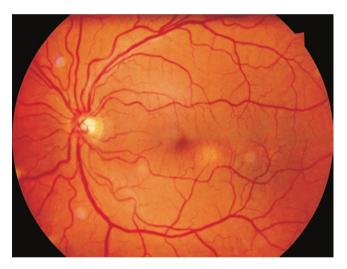
Fig. 10.106 Ganciclovir intraocular implant in AIDS patient



Fig. 10.107 Multifocal choroiditis associated with papilledema in patients with disseminated cryptococcosis



Fig. 10.109 Patient with aids showing conjunctival Kaposi's sarcoma



 $\begin{tabular}{ll} Fig.~10.108 & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and AIDS & Choroidiano nodule in patient with miliary tuberculosis and miliary tub$



Fig. 10.110 HIV positive patient, VDRL 1:32 reactor. Ulcerated lesion of hardened edges with 2 weeks of evolution; presence of inguinal adenoma hypertrophy with serous drainage of serous secretion.

Medicated with azithromycin 500 mg/day, for weeks, because at that time (2014) there was no supply of penicillin



Fig. 10.111 Patient with previous history of lesions in the anal area (note the scars), evolving to chronic lesion of exophytic growth. Laboratory tests concluded the diagnosis of HIV+ and hypertrophic herpes



Fig. 10.112 Similar to the previous cases of hypertrophic herpes in patients with aids without adherence to treatment, maintaining low levels of CD4+



Fig. 10.113 Sixty-four-year-old woman, HIV positive seeked emergency service due to multiple painful ulcers in the genital area. The lesions appeared 35 days ago and were treated with topical and systemic antibiotic therapy, without response. Definitive diagnosis was genital herpes and she was given intravenous acyclovir. Patients usually do not respond satisfactorily to the HSV oral medication



Fig. 10.114 Twenty-six-year-old patient, HIV positive, presents ulcerated vulvar lesion for 60 days, with intravenous antibiotics without success. Biopsy showed a chronic inflammatory process. Full resolution with 30 days of intravenous acyclovir. After collecting new lesion material and cytologic analysis, the diagnosis was of genital herpes. Usually, the assistance physician has the urge to medicate patients with antibiotics in these cases. It is worth remembering that basic research with cytology may provide opportunities for the correct diagnosis

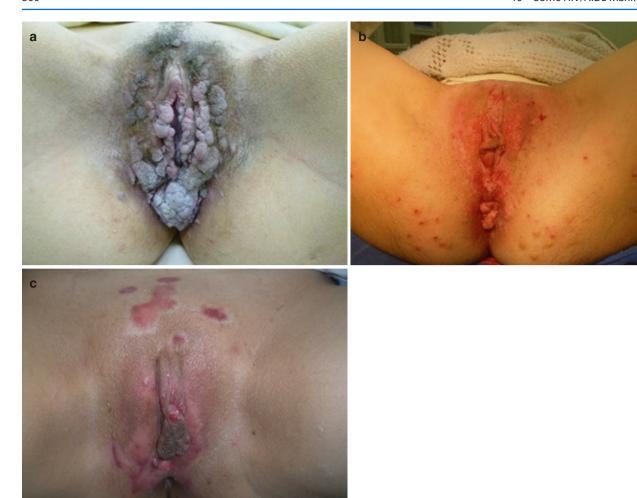


Fig. 10.115 (a) Patient with 20 years of age, HIV infected by vertical transmission. Irregular use of antiretroviral medication for the last 5 years. Six months ago presented extensive anogenital condylomatosis unresponsive to traditional treatments. Surgical treatment and supple-

mentation with topical medications were carried out. Patient was submitted to surgical treatment. (b) Photo after 45 days of surgery. Patient presented recurrence, treated with trichloroacetic acid and imiquimod (c)

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 Accessed 15 Feb 2017.
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Medical schools generally employ teaching and learning methods based on a series of summaries of the signs and symptoms that characterise each individual disease. With these they list a set of laboratory exams that are used to confirm diagnosis.

The super-specializations that are often excellent in bringing about technical and scientific improvement generally employ an arsenal of techniques that use cutting-edge technology, meaning that a doctor's knowledge acquired just 5 years previously can quickly become "outdated".

In addition, with globalization modern-day doctors are expected to recognize molecular biology exams as being the "ultimate" diagnostic tool.

However, this progress in automated technological exams is overtaking the basic practice of accumulating simple and structured basic knowledge involving low costs, small or almost non-existent side effects and the capacity to solve problems using reasoning and the integration of clinical facts with the medical history.

Obviously these exams are welcome and are necessary in order to bring about medical improvements. However, they are often used or interpreted incorrectly, leading to huge errors. The fact that these are often sold as foolproof worsens the situation. This is because the discovery of microorganism DNA in a certain body part or wound does not prove that it is the cause of the problem for that particular individual.

Various studies have indicated, for example, that research into genetic material using PCR can provide a false positive/false negative result in up to 4% of cases. Imagine your PCR results being positive (when they should be negative) for an STD, or the contrary.

As a part of routine practice, how many of our colleagues have access to bacterioscopy using the Gram technique (over 100 years old!), direct examination for *Trichomonas* (also available for over 100 years), serological screening for syphilis (also available for 100 years; Wasserman was already carrying out this exam in 1906), cell cultures for *Neisseria*, cytology using the Papanicolaou technique, histopathology

using paraffin blocks stained with hematoxylin-eosin, which can provide primary results at the time of consultation and others in up to a week?

Technically, all of these exams are very cheap and are historically very reliable. They are not foolproof, however, in terms of both the techniques and the technician.

On the other hand, how many of our colleagues know the epidemiology of STDs in their respective areas? What are the most prevalent STDs in their practice, clinic, health centre, city, state or in the country as a whole? What is the epidemiological pattern (if there is one) of the patient for each pathology?

We all have a lot of difficulty answering these questions. We shouldn't, because this data at a medical service level is not difficult to find. Appointment records can be tabulated, not necessarily with all of the variables but with basic data (syndrome, disease, normal results, gender, age, number of partners, level of education, condom use, contraceptive method), using a pencil, pen, paper and calculator.

Knowing simple data such as that cited is fundamentally important for planning prevention strategies, the provision of medication and other supplies for consultations, training and adequate staffing.

Therefore, we hope to progress to a mindset in which the discussion of cases and the exchange of clinical experience within health centres will generate new ways of teaching and learning, where problems and solutions are dealt with directly in the workplace. The benefits are enormous for healthcare teams and particularly for the patient.

Differential diagnosis is involved in all of these basic issues, both historically and now with more sophisticated modern technology. Using this together with common sense and intuition, both of which should be integral to all human activity, could increase the success of our consultations and significantly reduce human suffering, whether physical, emotional, social or economic.

In summary, we have long been trying to disseminate the following:

When seeing a patient with a suspected STD, perhaps it would be easier or more informative to recommend **what should NOT be done**:

- Maintain any kind of prejudice against sexuality, skin colour, level of education, social-economic and cultural level, profession, religious beliefs, neighbourhood, place of birth, etc.
- Diagnose and treat based on assumptions without investigating basic epidemiological, clinical and laboratorial data.
 Not everything found in the genital region is sexually transmitted. On the other hand, extra-genital signs and symptoms may (co)exist with an STD, particularly syphilis and HPV.
- Neglect to ask the patient to reflect on the situation and not provide basic information on the problem.
- Adopt a judgemental attitude (make judgemental comments about the patient and/or the case in question).
- Ignore the emotional and existential aspects of each case.
- Neglect to use the consultation as an opportunity to begin/ expand on the patient's education in health/prevention of other health problems. For example, try to obtain the patient's vaccine history (hepatitis B, hepatitis A, HPV, tetanus, 'flu, etc.).
- Avoiding, delaying or feeling embarrassed to ask the opinion of colleagues for cases that are chronic, recurring or resistant to previous treatment, especially but not restricted to situations in which a diagnosis has not been fully established. The wellbeing and full recovery of the patient is cardinal, not the doctor's "knowledge".
- Overvaluing publications on cost effectiveness. These are generally carried out in environments that are very different to those where most STD professional work is carried out, which are usually public health centres. Although general overviews are valid, medical practice should be personalised.

At least for us, quantifying the value (and wellbeing) of the people that we treat (and their families) is something that we are not able to do. This is not one of our objectives.

The great majority of actions that have caused and still cause a huge impact on large groups of people started with individual decisions and attitudes. Some examples include: the discovery of the tubercle bacillus, the discovery of penicillin, the proposed law obliging the Brazilian government to guarantee antiretroviral treatment within the public health system, the Australian government's free provision of vaccination programs against HPV for women and girls up to the age of 26 since 2007 and for young men in 2014, etc.

11.1 Hepatitis B

11.1.1 Synonyms

Viral hepatitis, chronic hepatitis, HBV, HB.

11.1.2 Concept

This is an infectious contagious viral disease that is systemic, and principally hepatic, transmitted parenterally, vertically (from the mother to the foetus), through sexual contact, blood transfusion, by accident via contaminated sharp objects, injection drug use, piercings and tattoos, the transplant of infected organs and occasionally via the faecal-oral route.

The World Health Organization (WHO) estimates that there are two billion cases of this across the world, with 400 million chronic cases. The rate of this disease becoming chronic varies from 5 to 10%.

11.1.2.1 Incubation period

Four weeks to 6 months (average of 12–14 weeks).

11.1.3 Etiologic Agent

The hepatitis B virus (HBV) is a 42 nm partially double stranded DNA hepadnavirus. It has a central part called the core (HBcAg), in which the nucleic acid of the virus, a DNA-polymerase enzyme and another purified fraction, antigen E (HBeAg), can be found. The core is covered by the surface antigen (HBsAg), which is important for the production of vaccines. HBV has universal dispersal, with a higher prevalence in the tropics and in developing countries.

11.1.4 Clinical Manifestations

Most symptoms appear during the acute and viral replication phase. There is a **prodromal or preicteric period**, that lasts between 3 and 5 days and is characterised by systemic symptoms such as asthenia, headache, nausea, vomiting, diarrhoea or constipation, a fever below 39.5 °C, pain in the right hypochondrium (caused by hepatomegaly and simulating cholecystitis or cholelithiasis), and may also present lymphadenopathy (mainly cervical and epitrochlear), splenomegaly, cutaneous rash (erythematous papular, mainly on the

trunk), myalgia, polyarthralgia and polyarthritis, respiratory problems (coryza, pharyngitis and interstitial pneumonia), as well as loss of desire to smoke associated with anorexia. Glomerulonephritis, nodose polyarthritis and papular acrodermatitis may also occur.

The **icteric period** then follows, which can last from 8 to 15 days and can involve acholic stools and choluria as a result of cholestasis. Around 70% of patients do not present icterus and are asymptomatic/oligosymptomatic. A **convalescence period** then follows, which can last up to 4 months and includes a progressive improvement in symptoms and laboratorial abnormalities until the patient is fully cured. On the other hand the disease may progressively worsen, characterizing fulminant hepatitis, which when lasting for more than 6 months indicates chronic illness.

11.1.5 Laboratory Diagnosis

This can be carried out via non-specific blood tests—blood biochemistry tests that show increases in bilirubin and aminotransferases, hypergammaglobulinemia, prolonged prothrombin time (TP), hypoglycemia and other common complications associated with hepatitis. Hemograms can be used with leukopenia and lymphocytosis, mainly during the preicteric phase.

Specific tests are based on screening for serological markers caused by infection by the B virus (antigens and antibodies) or on histopathology exams of liver biopsies and screening for HBV-DNA using PCR. We check for HBsAg, anti-HBs and anti-HBc (IgG and IgM) in initial screening, according to the following definitions:

Acute hepatitis: Diagnosis of acute hepatitis B is based on the detection of HBsAg and anti-HBc IgM. During the initial phase of infection, HBV, HBeAg and HBV DNA replication markers are also present. Recuperation is associated with the disappearance of HBV DNA, sero-conversion of HBeAg into anti-HBe and then seroconversion of HBsAg into anti-HBs.

Past HBV infection: previous or resolved HBV infection ("cure") is characterised by the presence of anti-HBs and anti-HBc IgG. Today we know that even in people considered to be cured there can be reactivation, mainly in patients with immunosuppression.

Immunity to HBV infection after vaccination: is indicated by just the presence of anti-HBs.

Chronic HBV infection: Diagnosis of chronic infection is based on the persistence of HBsAg for over 6 months. Additional tests to detect the replication of HBV— HBeAg, anti-HBe and HBV DNA, sometimes through liver biopsy—should be carried out to determine if the patient is in the replicative phase and can be recommended antiviral therapy. Patients are considered to be non-replicative, have low levels of replication or be inactive carriers when they present negative results for HBeAg and positive results for anti-HBe. HBeAg-negative patients with elevated levels of ALT should be tested with HBV DNA to determine if they have chronic hepatitis with precore mutations. It is important to remember that intermittent reactivations/exacerbations of the disease can occur, mainly in patients with immunosuppression. This is characterised by necroinflammatory effects: an increase in transaminases over 10 times the normal upper limit and two times the baseline value; or new histopathological alterations.

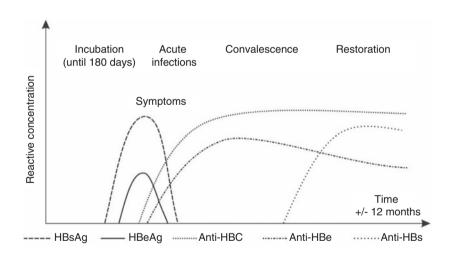
Occult HBV infection: There is a subgroup of patients that have occult HBV infection, defined as the presence of DNA HBV detected using PCR in patients that are HBsAg negative. These patients have been subclassified as "seropositive" or "seronegative", depending on whether they test positive or negative for other markers, most commonly anti-HBc. The majority of these patients have very low or undetectable levels of HBV DNA, which is why HBsAg cannot be detected. Mutant HBV infections that reduce HBsAg production or present mutations to the S gene that escape detection in serological screening for HBsAg are rare. Occult HBV infection has been associated with chronic liver disease and hepatocellular carcinoma.

Isolated anti-HBc positive: The isolated presence of anti-HBc, with no HBsAg or anti-HBs, can be found in 0.4–1.7% of blood donors in areas of low prevalence and from 10 to 20% in endemic countries. This can occur in the following situations: false positive (most common in areas of low prevalence—50 to 80%); during the window in acute hepatitis B when anti-HBc is predominantly of the IgM class; many years later the recuperation of acute hepatitis B when anti-HBs fall to non-detectable levels; and after many years of chronic HBV infection when HBsAg titers reach a level blow which they cannot be detected; HBV with mutation of the S gene. The loss of detectable HBsAg occurs in around 0.5% of patients with chronic hepatitis B per year.

Fig. 11.1 Interpretation of markers for hepatitis B

Interpretation of Serological Markers for Hepatitis						
HBsAg	Anti-HBs	Anti-HBc	HBeAg	Anti-HBe	Interpretation	
+ o r –	-	IgM	+ o r –	-	Acute phase	
+	-	IgG and IgM	+	_	Chronic phase with viral replication/reactivation	
+	-	lgG	_	+	Chronic phase with viral replication or high replication with precore or core mutation	
+	+	lgG	+ o r –	+ o r –	Chronic phase with Anti-HBs + (10-24% of cases)	
_	+	lgG	-	+ o r –	Immunological protection (cure)	
_	+	-	-	-	Vaccination	
_	_	lgG	_	_	False positive. Exceptions: See specific item above	

Fig. 11.2 Principal markers of hepatitis B infection and their serological expressions



Evaluation of Laboratory Methods

Exam	Sensitivity %	Specificity %
HBsAg	90	92
PCR	90	90

11.1.6 Treatment

In the acute phase, treatment basically consists of support: the objective is the fastest recuperation of hepatocytes through rest, maintaining homeostasis, correcting metabolic and electrolytic disturbances, diet and symptomatic medication (avoid sedatives, diuretics and tranquilizers). Drinking alcohol is prohibited. In case of intense pruritus use anti-histamines. Antiviral treatment is recommended just for acute hepatitis B with prolonged development; in cases of ascites, accentuated icterus/cholestasis and persistent or extrahepatic manifestations; in fulminant hepatitis; in candidates for liver transplant. The regular use of corticosteroids is not recommended.

In the chronic phase, an increasing range of medication is available: interferons, lamivudine, tenofovir, adefovir,

entecavir, telbivudine and other experimental drugs, as well as liver transplant. The duration of this can last from weeks to months. There are a range of therapeutic regimens, which vary according to the degree of severity, comorbidities, viral genotype and the local protocols of each country.

Active immunization (vaccine) should be carried out over three intramuscular doses (deltoid), the first within the first 12 h of life, in maternity, the second after 1 month and the third at 6 months. Adults are vaccinated in the same way (0, 30 and 180 days). Loss of dose does not mean the course has to be restarted.

A positive immunological response to the vaccine is defined as the development of hepatitis B surface antibodies (anti-HBs) at titers above 10 mIU/mL 1-3 months after the final dose. This is not recommended as a routine dose, as a response is observed in 95% of healthy vaccinated people. This is indicated for groups of people with a high risk of exposure to HBV and with immunosuppression: health professionals, homosexuals, sex professionals, partners of HBV carriers, HIV carriers, patients undergoing haemodialysis, etc. Those who do not respond should complete a second three-dose course of the vaccine. The second course is successful in around 50-70% of patients. Another approach is vaccination using a double dose, mainly in patients with immunosuppression. The regularity of this test is controversial, but it is recommended that this be carried out annually for those with chronic renal failure undergoing haemodialysis.

The need for reinforcement is also controversial. Those that benefit from this are those in which there is an indication of anti-HBs titration, as described above. In high-risk individuals (for example, health professionals), regular tests of anti-HBs levels and the use of an extra dose, where necessary, may be necessary in order to maintain immunity. Recommendations vary from country to country and from health service to health service.

Passive immunization (hyperimmune immunoglobulin—0.06 mL/kg of weight) must be carried out (even in pregnant women) up to 48 h after accidental exposure or up to 14 days, in cases where exposure is through sexual contact, and repeated after 30 days.

Concomitant vaccination should also be used according to routine dosage (use different muscular groups).

There is a range of new vaccines that have already been launched or that are being developed to improve immunogenicity and/or the convenience of administration: recombinant derived from mammal cells with antigens from the pre-S region; the combination of antigens S and C with intranasal administration; and vaccine combined with an adjuvant, such as a hepatitis A or HBV-ISS vaccine.

11.1.7 Therapeutic Protocols

We recommend the regular consultation of the some guidelines [1–4].

11.1.8 Complications

Fulminant hepatitis (0.1-1% of cases) with a mortality rate of 60%.

Chronic disease (1 to 10–90% in newborns), developing into cirrhosis of the liver or hepatocellular carcinoma in 25–40% of cases.

11.1.9 Vertical Transmission (VT)

Seroprevalence in pregnant women seen in the public health system can vary a lot. In Brazil this figure is around 1%.

Pregnant women with acute or chronic HB should be seen by an obstetrician and a clinical professional (a haematologist, gastroenterologist or infectologist).

HBsAg and HBeAg-positive pregnant women that do not receive immune prophylactic intervention present a 50–80% probability of vertical transmission (VT). In cases where the HBeAg marker is negative, the VT rate is around 10 times lower.

HB is the only viral hepatitis until today that is responsive to prophylaxis for VT (in both acute and chronic infections) if immunoprophylaxis is carried out adequately in both the mother and the newborn. Pregnant women with acute HB present increased rates of preterm labour, premature births and intrauterine growth restriction.

During hospital internment, good practice dictates that pregnant women infected with HBV (principally acute infections) are provided with individual and sanitary accommodation, just as attention to biosafety precautions should follow the same standards as for HIV infection.

The method of delivery should follow obstetric conditions and procedures that are invasive to the foetus should be avoided. The umbilical cord should be clamped as quickly as possible. In addition, the maternity team (perinatologists) should be aware of the mother's infection in order to know what conduct to use with the newborn.

11.1.10 Differential Diagnosis

Other viral hepatitis, protozoan, bacterial, fungal, druginduced and alcoholic hepatitis; diseases of the gall bladder and the pancreas.

