Diagnosing and Managing Vulvar Disease

John J. Willems, M.D.

FRCSC, FACOG

Chairman, Department of Obstetrics & Gynecology

Scripps Clinic

La Jolla, California

Objectives:

- Identify the major forms of vulvar pathology
- Describe the appropriate setup for vulvar biopsy
- Describe the most appropriate management for commonly seen vulvar conditions

Faculty Disclosure

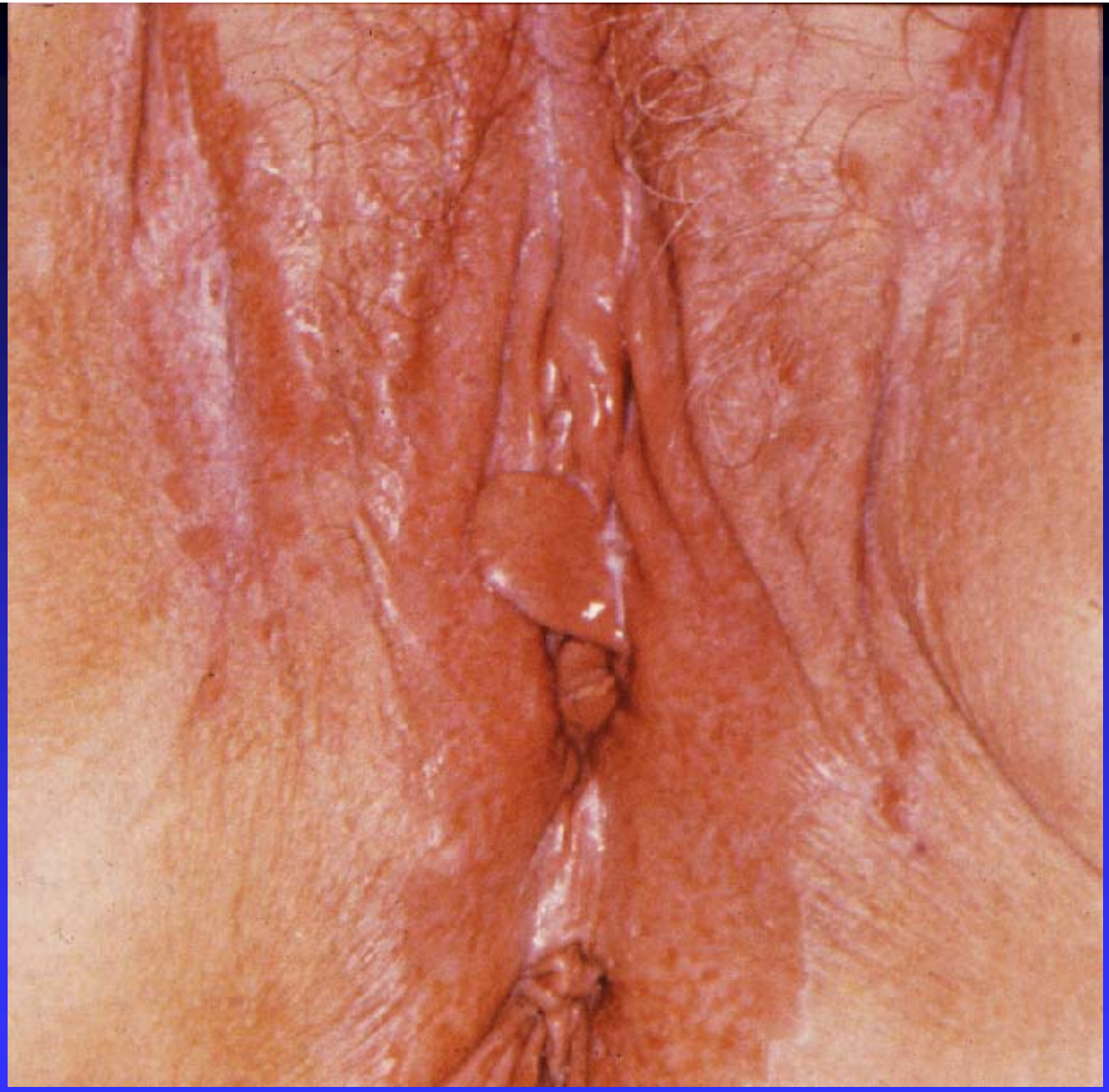
Company	Nature of Affiliation	Unlabeled Product Usage
• Warner Chilcott	• Speakers Bureau	• None

Classification of Vulvar Disease by Clinical Characteristic

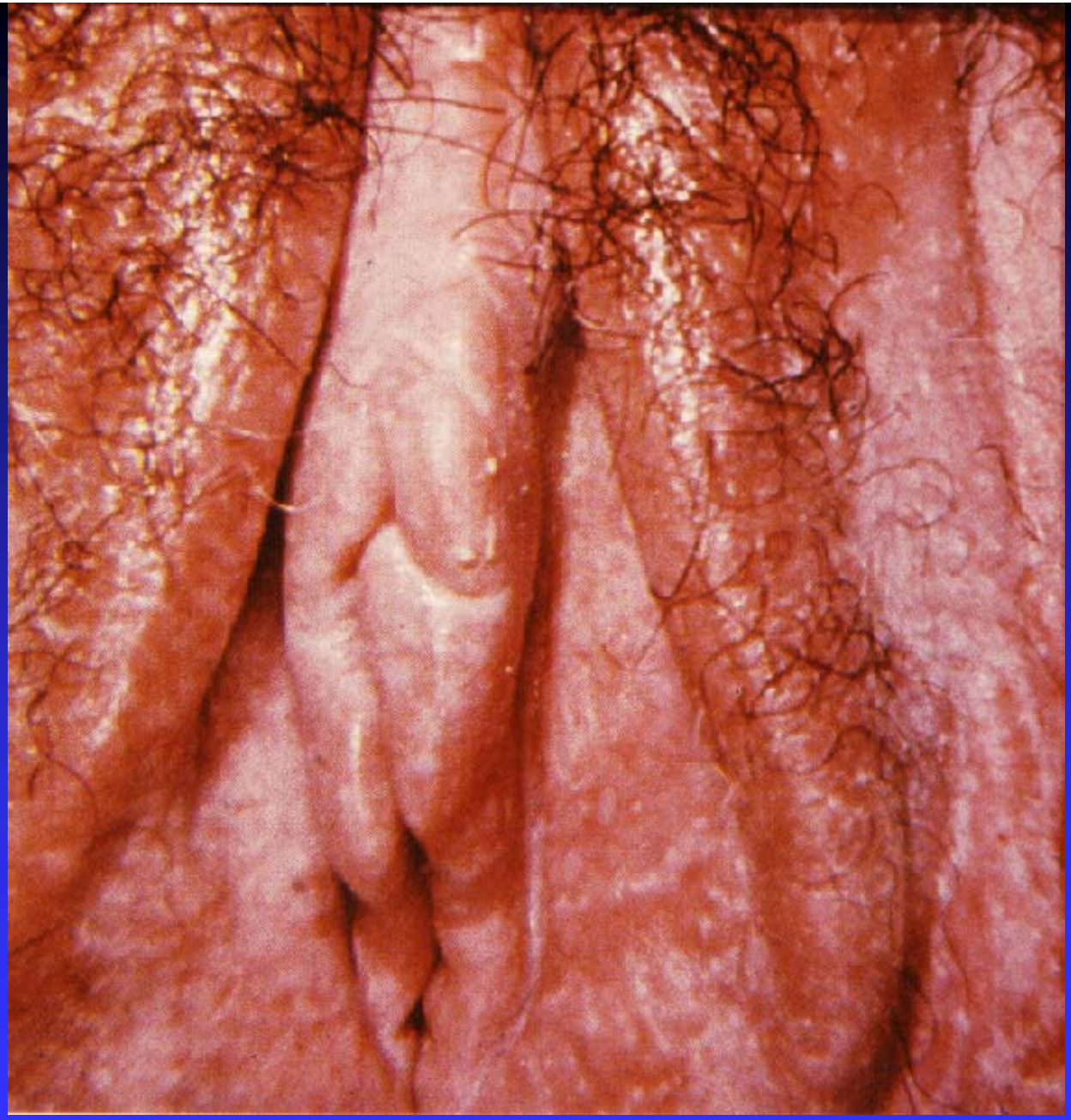
- Red lesions
- White lesions
- Dark lesions
- Ulcers
- Small tumors
- Large tumors

Red Lesions

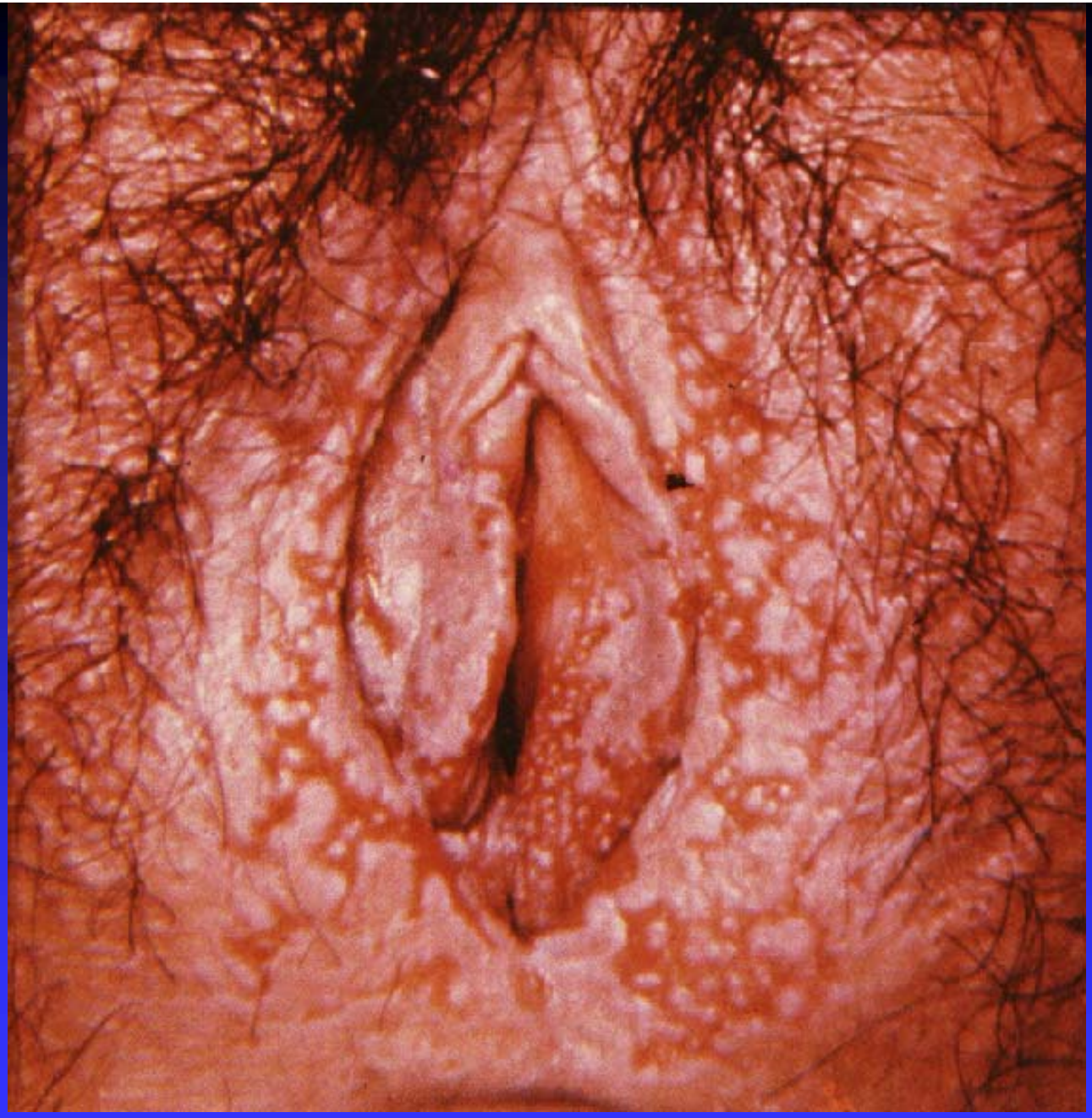
- Candida
- Tinea
- Reactive vulvitis
- Seborrheic dermatitis
- Psoriasis
- Vulvar vestibulitis
- Paget’s disease



