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2.1 Introduction

The clinical and laboratory diagnosis of male genital disorders, including a thorough review of the clinical exam and the laboratory tests currently available that might help in the differential diagnosis of the distinct pathologies affecting the region are detailed in this Chapter.

2.2 Medical History

2.2.1 General

Age.
Occupation.
Current and recent parenteral, oral and topical medications.
Concurrent illness or skin disorders (i.e., psoriasis, eczema).
Symptoms:
• Urinary: dysuria, meatal discharge, urethral pruritus

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Table 2.1 Useful recommendations for taking a sexual history

Explain the need for taking a sexual history and warn the patient that details about his/her sexual life will be discussed
Reassure the patient with regards to confidentiality
Respect and take a nonjudgmental attitude toward sexual habits of the patient, but advise when needed (i.e., regarding condom use)
Do not make assumptions (take a sexual history in every age group) (Richter et al. 1993; Cooperman et al. 2007)
Use specific language
Do not avoid a topic because you feel uncomfortable
Develop a routine approach to elicit the sexual history

- Genital: pruritus, soreness, pain, swelling, rash, blister, ulcer, nodule, tumor
- Details of present complaint:
- Duration of symptoms
 - First episode/Previous similar episodes (details)
 - Related to sexual activity:
 - If yes, details of sexual history is mandatory and the recommendations listed in Table 2.1 should prove helpful

2.2.2 Sexual History

Sexual identity (i.e., heterosexual, men who have sex with men [MSM], bisexual).

Marital status and extra-marital relationships (including sex of sexual contacts).

Date of most recent sexual contact and onset of symptoms.

Sex partner(s) complaining of anogenital symptoms?.

Sexual habits (oral, vaginal, and/or anal intercourse).

Condom use/lubricants/sex toys/other products.

Risky sexual behavior (intravenous drugs, STIs, alcohol or drugs in association with sexual activity, multiple partners and/or partners with STIs, hepatitis, blood transfusion).

2.2.3 Past Medical and Surgical History

Dermatological diseases.

Genitourinary diseases.

Surgical procedures (e.g., circumcision).

**Fig. 2.1** Alopecia areata**Fig. 2.2** Folliculitis

Allergies (drugs, atopy).

Sexually transmitted infections.

2.3 Physical Examination

Although the main focus of the physical exam is the genital region, a thorough skin examination under adequate illumination (natural light is ideal) is recommended.

2.3.1 Anogenital Region

2.3.1.1 Pubic Region

- Look for abnormalities of pubic hair (Fig. 2.1) and follicles (Fig. 2.2).
- Check for skin lesions covered by pubic hair (parasitic infestations, viral warts, molluscum contagiosum) (Fig. 2.3).



Fig. 2.3 Molluscum contagiosum

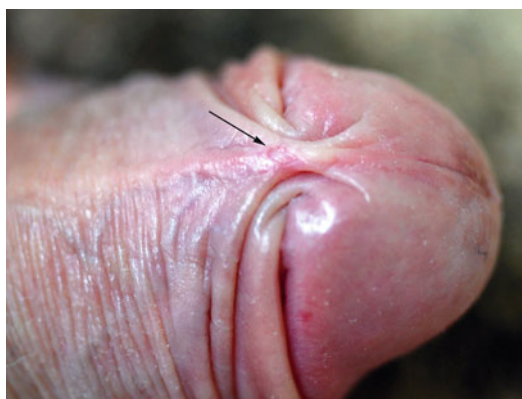


Fig. 2.4 Short frenulum with micro-ulceration (arrow)

2.3.1.2 Penis

In uncircumcised men.