Remember that there may be a coinfection/superinfection of hepatitis B with other forms that have become chronic: **hepatitis C and hepatitis D**. The main differential diagnosis, however, is with hepatitis C, estimated to occur in 250 million of the world's carriers, 25% of these experiencing a progression to the symptomatic form of the disease. This disease has a prevalence of 15–20% in North American homosexual men. Detection of HCV-RNA is carried out using PCR 3 weeks after contact with the HCV virus, while anti-HCV antibodies can only be detected after 3 months.

11.1.11 Observations

- Negative results for all markers: do not hesitate to prescribe a course of vaccines against hepatitis B. Many professionals forget to do this.
- Vaccines contain subunits and are genetic recombinants with HBsAg as an antigenic source (they present no risk to pregnant women or patients with immunosuppression).
- Do not hesitate to carry out serological screening of family members, especially for the sexual partner of the person with HBV.
- Safe sex using a condom (male or female) is imperative when one of the partners has HB.
- In countries with a high prevalence such as South Africa, Brazil, China, India and Russia (and many others) serological screening is recommended for all pregnant women whose serological and HBV vaccine status are unknown.

11.2 Scabies

11.2.1 Synonyms

Seven-year itch

11.2.2 Concept

Parasitic infestation of the skin caused by a mite. Transmission occurs predominantly through close contact with an infected person, and infection through clothes is rare. Sexual transmission of scabies is a possibility. It is a worldwide disease that is endemic in developing countries and cyclic in developed countries, with no preference according to gender, race or age and affecting all socioeconomic classes.

11.2.3 Incubation Period

The female creates a habitat by digging a tunnel into the skin. The male does not invade the skin and dies after mating. For 15–30 days, the female deposits from 40 to 50 eggs in the subcorneal tunnel and then dies. The biological cycle of the egg lasts for 2 weeks. Therefore, symptoms are expected to occur 3–4 weeks after infectious contact.

11.2.3.1 Etiologic Agent

Sarcoptes scabiei, variety hominis, is an arthropod from the Sarcoptidae family. It is difficult to visualize with the naked eye, has an oval-shaped body and its colour varies from grey to yellowy-brown, marked by parallel transversal grooves; it

has four pairs of legs and various setae and spines. This mite can survive for up to 2–3 days in warm humid environments, increasing the potential for indirect transmission. *Sarcoptes* is species specific, with transmission from domestic animals (dogs, cats, pigs, horses, etc.) to humans occurring occasionally, not progressing to other individuals.

11.2.3.2 Clinical Manifestations

Itching, particularly at night, is the principal symptom. This occurs as a result of the parasite tunnelling through the skin and/or through sensitivity to the components of *Sarcoptes*. Lesions are most commonly found on the vesicopapules and the papules, mainly located on the abdomen, buttocks, flanks, thighs, between the fingers, in the underarms and breasts. The pathognomonic lesion is represented by the scabies burrow, which is normally winding and measures between 5 and 15 mm with a vesicle at the end (protrusion of the mite). Abrasions, pustules and nodules may also be observed (more on the genitals and covered areas).

Crusted or Norwegian scabies occurs with the presence of numerous mites and in individuals with immunosuppression or who are malnourished or infected by the HTLV-1 virus. This manifests as stratified crusts, mainly on the bony protrusions and extremities. This form is very contagious. Itching may be discreet or absent.

11.2.4 Laboratory Diagnosis

Screening for the mite and its eggs must be carried out using scarification, shaving or curettage of the lesion, particularly the mite protrusion; dilute the material in mineral oil and identify the mite using an optical microscope. Triangular structures that seem to be "hang gliding" can be seen through the dermatoscope. Biopsy with a punch of 2 mm may reveal the parasite, as well as the eggs in its tunnel, and it may be necessary to take a series of sections from the block.

11.2.5 Evaluation of Laboratory Methods

We could not find any studies containing this data. However, specialist reports state that sensitivity does not exceed 60% but specificity is over 95%.

11.2.6 Treatment and Control of Cure

The topical therapeutic options below are effective and should be applied at night for three consecutive days and repeated after an interval of 1 week. Adults should apply medication to the whole body from the neck down and children under 10 should also apply it to the scalp. A common

error is to apply it just to the areas that are itching. The indiscriminate use of medications should be avoided as this may cause primary irritant dermatitis. In addition, it is not recommended that clothes and bedclothes are washed in boiling water, and these can simply be exposed to the sun or ironed. Concomitant treatment of all close family members is recommended in order to avoid reinfection, even of those who are asymptomatic. Domestic animals are not hosts of *Sarcoptes scabiei*, variety *hominis*, and therefore do not need to be treated.

Itching can be intense in some areas, particularly in the male genital region, and depending on the extent and intensity of this it can be treated with medium to high strength topical corticosteroids or systemic antihistamines in order to provide physical comfort to the patient and reduce the possibility of secondary infections via abrasions.

- Permethrin lotion 5%: there are no controlled studies on the use of permethrin in pregnant or breastfeeding women (risk category B); it is contraindicated in children under 2 months old.
- Deltamethrin lotion 10%: like permethrin this is a pyrethroid, a synthetic substance obtained from the esterification of chrysanthemic acid, which is extracted from the flower of the chrysanthemum (*Chrysanthemum cinerariaefolium*).
- Crotamiton lotion 10%: approved by the FDA just for the treatment of adults and contraindicated in pregnant and breastfeeding women. This drug is less effective than permethrin.
- Monosulfiram 25% in alcoholic solution: this should be diluted in water at a proportion of 1:2 (adults) and 1:3 (children); avoid alcohol for 10 days to prevent the antabuse effect.
- Benzyl benzoate 25%: often irritating and can cause contact dermatitis.
- Lindane lotion (gamma-hexachlorocyclohexane) 1%: a
 neurotoxin that should not be used in children or pregnant
 or breastfeeding women. Its sale has been suspended in
 Brazil and Europe. The FDA considers lindane to be a
 second-line therapy for scabies and lice.
- Precipitated sulphur 5–10%: a paste prepared in water or liquid vaseline; as it is not an irritant, it is used mainly in children younger than 2 months and pregnant women.
- Systemic options include:
- Ivermectin tablets 6 mg: oral treatment for adults and children over 15 kg and 2 years. Contraindicated in pregnant and breastfeeding women. The recommended dose is 200 μg/kg or according to the table: 15–24 kg = ½ tablet; 25–35 kg = 1 tablet; 36–50 kg = 1½ tablets; 51–65 kg = 2 tablets; 66–79 kg = 2½ tablets; >80 kg = 3 tablets. This should be taken as a single dose at night and repeated after 1 week.

11.2.7 Complications

Secondary infections and eczematization of the lesions. In breastfeeding women and patients with immunosuppression this may affect the face, scalp, palms of the hands and souls of the feet, an area where not usually affected in adults.

11.2.8 Differential Diagnosis

Hives, impetigo, syphilitic roseola, drug allergy and other pruritic rashes; crusted scabies can be confused with psoriasis, seborrheic dermatitis and eczema.

11.2.9 Observations

- There is no indication for the concomitant use of topical and systemic treatment for scabies.
- Frequent scabies infection is associated with STDs.
- Patients with AIDS may present atypical clinical manifestations.
- It is important that all family members living in the same house are treated at the same time and that guidance is offered on better hygiene/cleanliness of the home environment (mattresses, quilts, bed sheets...).
- In cases of secondary infection, topical or systemic antibiotics used principally for the treatment of streptococci or staphylococci are required.

11.3 Pediculosis Pubis

11.3.1 Synonyms

Public lice. Crabs.

11.3.2 Concept

Ectoparasitosis known for centuries, and for some this is the most contagious sexually transmitted disease. Mainly transmitted through intimate/sexual contact and occasionally through fomites.

11.3.3 Incubation Period

Although this parasite can take up to 27 days to reach the adult phase and that after fertilization egg laying can begin within around 36 h, symptoms usually start after around 1 week. All of this depends on the number of parasites transmitted and principally on the level of hygiene of the host.

11.3.4 Etiologic Agent

Pthirus pubis. This is an insect from the genus Pthirus and of the suborder Anoplura (sucking lice). It can be seen with the aid of a magnifying glass. Morphologically it has a short head embedded in a cavity in the thorax, and its abdomen, which is larger than the thorax, has six legs. The abdomen has four small elevations with various bristles. Its eggs are elongated and easily attach to hairs.

11.3.5 Clinical Manifestations

The patient's main complaint is intense itching. Urticarial lesions, vesicles or pigmented macules (bluish = cerulean macules) may be observed as a reaction to the saliva and/or anticoagulant that the parasite injects into the dermis while it is feeding. Historically this was the transmitter of endemic typhus and trench fever, as it can transmit rickettsia and borreliosis. The parasite can affect the pubic area, underarms, beard and eyelashes.

11.3.6 Laboratory Diagnosis

Removal of hairs and examination under a microscope to identify the adult insects or viable eggs. In more serious infestations the parasite can be seen with the naked eye.

11.3.7 Evaluation of Laboratory Methods

We could not find any studies containing this data.

11.3.8 Treatment and Control of Cure

Topical and systemic treatments follow the same application criteria used for scabies. Sexual partners should be evaluated and treated at the same time.

- Permethrin lotion 5%
- Malathion lotion 0.5%
- Benzyl benzoate lotion 25%
- Lindane lotion (gamma-hexachlorocyclohexane) 1%
- Solid vaseline: used to remove lice from the eyelashes; apply twice a day for 8 days.

- Ivermectin tablets 6 mg: oral treatment for adults and children over 15 kg and 2 years. Contraindicated in pregnant and breastfeeding women. The recommended dose is 200 μg/kg or according to the table: 15–24 kg = ½ tablet; 25–35 kg = 1 tablet; 36–50 kg = 1½ tablets; 51–65 kg = 2 tablets; 66–79 kg = 2½ tablets; >80 kg = 3 tablets. This should be taken as a single dose at night and repeated after 1 week.
- Trichotomy or physical removal of eggs attached to hairs using a fine comb.

11.3.9 Complications

Secondary infection and eczematization (rare) in very serious cases and infestation of the eyelashes, which may cause blepharitis.

11.3.10 Differential Diagnosis

Impetigo, microbial eczema, neurodermatitis, psoriasis, seborrheic dermatitis and contact dermatitis. Infestation of the eyelashes may resemble blepharitis.

11.3.11 Observations

- As the incidence of other STDs is common in carriers of pediculosis pubis, the relevant laboratory investigations are necessary in order to rule out any coinfections.
- In cases of secondary infection, topical or systemic antibiotics are recommended.

11.4 Molluscum Contagiosum

11.4.1 Synonyms

Water warts.

11.4.2 Concept

Disease caused by a poxvirus, characterized by the presence of a varying number of papules transmitted through direct contact with the skin. Autoinoculation can occur with new lesions appearing in other areas.

11.4.3 Incubation Period

Generally 3 weeks to 3 months after exposure.

11.4.4 Etiologic Agent

This is a poxvirus with four subtypes, with type 1 being the most prevalent. This virus has the capacity to reproduce in the cytoplasm of infected cells, provoking the appearance of cytoplasmic inclusions (Henderson-Patterson bodies).

11.4.5 Clinical Manifestations

Presence of hemispherical papules 3–6 mm in diameter that are isolated and well defined, either pink or the same colour as the skin, often with an umbilicated centre and a slightly erythematous base, more commonly found on the trunk and extremities in children and on the genitals in adults.

It is generally asymptomatic, and there may be itching or perilesional eczema. Generalized and persistent lesions may be found in patients with immunosuppression.

11.4.6 Laboratory Diagnosis

In case of uncertain diagnosis, carry out microscope investigations. Place the material obtained through curettage onto a slide, fix it with alcohol using the same method used for gynaecological examinations and request stained cytology using the Papanicolaou or Wright technique to screen for cytoplasmic inclusions.

For cytology using the Giemsa technique, leave the slide to air dry before sending it to the laboratory in a dry flask. Inclusions can also be seen via histopathological examination, but only as an exception.

11.4.7 Evaluation of Laboratory Methods

We could not find any studies containing this data.

11.4.8 Treatment and Control of Cure

- Curettage of lesions as the procedure of choice.
- Trichloroacetic acid 30–50% applied to lesions once a week.

- Cryotherapy with liquid nitrogen: this procedure is painful but should be used on larger lesions.
- Tretinoin cream 0.025–0.1%: may cause irritation to folded areas or areas exposed to the sun.
- Potassium hydroxide solution 5 or 10%: applied to lesions once a day for up to a week.
- Imiquimod cream 5%: applied three times a week every other night. Wash the area 8 h after each application. This should not be used by pregnant and breastfeeding women.
- Systemic medication: griseofulvin and cimetidine have been cited; cidofovir and intralesional interferon have been used in patients with immunosuppression.
- Specific treatment is often not necessary, as the lesions usually involute spontaneously after a few months.

11.4.9 Complications

Eczematisation, inflammation and secondary infection. Lesions on the eyelids may lead to conjunctivitis.

11.4.10 Differential Diagnosis

Acne vulgaris, prickly heat, chicken pox, basal cell epithelioma, lichen planus, milium, condyloma acuminata and other warts. In patients with AIDS, cutaneous cryptococcosis may present lesions similar to those for molluscum contagiosum.

11.4.11 Observations

- Patients should be re-examined after treatment at intervals of 15 days to 2 months.
- The sexual partners of adult patients should be examined it lesions are found in the anogenital region.
- Atypical extragenital lesions in adults, especially on the face, suggest coinfection with HIV or other immunodeficiencies.
- When lesions are observed on the genitals, some professionals often confuse them with HPV. Therefore, we believe that in some cases material from the lesions should be sent for histopathological examination.



Fig. 11.3 Traumatic lesion leading to petechiae on the junction of the hard and soft palate, contracted from performing fellatio. In this case, differential diagnosis includes herpes, other viruses and bacterial infection with streptococcus



Fig. 11.4 Ulcer on the buccal floor contracted from performing cunnilingus. Observe the sharp uneven borders of the anterior teeth. Differential diagnosis includes diseases that cause mouth ulcers, such as syphilis or herpes. In this case, as in the previous case, if the patient is HIV positive the infectiousness of the lesion will be higher. However, if the patient is HIV negative they will be more susceptible to contamination with HIV and other infections every time they practice oral sex



Fig. 11.5 Patient in her 50s referred to the STD clinic due to a genital tumour. She was very worried as she thought it was a malignant or serious venereal disease. This was simply a sebaceous cyst, which was at first treated by removal of the inner mass and then on another occasion by removal of the capsule. It is extremely important to keep in mind that we must consider STDs in our everyday practice. However, we must also remember that not everything found on the genitals is an STD. Establishing a diagnosis based on assumptions and without verifying the epidemiological history and performing thorough clinical and laboratory examinations represents low-quality medical practice. Therefore, we must follow global medical care routines in full



Figs. 11.6 and 11.7 Patient referred for peniscopy as his partner obtained oncological colpocytology results suggesting HPV. He did not present any lesion suggesting he was infected with this virus. He was diagnosed with a dermal cyst on the scrotum

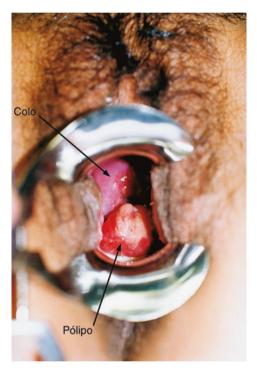


Fig. 11.8 Patient presenting large cervical polyps (*arrow*) that extends to the vaginal introitus. This was the reason for her referral. After a routine check up with direct examination of a vaginal swab we diagnosed vaginitis caused by *Trichomonas vaginalis*. Serological screening for syphilis, HIV, hepatitis B and C was non-reactive. We prescribed a course of injections against hepatitis B



Fig. 11.9 Patient referred to the Fluminense Federal University (UFF) STD clinic for treatment of bartholinitis. This was not a case of bartholinitis, but an abscess in the area close to the right labia majora. The patient reported that she had had similar symptoms on three previous occasions and that these had reduced upon local application of a stupe and antibiotic cream. Incision and drainage, as well as systemic antibiotic therapy, are the procedures that should be used to treat this. We must emphasize the fact that many of these processes start after depilation followed by folliculitis



Fig. 11.10 Twenty-six-year-old patient referred by the urology clinic presenting extensive balanitis with stinging. He reported this being the first time these symptoms had appeared. He denied receiving any previous treatment and said that the symptoms had appeared 24 h previously. Serological screening for HIV and syphilis was non-reactive. Bacteriology exams of a swab taken from the lesion using the Gram technique and dark field microscopy did not provide a clearer diagnosis. Stained cytology using the Papanicolaou and Giemsa techniques was non-specific. The patient was advised to wash using boric acid solution and topical application of *Uncaria tomentosa* gel 5%, which lead to complete cure within 4 days





Fig. 11.11 Patient seen at the UFF STD clinic after referral from the public health system, presenting classic symptoms of fungal balanitis (a). He reported that he sought medical attention for these symptoms and was given an IM dose of penicillin benzathine without being examined. Direct examination of a swab taken from the area did not provide a diagnosis of fungus. However, stained cytology was positive for hyphae. He was treated with itraconazol and given advice on hygiene. One week later he was fully recovered (b)



Fig. 11.12 Nineteen-year-old patient referred by a private health company for treatment of bartholinitis. The symptoms had persisted for over a week despite the use of oral antibiotics, azithromycin and ciprofloxacin. She was not experiencing fever or intense pain. She reported that the swelling did not hurt but was causing her discomfort (*sic*).

Note in panels (\mathbf{a}, \mathbf{b}) that there is no inflammation. The clinical diagnosis was Bartholin's cyst. Panels $(\mathbf{c}-\mathbf{f})$ show the marsupialisation of the gland. In (\mathbf{g}) , a drainage tube was left attached for just 24 h, as if left for longer this could facilitate a secondary infection of the gland

Fig. 11.13 Thirty-five-year-old patient, referred to the STD clinic at the Valença Faculty of Medicine in Rio de Janeiro by the Family Health Program (PSF) in the same city, with a history of vaginal tumours that were observed during sampling for oncological colpocytology carried out by a non-medical professional at this service. Examination carried out at the STD clinic revealed that this was a Gartner duct cyst (*a*), a disease with a low prevalence, and that it was not related to any STD. These are remnants of the mesonephric ducts on the lateral part of the vulva



Fig. 11.14 (a) Patient presenting a vegetating lesion on the vulva that had been present for a few months and on various occasions had been treated with trichloroacetic acid solution and podophyllin, as it was thought that it was a case of condyloma acuminata. (b) After examination, we proceeded to perform surgical exeresis. Histopathology revealed this to be a case of syringoma, a benign tumour that is rarely seen on the vulva. This is understood to be an adenoma on the ducts of the intra-epidermal eccrine sweat glands

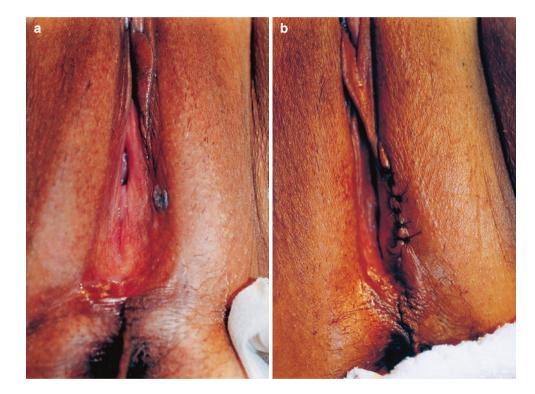


Fig. 11.15 (a) This is practically identical to the previous case. (b) This was also a case of syringoma. We consider exeresis of the tumour and histopathology to be good practice. There are both aesthetic and emotional aspects related to the presence of a lesion on the genitals. It is unusual for somebody to have a genital lesion and not think that this is associated with an STD. The previous case was worse, as the partner underwent two peniscopies to screen for HPV and it was established with certainty that he had contaminated his partner with HPV

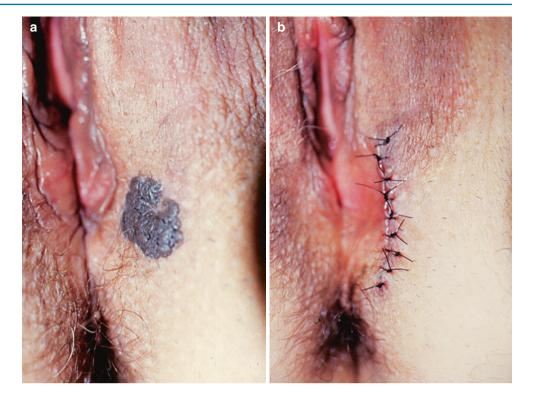




Fig. 11.16 Another case where histopathology was used to diagnose syringoma on the vulva