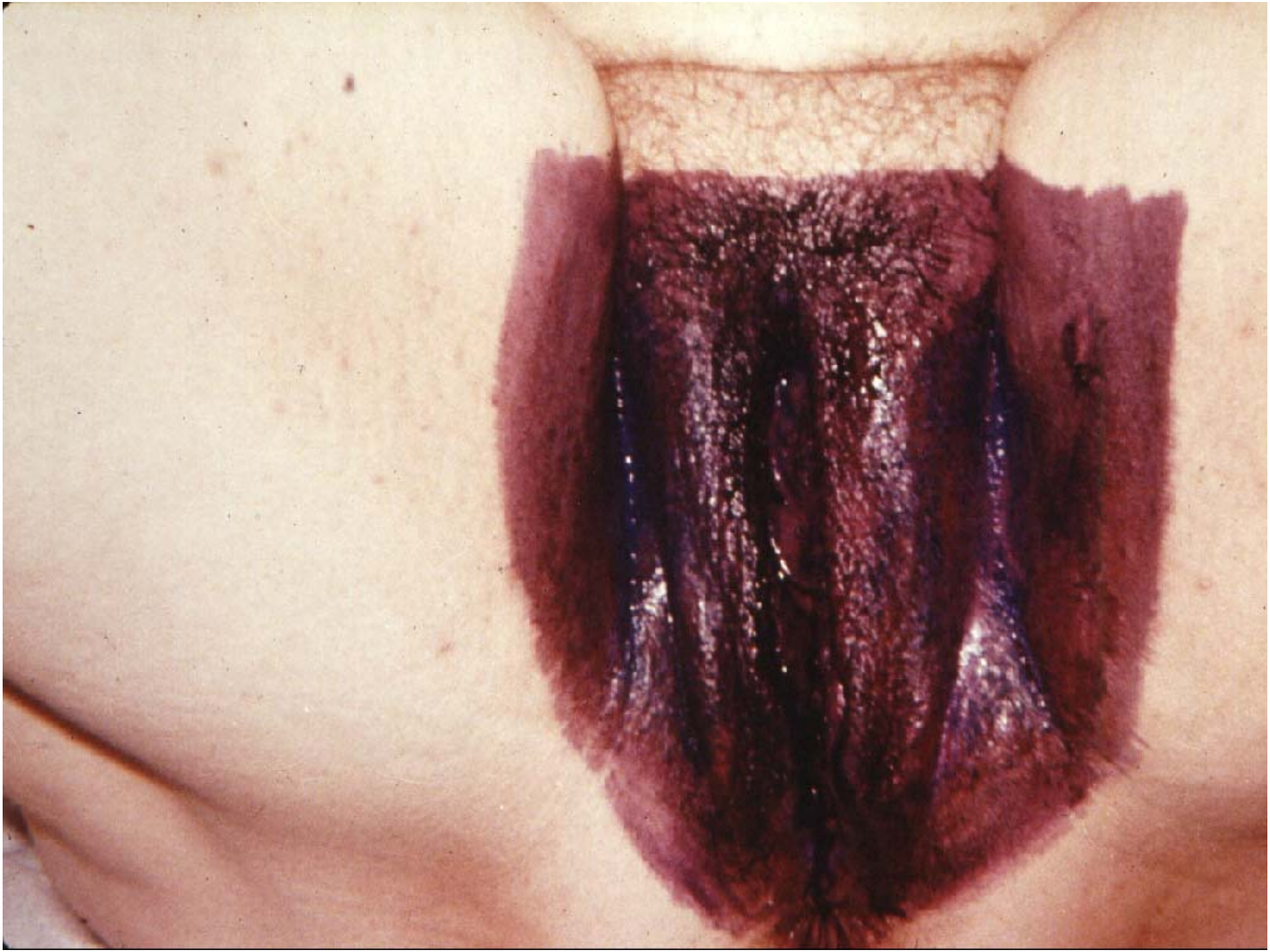
Candidal vulvitis

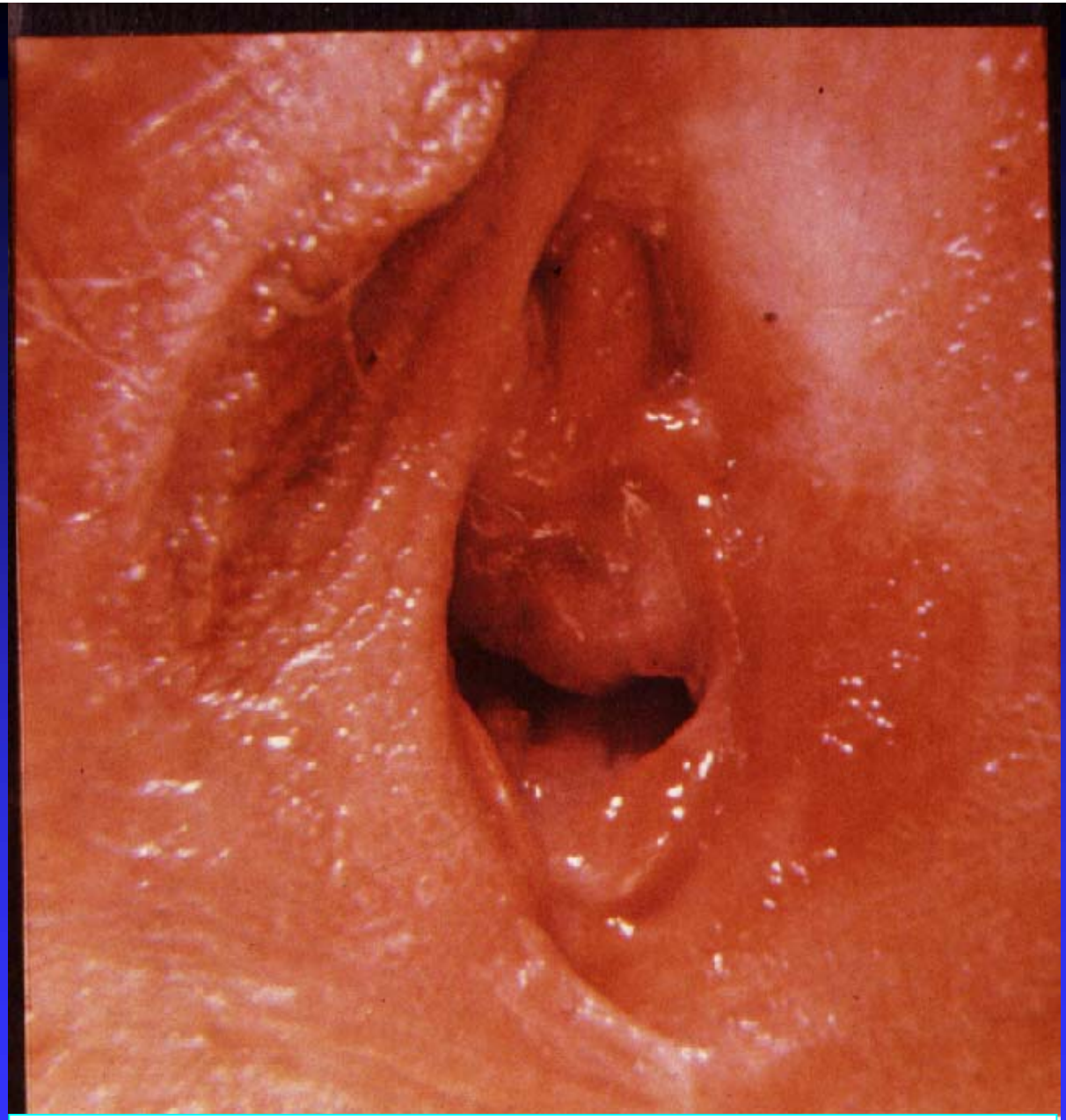


Superficial grayish-white film is often present

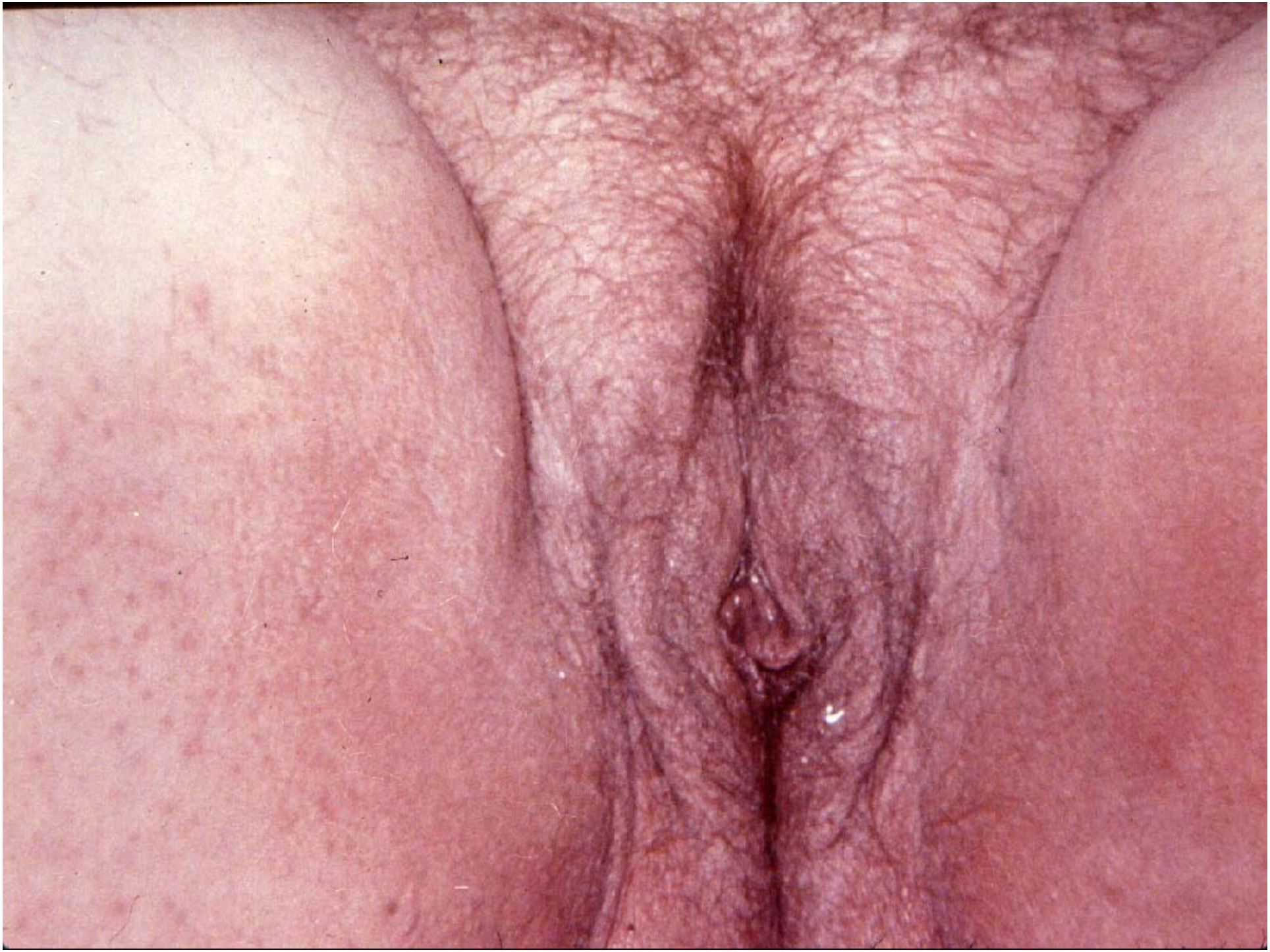


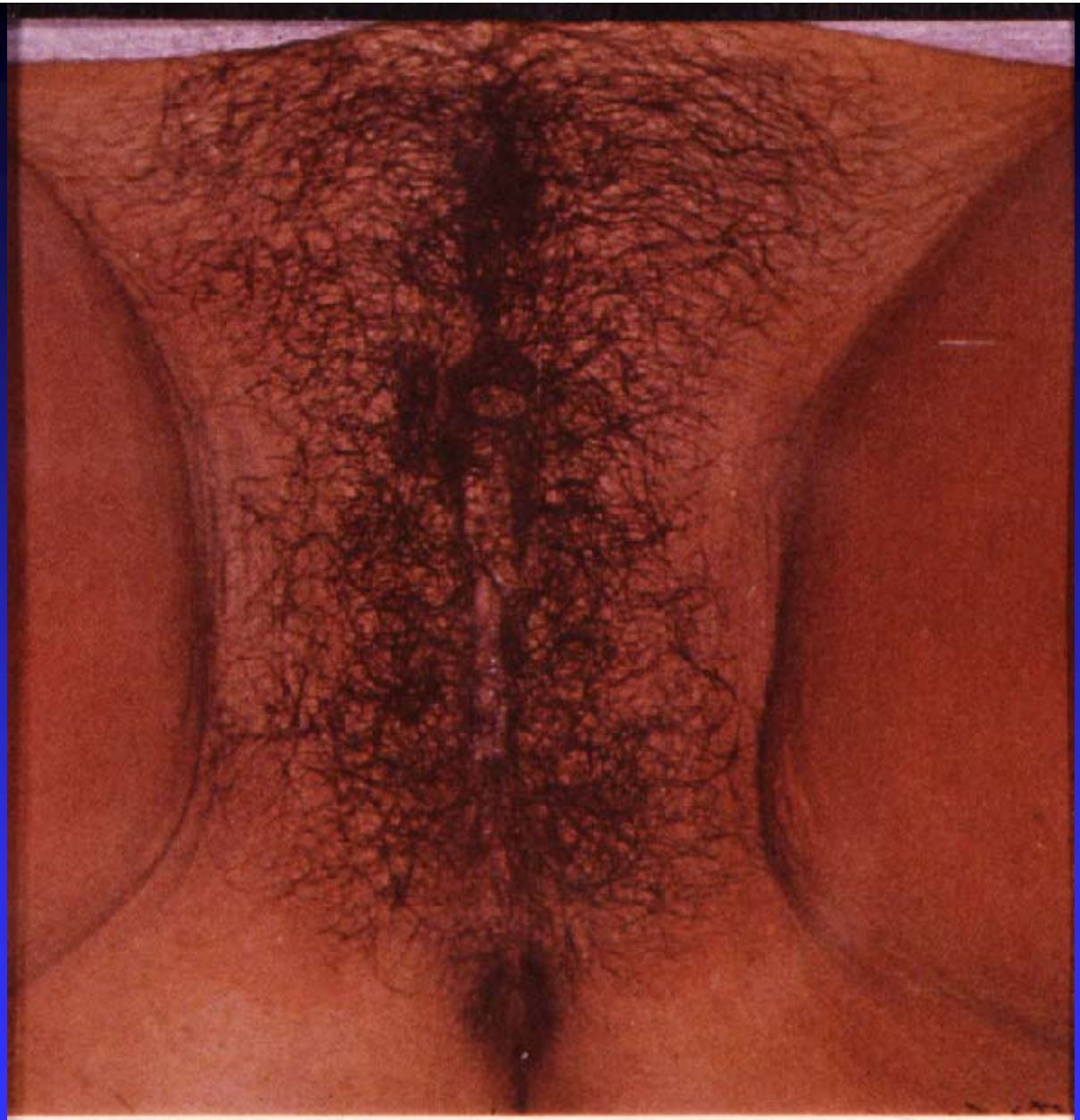
Thick film of candida gives pseudo-ulcerative appearance.