- Foreskin is retracted
 - Look for phimosis, waisting (Table 2.2), short frenulum (Fig. 2.4), frenular lesions (Fig. 2.5a, b), abnormal subpreputial discharge (observe secretion characteristics: color, thickness, odor, quantity)
- Urethral meatus.
 - Observe the position of the meatus.
 - Check for urethral discharge and secretion characteristics (color, thickness, odor, volume).
 - The urethral meatus is spread between the thumb and the forefinger (Fig. 2.6) and the fossa navicularis is examined: look for anatomical variations, stricture, acute and chronic inflammatory signs (Fig. 2.6), tumor, or viral warts (Figs. 2.5a, 2.7, 2.8, and 2.9).
- Glans and prepuce.
 - Look for inflammatory signs (i.e., erythema, edema, desquamation) (Fig. 2.10) (*see also* Balanitis and balanoposthitis in Chap. 9), fissures (Fig. 2.11), skin erosion, ulceration (observe ulcer morphology, base, border, distribution) (Fig. 2.12), tumor (Fig. 2.13), warts, atrophy (Fig. 2.14), hypopigmentation (Fig. 2.15), or hyperpigmentation (Figs. 2.16 and 2.17).

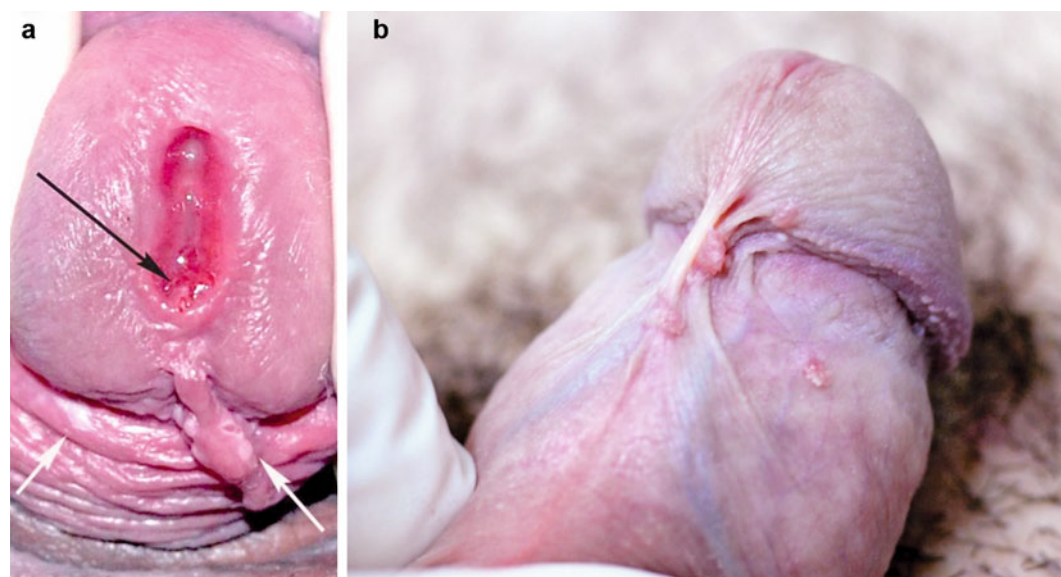


Fig. 2.5 (a) Urethral (black arrow), frenular (white arrow) and preputial HPV-related lesions. (b) Frenular and preputial warts