Fig. 11.17 Patient referred from a health centre after intramuscular administration of 500 mg of ceftriaxone to treat bartholinitis. She was very anxious and was complaining of pain and a tumour on her vulva. At the beginning of the consultation she denied any situation association with sexual activity. However, when there was just one doctor in the room and the patient was feeling more confident she reported that she had been raped by three men and had suffered violent injuries to her vulva. This is a learning point: many patients need time and confidence to talk about intimate details. Health teams should be careful to create an adequate environment in order to listen to their patients. Every one of us takes the time we need to speak



Fig. 11.18 This patient came to the clinic in an anxious state as he had been accused by his partner of having transmitted HPV to her. He just had some numerous sebaceous cysts on his scrotum. It is worth remembering that not everything on the genitals is an STD. It is not uncommon for a patient to receive colpocytological (PAP) results suggesting HPV and their partner not present anything. However, the complete routine should not be delayed, including serological screening and finding out the patient's vaccination status





Fig. 11.19 (a) Patient presenting a cyst containing a serous substance on his penis. (b) Totally cured after exeresis



Fig. 11.20 Patient seen at a private health clinic referred for treatment of warts on his penis. He actually presented small vegetative verrucous lesions on his penis, which are characteristic of condyloma acuminata. Histopathological examination proved this hypothesis to be correct. During the appointment, in line with our normal routine, we examined the penis, the scrotum and the perineal and perianal regions. We found some abnormalities in this area, however, they were just sebaceous granules (*a*), eliminating the possibility of this being a case of HPV infection in the perianal area



Fig. 11.21 Many men present these anatomical formations on the penis (*arrows*). Sometimes they are iatrogenically given "treatment" for HPV. As well as physical iatrogenesis, some of these patients are affected emotionally, as they are "labelled" as having an STD that develops into cancer. These anatomical formations are physiological



Fig. 11.22 This patient presented this genital epidermal cyst and a history of recurring genital herpes

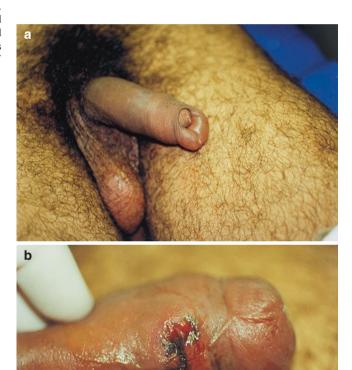


Fig. 11.23 (**a**, **b**) This patient arrived at the clinic with a case of edema on his foreskin and an ulcer on his penis. He reported that he had a cockscomb-type vegetative lesion on his penis. To cure this, he applied an unknown liquid sold by a pharmacy salesperson in his neighbourhood. He reported that soon after the first two applications the ulcer appeared, developing pain, necrosis and edema. As well as being caustic, this product caused topical irritation. We did not find out what the liquid was as the patient did not return for follow up

Fig. 11.24 (a, b) Patient referred to the STD clinic for treatment of a genital ulcer with a hypothetical diagnosis of lymphogranuloma. This was actually a case of paraphimosis. The patient claimed that it had been this way for 2 days and that when he went to the health centre he was referred to our clinic



Fig. 11.25 This is very similar to the two previous cases, although it was not paraphimosis but dermatitis caused by a primary irritant through the topical use of a solution for the treatment of mycosis. The product contained the metalloid iodine. Soon after using this medication to treat the itching caused by the mycosis, the patient noticed this severe edema





Fig. 11.26 What follows is a series of cases involving edemas on the penis with four different causes. All of these cases were seen at the STD clinic at the Federal University of Ceará University Hospital in the city of Fortaleza. The importance of anamnesis, clinical examination, classic STD laboratory examinations and an epidemiological approach are essential in deciding the therapeutic approach to be taken. (a) The edema appeared after the appearance of a genital ulcer noticed around 7 days after sexual relations with an occasional partner without protection. VDRL was 1:2 and serological screening for HIV and hepatitis B was negative. The patient was treated for syphilis and the symptoms disappeared the following week. (b) Edema on the penis that appeared after unprotected sex with his girlfriend, his exclusive partner. During the consultation he reported pain in his penis but no secretions or adenomegalies. He reported that he normally had a lot of difficulty externalizing his glans (phimosis). He was referred to the urology department and advised to apply a gold saline compress and an oral anti-inflammatory. The glans reduced in size after a urological procedure and the patient was later referred for postectomy. (c) Patient complaining of

edema and an ulcer on his penis that had appeared 24 h previously. He reported that the edema had appeared after an attack of severe genital itching. He reported itching in other areas of the body and that this worsened at night. When asked if other family members had displayed similar symptoms, he said that they had. In the photo there are traumatic ulcers on the penis, glans and hand. We also found lesions on the buttocks, abdomen and underarms. We recommended treatment for scabies with oral ivermectin 6 mg, 2 pills once a week repeated after 1 week, and advised that all symptomatic family members seek medical attention. (d) Patient presenting edema on his foreskin for 3 days. He had been experiencing stinging and purulent urethral discharge for 10 days, which began 6 days after having unprotected sex. Bacteriological examination of the urethral discharge was positive for intracellular Gram-negative diplococci in polymorphonuclears. We recommended oral ciprofloxacin 500 mg and oral azithromycin 1 g, both in a single dose. We advised his to use cold saline compresses and an oral antiinflammatory. The symptoms disappeared within 3 days

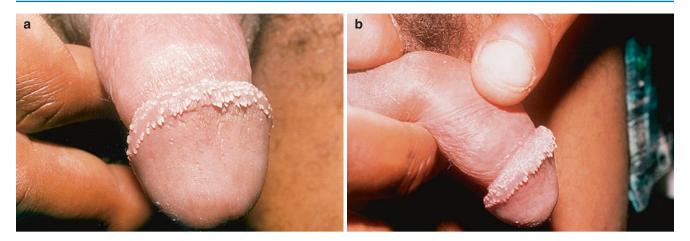


Fig. 11.27 (a, b) Young adult presenting a serious case of hypertrophy of the papillae, which can be easily confused with HPV infection. This patient had been seriously emotionally abused by their sexual partner, who accused him of having HPV



Fig. 11.28 Another case of hypertrophy of the papillae. It is obvious that in some situations the patient can present condyloma acuminata lesions in the middle of the papillae, and only these should be treated. However, care must be taken during examination to avoid causing iatrogenesis



Fig. 11.29 The same situation of hypertrophy of the papillae, also known as hirsuties coronae glandis





Fig. 11.30 (a-c) Hirsuties coronae glandis, which is often confused with condyloma acuminata, or HPV infection



Fig. 11.30 (continued)



Fig. 11.31 Another patient referred to the UFF STD clinic to treat HPV lesions. These were actually anatomical elements—Fordyce granules that have nothing to do with HPV infection. The patient insisted



that he did not want to continue with this "problem". He was given an explanation of what they are and that the best solution was to do nothing to avoid aggravating the area

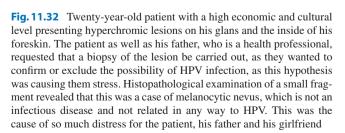




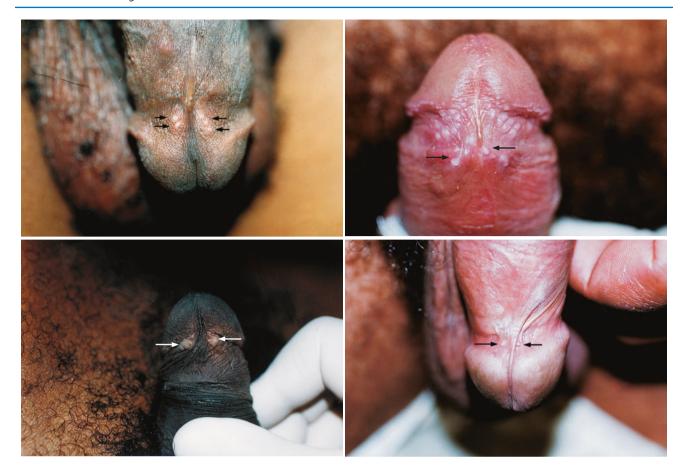


Fig. 11.33 Young adult patient seen at the UFF STD clinic referred for a peniscopy as his sexual partner presented oncological colpocytology (PAP) results showing cells with koilocytosis, suggesting HPV. The patient reported that he had already been examined by a urologist who had referred him for treatment for HPV at our clinic. This situation is actually physiological (pearly penile papules in the peroneal groove and Fordyce granules, which are sebaceous glands on the penile shaft) and is in no way related to HPV infection. Guidance on sexual and reproductive health should be given. We discovered from the patient history that he had not been vaccinated against hepatitis B. Therefore, we prescribed a course of injections for this. On March 9, 2011, an excellent article was published online in Nature 471 describing alterations in

human DNA that had made certain anatomical formations disappear, such as "spines" on the penis. These ridges exist in chimpanzees (and in various mammals) and increase sensitivity, making ejaculation happen faster. It is believed that these "spines" also remove the sperm of any rivals that have copulated with their mate previously. Therefore, this mechanical removal could help to ensure that pregnancy occurs as a result of the most recent coitus. On the other hand, the smoother penis of modern man may be linked to the adoption of monogamous relationships. Without these anatomical formations, man has made coitus last longer. Who knows, perhaps the formation of pearly penile papules/Fordyce granules/hirsuties coronae glandis are remnants of these old penile "spines"?

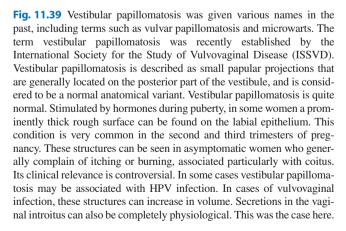
Fig. 11.34 Twenty-one-year-old single patient, a student, seen at the STD clinic of the Federal University of Ceará University Hospital in Fortaleza, complaining of genital warts he had suffered from for around 4 years. He reported having just one sexual partner in the last 2 years. He did not report any previous STDs. Examination of the genital area (peniscopy) after application of acetic acid 5% did not reveal any lesions suggesting HPV or any other infectious agent. He was informed that this was not an STD and that it was simply an enlargement of the glands in this region (*a*). Unfortunately, cases like this are sometimes "diagnosed and treated" as thought they were HPV infection. As well as physical trauma (to the local area), people can undergo significant emotional, social and marital stress, etc.





Figs. 11.35 to 11.38 Pearly penile papules. These are normal anatomical structures situated on the edge of the glans (the corona) or on the frenulum (*arrow*). They are common, with a reported incidence in 19% of the population. These are isolated skin-coloured papules that are 1–2 mm in diameter and form a circle on the edge of the glans, sometimes with a keratotic (spiculated) surface, and are often misdiagnosed as molluscum contagiosum or condyloma acuminata. They have a regular appearance resembling a riverbed covered in pebbles, which is

different to condyloma acuminata. Both conditions can take on a whitish appearance after application of acetic acid. Histology reveals the lesions to be angiofibromas. No treatment is required. In Fig. 11.37, although the patient's skin is black, the papules are very white and prominent. He reported difficulty in explaining to his partner that this was anatomically normal and was not a disease. In extreme cases, exeresis is recommended for emotional and aesthetic reasons





11.5 Behçet's Disease

11.5.1 Concept

Inflammatory disease with primary vasculitis affecting various systems and causing oral aphthous ulcers (always), recurring genital ulcers, uveitis, retinal vasculitis and skin lesions. It can also lead to arthritis, neurological alterations and thrombophlebitis.

11.5.2 Etiological Agent and Epidemiology

It has unknown etiology but is related to the presence of HLA-B51 and commonly found in populations in the Mediterranean and Middle East. It is prevalent in Turkey, Iran, Iraq, Saudi Arabia, Japan and South Korea. It mainly affects young men (from 20 to 40 years). Secondary immunological abnormalities towards bacterial and viral antigenic stimuli may be associated with its etiology.

11.5.3 Clinical Manifestations

Diagnosis follows the criteria established by the International Study Group for Behçet's Disease (Table 11.1), with the obligatory presence of one major criterion and two minor criteria.

The genital ulcers are painful, and in women may require fenestration of the labia.

11.5.4 Laboratory Diagnosis

Eminently clinical. IL-10 values are related to the intensity of clinical manifestations.

11.5.5 Treatment and Control of Cure

Genital lesions are treated with topical local injectable corticosteroids. This disease is recurring and may require systemic treatment with corticosteroids or immunosuppressants.

11.5.6 Differential Diagnosis

Differential diagnosis includes mouth ulcers, recurring aphthous stomatitis, herpes, syphilis, bullous pemphigoid, pemphigus, Crohn's disease and lymphogranuloma venereum, among others.

Table 11.1 Criteria by the International Study Group for Behçet's disease

Major criteria		Clinical picture
•	Recurring oral ulcers	Small, large or herpetiform aphthous lesions, observed by the doctor or the patient, recurring at least three times over the period of a year
Minor criteria		
•	Recurring genital ulcers	Aphthous ulceration or scarring observed by the doctor or the patient
•	Ocular lesions	Anterior or posterior uveitis or retinal vasculitis
•	Cutaneous lesions	Erythema nodosum, papulopustular or pseudofolliculitis-type lesions, or acneiform eruptions
•	Positive pathergy test result	Formation of a papule, 2 mm or larger, within 24–48 h of intradermal insertion of a needle in the forearm



Fig. 11.40 (a, b) Patient over 50 years old presenting a minor case of Behçet's disease, or Behçet's syndrome (arrow)

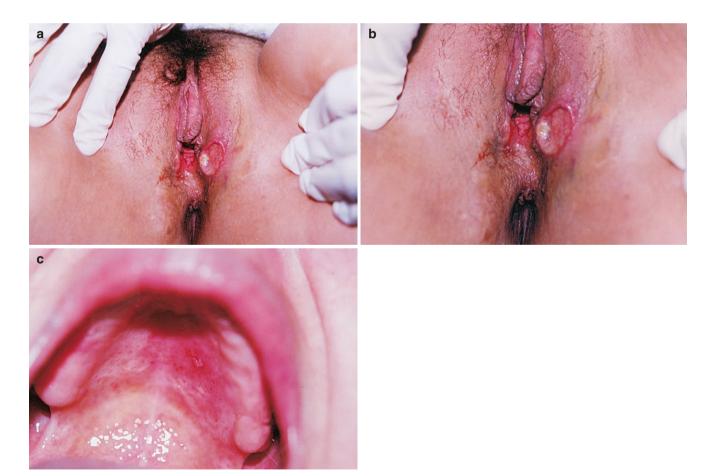


Fig. 11.41 (a, b) Behçet's syndrome. Young patient with a well-confined chronic ulcer with raised borders and a clean base. This was a very painful lesion. Serological screening for syphilis and HIV was negative, as was bacterioscopy of the lesion. It was treated with a corticosteroid after many treatments, including the syndromic approach for ulcers, but

with no success. (c) While examining the oropharynx, we noticed a small ulcer on the palate, over to the left, which was visible after removal of the patient's superior prosthetic denture. The patient did not present iritis uveitis, which is part of the triad of symptoms associated with Behçet's syndrome



Fig. 11.42 Behçet's ulcer (*arrow*). Unfortunately, many patients only receive correct diagnosis after initial approaches to treat STD ulcers have been applied

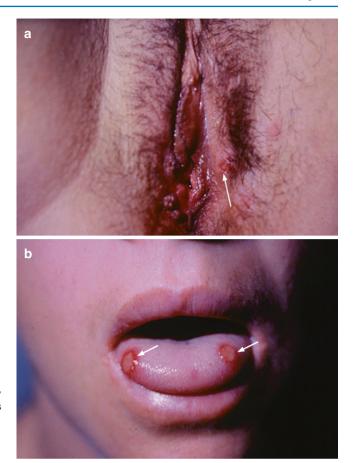


Fig. 11.43 (a, b) Vulvar and oral lesions associated with Behçet's disease (*arrow*)

Fig. 11.44 (a–c) Another case of orogenital Behçet's syndrome. Normally diagnosis is not simple and almost always a number of unsuccessful treatments are attempted with no success. Recurrence is a constant factor

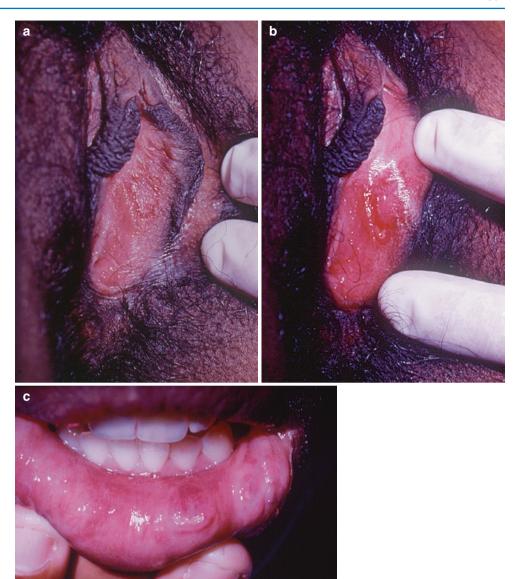






Fig. 11.45 (**a**, **b**) Although considering Behçet's Syndrome could be the classic approach, this case does not fit in with this kind of clinical picture. The patient reported that this was the third time that this problem had occurred. It was not possible to establish the etiology and the

lesions disappeared after a week without the patient using any medication. All routine examinations were negative. In 2 years of follow up the patient did not present any recurrence

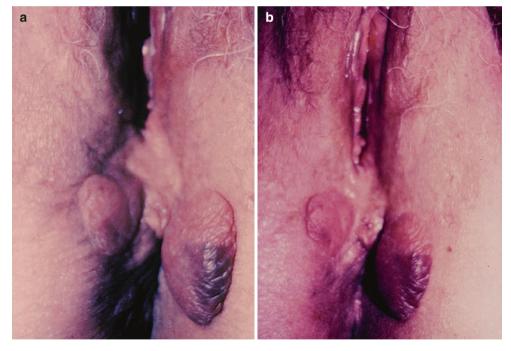


Fig. 11.46 (a, b) Perineal amyloidosis. Vegetative genital lesions are frequent, however etiological elucidation can be difficult as it involves clinical aspects that are unknown to gynaecologists. A 57-year-old white female smoker who had been pregnant eight times, given birth twice and undergone two abortions and had started her menopause at 48, was referred to the UNICAMP (Campinas University) Gynaecology Clinic after having been evaluated by various professionals, including a dermatologist and an oncologist, with no diagnosis being established. She presented two prominent violet-coloured lesions with a soft and fleshy consistency and a small inner haemorrhagic area, measuring approximately 2 cm and 5 cm respectively, stretching from the furcula to the left gluteal fold. The lesions were pruritic and presented spontaneous discharge of a bloody

and fetid secretion. The patient presented the following previous pathologies: diabetes, arterial hypertension and congestive heart failure, which developed after an acute myocardial infarction 5 years previously. Her symptoms included: dyspnoea, chest pain and edema of the lower limbs. She was taking NPH insulin, digoxin and furosemide. A diagnosis of eosinophilic granuloma had been suggested and two local biopsies were carried out that surprisingly confirmed a diagnosis of "primary cutaneous amyloidosis". Electron micrographs were obtained which revealed intracytoplasmic production of filamentous deposits (amyloid) in fibroblasts. Therefore, this excluded the possibility of this being a case of precursor lesions of plasmacytic dyscrasias, as the plasmocytes did not present any relationship with the etiology of the lesion

11.6 Erythema Multiforme, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

11.6.1 Concept

Acute syndromes with etiologies that are not always defined, sometimes related to infections or medication, sometimes to genetic predisposition (human leukocyte antigens (HLA)), with cutaneous, mucosal and sometimes systemic lesions.

Some authors describe a spectrum of manifestations including the mildest form, erythema multiforme minor $(EM_{m}),\,$ erythema multiforme major (bullous) $(EM_{M}),\,$ Stevens-Johnson syndrome (SJS), mixed clinical presentations of SJS/TEN and the most serious form which is the highly lethal toxic epidermal necrolysis (TEN), also known as Lyell's syndrome.