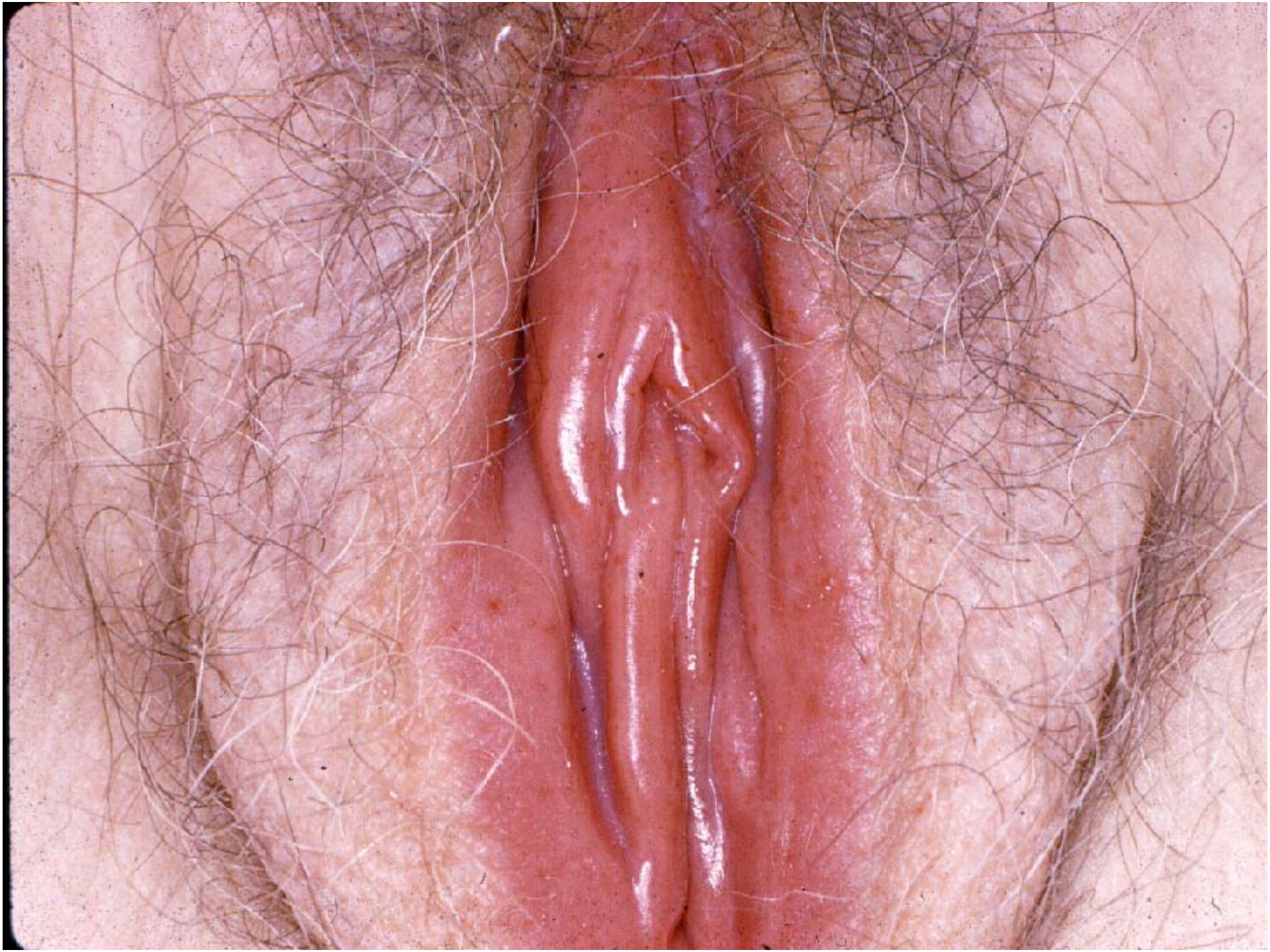


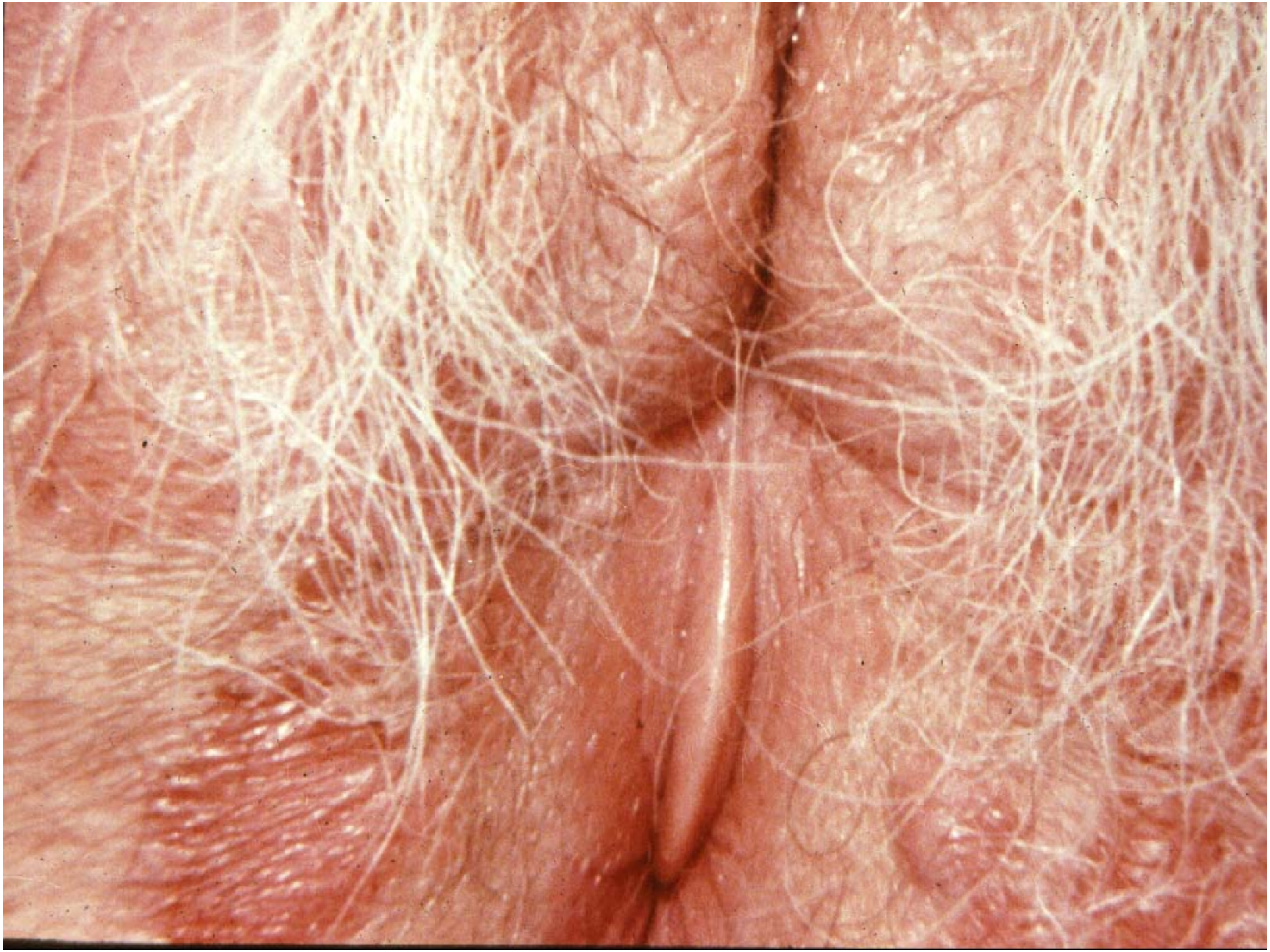
Acute vulvitis from coital trauma

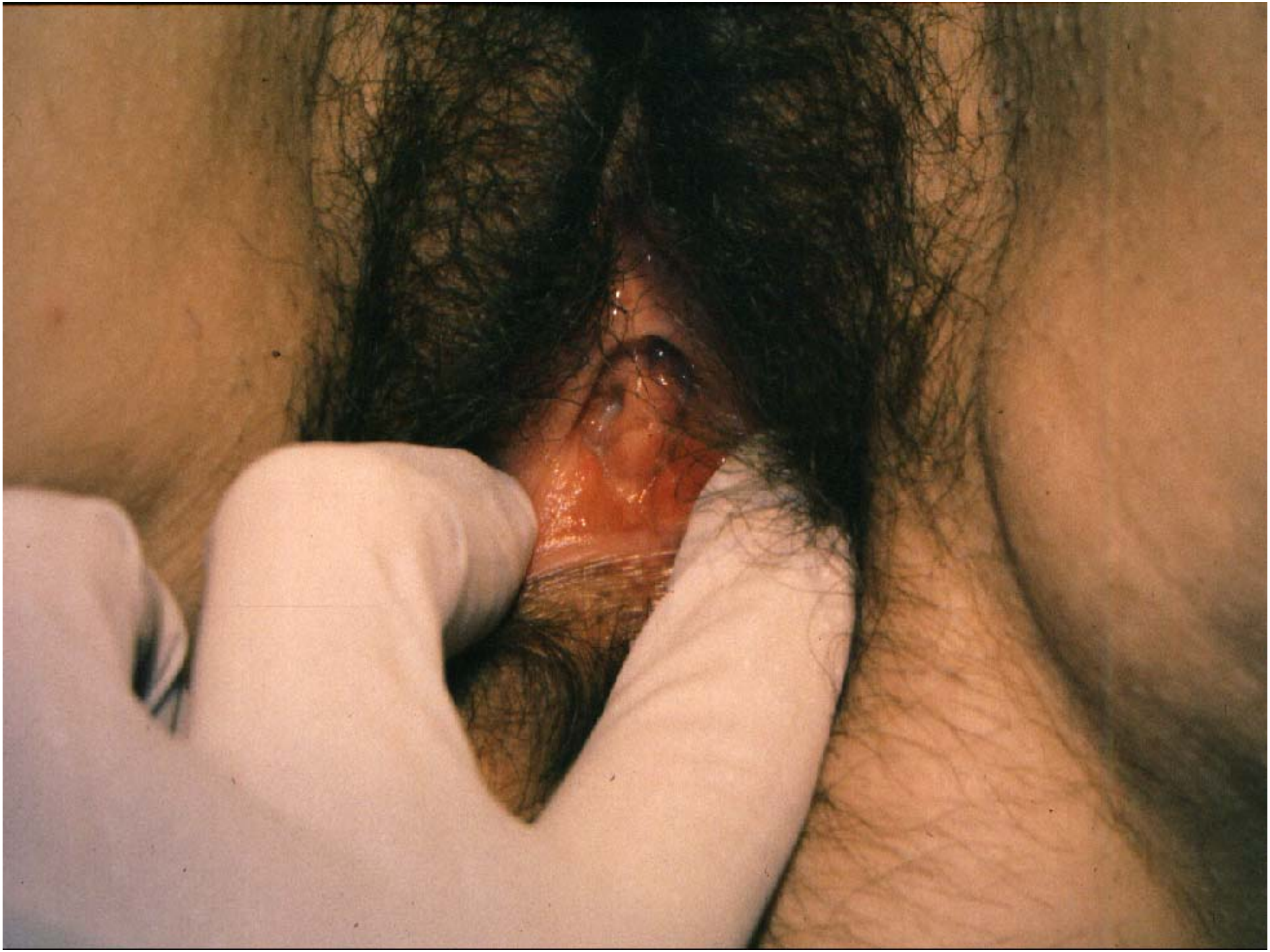




Contact irritation from synthetic fabrics







Nomenclature

Subtypes of Vulvodynia:

- Vulvar Vestibulitis Syndrome (VVS)

  also known as:

  - Vestibulodynia
  - localized vulvar dysesthesia

- Dysesthetic Vulvodynia

  also known as:

  - “essential” vulvodynia
  - generalized vulvar dysesthesia

Dysesthesia

- Unpleasant, abnormal sensation
  - examples include:
    - Burning
    - rawness
- Can be spontaneous or evoked
- Includes allodynia and/or hyperalgesia
  - Allodynia:

    Pain due to a stimulus that does not normally evoke pain
  - Hyperalgesia:

    Increased response to a stimulus that IS normally painful

Incidence of Dyspareunia

- **National Health & Social Life Survey**
  - **Adult Sexual Behavior**
- **1749 women - 18 to 59**
- **7% incidence of dyspareunia**

JAMA 1999;281,#6:537-544

Early Descriptions: Hyperaesthesia of the Vulva

1880

"…excessive sensibility of the nerves supplying the mucous membrane of some portion of the vulva; sometimes…confined to the vestibule…other times to one labium minus…"

Thomas, T.G., Practical Treatise on the Diseases of Women, Henry C. Lea's Son & Co., Philadelphia, 1880, pp. 145-147.