Fig. 2.6 Leukoplakic lesion inside the hypospadiac meatus

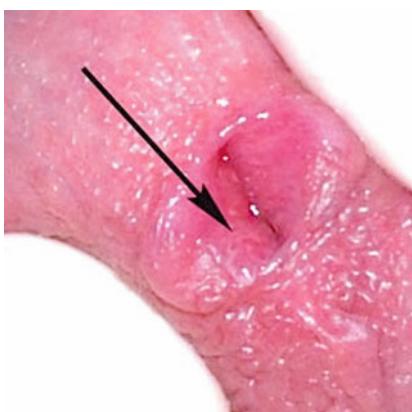


Fig. 2.7 Flat HPV-related lesion (*arrow*) in the fossa navicularis



Fig. 2.9 Exophytic HPV-related lesion at the urethral meatus



Fig. 2.8 Small HPV-related lesion in the fossa navicularis



Fig. 2.10 Balanoposthitis



Fig. 2.11 Balanoposthitis and fissures



Fig. 2.12 Genital ulcer – herpes simplex virus type 2



Fig. 2.13 Penile neoplasia

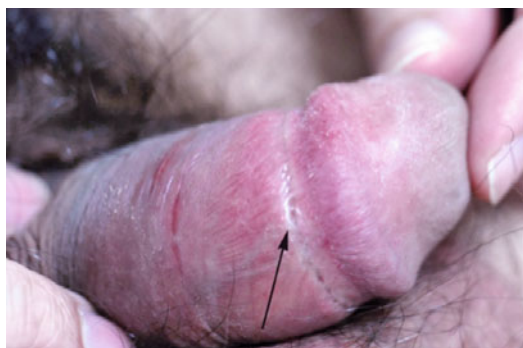


Fig. 2.14 Subcoronal postinflammatory atrophy (*arrow*) and preputial fissure



Fig. 2.15 Hypopigmentation (*arrows*) after topical podophyllin 25% use

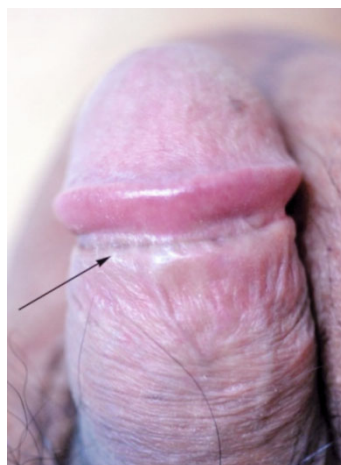


Fig. 2.16 Subcoronal postinflammatory hyperpigmentation (*arrow*) and scarring



Fig. 2.17 Preputial hyperpigmentation



Fig. 2.20 Folliculitis (arrow)



Fig. 2.18 Genital warts located at the penis base, scrotum, and pubic area

- Penile shaft and base.
 - Look for warts (Fig. 2.18), desquamation (Fig. 2.19), inflammatory (Fig. 2.20) and cystic lesions, ulceration, nodule, painful subdermal plaques (Peyronie's disease), tumors.

2.3.1.3 Inguinal Region (Including the Inguinocrural/Inguinoscrotal Folds)

- Palpate lymph nodes (check for inflammatory signs, fluctuation, nodal consistency), inguinal hernias (Fig. 2.21), and look for lesions that may be hidden under the pubic hair (Fig. 2.22).
- Move the skin folds and check for intertriginous dermatitis (i.e., intertrigo (Fig. 2.23), seborrheic dermatitis, seborrheic keratosis (Fig. 2.23) psoriasis, dermatophytoses, candidiasis, erythrasma), viral warts (Fig. 2.24), extramammary Paget's disease (*see* Parts II, III, and VI).



Fig. 2.19 Seborrheic dermatitis

Intertrigo is an inflammatory condition of body folds that clinically manifests as moist lesions, erythema, and scaling. Patients usually complain of soreness and itching, and heat, moisture, and the retention of sweat usually exacerbate symptoms.



Fig. 2.21 Inguinal hernia

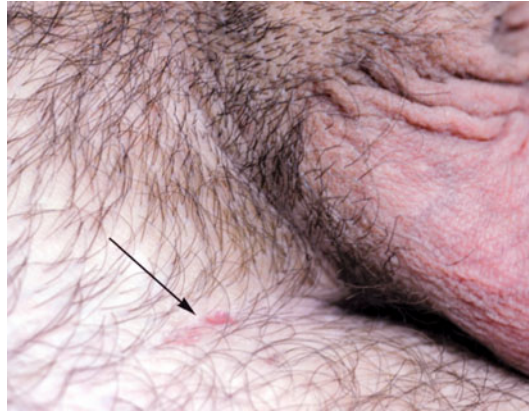


Fig. 2.24 Genital warts at right inguinal area (*arrow*)



Fig. 2.22 Squamous cell carcinoma



Fig. 2.25 Herpes zoster infection

- Check scrotal skin and appendages.
- Palpate scrotal contents (testes, epididymis, and the constituents of the spermatic cords).