11.6.2 Etiopathogeny

This condition is defined as a standard cutaneous reaction to intolerance to a stimulus, which in mild cases (erythema multiforme) is more frequently caused by infection by the human herpes virus (HSV), and in serious cases (Stevens-Johnson syndrome and toxic epidermal necrolysis), intolerance to drugs, especially beta-lactam antibiotics, sulfonamides, allopurinol, non-hormonal anti-inflammatories and aromatic anticonvulsants. The relation of some HLAs with determined drugs gives rise to genetic predisposition. The pathogenesis is not totally clear, but it involves a cell-mediated immune reaction leading to the destruction of cells infected with HSV or cells with the antigens related to the drugs with the presence of varying degrees of apoptosis. Patients with AIDS are more frequently affected.

11.6.3 Clinical Manifestations

The oral and genital mucosae are often affected across the whole spectrum of these different clinical presentations, with the skin being affected in the majority of cases. This can involve a range of cutaneous lesions: erythematous patches, target lesions (central purpuric patch surrounded by a pale

Table 11.2 Classification and characteristics of erythema multiforme major (EM_M), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

Classification/clinical characteristics	EM_{M}	SJS	SJS/TEN	TEN (with macules)	TEN (without macules)
Epidermal detachment (% skin surface)	<10%	<10%	10–30%	>30%	>10%
Typical target lesions	Yes	_	_	_	_
Atypical target lesions	Raised	Flat	Flat	Flat	_
Patches	_	Yes	Yes	Yes	_

raised halo and a peripheral erythema), epidermal detachment and blisters, which may be extensive in TEN, similar in appearance to a large burn. Exulcerations and pseudomembrane formations with ophthalmological, oropharyngeal-esophagial, laryngeal-tracheal-bronchial and genital (balanitis and vulvovaginitis) legions predominate on the mucosa, sometimes developing synechiae, particularly in TEN.

General wellbeing (high fever or hypothermia) and some organs (the lungs, kidneys and heart) are frequently affected in SJS and TEN, which may lead to death.

In order to assist non-specialist doctors with the classification of these syndromes, Bastuji-Garin et al. [5] have standardized their clinical presentations (see Table 11.2).

11.6.4 Laboratory Diagnosis

There is no laboratory examination that can confirm these diseases and diagnosis is clinical and based on the patient's anamnesis.

11.6.5 Treatment and Control of Cure

Treatment is symptomatic and principally offers general support in easing the hydroelectrolytic and caloric disturbances that can occur. There is no consensus on the use of corticosteroids and some authors say these should be limited to the first 48 h. Other studies advocate the use of human immunoglobin. Antiviral therapy and antibiotics can be used depending on the probable etiology or complications. It is imperative that the use of any suspicious or non-essential drug be suspended.

11.6.6 Differential Diagnosis

A range of clinical presentations can resemble EM, SJS and TEN, particularly bullous pemphigoid, pemphigus, Behçet's syndrome and collagenosis. The possibility of urethritis, conjunctivitis and stomatitis with other etiologies should also be excluded. In isolated genital lesions that do not occur in TEN, differential diagnosis includes ulcerative STDs and genital thrush.



Fig. 11.47 (a—e) This patient presented these monthly symptoms during menstruation. After receiving various treatments, biopsies, investigations and diagnostic hypotheses, dipirona was finally identified (used for dysmenorrhoea) as the cause of the orogenital symptoms. The patient reported that she started to take this medicine regularly the previous year

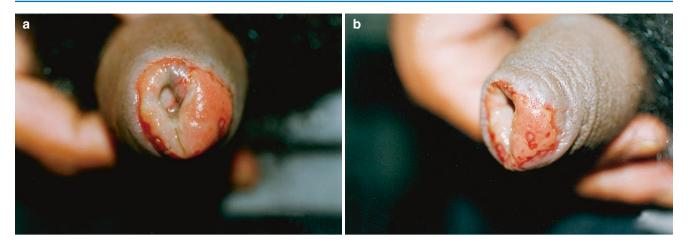


Fig. 11.48 (a, b) This patient reported recurring symptoms of genital herpes, but the situation shown here shows the genital symptoms after use of sulfa-based local medication for the "treatment" of the ulcers caused by HSV

Fig. 11.49 Woman seen at the maternity ward at the Valença Faculty of Medicine in Rio de Janeiro who was 32 weeks pregnant, with a history of pre-eclampsia, taking 1 g/day oral α -methyldopa (according to the client) presenting edema on the right labia minora. She was informed by the medical professional that was overseeing the prenatal appointment that this edema was characteristic of pre-eclampsia (sic). When questioned about her use of medication in the days leading up to the appearance of the ulcer, she reported that she had been using dipirona oral drops to alleviate pelvic pain. As this was a suspected adverse drug reaction, her use of dipirona was suspended and the symptoms improved 2 days later



Fig. 11.50 (a, b)
Dermatitis + pyodermitis in a patient with immunosuppression



11.7 Psoriasis

11.7.1 Concept

Recurring chronic inflammatory disease with a variable cutaneous-articular clinical presentation.

11.7.2 Epidemiology

This occurs universally in 1-3% of the population, at any age but predominantly in the thirties (in 75% of cases), is rare in people with black skin and occurs equally in both genders.

11.7.3 Etiopathogeny

Its etiology is multifactorial with genetic aspects of polygenic inheritance and environmental factors that influence its clinical manifestation. Twelve loci of susceptibility have already been mapped (PSORS1 to PSORS12) and it has a close relationship with HLAs (Human Leukocyte Antigens) -Cw6, especially in cases that occur before the age of 30. Its pathogenesis, which is not totally clear, involves increased epidermal proliferation and inflammation with participation of the immune system. Various studies have demonstrated the presence of inflammatory infiltrate T CD4 cells in its pathogeny, with a predominant Th1 response, the presence of dendritic and Langerhans cells in plaque psoriasis and alterations to levels of cyclic AMP and arachidonic acid. Environmental factors include cold, trauma, infection (viral and bacterial), endocrine and metabolic disorders, stress, smoking, alcohol, drugs (lithium, indomethacin, cloroquine, beta blockers and others).

11.7.4 Clinical Manifestations

Typical cutaneous lesions are well-defined scaly erythematous plaques that are either isolated or grouped, predominantly around the surfaces of the articular extensors, the trunk, the sacral region and the scalp (psoriasis vulgaris). There are also less common forms that predominantly affect the skin folds (inverse psoriasis) and generalized, pustular forms (erythrodermic psoriasis), among others. The nails are

affected in various ways and intensities in up to a half of patients with psoriasis vulgaris, however, the nails are affected in over 80% of psoriasis sufferers whose joints are affected (psoriatic arthritis). Symptomatically, itching is variable and occurs in around 80% of patients.

It mainly affects the folded areas of the genitalia (the inguinal regions, the foreskin and the keratinized parts of the vulva) and manifests as well-defined erythematous plaques without desquamation. Isolated genital lesions may be the initial manifestation of the disease and there may be a family history. Pustular psoriasis may occasionally affect the mucosa of the vulva, vagina and cervix.

11.7.5 Laboratory Diagnosis

Diagnosis involves clinical and histopathalogical examination of the skin: parakeratosis, uniform acanthosis, elongation of interpapillary cones, small clusters of neutrophils on the inside of the epithelium which may form intraepithelial abscesses (Munro's abscesses), hyperkeratosis or dermis with elongated, broad or twisted papillae with dilated capillaries.

11.7.6 Treatment and Control of Cure

Various drugs and therapeutic regimes may be applied to treat psoriasis, which would go beyond the scope of this text. Specific treatment for genital psoriasis is difficult to control, as it is based on medium-strength topical corticosteroids.

11.7.7 Differential Diagnosis

In most cases psoriasis has an easy clinical diagnosis and the semiotic technique of the Brocq cutterage method can also be applied. However, differential diagnosis for psoriasis includes seborrheic dermatitis, palmar-plantar eczema, erythrodermic cases with other etiologies, hanseniasis and various onychopathies, etc.

Differential diagnosis for vulvar and penile psoriasis includes candidiasis (which can also occur at the same time as psoriasis), dermatophytosis, seborrheic dermatitis and contact eczema.

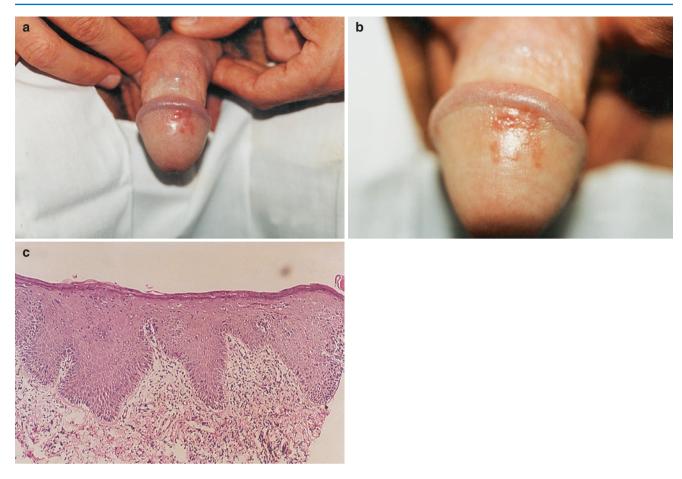


Fig. 11.51 (a–c) This young adult presented pruritic plaques with hyperaemia on his penis on various occasions, reporting that they had appeared after sexual intercourse. He reported that his girlfriend had vulvovaginal candidiasis. Direct examination for fungus on a swab taken from the lesion on the glans was positive. He was medicated with

an antifungal, which improved the symptoms, although they did not completely disappear. These procedures were repeated two or three times until a biopsy was proposed, which confirmed a diagnosis of psoriasis. This case of genital psoriasis resembling balanopostitis was described by Passos et al. in Brazilian Journal of STD [6].



 $\begin{tabular}{ll} \textbf{Fig. 11.52} & \textbf{Symptoms presented on the glans after use of oral sulfamethoxazole + trimethoprim } \\ \end{tabular}$



Fig. 11.53 Patient presenting fixed pigmented erythema caused by hypersensitivity to dipirona



Fig. 11.54 Symptoms on the penis that are already receding after use of oral acetylsalicyclic acid



Fig. 11.55 Patient with an ulcer on the glans that appeared regularly after the use of medication for migraine. He was medicated twice using the syndromic approach (with oral and intramuscular antibiotics) for genital ulcers, but with very slight improvement. All direct microbiological examinations were non-specific. The symptoms disappeared after he was instructed to stop taking his migraine medication



Fig. 11.56 Forty-nine-year-old patient who sought medical attention for redness on his penis. He reported that the symptoms had started around 30 days previously. He used polyvalent dermatological cream with antibiotics, corticosteroids and an antifungal but did not see any improvement. He said that he was very worried that it was an STD. It was actually balanoposthitis caused by an irritant-irritant contact eczema. This irritation could have been caused by accumulated urine, soap suds, substances eliminated in the urine or vaginal secretions after sex that were not removed properly, etc. In these cases, it is very important that the patient is asked to observe/look for the potential irritant. In the majority of cases, the discomfort can be reduced with the use of a thin layer of cream with benzalkonium chloride 0.1 mg and cetrimonium bromide 0.2 mg twice a day, dexpantenol 50 mg/g cream twice a day, or simply maintaining the area clean after urinating and washing and drying it after sex. We did not refrain from performing our full routine for all people presenting genital complaints



Fig. 11.57 Patient with 2-week old perianal ulcers and an extremely confusing clinical history. All microbiological examinations were nonspecific. VDRL reacted at 1:4. The patient was medicated according to the syndromic approach for genital ulcers caused by STDs and did not improve. She used oral dipirona regularly for dysmenorrhoea. She was advised to stop using this medication. Follow up after 4 months without using dipirona revealed an absence of lesions. VDRL continued at 1:4. Serological screening for HIV and hepatitis B was negative. She referred her fixed and exclusive sexual partner (as described by the patient) for a consultation at our clinic. We could not find anything relevant in his clinical or serological examinations. They were both prescribed a course of injections against hepatitis B. She later informed us that as an adolescent she had blotches on her skin and did some exams, although she couldn't remember which, and she received various injections (she did not know for what), which hurt a lot



Fig. 11.58 Patient presenting urethral preputial fistula with recurring infections and an increase in penile diameter. He was referred for urological surgery. However, until diagnosed by us he was medicated various times for "chronic venereal disease" for over a year



Fig. 11.59 This is not a case of condyloma acuminata. This is known as "molluscum pendulum" or fibroepithelial polyp of the vulva. It is not an infectious disease. However, this patient was referred to the gynaecological clinic for treatment for a "large genital wart" on the vulva





Fig. 11.60 Forty-five-year-old patient seen for treatment of CIN III. During the consultation she complained of a wart on her left thigh. She underwent a cone biopsy of the cervix and exeresis of the molluscum pendulum (fibroepithelial polyp), which had nothing to do with HPV, unlike the high-grade intraepithelial lesion on her cervix



Fig. 11.61 Patient referred for peniscopy at the UFF STD clinic as his fixed and exclusive partner had undergone oncotic colpocytology and presented a high-grade intraepithelial lesion on her cervix. Clinical examination of the genitalia did not reveal any typical HPV lesions. However, as shown in photos (**a**, **b**) and the videos, the patient pre-

sented plicomas on the penis (a) and the left thigh (b). The plicoma (fibroepithelial polyp) on the penis measured around 1.5 cm at its largest diameter. Surgical exeresis was proposed (c-e). Serological screening for HIV, syphilis, hepatitis B and C was negative. A course of vaccinations against hepatitis B was prescribed



Fig. 11.62 Extensive varicose tumour of the vulva in a pregnant woman. This was initially confused with genital warts



Fig. 11.63 This is also a case of varicose veins on the vulva in a pregnant woman who was referred to the STD clinic to receive a clear diagnosis

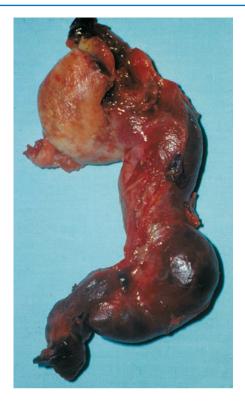


Fig. 11.64 This is a surgical specimen: an ovary and thrombosed ovarian veins. This was a case of postpartum acute abdomen where a laparotomy was carried out due to suspected abscessed postpartum pelvic infection. Note the immense thrombosis of the ovarian vessels that extended up to the vena cava, simulating the symptoms of pelvic infection

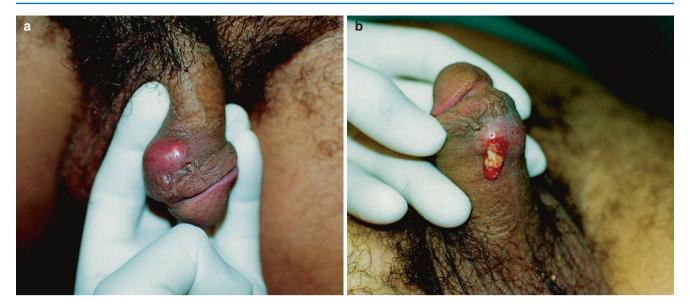


Fig. 11.65 (**a**, **b**) Retention cyst that developed into a large abscess on the penis. Whatever the initial aetiology, puncturing with a high calibre needle to drain the purulent material and carrying out the full routine for

patients with genital lesions should not be delayed. Microbiological examination of the pus revealed just *S. aureus*. All serological screening included in our routine was negative



Fig. 11.66 Due to the symptoms, at first it was thought that this was lymphogranuloma venereum. Examining the clinical history, it was discovered that the inguinal inflammation started a week before the consultation after a local trauma, followed by slight folliculitis that developed into a large abscess. Direct examination and serological screening was negative for *Chlamydia trachomatis*. Serological screening for syphilis and HIV was also negative for two tests taken with an interval of 30 days



Fig. 11.67 Child referred to the STD clinic, as shown in the photo after incision and drainage of "bartholinitis caused by an STD". The patient history revealed folliculitis, however, which developed into a genital abscess. Due to the location of the abscess, it is easy to imagine that this is not bartholinitis. The case was well investigated and data indicating sexual abuse was not found. According to the child, a "sore" appeared and grew into a lump after intense itching in the area



Fig. 11.68 Pyodermatitis on the shaft of the penis (*arrow*). Differential diagnosis must be carried out for scabies lesions. Obviously, the whole routine for genital lesions should be followed. Nothing impedes the patient from testing positive in serological screening for syphilis or HIV



Fig. 11.69 Patient with symptoms of pyodermatitis presenting relatively high reactivity in serological screening for syphilis, 1:128. Serological screening for HIV was negative. No spirochete-type bacteria were identified in swabs taken from the lesions and observed using dark field bacterioscopy. The patient was medicated with just penicillin benzathine and was cured



Fig. 11.70 Case of pyodermatitis in a male patient: scrotum and base of the thigh. He also presented dermatomycosis. The patient spontaneously sought out our services after reading an article in a newspaper stating that any genital lesion can be an STD. It is worth remembering that the first step in health education with diagnosis and early treatment involves providing information to the population. And obviously having a specialist service providing a fast and high-quality service

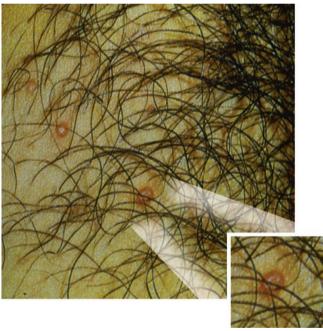


Fig. 11.71 Folliculitis in the genital area. However, the lesion in the close up is very similar to a molluscum contagiosum lesion. We collected a sample from this lesion to perform laboratory exams, the result of which was pyogenic inflammation, without the cytopathic effects of viral infection



Fig. 11.72 Large inclusion cyst on the labia majora of the vulva similar to bartholinitis

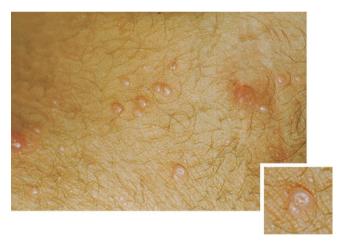


Fig. 11.73 Note the central umbilication of the typical lesions of molluscum contagiosum





Fig. 11.74 Adolescent patient with a paraurethral cyst. Observe the vaginal discharge, which examination showed to be of fungal origin. This clinical picture should not be confused with bartholinitis. After treatment for vulvovaginitis and screening for other STDs, the cyst can be punctured and emptied. However, recurrence is not uncommon



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Fig. 11.75 Many cases of molluscum contagiosum on the genitals are confused with HPV. The characteristic central umbilication that when pressed produces a white paste-like material is typical of molluscum contagiosum, which is caused by the poxvirus



Fig. 11.76 This was a case of molluscum contagiosum on the penis of a patient who underwent peniscopy as his partner had a history of a HPV result from oncological colpocytology

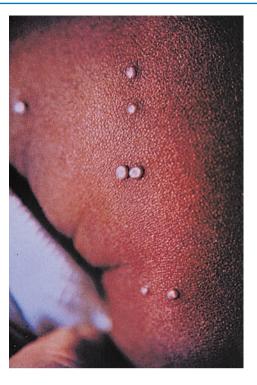


Fig. 11.77 Molluscum contagiosum in a child. This is actually a common disease at this age. However, we have often observed molluscum contagiosum lesions on the genitals of adults



Fig. 11.78 Papular lesion with the central umbilication that is typical of molluscum contagiosum. One form of treatment is the curettage of lesions and the application of iodine onto the curetted area

Fig. 11.79 (a–d) Twenty-four-year-old man referred to the UFF STD clinic for treatment of genital lesions. As his sexual partner was being treated for vulvar warts, the patient in question arrived stating he had HPV. This was actually a case of molluscum contagiosum





Fig. 11.80 Another case of molluscum contagiosum that was being treated as if it were HPV infection. At this time in which many cases of HPV are seen, various professionals hold the false belief that growths on the genitalia are basically caused by HPV. It is essential that differential diagnosis is established, even if some diseases are much more prevalent than others. Considering that many patients and their partners believe that they have HPV, laboratory diagnosis should be used to better deal with such cases



Fig. 11.81 Molluscum contagiosum in a woman who was being incorrectly medicated using the syndromic approach for genital ulcers with antibiotics. Once again it is clear that technical training for the treatment of STDs (in any area of medicine) is essential for good medical practice. The following should be avoided at all cost: providing diagnosis and treatment based on assumptions without assessing epidemiological, clinical and laboratory data. Not everything that is found on the genitalia is sexually transmitted