1888

"This disease…is characterized by a supersensitiveness of the vulva…No redness or other external manifestation of the disease is visible…When…the examining finger comes in contact with the hyperaesthetic part, the patient complains of pain, which is sometimes so great as to cause her to cry out…Sexual intercourse is equally painful, and becomes in aggravated cases impossible."

Skene, A.J.C., Diseases of the external organs of generation, In: Treatise on the Diseases of Women, New York, D. Appleton and Co., 1888, 77-99.

Vulvar Vestibulitis: History

Skene's surgical notes state: "The sensitive tissue has been dissected off and relief obtained for a time, the hyperesthesia returning, however, as before the operation."

Vulvar Vestibulitis: History

1942 Minor vestibular glands identified by Hunt

1976 Erythematous Vulvitis in Plaques (Pelisse & Hewitt)

1983 Extensive perineoplasty advocated by Woodruff & Parmely

1987 Vulvar vestibulitis syndrome coined and defined by Friedrich

1988 Histopathology – chronic periglandular inflammatory response without direct glandular inflammation (Pyka)

NIH Holds First Symposium

Vulvodynia Workshop:

Current Knowledge and Future Directions

- April 2-3, 1997
- More than 200 medical specialists attended
- Led to first federal funding of vulvodynia research in FY 2000

Coexisting Medical Conditions

Results from a self-report survey of vulvodynia patients administered by the National Vulvodynia Association

Disorder	Number surveyed	Have It	Suspect It
Chronic Fatigue	1566	12.6%	19.9%
Endometriosis	1452	15.6%	4.4%
Fibromyalgia	1547	20.0%	15.4%
Interstitial Cystitis	1662	25.2%	22.0%
Irritable Bowel	1675	34.9%	15.8%
Low Back Pain	1729	55.5%	-
Migraine Headaches	1564	31.2%	-
Chemical Sensitivities	1595	27.2%	18.2%
Other Chronic Pain	2150	40.5%	-

Vulvar Vestibulitis: Associations

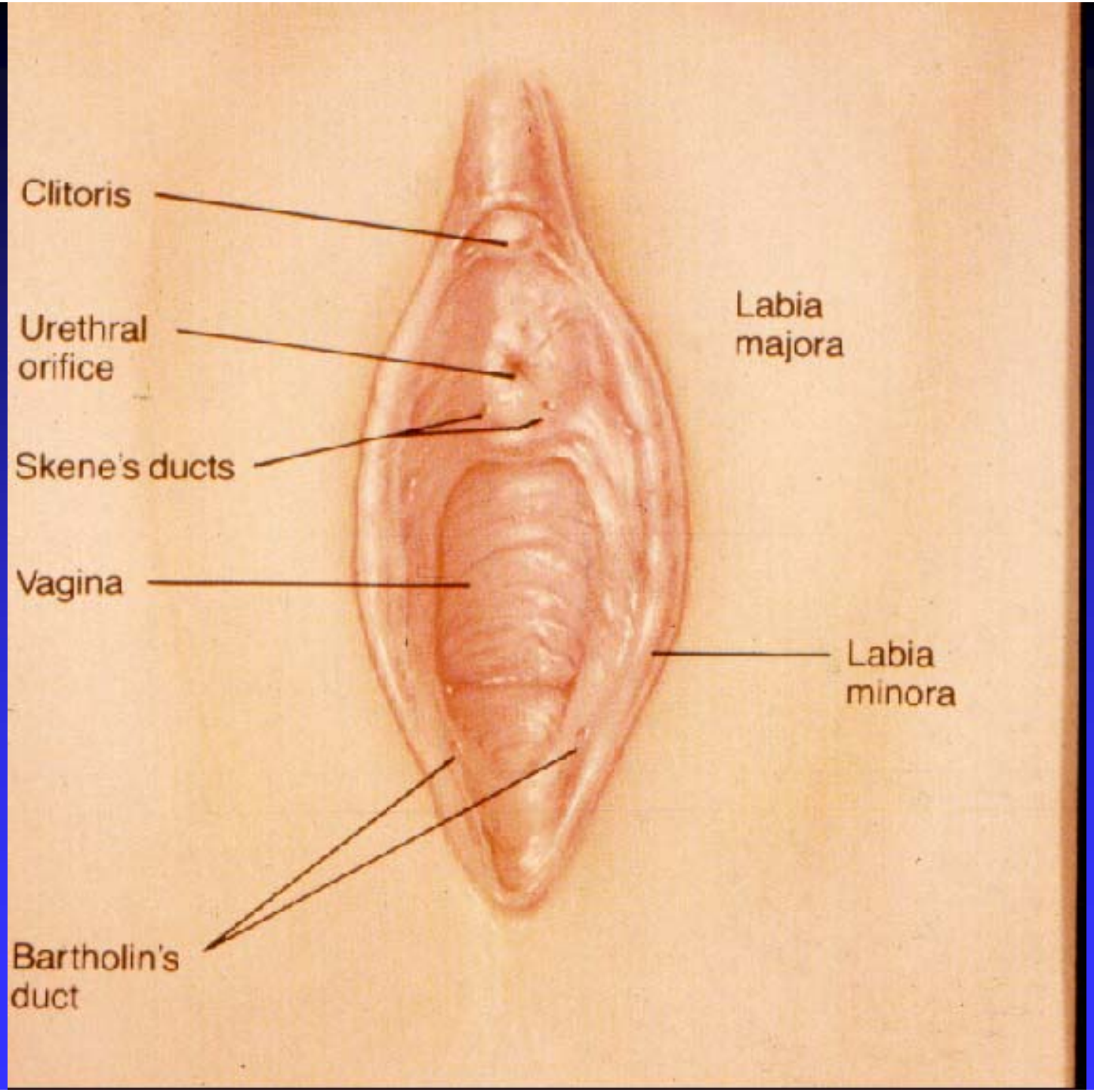
- **Allergies**
- **Chronic Fatigue**
- **Fibromyalgia**
- **Interstitial cystitis**
- **Irritable Bowel**
- **Sensitive Skin**
- **Multiple Chemical Sensitivities**

Vulvar Vestibulitis Syndrome (VVS)

Also known as:

localized vulvar dysesthesia

vestibulodynia


Clitoris
Urethral orifice
Skene's ducts
Vagina
Bartholin's duct
Labia majora
Labia minora

VVS: Diagnosis

- Rule out infection, dermatoses (biopsy or colposcopy may be necessary) and any other cause of pain
- Diagnosed using Friedrich's Criteria:
  - Severe pain on vestibular touch or attempted vaginal entry
  - Tenderness to pressure localized within the vulvar vestibule
  - No evidence of physical findings except for varying degrees of erythema

Friedrich Jr., E.G., Vulvar vestibulitis syndrome, Journal of Reproductive Medicine, 32 (1987) 110-114.

Vulvar Vestibulitis: Patient Profile

67 Patients

Average age at onset	**25**
Caucasian	**100%**
Nulliparous	**49%**
Prior abortions	**26%**
Primiparous	**11%**
Multiparous	**13%**
Onset - Acute	**80%**
- Gradual	**20%**

Peckham 1986

Vulvar Vestibulitis: Etiology

57 Women with Vulvar Vestibulitis

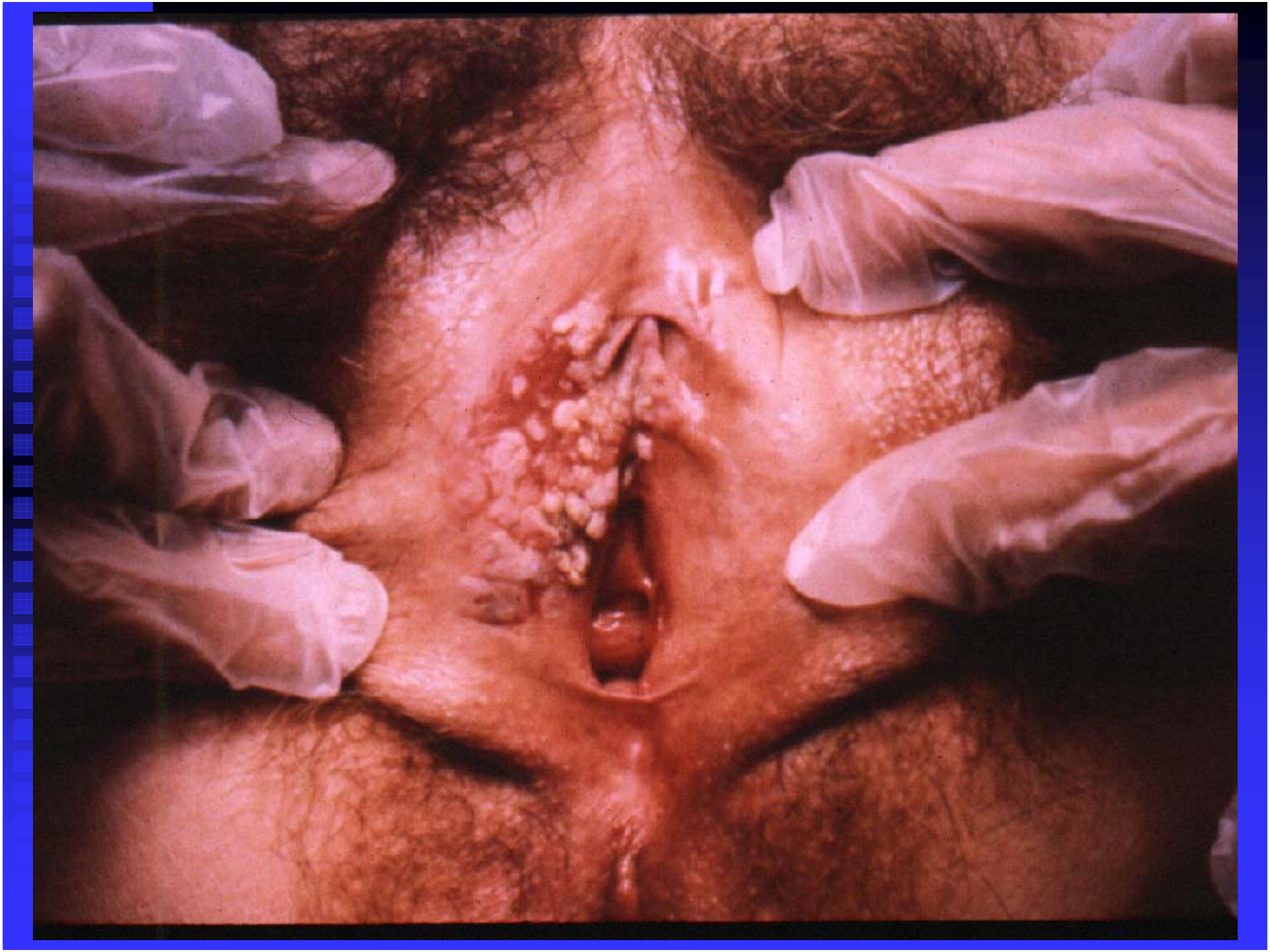
Gonorrhea	**0.0%**
Chlamydia	**0.0%**
Trichomonas	**0.0%**
Mycoplasma	**0.0%**
Gardnerella	**14.0%**
Candida	**8.8%**
HPV DNA	**5.3% (by PCR)**

Bazin et al.1994

Vulvar Vestibulitis: Etiology

Vulvar Vestibulitis is rarely associated with HPV infection.

Wilkinson et al. 1993



Vulvar Vestibulitis: Etiology

31 Women with Vulvar Vestibulitis

- **32% had a female relative with dyspareunia or tampon intolerance**
- **21% date symptoms to postpartum period**

Goetsch 1991

Vulvar Vestibulitis: Etiology

The Candidal Trigger

63% Friedrich (1988)

67% Peckham (1986)

80% Mann (1992)

Vulvar Vestibulitis: Etiology

Antigens of Candida Albicans

cross-react with certain

vulvovaginal tissue antigens

in predisposed patients.

Ashman & Ott 1989

The Telephone is Neither a Diagnostic Nor a Therapeutic Tool, and the Temptation to Use it as Such Should be Resisted.

Eduard G. Friedrich, Jr, MD

If the Treatment isn't Working, Reconsider the Diagnosis.