2.3.1.4 Perineal, Anal, and Perianal Region

Patient can be examined in either dorsal decubitus with legs widely folded and scrotum lifted upwards, or rolled sideways with both legs flexed against the abdomen and the buttocks spread apart:

- Look for cutaneous and mucocutaneous inflammatory signs, anal discharge (see Sect. 10.5), viral infections (Figs. 2.25, 2.26, and 2.27), fissures, ulcerations, tumor (Fig. 2.28).
- Perform a rectal exam, if needed, at the end of the physical examination.



Fig. 2.23 Intertrigo (note also cutaneous vascular lesion [*blue-colored*] and seborrheic keratosis [*brown-colored*] involving the left hemiscrotum)

The ability to identify cutaneous lesions is the key determinant for facilitating an accurate dermatologic diagnosis. Description of skin and mucosal lesions includes documenting its distribution (i.e., symmetrical or asymmetrical, localized, grouped, intertriginous), configuration (i.e., linear, annular, circinate, serpiginous, zosteriform), size, color (including pigmentation changes, such as hyperpigmentation and hypopigmentation), number, and morphology (Table 2.2)

2.3.2 Extragenital Skin

- Look for skin and mucosal (i.e., oral cavity) lesions.
- Color digital photography of skin lesions may provide useful information for baseline reference and follow-up evaluation.



Fig. 2.26 Perineal HPV-related lesion (Source: Rosenblatt and Campos Guidi 2009a. Courtesy of Dr. Carlos Walter Sobrado. Reproduced with permission from Springer)

2.4 Laboratory Evaluation

The following diagnostic tests, imaging studies, and procedures may help in the diagnosis of both primary genital conditions and systemic disorders that involve the male genitalia (see Part V).



Fig. 2.27 Perianal HPV-related lesion (Source: Rosenblatt and Campos Guidi 2009a. Courtesy of Dr. Carlos Walter Sobrado. Reproduced with permission from Springer)

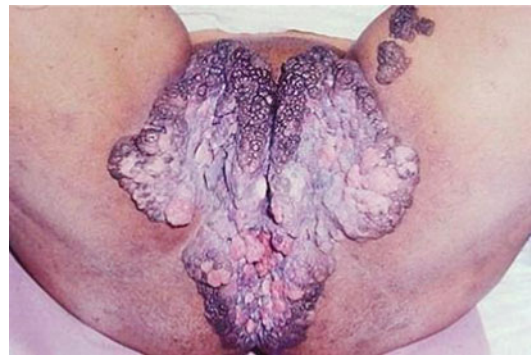





Fig. 2.28 Extensive Buschke-Löwenstein tumor (Source: Rosenblatt and Campos Guidi 2009a. Courtesy of Dr. Carlos Walter Sobrado. Reproduced with permission from Springer)

Table 2.2 Nomenclature of cutaneous and mucosal lesions

Lesion	Description	Figure(s)
Macule	A circumscribed, small, flat lesion (Fig. 2.29)	 Fig. 2.29 Contact allergy
Papule	A small (up to 0.5 cm in diameter), elevated, solid lesion (Fig. 2.30). Papules may coalesce to become plaques (Fig. 2.31).	 Fig. 2.30 Molluscum contagiosum and Fordyce spots
Plaque	A circumscribed, large (>0.5 cm in diameter), raised, superficial, and solid lesion (Fig. 2.31)	 Fig. 2.31 Psoriasis plaque

(continued)

Table 2.2 (continued)