Fig. 11.82 Although diagnosis of syphilis should never be dismissed, pruritic papular lesions that become itchier at night are typical of scabies. However, according to good practice, when seeing patients with genital lesions, exams for syphilis and HIV should be offered. In this case VDRL was reactive at 1:32



Fig. 11.83 Pruritic papular scabies lesions on the glans and scrotum

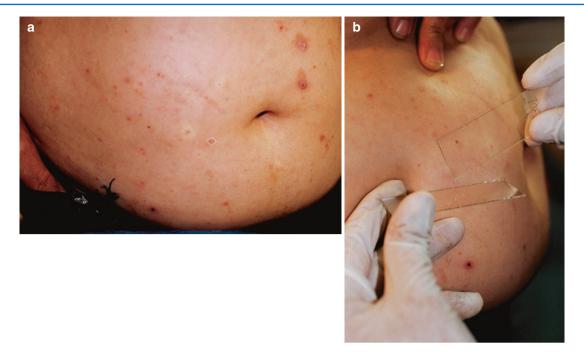


Fig. 11.84 (**a**, **b**) The skin of the abdomen is a common location for the arthropod of the Sarcoptidae family; *Sarcoptes scabiei var. hominis*. To visualize the etiological agent, swabs must be taken from the lesion,

attempting to remove the ectoparasite for direct examination with an optical microscope. However, visualizing the parasite in a laboratory exam is not an easy task. A negative result should not exclude clinical diagnosis

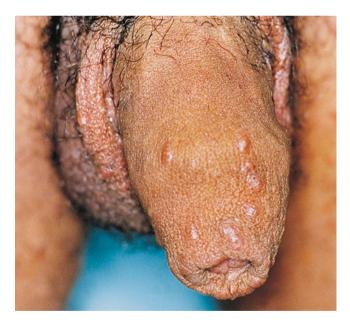


Fig. 11.85 Another case of scabies. Various topical treatments are proposed, such as benzyl benzoate 25%, lindane 1% and monosulfiram. In one way or another, each of these products causes irritation to the area that it is applied to a larger or lesser degree. In order to avoid this collateral effect we always try to recommend oral treatment with ivermectin at a dose of 12 mg (two 6 mg tablets) for adults weighing 51–65 kg. In addition, guidance on hygiene related to underwear, bed sheets, bed covers and mattresses should not be forgotten



Fig. 11.86 Case of scabies together with a significant suppurating inguinal adenitis, with secondary infection. Local treatment normally provokes stinging and irritation. Systemic treatment with ivermectin together with personal, family and household measures relating to hygiene provide good success rates. The full routine for genital lesions should never be delayed, in this case extending to family members living in the same household



Fig. 11.87 (a) Father with scabies. (b) Mother with scabies. Also see other photo



Fig. 11.88 Child with scabies. When seeing a patient with scabies, a lot of attention must be given to the other individuals living in the same household, whether family members or not



Fig. 11.89 Patient seen at the STD clinic with these symptoms. He reported slight itching. This was a case of dermatomycosis on the penis. These patients generally apply polyvalent creams/pomades for a few days. They get better and then interrupt the treatment before total cure has been achieved



Fig. 11.90 Extensive dermatomycosis on the vulva, inguinal region and up to the lower abdomen. Despite the clinical appearance and localization on the genitals, this is not an STD. It is important to emphasize that patients complete their treatment even if the symptoms improve after a few days. In addition, the full routine should be followed. This patient, for example, presented a positive result for serological screening for syphilis, with VDRL 1:64



Fig. 11.91 Similar to the previous case, the only difference being the patient's sex



Fig. 11.92 As well as symptoms on the nipple, this patient sought out our services due to vaginal discharge typical of candidiasis. She was breastfeeding and her child also presented candidiasis in the buccal cavity. Examination of both revealed the presence of *Candida albicans*



Fig. 11.93 (a–c) This patient was the husband of the previous patient. Examination of the lesions also revealed *Candida albicans*. After providing advice, serological screening was performed that was non-reactive for VDRL and HIV. Both related having extramarital relations in

the recent past. However, candidiasis is not classified as a classic STD. The mother, father and child had not been vaccinated against hepatitis B. We then followed the global care routine



Fig. 11.94 Dermatomycosis in a patient who came to our service for a HIV test. During the interview we observed these and other fungal lesions that had specific treatment. Serological screening (VDRL, hepatitis B and anti-HIV) was negative. However, anti-HCV serological screening (hepatitis C) was reactive. He was referred to the specialist medical service. Once again we see that opportunities should not be missed. Early diagnosis and treatment are important steps in controlling disease, especially infectious contagious diseases



Fig. 11.95 (a–d) Young patient, a sex professional, who sought out our services with these extensive dermatomycosis lesions covering areas of the vulva, buttocks and thighs. She also presented secondary bacterial infection and scabies lesions. Screening for fungus can be performed by carefully scraping the lesion with a blade and trimming the material with another. This material should be processed for direct

examination and cell culture by a qualified team. The patient in question agreed to carry out exams such as serological screening for HIV, syphilis, hepatitis B, hepatitis C, gonococcus and chlamydia, oncological colpocytology and parasitology of the faeces. The only abnormal results were for *Candida sp.* hyphae in the vaginal swab and *Strongiloides estercoralis* in the faeces

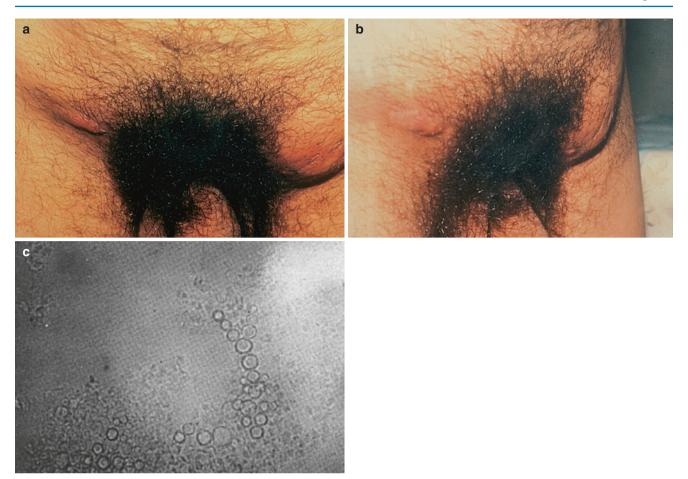


Fig. 11.96 (a, b) Young adult with these inguinal symptoms for over a year, which sometimes discharge a purulent material. He reported numerous treatments and taking various antibiotics for a maximum of 2 weeks, especially penicillin benzathine, with no significant improvement. He reported that he had a positive VDRL result of +++ and ++++ (according to the patient). For this reason, he had received various doses of penicillin benzathine. He also said that he underwent a biopsy of the right inguinal region, and the result of this was non-specific chronic

infection. Serological screening at our clinic for HIV, chlamydia and syphilis was negative. (c) Direct examination and cell cultures of the purulent material that was being spontaneously discharged revealed paracoccidioidomycosis. The patient was given a special referral for this serious mycosis. Not everything on the genitals is sexually transmitted. A detailed report of this case can be seen free of charge in the Brazilian Journal of STD [7]

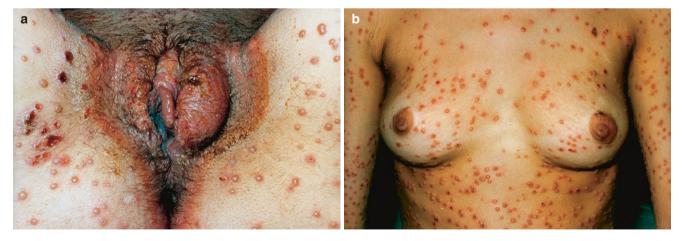


Fig. 11.97 (a, b) This patient with a serious case of adult chickenpox was asked to attend out STD clinic for these symptoms on her vulvar. This was simply a secondary impairment of the genitals caused by the systemic viral infection that often presents as associated bacterial infection

11.8 Lymphogranuloma Venereum and Non-Hodgkins Lymphfoma: Case Study [8]

A 17-year-old mixed race male high school student living in the city of São Gonçalo (Rio de Janeiro) who was single with a fixed and exclusive partner and heterosexual. He reported having his first sexual experience at 14 and not using condoms. He was referred by the Azevedo Lima State Hospital (HEAL) in the city of Niterói to be seen at the UFF STD clinic due to the presence of a painless unilateral inguinal ulcer he had had for 2 months. The patient described the onset of symptoms as the appearance of a small papule with a purulent liquid discharge that developed into an ulcerating nodule, along with a low fever 1 week before the consultation that he did not measure. Clinical examination revealed an ulcerating tumour with raised borders in the right inguinal region and with areas of necrosis, measuring approximately 10 cm at its widest diameter (Fig. 11.98a).

At the STD clinic we performed laboratory exams with the following results: serological screening for *Chlamydia trachomatis* reacted 1:32; cytopathology of a sample of the inguinal lesion: inconclusive morphology for the malignancy; VDRL non-reactive; anti-HIV non-reactive.

Using the clinical and laboratorial evidence, lymphogranuloma venereum was diagnosed and treatment of erythromycin 500 mg every 6 h for 21 days was prescribed. The clinical symptoms totally disappeared after this therapy. This occurred very quickly while the patient was taking the antibiotics.

Three months after the first consultation, the patient returned to the UFF STD clinic presenting a new ulcerating lesion similar to the previous one, this time on the right supraclavicular region. He also reported that 70 days previously he had suffered a fall and fractured his right clavicle, causing pain and local edema, with radiography of the thorax presenting a lytic lesion on his right clavicle and morphostructural abnormalities, caused by an insufflating lesion with formation of mass and density of the soft parts.

Upon physical examination, the clavicular region presented an ulcerating lesion with raised borders, a vegetative base and a purulent secretion that was not painful upon palpation, measuring approximately 4 cm (Fig. 11.98b).

There were no lesions in the inguinal genital region and the inguinal lesion had completely healed (Fig. 11.98c).

These new symptoms led to the strong suspicion that this was a case of systemic neoplastic disease. Therefore, it was decided that the patient should be immediately referred to the National Cancer Institute (INCA) in the city of Rio de Janeiro for clinical investigation and follow up.

The following examinations were requested at the INCA with the following results: tomography of the thorax revealing a bone lesion on the right clavicle, a small nodule with

dense soft areas located on the lung periphery, on the right upper lobe (sarcoma); tomography of the pelvis and abdomen with normal results; skeletal scintigraphy carried out 2 h after intravenous administration of 99mTc-MDP revealing hyperfixation of the radiopharmaceutical across the whole of the right clavicle, the 6th costovertebral joint to the right and the rest of the skeleton with a regular distribution; serological screening for hepatitis A, B and C all negative; anti-HTLV1 and anti-HIV non-reactive; radiography of the right shoulder presenting a significant insufflating lytic lesion on the right clavicle; TGO 16 mg/dL; beta-2microglobulin 2.24; alkaline phosphatase 120 mg/dL; LDH 260; gamma-GT 46; total bilirubin with no abnormalities; hemogram and clinical examination of urine with no abnormalities; incisional biopsy of the right clavicle revealing granulomatous tissue with no malignancy; bone marrow biopsy presenting 70% cellularity involving all three series and exhibiting maturation; incisional biopsy of the supraclavicular ulcerovegetative lesion revealing high grade non-Hodgkin's lymphoma. Immunohistochemistry presenting diffuse non-Hodgkin's lymphoma with large B cells.

Given this confirmed diagnosis, the treatment selected was chemotherapy. We tried to find the patient to find out how the case developed but were unsuccessful.

11.8.1 Comments

This report is important as this is a rare pathology and a challenging diagnosis. Although extracutaneous B-cell lymphomas are more common than the T-cell type, on the skin this is the opposite and T-cell lymphomas are more common. Cutaneous B-cell lymphomas are slightly more prevalent in men and have a higher incidence around the age of 59, its occurrence in younger patients and adolescents being very rare.

Despite the clinical evidence, it is always important that diagnosis is confirmed to exclude other pathologies that have similar characteristics, such as cutaneous tuberculosis, paracoccidioidomycosis, Jessner lymphocytic infiltration of the skin, insect bites, cutaneous leishmaniasis, drug eruption (diphenylhydantoin, carbamazepine, salicylates, nitrofurantoin and cyclosporine) and cutaneous lymphocytoma.

The first lesion described that was treated as lymphogranuloma venereum (inguinal lesion) had various similarities with the second lesion (clavicular), and even though it completely healed very quickly with specific treatment for lymphogranuloma, cutaneous B-cell lymphoma can also recede and reappear.

This means there is a doubt if the two lesions had the same cause, as a biopsy was not carried out on the inguinal lesion, just cytology, which gave a negative result for malignancy.

Another case was seen by the authors at the same STD clinic with a patient from the state of São Paulo presenting a large inguinal mass (bubo), who reported receiving previous treatment with doxycycline and tetracycline, which was unsuccessful, and that the final diagnosis was paracoccidioidomycosis (Fig. 11.96).

Therefore, for patients with any inguinal genital lesions, medical assistants should not forget that many systemic diseases can have localized manifestations that can look like an STD. On the other hand, the presence of STDs with other infectious or non-infectious diseases is a common occurrence.



Fig. 11.98 (a) Ulcerovegetative lesion on the right groin. (b) Ulcerovegetative lesion very similar to that shown in figure (a), on the right clavicular region. (c) Lesion presented in figure (a) completely healed

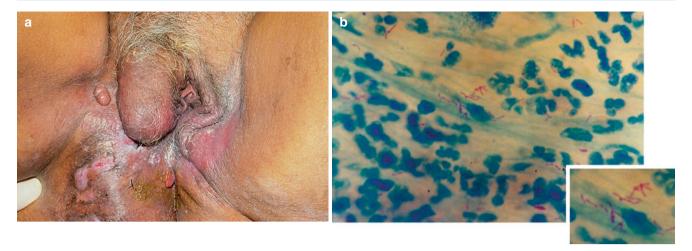


Fig. 11.99 (a) Elderly patient presenting a case of esthiomene: fistulas, ulcers and vulvar elephantiasis. We made a clinical diagnosis of chronic lymphogranuloma venereum (genitorectal syndrome). However, we collected material from the affected area and blood for serological screening. All of the exams were negative for STDs. Since the patient had maintained the symptoms by eliminating the material

contained in the fistulas, we carried out another biopsy and included mycobacterial screening. We then advised the patient to go without antibiotics for a week. Acid-alcohol resistant bacillus (AARB) screening was positive, as shown in figure (b) (thin bacilli stained red) among various polymorphonuclears. The diagnosis was vulvar tuberculosis and the appropriate measures were then taken



Fig. 11.100 Case described in the chapter on HPV. This was a case of Buschke-Löwenstein tumour

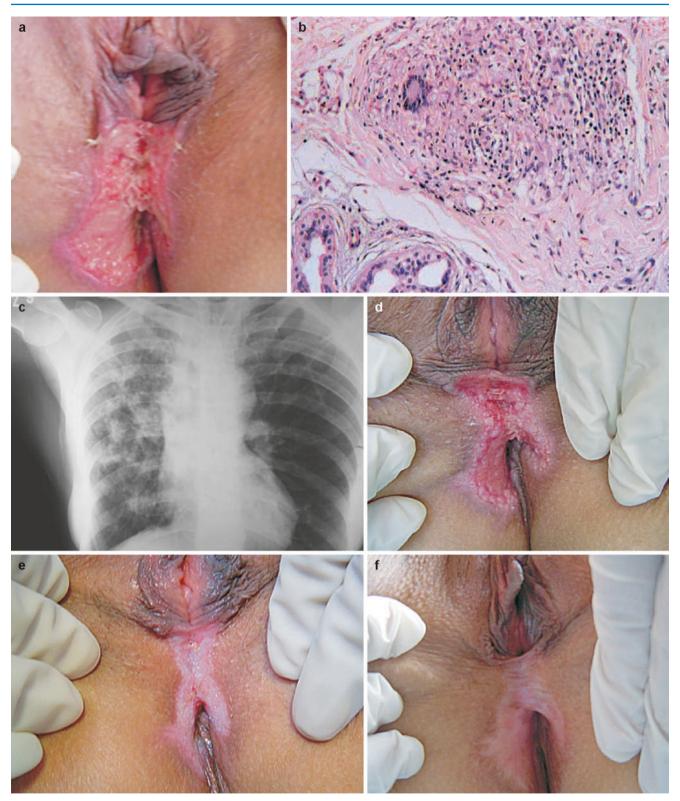


Fig. 11.101 Fifty-four-year-old patient seen at the Santa de Misericórdia Gynaecology Clinic in Vitória, Espírito Santo. She presented a chronic genital ulcer over 7 cm at its largest diameter after an initial erythematous spot in the perineal region associated with light stinging and itching. The lesion had a dirty, granulous base with regular well-defined contours and raised borders (a). Biopsy of the lesion revealed a granuloma made up of giant Langehans-type multinucleated cells with epithelioid cells and permeating lymphocytic infiltrate, suggesting investigation for tuberculosis (b). Radiography of the thorax revealed fibrocystic lesions

on the upper half of the right lung with permeating condensation, highly suggestive of pulmonary tuberculosis (c). Bacilloscopy of the sputum was positive. Triple treatment (rifampicin, isoniazid and pyrimethamine) for tuberculosis was started in April 2005. Once week after starting treatment, the genital lesion improved significantly (d). Twenty-six days into treatment the ulcer disappeared, leaving behind just an area of hypochromia (e). After 42 days the skin was totally epithelized (f). This case was published in the Brazilian Journal of STDs and can be accessed for free at http://www.STD.uff.br/revista18-1-2006/16.pdf



Fig. 11.102 (a, b) Thirty-five-year-old married patient working in general services interned at the hospital at the Federal University of Ceará (UFC) in Fortaleza for hairy cell leukaemia. He presented ulcers with a seropurulent secretion and penile warts that had appeared 3 months previously when he stopped having sexual relations. Examination revealed fistulization with communication between the ulcers. Treatment was started with intramuscular penicillin G benzathine 2,400,000 U.I., and oral doxycycline 100 mg twice a day. Biopsy of the ulcer revealed a light chronic non-specific inflammation and condyloma acuminata. (c) One week after initial therapy. (d) Two weeks after the use of doxycycline and surgical removal of the warts, after

which specific staining for tuberculosis and donovanosis was requested for samples taken from the ulcerating lesions. (e) Positive AARB exam. Acid-alcohol resistant bacilli stained red are indicated by the *arrow*. (f, g) After treatment for tuberculosis with pyrazinamide 2.0 g per day for 2 months, isoniazid 400 mg and rifampicin 600 mg per day for 6 months. This case once again demonstrates the need to carry out laboratory exams and for medical assistants to remember that not everything that is observed on the genitalia is related to a classic STD. Other infectious or non-infectious diseases can occur together with an STD. The patient turned down surgical correction after the infectious disease had been cured

Fig. 11.103 Fournier gangrene. This is a gangrenous cellulitis and a variant of necrotizing fasciitis that affects the anogenital region. It develops quickly into tissue necrosis, with an absence of any obvious suppuration but with systemic toxicity. It affects men around 50/60 years old. It presents mixed aerobic and anaerobic microbiota in cell cultures. The causes include periurethritis, lower urinary tract instrumentation and penis surgery. It progresses into urinary retention, abdominal discomfort and perianal pain disproportional to the local impairment, edema, erythema, skin necrosis, crepitation, blisters and fever. Diagnosis is clinical and laboratorial. The pathogenesis is not clear, but it starts as a periurethral or cryptoglandular infection with local or faecal bacteria. Differential diagnosis is carried out for non-necrotizing cellulitis, streptococcal gangrene, ischemic necrosis or by warfarin. The mortality rate is 10–30%. Treatment must be immediate, surgical (debridement) and with systemic antibiotics