Rules for the Evaluation of Vulvar Symptoms

- **Rule #1**
  - **Everything feels like a yeast infection**
- **Rule #2**
  - **Not everything that feels like a yeast infection is a yeast infection**
- **Rule #3**
  - **Remember Rule #1**

VVS: Treatment

- Eliminate irritants
- Topical estradiol may decrease severity of symptoms
- Tricyclic antidepressants (e.g. amitriptyline) or anti-convulsants (e.g. neurontin) may be helpful for their pain-blocking qualities
- Counsel patient on vulvar self-care and self-help tips
- Topical anesthetics (e.g. lidocaine)
- Pelvic floor therapy (for those who have pelvic floor muscle abnormalities as measured by surface electromyography)
- Physical therapy
- Surgery (vestibulectomy with vaginal advancement) usually used after more conservative therapies are exhausted (high success rates of 70%+)
- Interferon injections – not recommended
- **CO2 LASER VAPORIZATION NO LONGER RECOMMENDED**

Vulvar Vestibulitis: Therapy

"The biases of eminent men are still biases."

M. Crichton 1971

Vulvar Vestibulitis: What Does Not Work

Laser

Topical steroids

5 Flurouracil (Efudex)

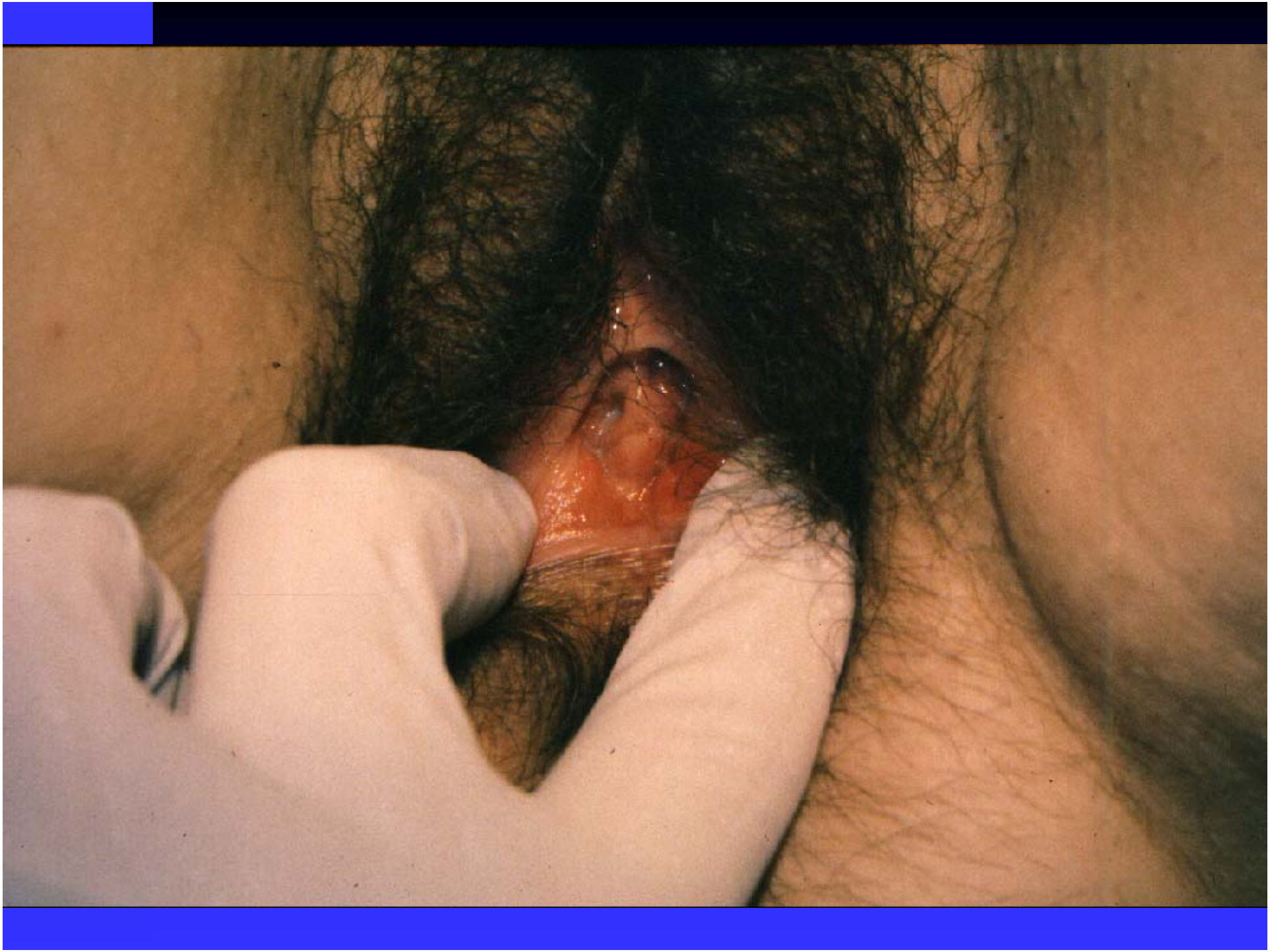
Trichloroacetic acid (TCA/BCA)

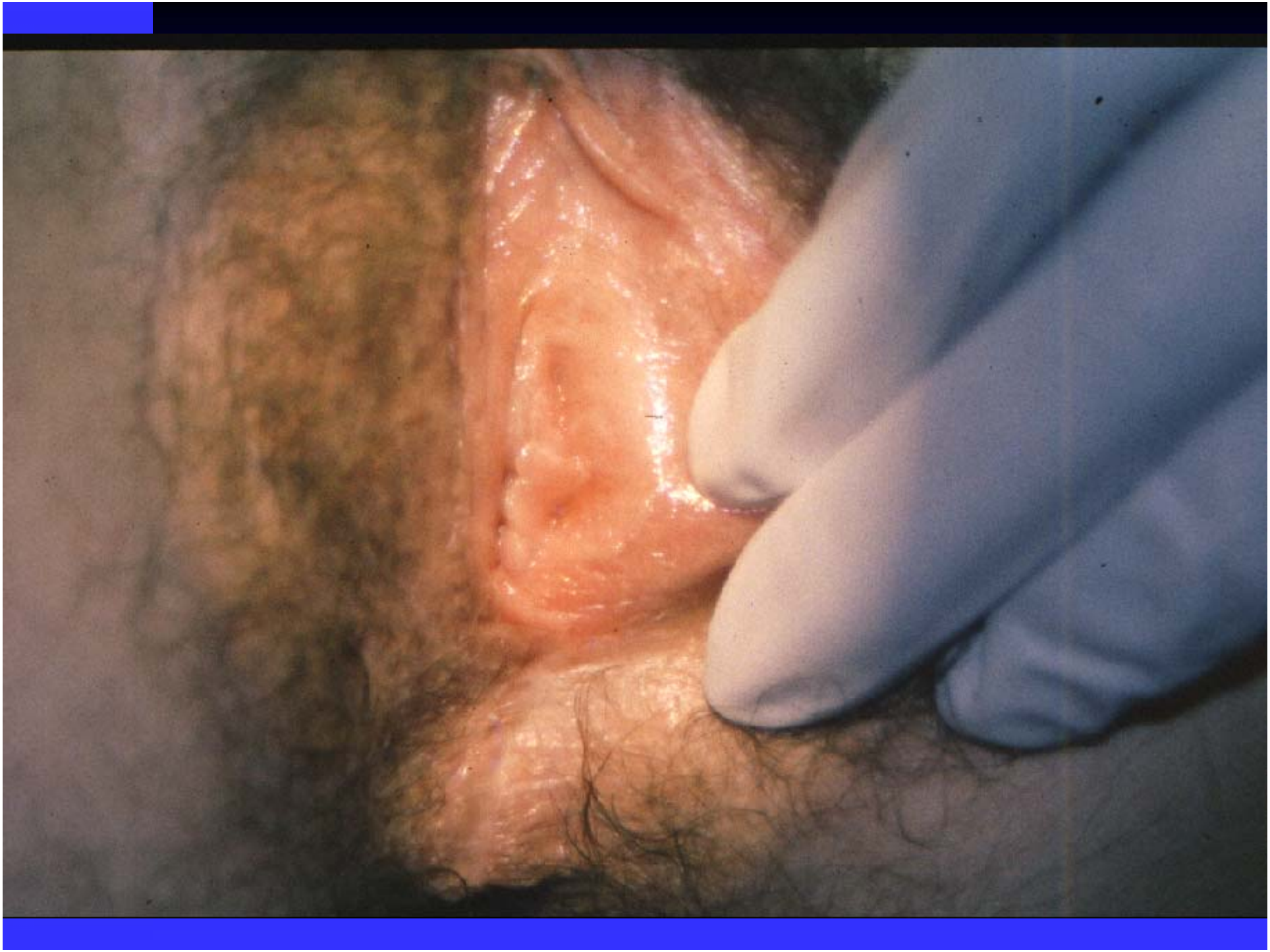
Interferon

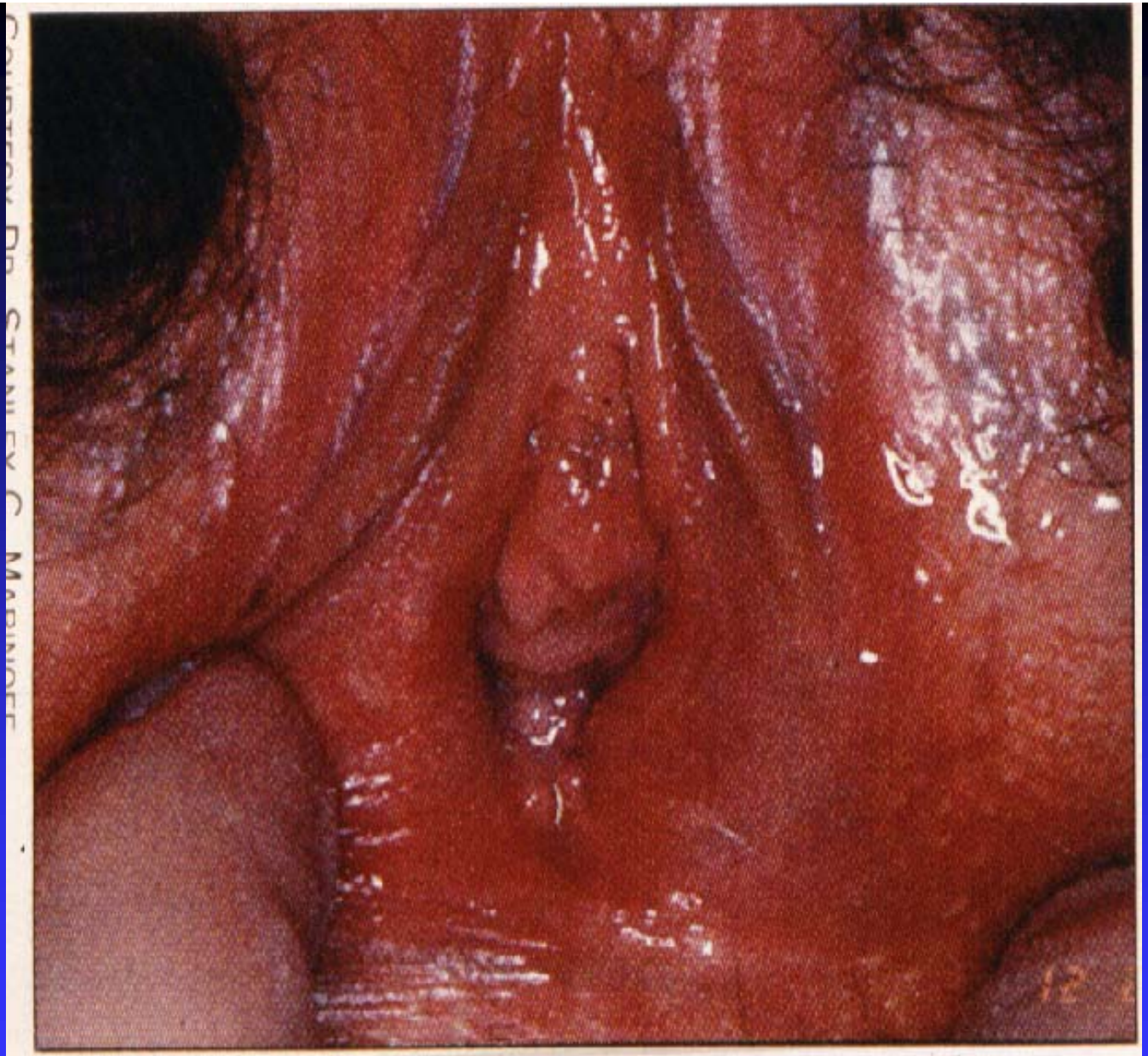
? Surgery

Vulvar Vestibulitis: Therapeutic Approach

- **Topical estrogen b.i.d.**
- **Biofeedback**
- **Antihistamines**
- **Reduced oxalate diet**







This is what the genitalia look like after vestibulectomy with vaginal advancement.