Lesion	Description	Figure(s)
Nodule	A circumscribed, palpable lesion of varying size (typically between 0.5 and 2 cm in diameter) (Fig. 2.32)	 <p>Fig. 2.32 Inguinal keloid</p>
Tumor	A raised, large (>2 cm in diameter), solid lesion (Fig. 2.33)	 <p>Fig. 2.33 Penile carcinoma</p>
Vesicle	A circumscribed, small (up to 0.5 cm in diameter) collection of free fluid (Fig. 2.34)	 <p>Fig. 2.34 Herpetic lesions (first clinical episode)</p>

Table 2.2 (continued)

Lesion	Description	Figure(s)
Bulla	A circumscribed, large (>0.5 cm in diameter) collection of free fluid (Fig. 2.35)	 <p>Fig. 2.35 Bullous pemphigoid (note bullous lesions in various stages)</p>
Pustule	A circumscribed, small collection of pus (Fig. 2.36)	 <p>Fig. 2.36 Genital herpes</p>
Cyst	Papule or nodule with an internal lining and containing liquid or semisolid content (Fig. 2.37)	 <p>Fig. 2.37 Median raphe cyst</p>

(continued)

Table 2.2 (continued)




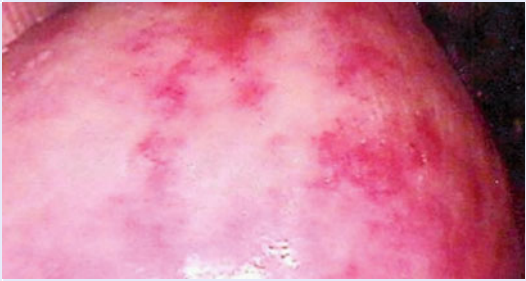
Lesion	Description	Figure(s)
Erythema	Redness (Fig. 2.38)	 <p>Fig. 2.38 Nonspecific balanoposthitis</p>
Edema	Abnormal accumulation of fluid in the tissues (Fig. 2.39)	 <p>Fig. 2.39 Allergic contact dermatitis causing penile edema</p>
Purpura	Purple-colored spots and patches on the skin, mucus membranes and internal organs, which result from the leaking of small blood vessels (Fig. 2.40)	 <p>Fig. 2.40 Purpuric-like lesions following topical corticosteroid use</p>

Table 2.2 (continued)

Lesion	Description	Figure(s)
Petechiae	Small purpura spots (Fig. 2.41)	
		Fig. 2.41 Petechiae-like glanular lesions
Ecchymosis	Larger area of mucocutaneous bleeding, forming a flat, rounded or irregular, blue or purple-colored patch (Fig. 2.42)	
		Fig. 2.42 Ecchymosis following intercourse (note associated lichen sclerosus involving glans and frenulum)
Erythroplasia	Red patches or plaques (nonulcerated) on mucous membrane, often designating cellular dysplasia or a premalignant condition (Fig. 2.43)	
		Fig. 2.43 Erythroplasia of Queyrat

(continued)

Table 2.2 (continued)







Lesion	Description	Figure(s)
Leukoplasia	White patches or plaques on the mucous membranes, often designating cellular dysplasia or premalignant condition (Fig. 2.44)	
		Fig. 2.44 Preputial leukoplakia
Scale	Excess dead stratum corneum or keratin produced by abnormal keratinization and shedding (Fig. 2.45)	
		Fig. 2.45 Ichthyosis vulgaris
Lichenification	Thickening and hardening of the skin, usually the result of constant scratching and rubbing (Fig. 2.46)	
		Fig. 2.46 Scrotal lichenification

Table 2.2 (continued)

Lesion	Description	Figure(s)
Fissure	A linear loss of epidermis and dermis with sharply defined borders (Fig. 2.47)	
		Fig. 2.47 Balanoposthitis – diabetes mellitus
Erosion	A focal loss of epidermis (above the basal layer) that usually heal without scarring (Fig. 2.48)	
		Fig. 2.48 Erosion after topical Efurix application
Crust	A collection of dried exudates (blood serum) and cellular debris (Fig. 2.49)	
		Fig. 2.49 Crusts forming after CO ₂ laser treatment for genital warts