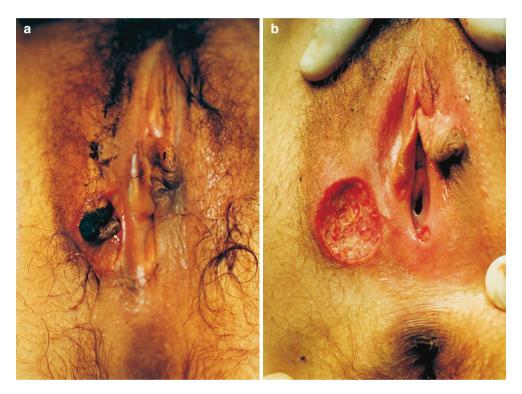


Fig. 11.104 (a) Adolescent with an excellent social and economic level and not sexually active presenting an extensive ulcerating lesion with very painful areas of necrosis that had appeared 4 days previously. She was using oral ampicillin for recurring tonsillitis. All exams for STDs were negative. She was extremely emotionally distressed due to family problems, legal processes and the separation of her parents. She was not

a drug user. (b) We proceeded by cleaning and debriding the lesion in a hospital environment under short-duration general anaesthetic and suspended her use of ampicillin. Examination of material revealed the "pure" presence of bacteria with *Clostridium* morphotypes. Systemic antibiotics with clindamycin was prescribed for 10 days. The lesions healed quickly. Serological screening for syphilis, HIV and hepatitis was non-reactive



Fig. 11.105 Twenty-two-year-old patient interned at the gynaecological clinic at the Federal University of Paraná Hospital in Curitiba presenting the following history. Sixteen days previously she had sought medical attention complaining of axillary folliculitis and was medicated with a non-hormonal anti-inflammatory (NHAI). Two days later she returned to the health centre complaining of vulvar lesions. The initial diagnosis was genital herpes and oral acyclovir was recommended. Serological screening for syphilis, HIV and hepatitis was non-reactive. The symptoms progressed, including an increase in the areas of necrosis on the left labia majora, and as this was thought to be a

reaction to the medication, an oral corticosteroid was prescribed (oral prednisone, 40 mg per day). Two days after starting treatment with corticosteroids, the patient reported an improvement and the symptoms stabilized (a, b). Returning 15 days after starting treatment with the corticosteroids, the patient was asymptomatic and there was a significant regression of the lesions, as shown in Panel (c). The areas of necrosis led to loss of tissue of the right labia majora, which will require reconstructive surgery. Pharmacodermia caused by NHAIs imitates other diseases, leading to incorrect diagnosis of STDs, especially when the lesions occur on the genitals, in both men and women



Fig. 11.106 Genital tumour in an elderly patient referred to the STD/vulvar pathology clinic. This was a case of genital and rectal prolapse



Fig. 11.107 (a–e) This adolescent presented vulvar myiasis, syphilis, trichomoniasis, candidiasis, HIV and was pregnant. She was taken for surgery and the area was cleaned under anaesthetic. After maturation, the larvae were identified as belonging to the *Sarcophaga* genus. She was medicated specifically for each STD. For the HIV she was given antiretroviral medication according to protocol 076. The birth was normal and the baby was born healthy, without any syphilis or HIV infection. We will

now present some cases that we managed to record of people with genital myiasis. Based on personal experience, we have noticed that various doctors that see these types of cases are too "embarrassed" to document them. Some say that it makes the country look bad. We think differently. We believe that seeing, documenting and publishing these cases in a scientific way means we are better prepared to improve society's problems. This actually occurs in every corner of the world

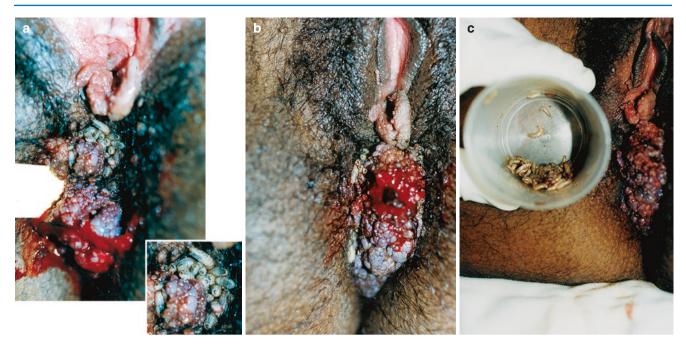


Fig. 11.108 (a-h) The following case of vulvar myiasis is in a 17 year old. She was 10 weeks pregnant and had one fixed sexual partner. The patient had already been to four public health centres: three in the municipality of São Gonçalo and one in Niterói, on the same day, before arriving at the UFF STD clinic. At the fourth health centre the patient could not be seen by the doctor as he was overseeing a birth at the time. At the second she was "seen" but not examined. She was advised to look for another centre. At the third, the emergency unit of a public hospital, she asked to be examined on a bed but this was not permitted. The exam was carried out with the patient standing up. She was prescribed a nonsteroidal anti-inflammatory. At 11 pm she went to another emergency unit in which parasitological examination was requested. She was advised to return the following day to the hospital's medical clinic. The following day, she was advised by a relative to come to the UFF STD clinic in Niterói, where she complained of intense pain in the genital region that made it hard for her to walk. Gynaecological examination revealed condyloma acuminata lesions on her vulva, vaginal introitus and perineum associated with infestation of multiple larvae. Some had penetrated her vagina, anus and urethra. The patient was cooperative and the lesions showed signs of secondary infection. Taking this into consideration, the team opted to immediately remove the larvae using an anatomical clamp. Approximately 50 larvae were removed during the first intervention. After cleaning, the area was covered with solid vaseline in an attempt to close the ostia through which the larvae could get to the surface, as the condyloma lesions made the surgical cleanup very difficult. The patient was medicated with an oral anaesthetic and 1 g oral azithromycin. We asked her to return to the clinic 24 h later. The following day, the pain had improved; approximately 15 larvae were removed. On the third day, another two larvae were removed. Treatment was started for vulvar condylomatosis with trichloroacetic acid solution 60%. Samples were taken for serological screening for syphilis and HIV, for oncotic colpocytology and bacterioscopy of vaginal content using the Gram technique. The patient came to the clinic on various occasions; the condyloma lesions did not totally disappear, however. There was no secondary infection. We decided to surgically remove the remaining HPV lesions under local anaesthetic, which we carried out at the clinic. The tissue fragments were sent for histopathological analysis. After maturation, the larvae were identified as Cochliomya hominovarax. Colpocytology revealed CIN I; staining using the Gram technique and direct cytology of the

vaginal content revealed numerous pus cells and an exuberant mixed microbiota. Serological screening for syphilis and HIV was negative. During follow up of the treatment for the condyloma lesions and vaginitis, the patient suffered a miscarriage and was treated for this at another health centre. Myiasis is seen more frequently in rural areas. In urban areas it mainly affects people with substandard hygiene, those with a low level of education and children. Infestation is most common in uncovered areas of the body. There are only a few reports of vulvar myiasis in the literature. We emphasize the importance of carrying out careful gynaecological examination in order to detect less common diseases. Reinforce with patients that simple hygiene habits can help to prevent this type of disease. The patients described here had substandard levels of hygiene, although they were not homeless. In our opinion, the flies deposit their eggs in the genitals as they are probably attracted by the odour caused by bad personal hygiene and coexisting genital infections. If these are not removed by washing, the larvae grow and cause inflammation. We emphasize the importance of offering serological screening for syphilis and HIV to all patients with genital infections. It is interesting to note that the patient (Fig. 11.107a-e) with multiple genital infections (vulvar myiasis, candidiasis, trichomoniasis, syphilis and HIV) had a normal birth, while the patient with vulvar myiasis and extensive condyloma lesions suffered a miscarriage. The first patient, with a larger genital lesion, who at first did not want to be examined, required general anaesthetic in an operating theatre so that the lesions could be cleaned. The second patient was very cooperative, her lesions contained a lower number of larvae and she was treated in the clinic. The first patient had difficulty communicating and expressing herself and the second demonstrated that she was not accepting her pregnancy very well. We believe that although myiasis in humans is rare, it must occur more frequently than is thought as many cases must be seen in rural areas of many countries, including those that are more developed, or in the areas surrounding large cities, where the doctors do not always have sufficient resources or the habit of registering and publishing these cases. The cases presented here show the importance of paying particular care to patients, which starts with basic medical procedures such as careful physical examination. The negligence towards these patients described is as shocking as the disease itself. These diseases are also reported in developed countries, which are also deficient in treating the poorer members of their populations



Fig. 11.108 (continued)

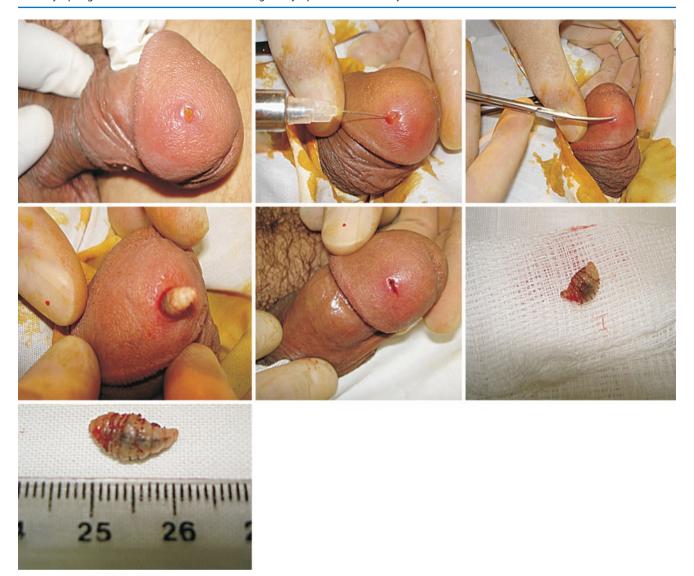


Fig. 11.109 Man over 60 years old, retired soldier, living in a rural area in the municipality of São Gonçalo, Rio de Janeiro, who was referred to the UFF STD clinic by a urologist for the treatment of a genital lesion. During the consultation, the patient reported that he felt "a twinge inside the head of his penis, as though there is an insect inside". He also said that 20 days previously he noticed a nodular lesion and hyperaemia in his glans. He self-medicated for 2 days with polyvalent dermatological creams (corticosteroid, antibiotic, antifungal and antiallergic). He later went to a doctor who according to the syndromic approach for genital ulcers prescribed third-generation quinolone for 7 days. However, he did not improve and the symptoms continued.

During clinical examination we found a nodular lesion on his glans 2 cm in diameter, with a central ulcerated area and an orifice of around 3 mm. It was then possible to diagnose this as a case of myiasis. A small amount of local anaesthetic was applied to widen the orifice and extract the larva through light compression of the base of the cavity. We carried out extensive cleaning of the cavity that had contained the larva with saline and iodopovidone solution. We prescribed ciprofloxacin 500 mg three times a day, an emergency analgesic and vaccination against tetanus. The fly larva was later classified as *Dermatobia hominis*. This case can be visualized for free [9]

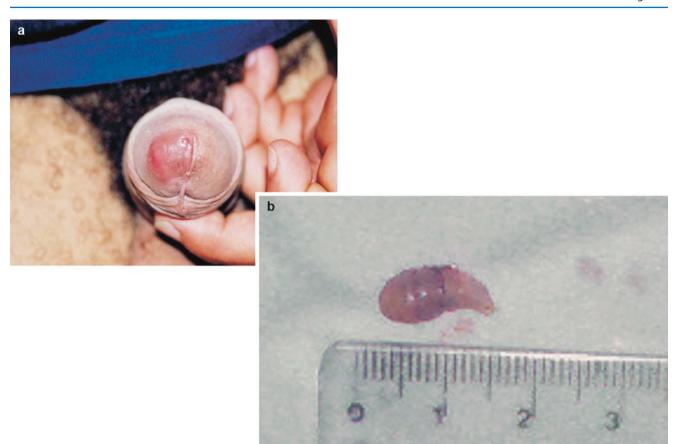


Fig. 11.110 Twenty-one year old man living in an urban area of the municipality of São Gonçalo, Rio de Janeiro, who came to the UFF STD clinic with a lesion and pain in his penis. He said that the lesion had appeared a month before with itching, pain and a small lump on his glans. After a few days, the patient reported that the lesion started to eliminate a serosanguineous secretion from a small orifice in its centre. He said that he sought medical attention 2 weeks previously and had been treated for primary syphilis. He reported that a little before presenting the lesion he noticed that there were more flies than normal in his home. He also said that he sometimes slept naked, that he took a quick shower before going to work and that he used condoms infrequently during sex. Clinical examination revealed a 1 cm × 2 cm hyperemic area next to the urethra (a). The lesion contained an orifice 3 mm

in diameter with a serosanguineous secretion. From the orifice it was possible to see the movement of the larva. We then proceeded to apply local anaesthetic around the orifice and widen it with surgical scissors to around 5 mm. After light and continuous compression of the base, the larva came out of the cavity. The cavity was cleaned extensively with saline solution and we prescribed rifocin 150 mg/mL. We administrated oral azithromycin 1 g. Serological screening for syphilis and HIV was negative. We prescribed vaccination against tetanus. The larva was classified as *Dermatobia hominis* (b). This is another case that demonstrates that the syndromic approach for STDs without good clinical examination can lead to huge errors. This case was published in STI 2004 [10]. In 2007, it was classified in the Top Ten with 4562 Total Full-text Accesses





Fig. 11.111 (a–c) This case was described in the chapter on HPV and illustrates a case of epidermodysplasia verruciformis and vulvar intraepithelial neoplasia (VIN) in the same patient. Epidermodysplasia verruciformis consists of a particular susceptibility to cutaneous infection by HPV. The lesions normally start to manifest during infancy and are generalized, with the appearance of flat warts or scaly erythematous lesions that resemble tinea versicolour or pink psoriasis. The types of HPV related to the first type are 3 and 10, and those related to the second type are 5 and 8. Many patients present infection by multiple types

of HPV. Half of these cases are inherited through an autosomal recessive inheritance pattern. Recurrence of the lesions is common, even after treatment. The types of HPV linked to epidermodysplasia verruciformis can be oncogenic in susceptible individuals. Lesions can occur on the cervix and oropharynx, but this is not common. The existence of an immunological defect specific for HPV has been proposed. Some patients have a high risk of the appearance of squamous cell carcinomas, which usually occur in tinea-type lesions in areas exposed to the sun (mainly in those caused by types 5 and 8)

11.9 Lichen Sclerosus or Scleroatrophic Lichen

11.9.1 Concept

Chronic dermatosis that can occur on the genitalia of both sexes and that is characterized by atrophic, confluent, whitish shiny papules or plaques with a hard dry surface.

11.9.2 Etiopathogeny

Its aetiology is unknown although there is evidence of genetic alterations (association with human leukocyte antigens (HLA)), autoimmune disease or peripheral metabolism of androgenic hormones. It is more common in woman than in men with a proportion of 10:1. It is more common in adults but can occur at any age.

11.9.3 Clinical Manifestations

In men the condition is usually asymptomatic, with the development of erythematous lesions into typical lesions taking months or years. Uncircumcised men more frequently present stinging, itching, dysuria, painful erections and strips of sclerotic tissue of 1–2 cm can form on the distal part of the foreskin. In these men, the final stage of balanitis xerotica obliterans can occur.

In women, this mainly occurs on the vulva and the anus, starting with few or no symptoms and developing to itching that becomes very intense, fragile skin with erosions, pain, formation of scar tissue and finally constriction of the vaginal introitus (kraurosis vulvae).

Extragential cutaneous lesions can sometimes occur in both sexes.

11.9.4 Laboratory Diagnosis

Diagnosis is made through biopsy of the affected skin. Histopathological examination reveals hyperkeratosis, atrophy of the malpighian layer and vacuolization of the basal layer, dermis with mononuclear inflammatory infiltrate (lymphocytes) in strips, edema and homogenized collagen fibres.

11.9.5 Treatment and Control of Cure

Treatment involves high-strength corticosteroid creams for up to 6 months. Topical immunomodulators (tacrolimus) have a good response. Creams with antibiotics or antifungal medication can be used for secondary infections and circumcision where necessary. The application of topical testosterone for lesions on the vulva is no longer used. Surgery in women has a high rate of recurrence. Topical corticosteroids do not bring about cure but can control symptoms.

There are reports that itching can be improved by taking high doses (800,000 U.I.) of oral vitamin E for long periods.

11.9.6 Differential Diagnosis

Differential diagnosis includes lichen simplex chronicus, vitiligo and lichen planus. Squamous cell carcinoma can develop in up to 5% of women with untreated vulvar lichen sclerosus.

Fig. 11.112 (a, b) Patient with hypochromia and intense vulvar itching which sometimes caused fragility of the skin leading to bleeding. Histopathological examination led to a diagnosis of lichen

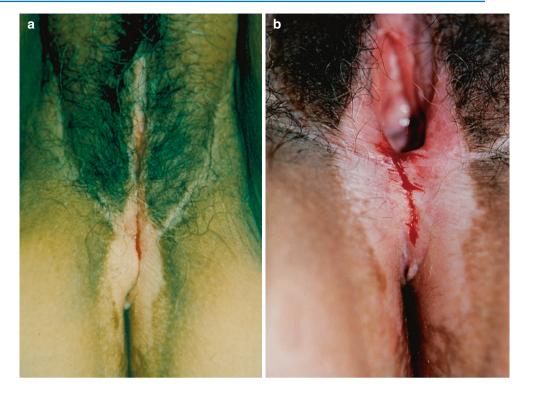




Fig. 11.113 Another case of lichen sclerosus. Although these may seem to be simple cases, various patients with similar symptoms are referred to STD clinics



Fig. 11.114 Lichen sclerosus

Fig. 11.115 Patient with vulvar lichen sclerosus. Sometimes patients with these symptoms are initially investigated and receive treatment for HPV infection. Clinical experience and histopathological exams are important for dealing with these cases



Fig. 11.116 (**a**, **b**) The Collins test, application of toluidine blue stain followed by the application of acetic acid, can help to identify areas of high mitotic activity, helping to provide a better biopsy. Intraepithelial vulvar neoplasia (VIN) is a flaky intraepithelial process characterized by proliferation and abnormal epithelial maturation with an increase in nuclear volume and nuclear atypia. Based on the extension of the intraepithelial neoplasia, this can be histopathologically classified into VIN I (light dysplasia), VIN II (moderate dysplasia) or VIN III (accentuated dysplasia/carcinoma in situ)





Fig. 11.117 Patient with intraepithelial neoplasia II associated with HPV infection. It is worth noting that this patient was submitted to numerous topical applications of podophyllin solution, trichloroacetic acid for over a year for the treatment of the "HPV lesion" (according to the patient). The first time that we saw this patient we carried out biopsies of distinct parts of the lesion in order to better evaluate the case



Fig. 11.118 Another patient presenting VIN II. The history of the clinical evolution of this patient is similar to that for the previous patient

Fig. 11.119 Cervical cancer with uterine prolapse in a 76-year-old patient referred for evaluation by an STD specialist





Fig. 11.120 Cervical cancer in an elderly woman with genital prolapse. We now know that almost all these cases had persistent HPV infection as their cause, mainly types 16 and 18

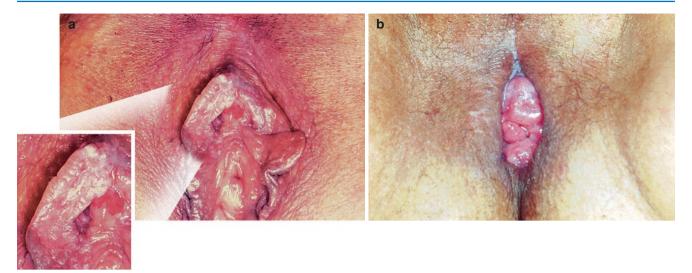


Fig. 11.121 (a) This patient over 50 years old was treated for months with podophyllin solution 25% for a lesion on the labia minora close to the clitoris. She went to the STD/vulvar pathology clinic at the Institute of Gynaecology at the Federal University of Rio de Janeiro, where after

undergoing a biopsy she was diagnosed with in situ vulvar carcinoma. (b) Treatment was surgical: vulvectomy. We believe that chronic, recurring lesions that are resistant to treatment should undergo histopathological analysis



Fig. 11.122 Similar to the previous case. This patient was treated with "a liquid that burned a lot" (she didn't know the name of the solution) for vulvar tumour. Biopsy revealed this to be vulvar cancer

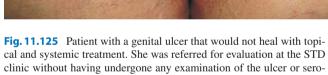


Fig. 11.123 Very elderly patient referred for treatment for an STD as she presented a vulvar ulcer that had been present for more than a year and had not healed with topical products and systemic antibiotics. This was a case of vulvar cancer in the area around the clitoris