Vulvar Vestibulitis: Topical Estrogen

Effect of Topical Estrogen on the Vulvar Vestibule

Thirty-nine postmenopausal, unestrogenized women evaluated for sensory threshold by mechanoreceptor analysis

"lowering the mechanoreceptor threshold of the vulvar vestibule results from a rapid-acting, direct effect of topical estradiol cream upon mechanoreceptive nerve fibers" ***Foster - ISSVD abstract 1997***

Vulvar Vestibulitis: Current Results

971 Consecutive Vestibulitis Patients

- **Follow-up from 3 months to 23.2 years**
- **Average follow-up – 11.1 years**

Vulvar Vestibulitis: Current Results

Diagnostic Criteria

- **Severe pain on vestibular touch or attempted vaginal entry**
- **Tenderness to point pressure localized within the vulvar vestibule**
- **Physical findings confined to vestibular erythema of various degrees**

J Reprod Med 1987;32: 110-114

Vulvar Vestibulitis: Current Results

971 Consecutive Vestibulitis Patients

Caucasian	**949**	**–**	**97.7%**
Premenopausal	**806**	**–**	**83.0%**
Nulliparous	**487**	**–**	**50.2%**
Prior abortions	**105**	**–**	**10.8%**
Primiparous	**126**	**–**	**13.0%**
Multiparous	**252**	**–**	**26.0%**

Vulvar Vestibulitis: Current Results

971 Consecutive Vestibulitis Patients

Urologic Symptoms	**436**	**–**	**44.9%**
Yeast History	**667**	**–**	**68.7%**
HPV History	**119**	**–**	**12.3%**
Irritable Bowel	**166**	**–**	**17.1%**
Fibromyalgia	**249**	**–**	**25.6%**

Vulvar Vestibulitis: Current Results

971 Consecutive Vestibular Patients

- **64 with prior perineoplasty**
- **41 with prior laser surgery to vestibule**
- **15 with multiple vestibular surgeries**
- **8 with multiple laser surgeries to the vestibule**
- **27 with combinations of laser and scalpel surgery**
- **23 with prior topical 5-flurouracil exposure**
- **15 with prior vestibular interferon injections**

Vulvar Vestibulitis: Current Results

Definition of Response

- **Complete response: substantially improved**
  - **Full activities of daily life**
  - **Able to wear fitted clothing**
  - **Urinary symptomatology cleared**
- **Partial response: moderately improved**
  - **Comfortable coitus at least one third of the time**
  - **Quality of life significantly better**

Vulvar Vestibulitis: Current Results

Objective Correlates of Response

- **Q-tip testing normalized**
- **Vestibular erythema absent**
- **Pelvic floor muscle tension reduced**
- **Enhanced voluntary control of the pelvic floor musculature**
- **Pelvic musculature non-tender to palpation**

Vulvar Vestibulitis: Current Results

971 Consecutive Vestibular Patients

884 Evaluable Patients

- **711 patients (80.4%) - complete response**
- **150 patients (17.0%) - partial response**
- **23 patients (2.6%)- no response**
- **87 patients (9.0%)- lost to follow up**

Vulvar Vestibulitis: Current Results

971 Consecutive Vestibulitis Patients

884 Evaluable Patients
711 Responders

- **63.7% - topical estradiol & biofeedback & reduced oxalate diet / oral calcium citrate**
- **34.9% - topical estradiol & biofeedback**
- **1.4% - biofeedback & reduced oxalate diet / oral calcium citrate**

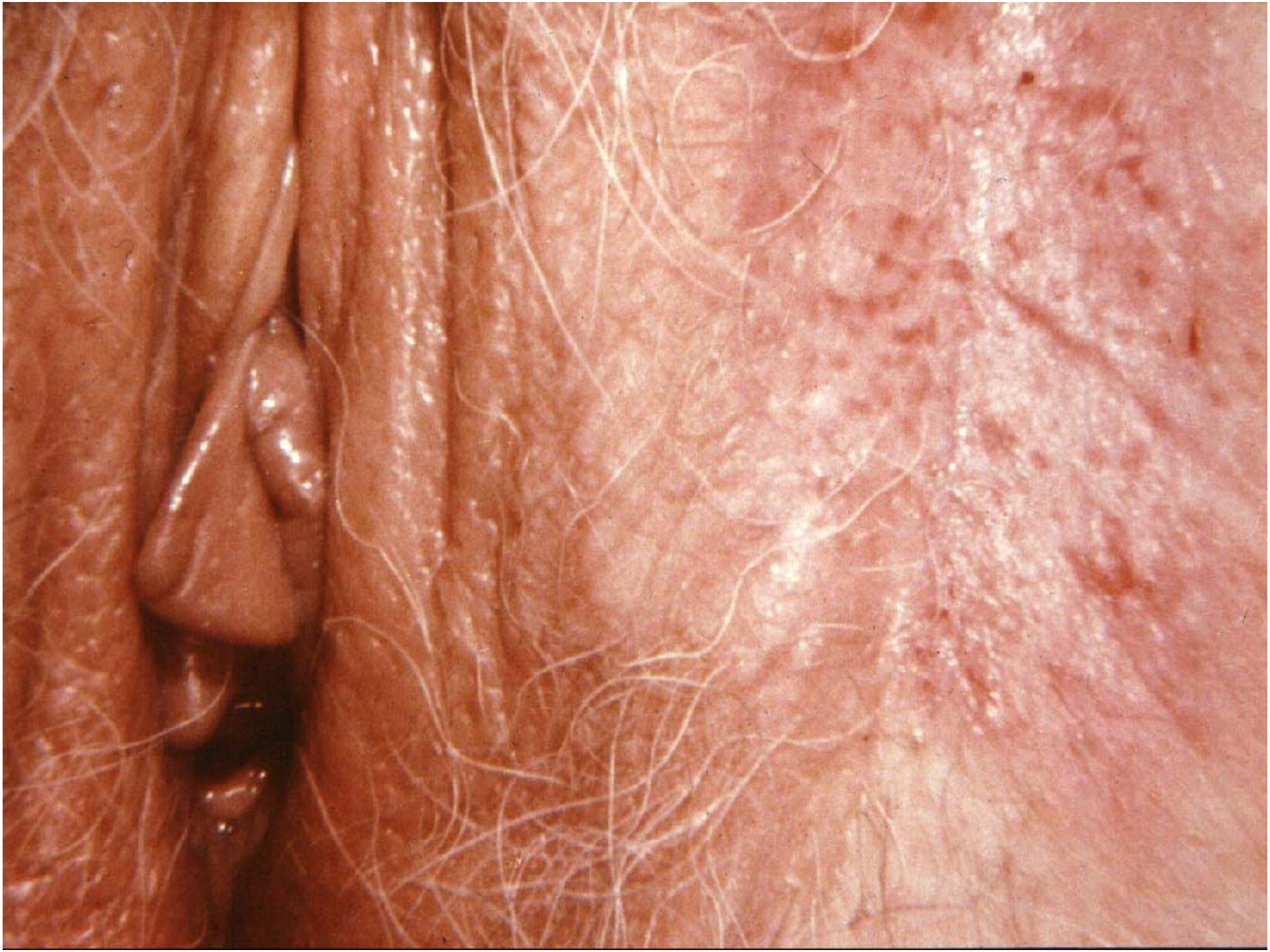
Vulvar Vestibulitis: Current Results

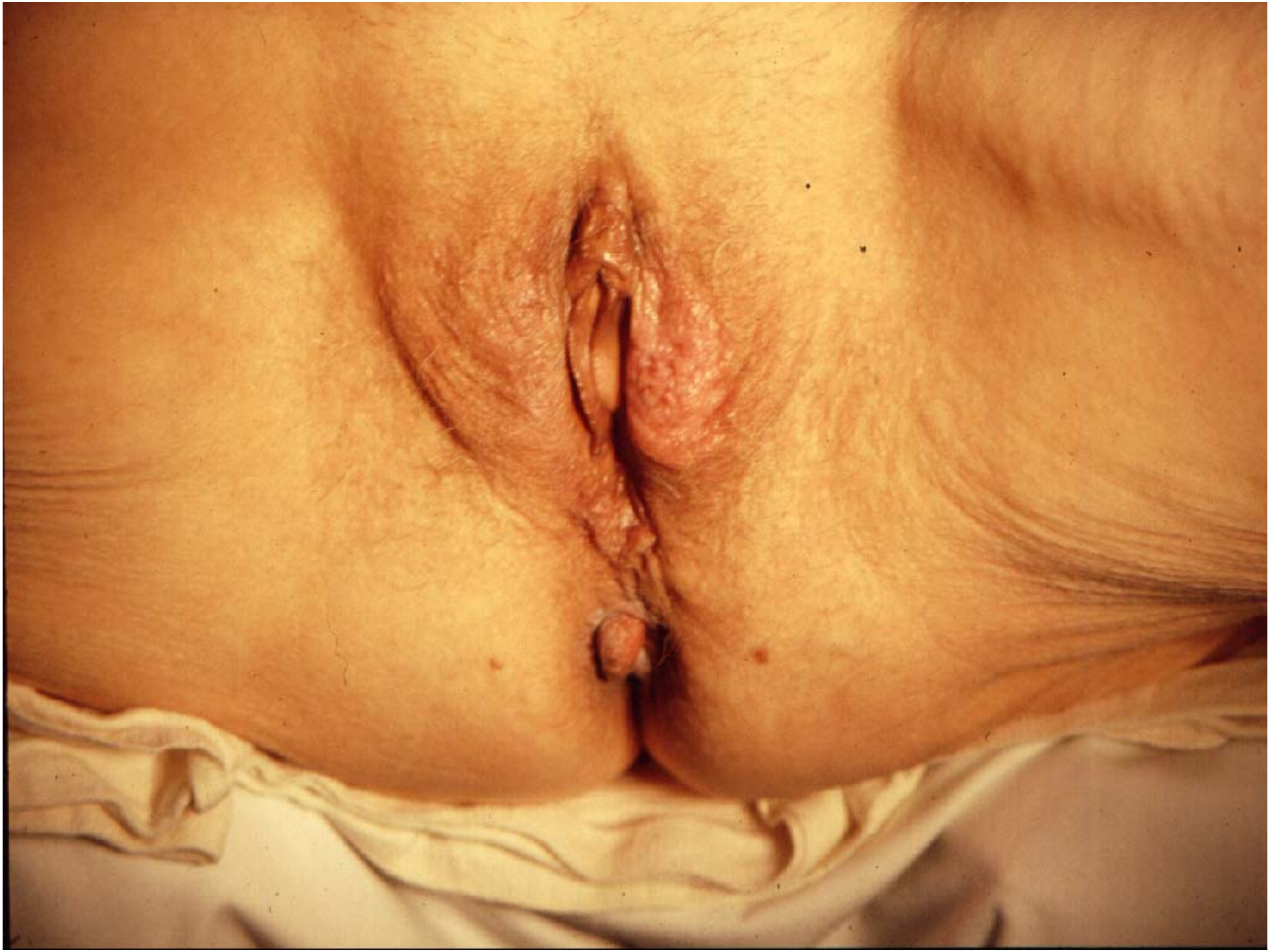
- 249 Patients with fibromyalgia
  - no response in 9 (3.5%)
  - partial response in 104 (41.9%)
  - complete response in 136 (54.5%)
- 2 Patients with reflex sympathetic dystrophy
  - no response in 1
  - partial response in 1