(continued)

Table 2.2 (continued)




Lesion	Description	Figure(s)
Ulcer	A focal loss of epidermis and dermis that often heals with scarring (Fig. 2.50)	 <p>A clinical photograph showing a well-demarcated, circular ulcer on the penile shaft. The ulcer bed is deep and contains a red, fibrinous exudate. The surrounding skin is normal in color and texture. A finger is visible at the top, holding the penile skin to expose the lesion.</p> <p>Fig. 2.50 Topical 5-fluorouracil side-effect</p>
Atrophy	A skin depression resulting from the loss or thinning of the epidermis or dermis (Fig. 2.51)	 <p>A clinical photograph of the glans and corona of the penis. The skin appears thin, pale, and wrinkled, with some areas of white discoloration and redness, characteristic of lichen sclerosus.</p> <p>Fig. 2.51 Lichen sclerosus – atrophic changes at glans and corona</p>
Scar	An abnormal formation of connective tissue replacing normal skin (usually appearing following skin injury) (Fig. 2.52)	 <p>A clinical photograph of the penile shaft showing a prominent, raised, and irregular scar. The scar is surrounded by a white, flat, HPV-related lesion. An arrow points to the white lesion.</p> <p>Fig. 2.52 Scar resulting from topical Aldara application (note white HPV-related flat preputial lesion – arrow)</p>

Table 2.2 (continued)


Lesion	Description	Figure(s)
Waisting (Singh and Bunker 2008)	Preputial fibrotic and stenotic ring (Fig. 2.53)	

Fig. 2.53 Lichen sclerosus and waisting (arrow)

2.4.1 Blood Tests

- Blood glucose levels and glycated hemoglobin (HbA1c) are helpful to exclude candidal balanoposthitis caused by poorly controlled diabetes mellitus.
- Creatinine and blood urea nitrogen (BUN) measurements are essential for the monitoring and management of systemic diseases that course with acute or chronic renal failure (i.e., Henoch-Schönlein purpura, Wegener’s granulomatosis) (see Part V).
- Serum IgE levels may suggest an atopic disorder.
- Eosinophilia (see Sect. 15.16).
- Serologic testing may aid in the diagnosis of infectious pathogens (i.e., syphilis) (see Part III).
- Immunodeficiency virus (HIV) testing.
- Lymphocyte, CD-4+, and CD-8+ counts in HIV infection.
- Antineutrophil cytoplasmic antibodies (ANCA) (see Sect. 15.10).
- Detection of amyloid protein in serum may diagnose amyloidosis (see Chap. 15).

2.4.2 Urine Tests

- First-void urine and mid-stream urine specimen may help exclude urinary tract infection.
- Proteinuria and microscopic hematuria can diagnose nephritis (see Sects. 5.8 and 5.9).

A nucleic acid amplification test in first-void urine may detect urethral infection with *Chlamydia trachomatis* and *Mycoplasma genitalium* (see Chap. 10)

- Detection of amyloid protein in urine may diagnose amyloidosis (see Part V).

2.4.3 Skin Scraping Test, Potassium Hydroxide (KOH) Preparation, and Mycological Analysis

- Useful test to diagnose fungal infection (see Part III).
- Skin scraping exam and mineral oil drops may help visualize mites, eggs, and/or parasite excreta under light microscope.
- Microbiological swabs are often taken from the groins and glans penis, particularly looking for evidence of yeast and/or anaerobic bacterial infection (particularly in persisting, recurrent, or nonspecific balanitis).

2.4.4 Bacteriological Gram Staining and Cultures of Body Fluids and/or Secretions

- These tests may detect viral, and fungal infections (see Part III).