Fig. 11.124 Invasive cancer of the vulva. The clinical history was very similar to that for the previous patient









logical screening. Biopsy revealed this to be carcinoma of the vulva. We now know that at least half of cases of cancer of the vulva are caused by HPV



Fig. 11.126 Cancer of the vulva and lichen sclerosus



Fig. 11.127 Patient with a chronic vulvar ulcer who had already been submitted to various treatments. Biopsy revealed this was cancer of the vulva



Fig. 11.128 Another case of chronic vulvar ulcer with a diagnosis of cancer of the vulva. It must be repeated: we believe that chronic, recurring lesions that are resistant to treatment should undergo histopathological analysis as soon as possible. Delaying decent medical attention trivializes the value of life, quality of life and the resources made available by the government. We say this because the absolute majority of these cases are seen in poorer members of society who use the public health system



Fig. 11.129 Recurrence of cancer of the vulva in a patient who had undergone vulvectomy and radiotherapy



Fig. 11.129 (continued)



Fig. 11.130 Another case of chronic vulvar ulcer in which the diagnosis was cancer of the vulva and the clinical history was the same as the various cases related above





Fig. 11.131 Eighty-two-year-old woman seen at the vulvar pathology clinic at the gynaecology service at the UFF's Antônio Pedro University Hospital, with diagnosis of the underlying disease being chronic lymphocytic leukemia (CLL) and histological examination revealing a her-

pes simplex vulvar ulcer + CLL. Before being diagnosed at the UFF gynaecology clinic, the patient received various "treatments" without any laboratory examination

Fig. 11.132 Sixty-two-year-old patient who sought medical attention at the family health program in the municipality of São Gonçalo, Rio de Janeiro, complaining of vulvar pain and the sensation that she had a "ball" in her vagina. She had been to an emergency clinic 10 days before, where she was seen by a gynaecologist who did not examine her but prescribed penicillin benzathine 2,400,000 U.I. and asked her to go to a health centre, as her case was not an emergency (according to information from the patient). A biopsy was performed on the lesion and the histopathological result was squamous cell carcinoma of the vulva. The patient was referred to the specialist service but died 4 months later. It is worth noting that the patient had been presenting these symptoms for many years and that she sometimes sought medical attention and was medicated with "creams and pills"





Fig. 11.133 Fifty-five-year-old woman presenting these lesions that had appeared 8 months previously (a, b). She said that she was seen by a doctor on the family health program and was medicated with topical nystatin cream and ketoconazole pills. She said that no laboratorial exams had been carried out to confirm the diagnosis. After cytology and histopathology (c-e) of the lesion, we were unable to identify the aetiology. However, the lesions reduced in size considerably with the use of oral ciprofloxacin 500 mg twice a day for 15 days and doxycycline 100 mg twice a day for 30 days. In fact, at the start of the treatment the

patient used the medication inconsistently. Only after we provided all of the medication was there an improvement in the symptoms. However, the lesions increased in size again. Another biopsy was carried out and the result was inconclusive. (f) shows a significant improvement with the use of prednisone 40 mg every morning for 2 weeks. Various exams, including colonoscopy, did not reveal any alterations. Examinations by other professionals including a dermatologist and a proctologist were requested. However, a diagnosis was still not confirmed



Fig. 11.134 This warty clinical appearance resembles condyloma acuminata; however, data such as age, length of development and histopathology of the lesion revealed this to be warty carcinoma of the vulva



Fig. 11.135 Typical case of melanoma of the vulva diagnosed through biopsy of the lesion



Fig. 11.136 Similarly to the previous cases, this patient was being treated for HPV. Biopsy indicated this was an invasive malignant lesion. It is routine for us to perform histopathological analysis on any lesion that has been present for 4 weeks or more, principally if they do not recede with clinical treatment



Fig. 11.137 This patient, who had lesions for years, was having an ulcerovegetative lesion treated with podophyllin for months. It was a case of squamous cell carcinoma of the penis

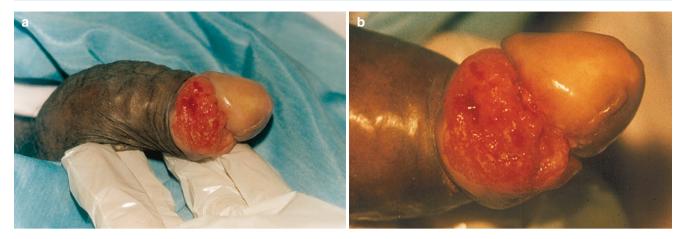


Fig. 11.138 (a, b) This was the case of an 82-year-old man who had this lesion for over a year. He used healing pomades and antibiotics for "venereal disease". He was referred from another health centre to the STD clinic. Biopsy revealed this to be cancer of the penis



Fig. 11.139 (a) Identical to the previous cases. Cancer of the penis being "treated" as a genital wart caused by HPV. (b) Thirty-five-year-old patient who had a lesion on his glans for 3 years that progressively increased in size despite treatment with podophyllin. Biopsy revealed this to be squamous cell carcinoma. Delaying biopsy of chronic genital lesions generally delays correct diagnosis and reduces the chances of efficient treatment being administered. (c) This patient was submitted to surgical treatment for amputation of the penis (Photos 11.137b, c by Edison Natal Fedrizzi)



Fig. 11.140 (a) This patient, who was from a rural area, reported that for 6 years he had vegetative lesions on his penis that were treated by being strung with horsehair (according to the patient). We examined him during an STD training session for doctors from the northeast of Brazil. (b) Biopsy revealed this to be cancer of the penis. Note the severe inguinal lymphatic impairment indicating invasive disease

Fig. 11.141 Middle-aged patient presenting cancer of the penis. It is worth noting that all of these cases of cancer of the penis and cancer of the vulva could have been diagnosed and treated a long time before these photos were taken. In addition, we hope that in the near future many cases of genital cancer will be avoided through the consistent use of condoms, progress in health education and vaccination against HPV. This is the case all over the world





Fig. 11.142 Another case of cancer of the penis with locoregional lymphatic impairment associated with advanced disease



Fig. 11.143 Patient who had already had an operation for cancer of the penis (amputation) presenting inguinal impairment and scabies



Fig. 11.144 Young patient who had these symptoms for 2 weeks. Screening for possible sexual transmission agents was negative, including serological screening. He was medicated with a single dose of oral azithromycin 1 g and the symptoms cleared up within a week. We carried out clinical and serological follow up for more than a year and the symptoms never returned

Fig. 11.145 In (a), a patient over 50 years old referred to the STD clinic as he was presenting a pedunculated lesion on his left buttock that was years old. The patient was extremely anxious, as the hypothesis he had been given on various occasions was that it was an STD; probably condyloma acuminata. In (b), through very careful clinical examination it can easily be seen that this is just a case of "molluscum pendulum", a plicoma approximately 3 cm long. In (c), suture of the skin after exeresis under local anaesthetic. As is good practice, the material was sent for pathological examination. Serological screening was negative





Fig. 11.146 (a–e) Fifty-four-year-old patient presenting these symptoms for over 3 years, including fistulas in the area close to the anus that trailed off towards the adipose tissue on the left buttock. He reported that he had used "all antibiotics". He also informed us that the first week he had used antibiotics the symptoms had improved and the elimination of the purulent secretion had reduced. However, all of the symptoms

returned after 2 weeks. We identified just *Staphilococcus aureus* in the secretion. Exams for STDs, including serological screening for chlamydia, syphilis and HIV were non-reactive. We opted to perform surgical exeresis of the area. In (e), note how it trailed off. Histopathology concluded that this was pyogenic granuloma



Fig. 11.147 (a–d) Identical to the previous case, the only difference being the sex of the patient. No links to any STD could be established. However, both patients did not have sexual partners but were "labelled as carriers of chronic and untreatable venereal diseases"



Fig. 11.148 Patient with hidradenitis suppurativa (HS). This is a disturbance of the apocrine sweat glands. It is more common in women and the reason for this is unknown. It can develop in any area, but the genitofemoral lesions are more common in women. HS is currently considered to be a disease of the follicular epithelium, with follicular occlusion and subsequent inflammation causing clinical problems. Studies suggest that it involves a dominant autosomal inheritance pattern with the transmission of just one gene. However, no genetic locus has been discovered. Differential diagnosis includes: furuncles, abscesses, actinomycosis, donovanosis, lymphogranuloma venereum, Crohn's disease and tuberculosis, including others. The quality of life of people with severe symptoms is significantly affected. In the case in question, the patient was totally excluded from work, social and family life. Her husband threw her out of the house believing that she had an incurable venereal disease. To treat HS, surgery involving skin grafts can lead to cure in some cases. Antibiotics, retinoids (isotretinoin, acieration and etretinate), hormonal treatments (cyproterone acetate 50 mg + ethinyl estradiol 50 g), immunosuppressants and even radiotherapy can be used. The patient in question had been submitted to almost all of these treatments with little improvement and in small intervals. We could not maintain this patient's follow up



Fig. 11.149 (a–c) Adolescent presenting a case of genital elephantiasis. Although he had been screened for chlamydia and even filariasis, these exams were negative. The patient was resident in sub-Saharan Africa. This impairment of lymphatic drainage is irreversible and in some cases can even be congenital. This was a 13-year-old boy who reported that the problem started when he was 10 after some slight peeling on his penis. He reported having had some sexual experiences. Serological screening for syphilis and HIV was also negative





Fig. 11.149 (continued)



Fig. 11.150 Fifty-six-year-old patient from a rural area in the state of Rio de Janeiro reporting that she had had a single fixed partner for over 20 years. She was referred to us presenting extremely painful vulvar ulcers that had appeared 2 months previously. All of the correct examinations, including biopsy, were non-specific. She had already been medicated with various antibiotics without any significant improvement. This patient was seen in 1988. Owing to her history, we followed up the husband who was around the same age, apparently healthy, and to begin with we had some difficulty broaching the subject of HIV with him. However, after three consultations over the period of a month we also overcame our prejudices and managed to perform a HIV test. The results were positive for both the husband and wife. He then reported sometimes having sexual relations without a condom with some "girls" in the city. For the whole team and for me in particular, this case was a turning point in us never delaying HIV exams in any patient with any type of genital abnormality, even if the clinical history does not at first indicate any form of risk. The etiology of the ulcer was not established through exams, but it improved with high doses of acyclovir. The patient died due to various complications before the ulcer had healed completely. It was highly probable that this was a case of genital herpes or a cytomegalovirus lesion caused by HIV



Fig. 11.151 (a) Adult man with painful chronic penile ulcers. He claimed that the pain diminished if he tightened a strip of gauze around his penis. As this had been present for months, it ended up causing significant edema and increasing the volume of the organ. He reported having already used various creams and pomades on the area, as well as systemic antibiotics and anti-inflammatories. He stopped having sex just the previous month. We advised him to stop taking any systemic or local medication for a week. We then carried out our routine procedure for chronic genital ulcers, including direct examination, the Gram technique, AARB, the Giemsa technique, dark field microscopy, the Papanicolaou technique, histopathology and reserve slides. Serological

screening for syphilis and HIV was also performed. None of the exams identified the etiological agent. (b) The patient was medicated with oral azithromycin 1 g per week for 4 weeks. The results were highly satisfactory, as the lesions were almost healed by the third week. General measures relating to diet and hygiene were advised and he was asked to remove the gauze that he used to compress the area. Oral tramadol was prescribed for the pain, which the patient described as intense. Both the patient and his partner asked if mastic tea baths could be used on the area, which had been recommended by a family member. We did not object to such a practice. We just advised that if this caused any irritation he should stop doing this and return to the clinic immediately



Fig. 11.152 Patient with elephantiasis, ulcers and fistulas. Saxophone penis indicates problems, probably involving fractures to the tunica albuginea of the penis. This could be a sign of Peyronie's disease



Fig. 11.153 (**a**, **b**) Forty-seven-year-old patient from a rural area of Rio de Janeiro state presenting these lesions that had appeared 20 years previously. She had already been submitted to various treatments for HPV without any improvement. Serological screening for syphilis and HIV was non-reactive. The patient denied having multiple partners or having had any STD. Following our routine of performing biopsies on any lesions that are over a month old, we were able to obtain a histopathological diagnosis of Mibelli's porokeratosis (Vittorio Miybelli, Italian dermatologist, 1860–1910). This non-infectious pathology affects mostly the skin in the genital region. It represents a keratiniza-

tion disorder histologically characterized by the presence of a cornoid lamella. Clinically this creates a wall of cells through the stratum corneum of the lesion. This disease follows a dominant autosomal inheritance pattern. In a small percentage of patients this can develop into malignant degeneration: squamous cell carcinoma or basal cell epithelioma. Treatment should concentrate on the individual destruction of the lesions (using physical or chemical means). Some use 5-fluorouracil 5% cream twice a day for 15 days. Recurrence is not uncommon and it can worsen with exposure to the sun or immunosuppression





Fig. 11.154 Twenty-five-year-old patient seen at the STD clinic at the Valença Faculty of Medicine in Rio de Janeiro with a history of warty lesions on her vulva, the base of her thighs and her left hand. She said she had these lesions for around 8 years and had been submitted to various topical treatments (podophyllin, trichloroacetic acid 90% and podophyllotoxin) without any improvement in her symptoms. She reported to have undergone two surgical procedures to remove part of the lesions. A biopsy of the lesion was carried out providing a diagnosis of inflammatory linear verrucous epidermal naevus (ILVEN). Note the linear lesions on her left hand and left hemivulva. In 1896, Unna was the first person to propose the term inflammatory linear verrucous epidermal naevus. The specific histopathological characteristics described are:

alternation between hypergranulosis associated with areas of orthokeratosis and agranulosis associated with areas of parakeratosis. The nonspecific characteristics described are: papillomatosis, acanthosis and chronic perivascular and dermal lymphomonocytic infiltrate. The following findings may also be seen in cases of psoriasis. Nonhistopathological criteria for diagnosis of ILVEN: — Early age of appearance (in 75% of cases this appears before the age of 5 and in 50% of cases before 6 months) — Predominance in women with a proportion of 4:1 — The left side is more commonly affected — Itchin g — Psoriasiform appearance — Persistence and resistance to treatment. Martins et al. also describe an excellent case ILVEN [11]

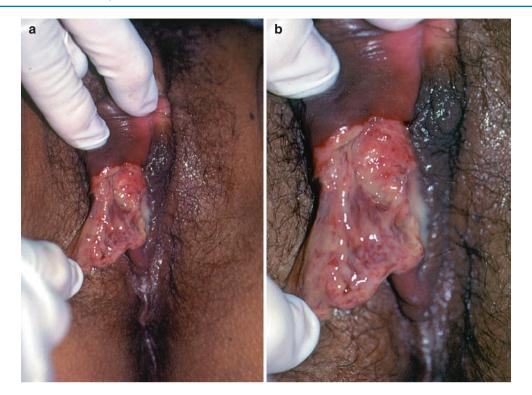


Fig. 11.155 (**a**, **b**) Patient with a chronic ulcerovegetative ulcer. None of the exams carried out, including direct bacterioscopy, cytology, histopathology and serological screening, provided a diagnosis. These cases are labelled genital ulcer of unknown etiology. In these situations, the syndromic approach for ulcers should be used. If this does not work, we usually recommend long-term antibiotic treatment, which may involve doxycycline, sulfa, lincomycin or azithromycin.

The combination of lincomycin and amoxicillin for 30 days has already healed some of these lesions. General advice on hygiene, diet and screening for general chronic disease should not be forgotten. Even with the best laboratory resources, approximately 20% of ulcers do not receive a defined etiological diagnosis. However, we must use the laboratory resources that we have and ask for the expert advice of our colleagues



Fig. 11.156 Another case technically labelled genital ulcer of unknown aetiology. However, this case could also be called "I don't know what this is"



Fig. 11.157 Patient in her 50s with a chronic case of genital lesions who was initially medicated with numerous topical treatments. Histopathology of a genital biopsy revealed this to be Hailey-Hailey disease (HHD). HHD, also called benign familial pemphigus, is clinically characterized by flaccid blisters and erosions, mainly in intertriginous areas as seen in this case. This is a rare acantholytic condition involving a dominant autosomal process (mutations to the ATP2C1 gene). The main alteration results in the loss of cellular adhesion in the epidermis, which alongside local factors (friction, humidity, heat, microbial colonization and secondary infections) leads to the appearance of lesions in intertriginous regions. Eight people in the same family presented this disease. Differential diagnosis includes Darrier's disease. Treatment generally involves corticosteroids and systemic antibiotics, as secondary infections exacerbate acantholysis. Surgical methods can also be used, such as exeresis of the area and healing by secondary intention, exeresis with skin grafting, dermoablation and laser ablation. In a well-documented study, Bessa et al. (http://www. scielo.br/pdf/abd/v85n5/v85n05a21.pdf) describe the use of type A botulinum toxin for the treatment of HHD in two women



Fig. 11.158 This patient had also been submitted to various treatments before undergoing an adequate biopsy, the histopathological diagnosis from which was Darier's disease (DD). DD is also a disease inherited by a dominant autosomal process (mutation to the ATP2A2 gene). Histopathology of DD revealed hyperkeratosis and focal dyskeratosis (abnormal keratinization and premature keratinocytes) associated with acantholysis and suprabasal fissure. Differential diagnosis for DD includes seborrheic dermatitis, Grover's disease, Hailey-Hailey disease, pemphigus vulgaris, Candida infection, impetigo and flat warts. Treatment involves topical steroids, oral retinoids, antiseptics and antibiotics to treat secondary infections. The use of topical tacrolimus to treat extensive Darrier's disease has been cited. Psychological follow up is required as a result of social disability



Fig. 11.159 Elderly patient with a chronic hypochromic vulvar lesion and ulcerative areas. Note the vulvar atrophy. Biopsies of different areas were carried out and the syndromic approach for genital ulcers was avoided without previous detailed evaluation of epidemiological aspects. This was diagnosed as lichen sclerosus



Fig. 11.160 Patient with systemic lupus erythematosus (SLE), which was the underlying cause of this extensive genital condylomatosis (HPV). The systemic disease increases the recurrence of condylomas and hinders treatment, as it makes secondary infection more likely after chemical or electric cauterization and/or exeresis



Fig. 11.162 Young female patient with seborrheic dermatitis on her buttock. This case was initially confused for HPV at a different health centre



Fig. 11.161 Young woman with a significant case of molluscum contagiosum who was referred for treatment of genital blisters caused by HPV. Note the lesions with central umbilication that are characteristic of molluscum contagiosum, which is totally unrelated to HPV. Although this is not a classic STD, the full routine for genital lesions should be followed. Especially serological screening for syphilis, HIV and hepatitis



Fig. 11.163 Young female with a urethral cyst referred for treatment of misdiagnosed bartholinitis



Fig. 11.164 Forty-eight-year-old patient presenting a vegetative lesion on her cervix and at the back of her vagina. Biopsy revealed invasive carcinoma of the cervix. For a long time we have known that cases such as this can be avoided with serial oncotic colpocytology. We currently believe that these situations can be eliminated using the vaccination against HPV and the consistent use of condoms, as well as the other measures cited above





Fig. 11.165 Patient with American cutaneous leishmaniasis (ACL) on the face. Note that in its initial form this abnormality can be confused with labial herpes. ACL is a chronic non-infectious parasitic disease caused by protozoa of the genus Leishmania, with the involvement of various species of this parasite. Transmission occurs through vectors (rodents, canines, horses, marsupials, etc.). This is a zoonosis that secondarily affects humans. Diagnosis can be obtained, as it was in this case, through the Montenegro skin test, serological reactions including indirect immunofluorescence (RIFI) and ELISA, PCR and flow cytometry. The best diagnosis is demonstration of the presence of the parasite in the lesion. The material can be scraped or biopsied from the lesion, preferably from the borders, and stained cytology analysis using the Giemsa, Leishman or Panoptic techniques should be used. This patient was treated with N-methylglucamine antimoniate (the WHO's drug of choice), but amphotericin B and pentamidine isethionate may also be used



Fig. 11.166 These cases of cancer of the penis in men from the state of Alagoas are in patients around 50 years old. All of them had a history of chronic warty lesions, treatment with local and systemic antibiotics and the absence of biopsies



Fig. 11.167 Patient with lymphangiectasia after surgery to treat cancer of the penis. He also presented dermal sequelae from radiotherapy. We now know that the majority of cases of this tumour involve HPV. Molecular epidemiology studies indicate type-6 HPV as the second most identified type of HPV in biopsies for cancer of the penis. Therefore, vaccination against HPV should not be delayed in young men as a preventative measure for this disease. Together with the use of other preventative measures such as the consistent use of condoms