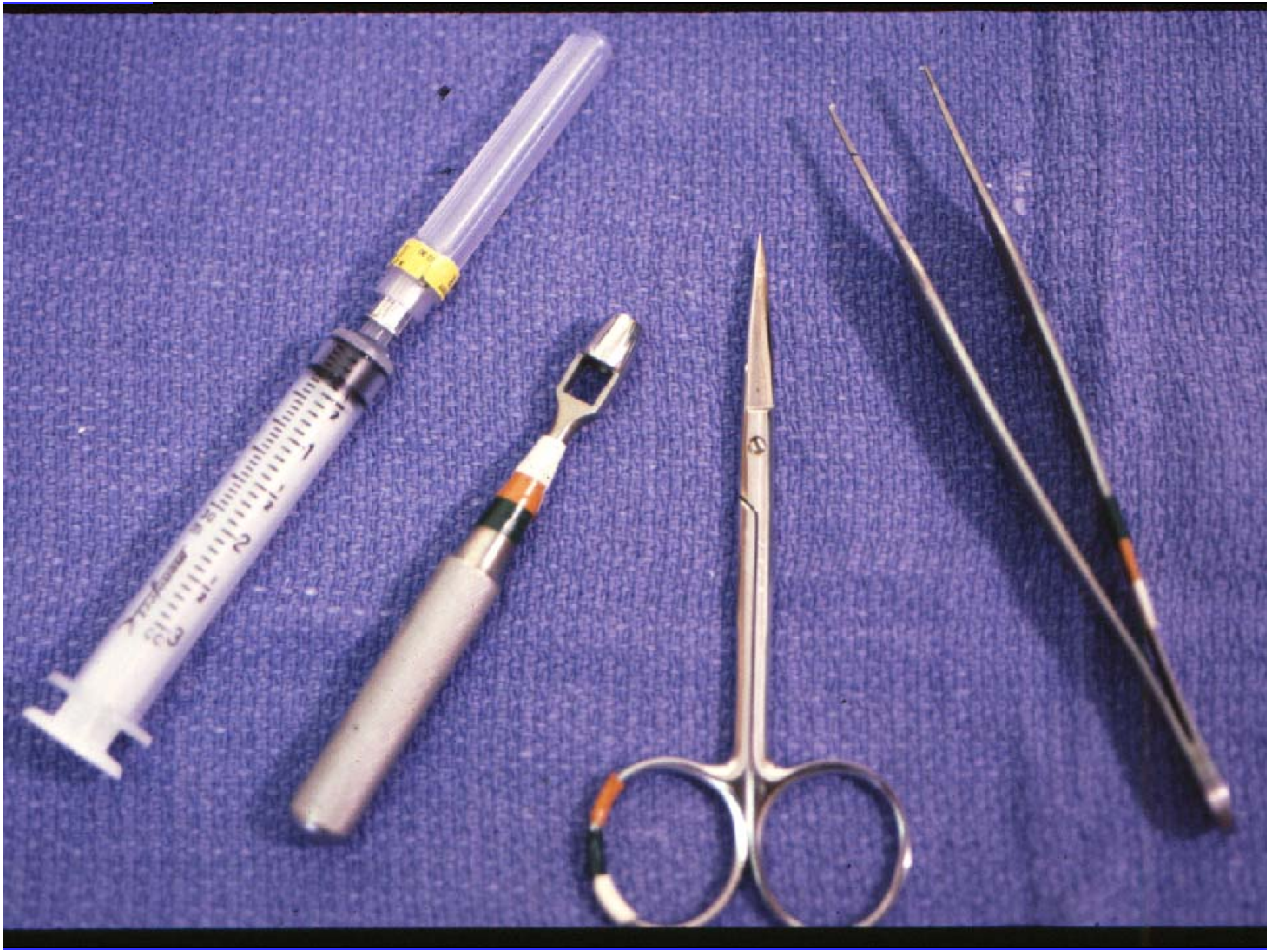
Vulvar Vestibulitis: Beyond 2011

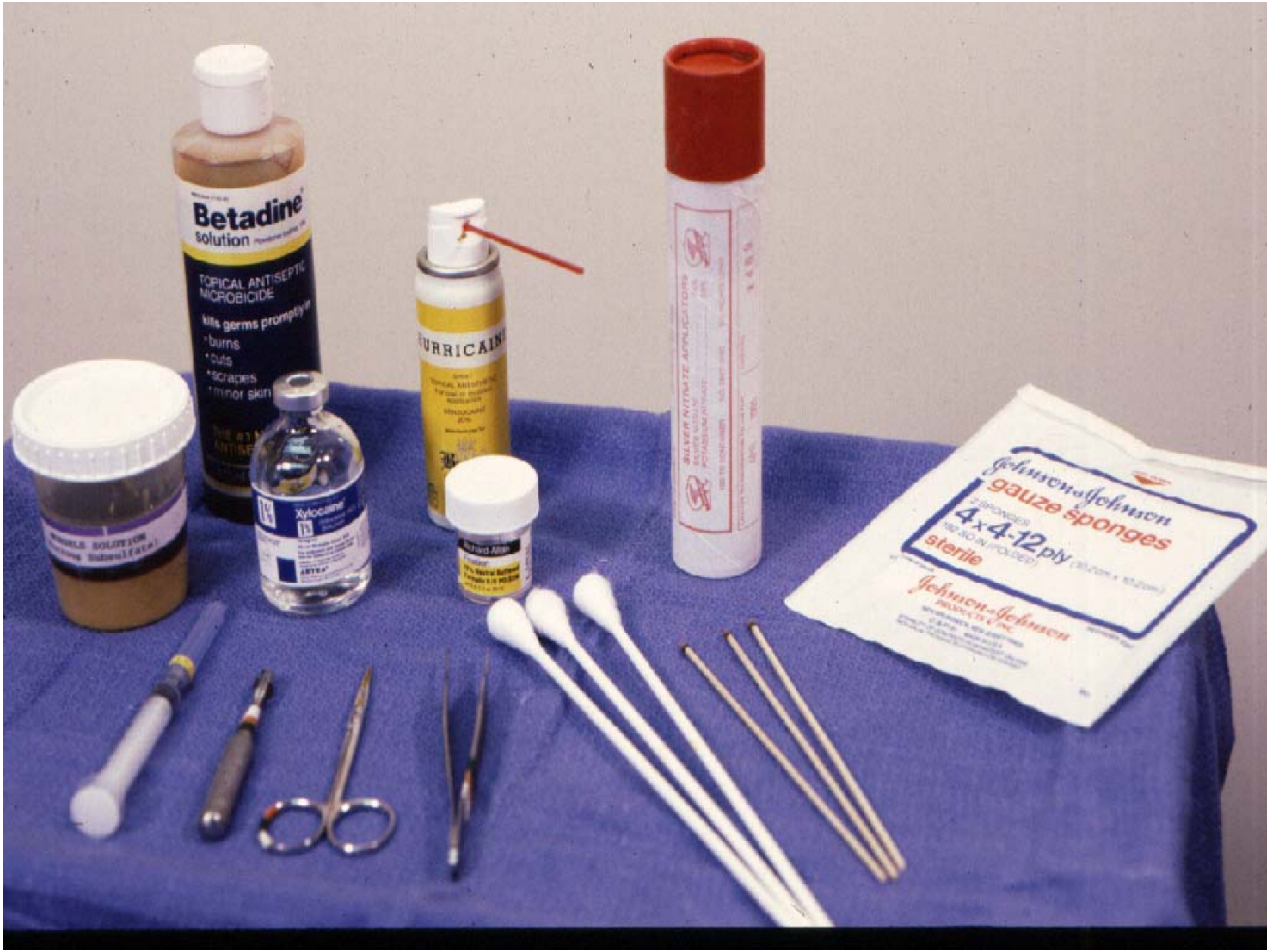
Research Directions

- **Genetic Basis**
  - **Further familial evaluation**
  - **Human genome project**
- **Mast cell management - linolenic acid**
- **Improved neuropharmaceutical agents**
- **Improved combined topical therapies**
- **Urinary symptomatology and oral heparinoids**








Betadine
solution
TOPICAL ANTISEPTIC
MICROBICIDE
Johnson&Johnson
gauze sponges
4x4-12ply
sterile
Johnson&Johnson

Lichen Simplex Chronicus (LSC)

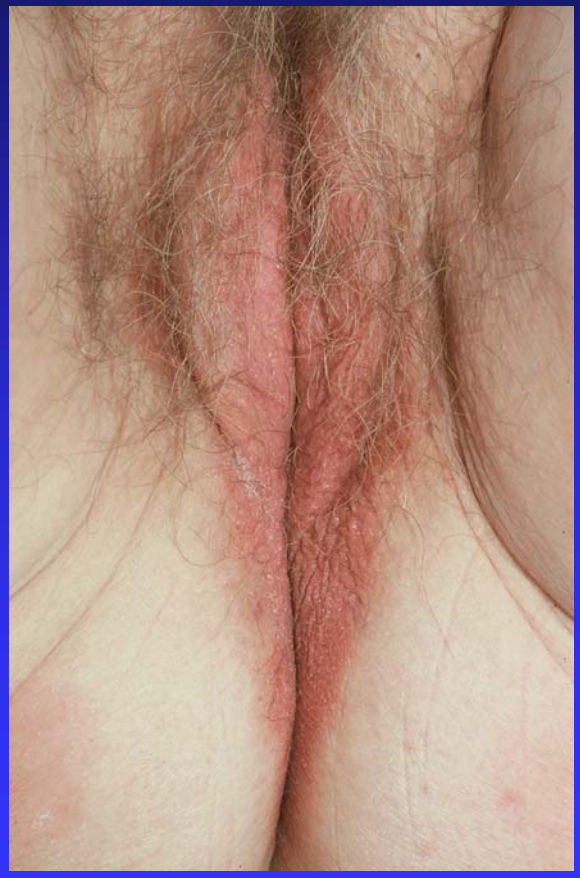
LSC: General Information

- End stage of itch-scratch-itch cycle in predisposed patients due to:
  - Irritants
  - Infections
  - VIN
- Patients often frustrated by long course of symptoms and having seen many physicians
- Recurrence is common

LSC: Diagnosis

- Patient reports intense pruritus with relief upon scratching
- Thick, lichenified skin – often reddened
- May exhibit erosions or fissuring
- Culture for yeast and bacteria

LSC – Classic Presentation



Usually, the skin abnormalities of lichen simplex chronicus (aka eczema, atopic dermatitis, neurodermatitis) are caused by rubbing or scratching, as can be seen from the rubbed and thickened skin in this woman.

LSC: Treatment

- Treat any underlying infection
- Remove potential irritants or allergens; stop all topicals, soaps, douches, etc.
- Sitz baths or compresses 1-2x/day for 10-15 minutes
- Mid-to-high potency topical corticosteroid
- Counsel patient about vulvar self-care measures to minimize risk of recurrence

White Lesions

- Dystrophy
  - Lichen sclerosus
  - Squamous cell hyperplasia
  - Mixed/other dermatoses
- Vitiligo
- Leucoderma
- Cancer in situ

Classification of Vulvar Dystrophy (ISSVD - 1975)

- Hyperplastic dystrophy
  - Without atypia
  - With atypia
- Lichen sclerosus
- Mixed dystrophy - lichen sclerosus with epithelial hyperplasia
  - Without atypia
  - With atypia

Classification of Vulvar Dystrophy (ISSVD - 1987)

- Squamous cell hyperplasia
  (formerly hyperplastic dystrophy)
- Lichen sclerosus
- Other dermatoses

Vulvar Dermatoses

Lichen Sclerosus (LS)

LS: General Information

- Etiology unknown, generally believed to be autoimmune
- Occurs on genital skin in about 80% of cases
- Females of any age can develop LS, including young children, toddlers and infants (as can males) but most symptomatic are post-menopausal women
- Childhood LS can resolve at puberty (children should be followed very carefully throughout adolescence – do not assume that no symptoms equals no disease)
- Sometimes improves during pregnancy (usually 2nd tri)
- Often misdiagnosed as yeast infections, herpes or vitiligo
- 2-5% risk of developing vulvar squamous cell carcinoma

LS: Diagnosis

- Pathognomonic sign is texture change – crinkling, occasionally looks waxy
- Punch biopsy typically used
  - in women with severely fragile skin or in children, treatment is sometimes initiated without a biopsy
- Histological findings:
  - hallmark is liquefaction degeneration of the basal cell layer with homogenization of collagen in the dermis (epidermis can be atrophic or thickened)
- Hypo-pigmentation – “butterfly” or “keyhole” appearance
- Pruritus, sometimes burning or pain
- Atrophy and increased risk of fissures
- In advanced or untreated cases: clitoral hood fuses; labia minora fused to majora; narrowing of the introitus; dyspareunia

LS – Classic Presentation

Severe lichen sclerosus is itchy and it can be identified by the white color and easy bruising and tearing when rubbed, obviously a cause of symptoms.

LS: Treatment

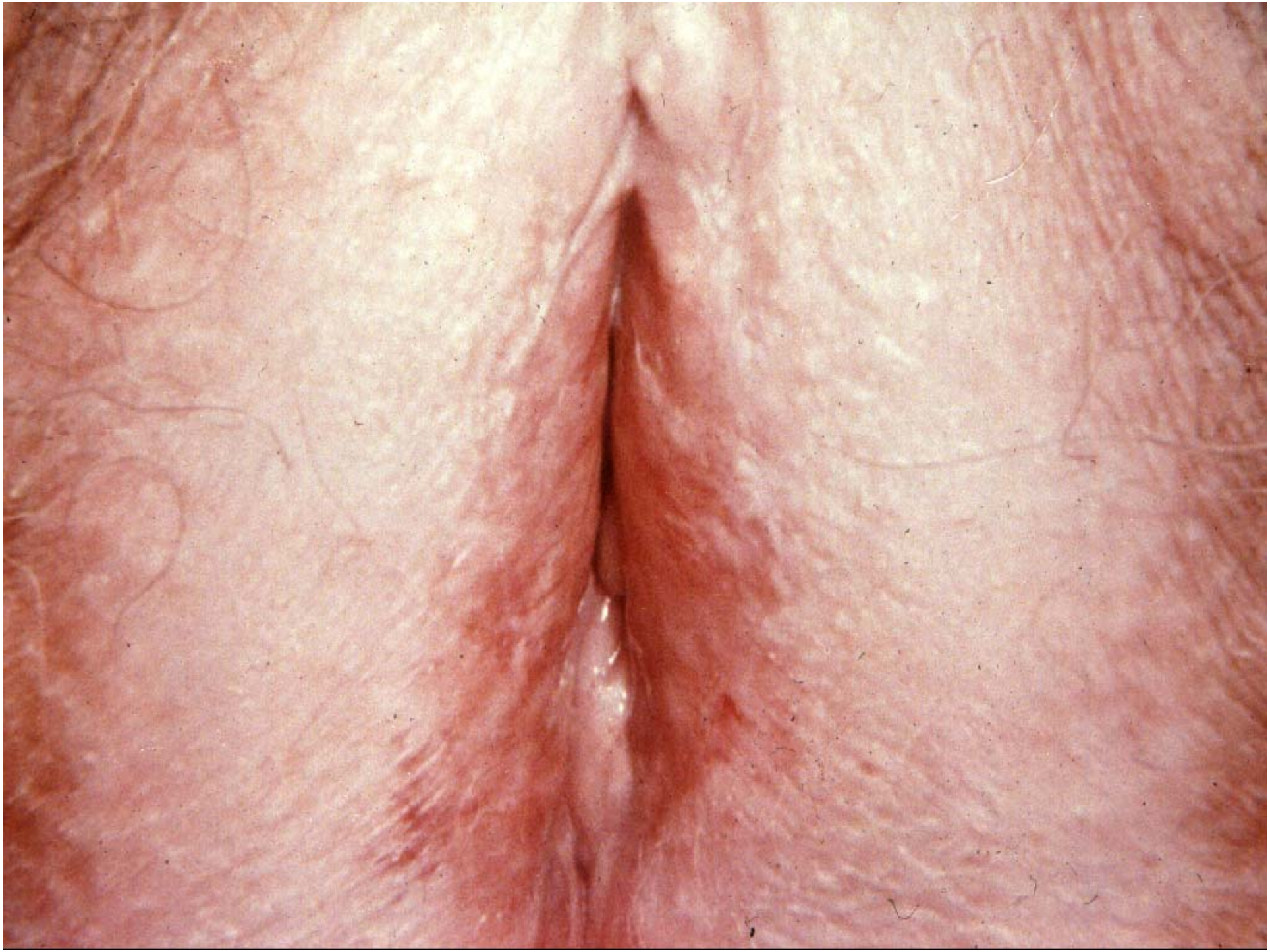
- Topical clobetasol propionate 0.05% 1-2x/day
  - Reduce frequency and/or potency when texture and/or symptoms normalize
- Testosterone and progesterone do not work better than petrolatum ointment (Vaseline) alone
- Some are beginning to prescribe topical tacrolimus with good results – research is needed
- Dilator and/or sex therapy may be helpful for women who experience dyspareunia
  - first treat the vulvar skin to help restore elasticity – and recommend using lubrication
- Counsel patient on vulvar self-care measures
- Skin grafting not recommended due to high rate of recurrence