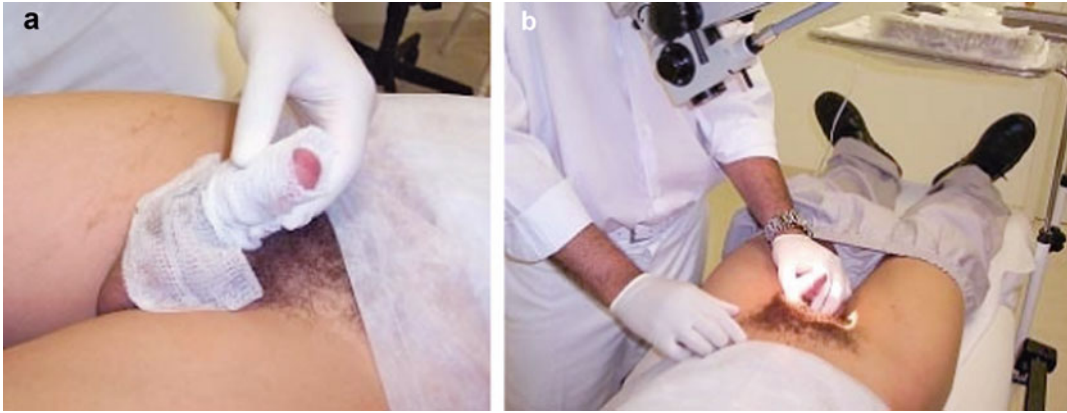


Fig. 2.54 Acetowhite test – (a) Genital skin is wrapped in gauze soaked in 5% acetic acid solution. (b) Subsequent exam with a magnifying hand lens or microscope/

colposcope (Source: Rosenblatt and Campos Guidi 2009b. Reproduced with permission from Springer)

2.4.5 Dark-Field Preparation

Dark-Field Preparation (See Sect. 10.2).

2.4.6 Acetowhite Test

- Test may help detect genital skin abnormalities caused by infection with human papillomavirus (HPV) (see Chap. 10).
- The *acetowhite test* is associated with a high number of false-negative and false-positive results (Mansur 2002), and the latter situation commonly occurs when coexisting inflammatory conditions are present. However, test can be useful for identifying flat genital lesions (Bleeker et al. 2006) and to evaluate male sexual partners of women with vulvar lesions (Taner et al. 2006), but association with molecular studies and/or histopathologic confirmation is required.

Acetowhite test

The warts and adjacent normal penile skin/mucosa (as well as scrotal, perineal, and perianal area) are wrapped in gauze soaked in 5% acetic acid solution for about 3–5 min (Fig. 2.54a)

The whole area is subsequently examined with a magnifying hand lens or microscope/colposcope (between 8× and 40×) (Fig. 2.54b). Highlighted HPV-related

lesions develop a white color (Fig. 2.55a, b), which is attributed to an overexpression of cytokeratin in the HPV-infected suprabasal cells. These are undifferentiated cells rich in protein content and the whitening might be caused by protein denaturation. HPV lesions often exhibit well-demarcated punctuated capillary patterns. Acetowhite test in inflammatory conditions (i.e., *Candida* infection) usually presents with a more irregular and diffuse pattern (Fig. 2.56).

2.4.7 Brushing Cytology

- May detect cytological abnormalities caused by infection with human papillomavirus (HPV) (Fig. 2.57).

2.4.8 Molecular Studies (i.e., Polymerase Chain Reaction (PCR))

- Useful for the detection of virus (i.e., human papillomavirus, herpes simplex virus) and bacteria (i.e., syphilis, Chlamydia, and Mycoplasma).

2.4.9 Patch Testing

- Useful test to exclude contact dermatitis (see Sect. 4.4).