Fig. 11.168 Eighty-three-year-old patient seen just for a biopsy of a vegetative lesion on her vulva. Histopathological examination revealed this to be condyloma acuminata with areas exhibiting atypia but with no malignancy. Surgical exeresis was proposed







Fig. 11.169 Patient from a rural area of Alagoas with a case of systemic lupus erythematosus. Note that the dermatological abnormalities mean that differential diagnosis should include exanthematic syphilis, also known as secondary syphilis



Fig. 11.170 Patient referred to the Salgadinho Medical Centre in Maceió, Alagoas, to treat a lump on her vulva. This was not in fact an STD but an epidermal inclusion cyst and it was treated by removing the cyst



Fig. 11.171 Fifteen-year-old patient seen at the Salgadinho Medical Centre in Maceió, Alagoas, with various papular and hyperchromic lesions with a rough surface on her vulva. Biopsy revealed this to be condyloma + VIN 1

Fig. 11.172 Young adult male, rural worker, with reddish papular dorsal lesions, each presenting a central orifice. He described "twitching and stinging" in the lesions. He said he had previously had larvae in his scalp. He was medicated with oral ivermectin. He returned for a consultation 3 weeks later saying that the upper lesion had "opened" after 3 days and a dead larva had come out of it. The rest of the lesions receded



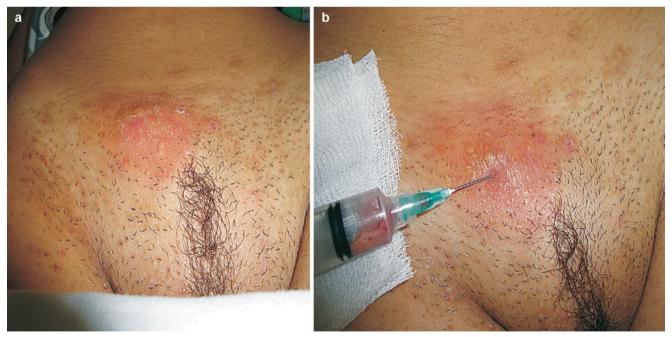


Fig. 11.173 University student that came to the UFF STD clinic complaining of pain, heat and redness in her pubic region (a). She reported that she had similar yet less intense symptoms around a year ago after using a razor in this area. A week previously she noticed that the inflammation had worsened. She went to a gynaecologist, who prescribed amoxicillin 500 mg three times a day and told her this was an STD—lymphogranuloma—but they did not request any serological screening and did not ask the sexual partner to arrange a consultation. After the

anamnesis we discovered that the patient always used a condom and that she had not had sex for over 6 months. Emptying of the abscess was proposed (b) and we requested serological screening for chlamydia, syphilis, HIV and hepatitis B (she did not know her vaccination status). We also performed direct immunofluorescence on the purulent content to screen for chlamydia. All exams were negative. A course of vaccinations against hepatitis B was prescribed

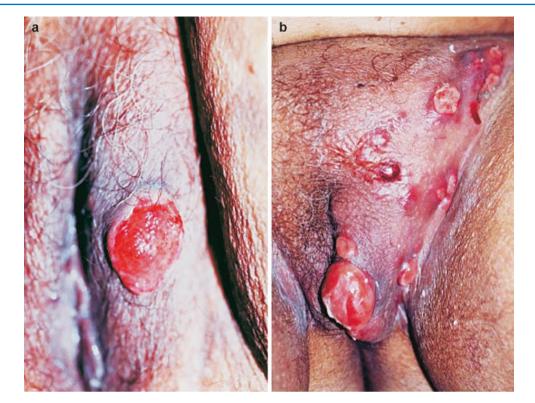


Fig. 11.174 Sixty-five-year-old patient seen at a private clinic with a slightly painful erythematous ulcer with a clean base and raised borders (a). She had already been submitted to antimicrobial treatment according to the syndromic approach for genital ulcers without success and she was still taking oral ciprofloxacin 500 mg twice a day. She said that the histopathological results for a biopsy of the lesion would be ready in a week. She reported that the lesion had appeared 2 months previously. During the anamnesis we discovered that she had fever in the evenings and the hemogram revealed leukocytosis with deviation to the left. Although she said she had lost weight in recent months, this was not exaggerated (according to the patient). One week later she brought the results of the biopsy: pyogenic granuloma. As the symptoms had not improved, we called the laboratory that carried out the histopathology and asked for the slide to be re-examined. We were told that this

would take 2 weeks. We therefore decided to perform some other biopsies (one from the middle of the lesion and two from two different borders) and send these to a known professional. The result was lymphoma and the patient developed unsatisfactorily (vulvar lesion (b) and dying a few months afterwards). A month after we requested that the slide be re-examined, the laboratory got in touch to say that the result was incorrect and that it must be something malignant. We asked them about the delay in correcting the error and they informed us that "dealing with health plans sometimes leads to this". Once again it is clear that the syndromic approach for STDs should be monitored. It also shows that many genital abnormalities are local symptoms of a systemic disease and that asking for re-examination of slides and carrying out new exams for analysis by a well-known professional are attitudes that should be put into practice and not delayed

Fig. 11.175 Sixty-eight-year-old patient submitted to vulvectomy some years ago for VIN III and who has been undergoing follow up and treatment for lichen sclerosus for 4 years. Eight months previously she noticed a round lesion on the right of her vulva with a warty appearance, and this was treated as condyloma acuminata without success. Exeresis of the lesion was performed, which revealed a diagnosis of warty carcinoma. It is worth noting that chronic lesions should be biopsied (Photo by Edison Natal Fedrizzi)



11.10 Vulvar Paget's Disease (Recurring Extramammary Paget's Disease of the Vulva)

Recurring extramammary Paget's disease of the vulva (EMP) is a rare adenocarcinoma characterized by glandular differentiation and an insidious course. With standard treatment there is the risk of loss of tissue function and recurrence of the disease. Recurrence rates of EMP are high despite aggressive surgical intervention. Diagnosis is carried out through histopathological examination and the recommended treatment is currently extensive surgical excision. Histopathological characteristics are similar to Paget's disease of the breast and Paget's disease of the vulva. Paget cells are present either in isolation or in small groups, and they are characteristically stained with hematoxylin and eosin. New therapeutic strategies that are less mutilating and aggressive than excision, X-ray therapy or chemotherapy would be good options.

Here we report a case in which complete clinical and histological resolution of non-invasive EMP of the vulva was achieved with minimum adverse effects after 6 weeks of application of imiquimod. Imiquimod is an immunomodulator that stimulates the production of a series of cytokines, including IL-1, IL-6, IL-8 and IL-12, and particularly IFN $-\alpha$ and TNF. Imiquimod is generally well tolerated without any serious secondary effects or tissue damage. This can be a useful alternative or adjunctive in the treatment of EMP.

11.10.1 Case Study

Here we present the case of a patient with recurring EMP who responded to treatment with topical imiquimod. She is a 72-year-old woman with a history of hypertension and diabetes, and in 1995 she underwent a vulvectomy (with disease-free margins) for EMP. She abandoned her follow up but returned 8 years later with a benign lesion, an erythematous papule close to her surgical scar. Once the symptoms had been alleviated with a topical corticosteroid, the patient did not turn up for her scheduled vulvoscopy.

The patient reappeared 2 years later with a larger lesion (Fig. 11.176a). Upon examination, a lesion with hypopigmentation and leukoplakia was observed on her vulva and the gluteal region. Biopsy was positive for EMP and differential diagnosis was confirmed through histopathological

examination (HE—Fig. 11.176b) and immunohistochemistry (Table 11.3). Immunohistochemistry was positive for CK 7 (Fig. 11.176c), EMA (Fig. 11.176d) and CEA (Fig. 11.176e). As a result of her chronic secondary diseases (diabetes and arterial hypertension), we did not propose another operation. The therapeutic options were discussed with the patient and she agreed to undergo treatment with imiguimod cream 5% for 6 weeks. The treatment started on 10.08.2005. One week later, she returned to the emergency room with headache and flu-like symptoms, where she received medical attention and gynaecological evaluation (Fig. 11.177). Owing to the pain, stinging and ulceration in the treated area, she returned 14 days later (Fig. 11.178) and the topical medication was suspended for 2 weeks. On her next visit, she presented a significant improvement with just slight hyperaemia (Fig. 11.179) and her medication was restarted. After the course of medication was completed, the patient evaluation and biopsy were negative (Fig. 11.180a, d). Follow up confirmed that this approach had been successful (Fig. 11.181). The patient remained clinically free of EMP for around 1 year.

11.10.2 Conclusion

The management of EMP of the vulva can be challenging and sometimes frustrating. Various factors contribute to recurrence and failures in treatment. This report suggests that topical imiquimod can used as an alternative for patients with recurring extramammary Paget's disease in order to avoid suffering, permanent disfiguration and functional deficits. Imiquimod cream works as a modifier of the immune response and seems to be a promising additional option for therapy.

Table 11.3 Immunohistochemical colouration

Immunohistochemical	Results
CK 7	Positive
EMA	Positive
CEA	Positive
GCDFP-15	Weak positive
HMB-45	Negative
Protein S-100	Negative
Melan-A	Negative
c-erbB-2	Negative
p53	Negative

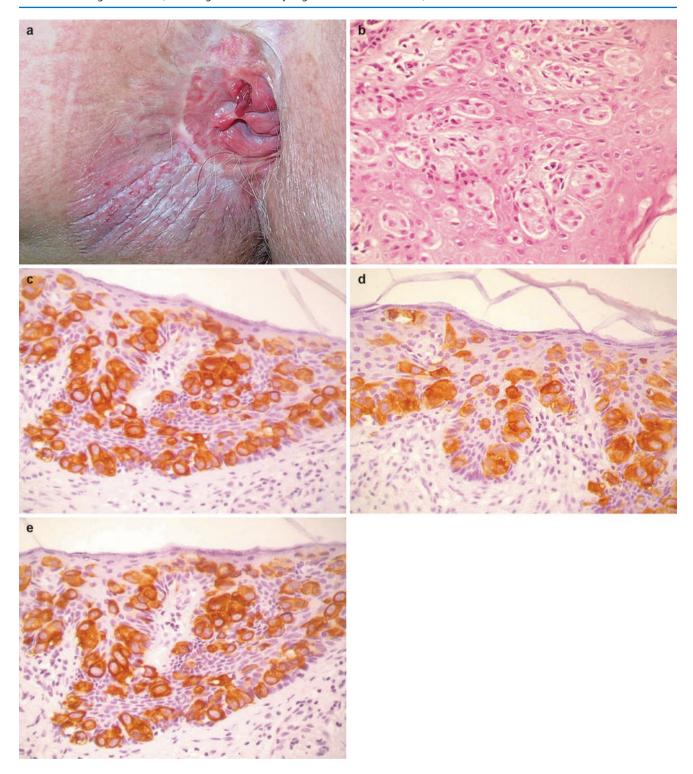


Fig. 11.176 (a) Paget's disease involving the vulva and the gluteal region. Clinical evaluation; (b) biopsy representative of EMP of the vulva with Paget cells—coloration with hematoxylin and eosin; (c) CK 7; (d) EMA; (e) CEA. This case was published in the Brazilian Journal of STD [12]



Fig. 11.177 Evaluation 1 week after topical treatment with imiquimod 5%



Fig. 11.179 Improvement of lesions using local treatment—2 weeks of treatment followed by 2 weeks of temporary interruption of topical imiquimod



Fig. 11.178 Local adverse events associated with the use of imiquimod, leading to discontinuation of treatment



Fig. 11.180 (a) Remission after completion of topical therapy with imiquimod. Clinical evaluation. (b) To confirm the absence of the accentuated disease, seven punch biopsies were performed, none of

which showed any sign of the recurring disease. (c) Light chronic inflammation and absence of Paget cells. (d) Light chronic inflammation and absence of Paget cells



Fig. 11.181 Image representative of clinical follow up of treatment with imiquimod leading to the remission of EMP of the vulva

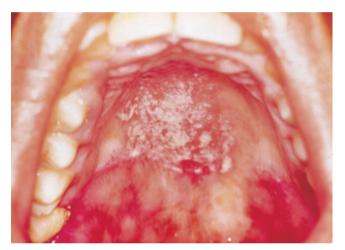


Fig. 11.182 Twenty-two-year-old bisexual male patient seropositive for HIV presenting intraoral lesions, represented by extremely painful erythematous areas as a result of herpes simplex infection. Note the presence of white necrotic material in some areas as a result of overlying pseudomembranous candidiasis. Until proven otherwise, adults with oral candidiasis should be screened for diseases that lead to immunosuppression, such as HIV



Fig. 11.183 Thirty-one-year-old male patient presenting erythematous areas covering the buccal mucosa, labial mucosa and the back of the vestibule and gingiva, as shown in the image, which is covered with a whitish necrotic material as a result of pseudomembranous candidiasis. Various people with immunosuppressive disease initially present or "start their symptoms" with oral candidiasis



Fig. 11.184 Twenty-eight-year-old female patient presenting irregular erosive erythematous lesions on the upper labial mucosa, alveolar mucosa and attached gingiva, that had suddenly appeared 15 days after the regression of a recurring herpetic labial infection. Other areas of the mouth were affected with the appearance of erythematous lesions preceded by vesicles and blisters on the palms of her hands and souls of her feet, and other cutaneous areas presented lesions in the form of concentric circles, resembling a "bull's-eye" or "target", characterizing the clinical symptoms of erythema multiforme



Fig. 11.185 Forty-eight-year-old female patient presenting erosive erythematous lesions on the buccal mucosa covering the vermilion, gingiva and buccal mucosa, as shown in the image. Note that the periphery of the lesion presents irradiated keratotic white lines. As well as these intraoral aspects, the patient presented cutaneous lesions with an erythematous appearance with flaking, and on the face she presented an eruption in the shape of "butterfly wings", confirming the diagnosis of this case as lupus erythematosus



Fig. 11.186 Twenty-year-old female patient presenting an erythematous area covering the right lingual edge and belly, with keratotic white lines with striations on the periphery, representing the clinical symptoms of erosive lichen planus, which resembles the clinical appearance of the oral manifestations of secondary syphilis







Fig. 11.187 In (a), an ulcerodestructive lesion causing perforation of the middle line of the hard palate, the result of the presence of rhinoscleroma, which resembles the bucconasal communication caused by tertiary syphilis (gumma). Diagnosis is possible through histopathological analysis of a biopsy of the lesion. In (b), an image of the perforation of the middle line of the hard palate, caused by nasal tuberculosis, which requires differential diagnosis with gumma. Biopsy of the protuberance clarified the diagnosis. In (c), image obtained by optic oral endoscopy with a Hopkins 30-degree fiber optic endoscope, which revealed an ulcerative perforating lesion on the soft palate cause by *Cancro oris* (noma—see Chap. 9), which requires differential diagnosis with hard chancre



Fig. 11.188 Sixty-one-year-old female patient presenting an ulcerodestructive lesion on the middle line of the hard palate provoking bucconasal perforation and communication, caused by tuberculosis. Malignant tumours in the nasal cavities such as carcinomas and lymphomas, American cutaneous leishmaniasis, paracoccidioidomycosis, histoplasmosis, intraoral squamous cell carcinoma, malignant tumours of the accessory salivary glands on the palate, necrotizing sialometaplasia and rhinoscleroma are the main causes of destructive lesions of the palate that lead to bucconasal communication

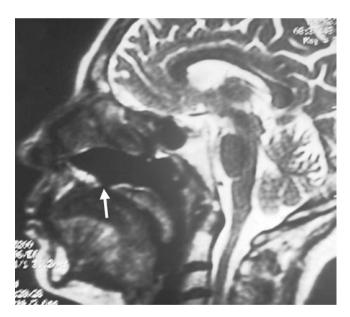


Fig. 11.189 Image of a sagittal CT slice showing perforation of the middle line of the palate caused by the tuberculosis shown in the previous image and indicated by the *arrow*. Note the destruction of the nasal bone structures and cartilage. Why did we include these cases in this publication? Because all of them enter into the differential diagnosis of sexually transmitted diseases, especially late syphilis lesions





Fig. 11.190 (a) Thirty-six-year-old patient who had been diagnosed with systemic lupus erythematosus 11 years previously. She was using high doses of oral corticosteroids. Eight months previously she noticed warty lesions in her anogenital region and carried out various treatments for condyloma acuminata (HPV). She underwent surgery to remove the lesions. Histopathological examination of the surgical specimen confirmed that this was a Buschke-Lowenstein tumour (a). (b) This patient underwent surgical treatment. She experienced recurrence and was treated (b) with imiquimod (Photo by Edison Natal Fedrizzi)



Fig. 11.191 Forty-nine-year-old white married female homemaker. Five years previously she noticed extensive vulvar ulcers that partially responded to the use of an intravenous antibiotic. This recent attack did not respond to treatment. A biopsy performed in her city revealed acute folliculitis. Another biopsy was performed that revealed necrotizing

vasculitis compatible with a diagnosis of Behçet's disease. The patient took a systemic corticosteroid having presented an excellent response with complete healing of genital and lingual ulcers (Photos \mathbf{c} and \mathbf{d}). Results of histopathological examination of the lesion revealed necrotizing vasculitis (Photo \mathbf{e}) (Photo by Edison Natal Fedrizzi)

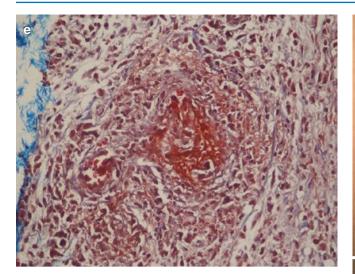


Fig. 11.191 (continued)



Fig. 11.192 Forty-two-year-old patient complaining of an occasionally pruritic reddish lesion in her genital region that had not responded to various treatments using polyvalent topical medications. General examination revealed similar lesions on her elbows and scalp. This case was discussed with a dermatologist colleague and after biopsy of the vulvar lesion it was established that it was a case of psoriasis. Treatment for this disease was started and it was brought under control (Photo by Edison Natal Fedrizzi)





Fig. 11.193 Nineteen-year-old adolescent with an asymptomatic partner who had noticed multiple lesions in her genital region 3 weeks previously (Photo **a**). These were painful and did not respond to treatment with oral antibiotics and oral acyclovir. Note the ulcers on her lips and the inner side of her tongue (Photo **b**). After various clinical and laboratorial analyses it was established that this was a case of Behçet's disease. It is worth remembering that not everything that appears on the genitalia is an STD (Photo by Edison Natal Fedrizzi)





Fig. 11.194 Thirty-two-year-old patient who observed a painless lesion close to her clitoris 6 months previously that slowly started to increase in size. She reported feeling discomfort during sex. The preoperative diagnostic hypothesis was sebaceous cyst. However, the results of histopathological examination of the surgical specimen

revealed leiomyoma. We believe that histopathological examination of all surgical specimens should be mandatory. In many cases this does not change the form of follow up, but the correct diagnosis is documented (Photo case by Edison Natal Fedrizzi) Photo in the immediate postoperative period



Fig. 11.195 Sixty-one-year-old patient who had been treated for 8 months for vulvar condylomatosis but had not responded to various medications. Clinical examination of the vulva revealed a large vegetative lesion with infiltrate, and biopsy revealed a histopathological diagnosis of warty carcinoma (Photo by Edison Natal Fedrizzi)



Fig. 11.196 Sixty-nine-year-old patient who had a warty lesion on her right labia majora for 4 years that had not improved with various treatments, including cauterization. However, she had not undergone any laboratory exams of her vulva before her consultation at the Federal University of Santa Catarina Gynaecology Clinic. Biopsy of the lesion revealed warty carcinoma (Photo by Edison Natal Fedrizzi)







Fig. 11.197 (a) Eighteen-year-old patient who reported starting sexual activity 6 months previously with just one partner. Soon after becoming sexually active, warty lesions appeared in her genital region that rapidly increased in size. No immunosuppressive disease could be identified during examination. She underwent surgical treatment and the histopathological diagnosis was Buschke-Löwenstein tumour. (b) Photo during the operation. (c) Photo 60 days after surgery (Photo case by Edison Natal Fedrizzi) (See which photo has the best resolution)

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