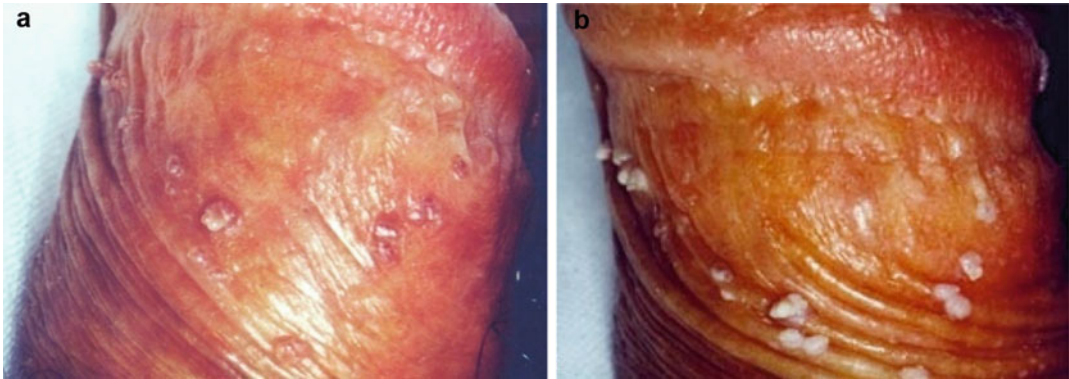


Fig. 2.55 (a) HPV-related lesions before acetowhite test (b) HPV-related lesions develop a *white color* following acetowhite test (Source: Rosenblatt and Campos Guidi 2009b. Reproduced with permission from Springer)

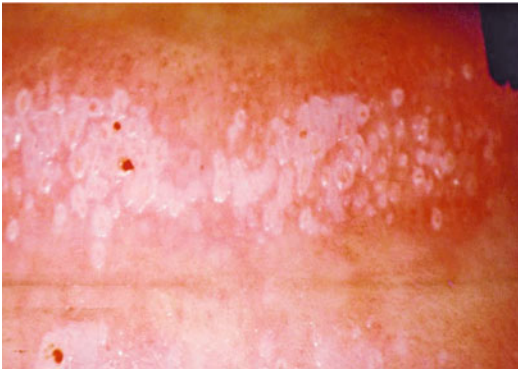


Fig. 2.56 Acetowhite test shows irregular and diffuse pattern in inflammatory conditions (Source: Rosenblatt and Campos Guidi 2009b. Reproduced with permission from Springer)



Fig. 2.57 Brushing cytology of penile skin – saline drops increase cellularity (Source: Rosenblatt and Campos Guidi 2009b. Reproduced with permission from Springer)

2.4.10 Skin Pathergy Test

- Helpful test to diagnose Behcet's disease (see Chap. 6).

Skin pathergy test

The forearm is pricked with a small, sterile needle and the site is examined 1–2 days after the test. The presence of a small red bump or pustule constitutes a positive test.

2.4.11 Dermoscopy (Also Known as Dermatoscopy or Epiluminescence Microscopy)

- Useful test for monitoring nevic lesions suspicious of melanoma, but it may also aid in the diagnosis of other common skin tumors (i.e., basal cell carcinomas, squamous cell carcinomas, dermatofibromas, seborrheic keratosis, angiomas, cylindromas).
- Test may also aid in the diagnosis of parasites (scabies, pubic louse, tungiasis), fungal infections, and common warts.

2.4.12 Skin Biopsy with Histopathological Evaluation (See Chap. 3/Appendix A)

- Direct and indirect immunofluorescence may help in the differential diagnosis of vesiculobullous dermatoses (see Chap. 7).



Fig. 2.58 Vitiligo-affected skin fluoresce (blue color) under Wood's light

- Specific staining techniques may aid in the diagnosis of infectious pathogens (i.e., tuberculosis) (*see* Chap. 9).

2.4.13 Wood's (Ultraviolet) Light

- Useful test to detect areas of skin that may fluoresce (i.e., vitiligo (Fig. 2.58), erythrasma, and fungal infections) (*see* Parts III and IV).

2.4.14 Imaging Studies

- Ultrasonography (US), computed tomography (CT) and nuclear magnetic resonance (NMR) imaging may help in the diagnosis of specific

primary genital conditions as well as genital lesions secondary to systemic diseases (*see* Parts II, IV, V, and VI).

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Male Genital Lesions

The Urological Perspective

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