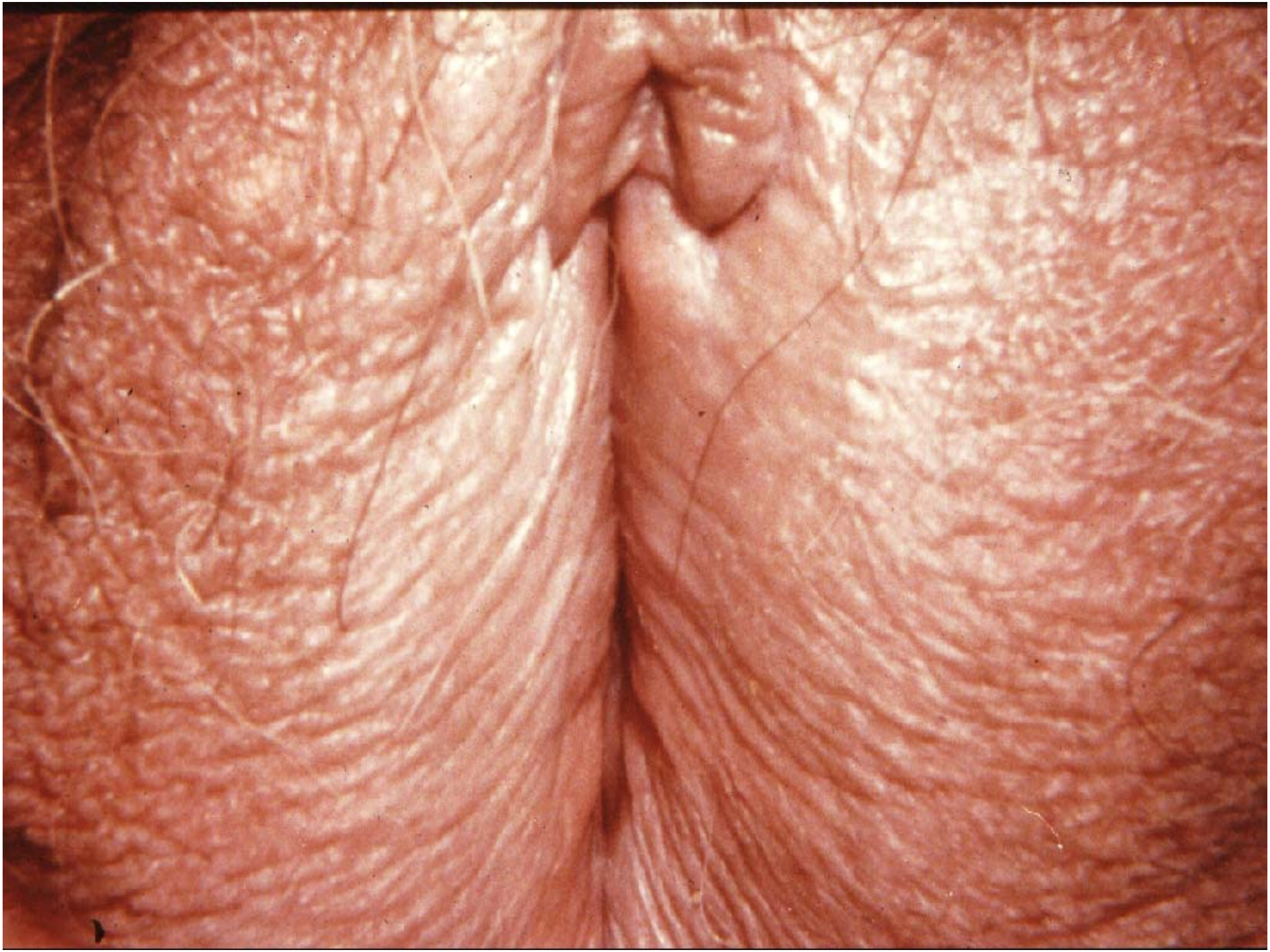
Suggestions for instructing patients in applying topical treatments

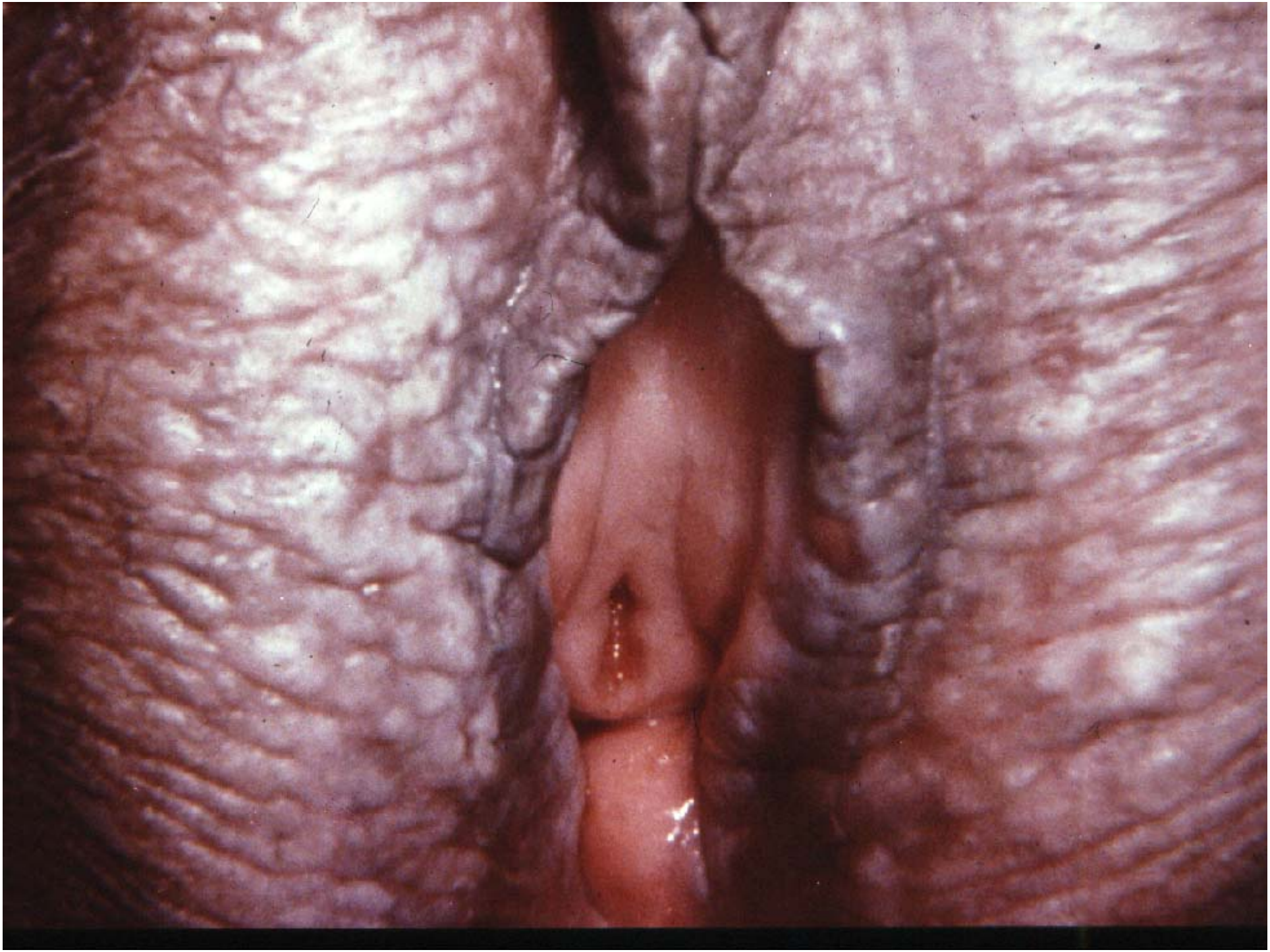
Some topical treatments are very effective, however caution should be used in their application.

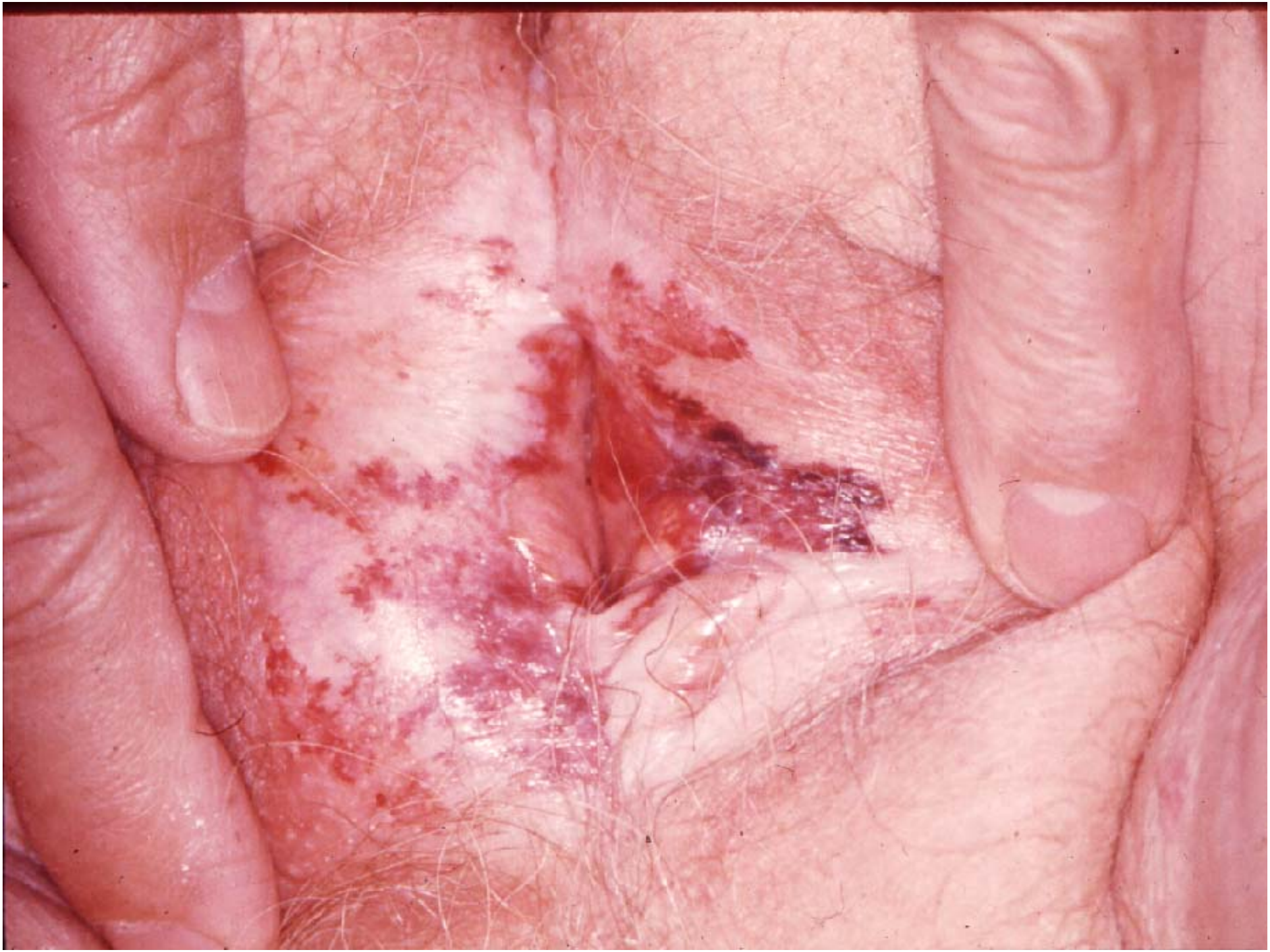
Give specific instructions for applying topical treatments for the vulva:

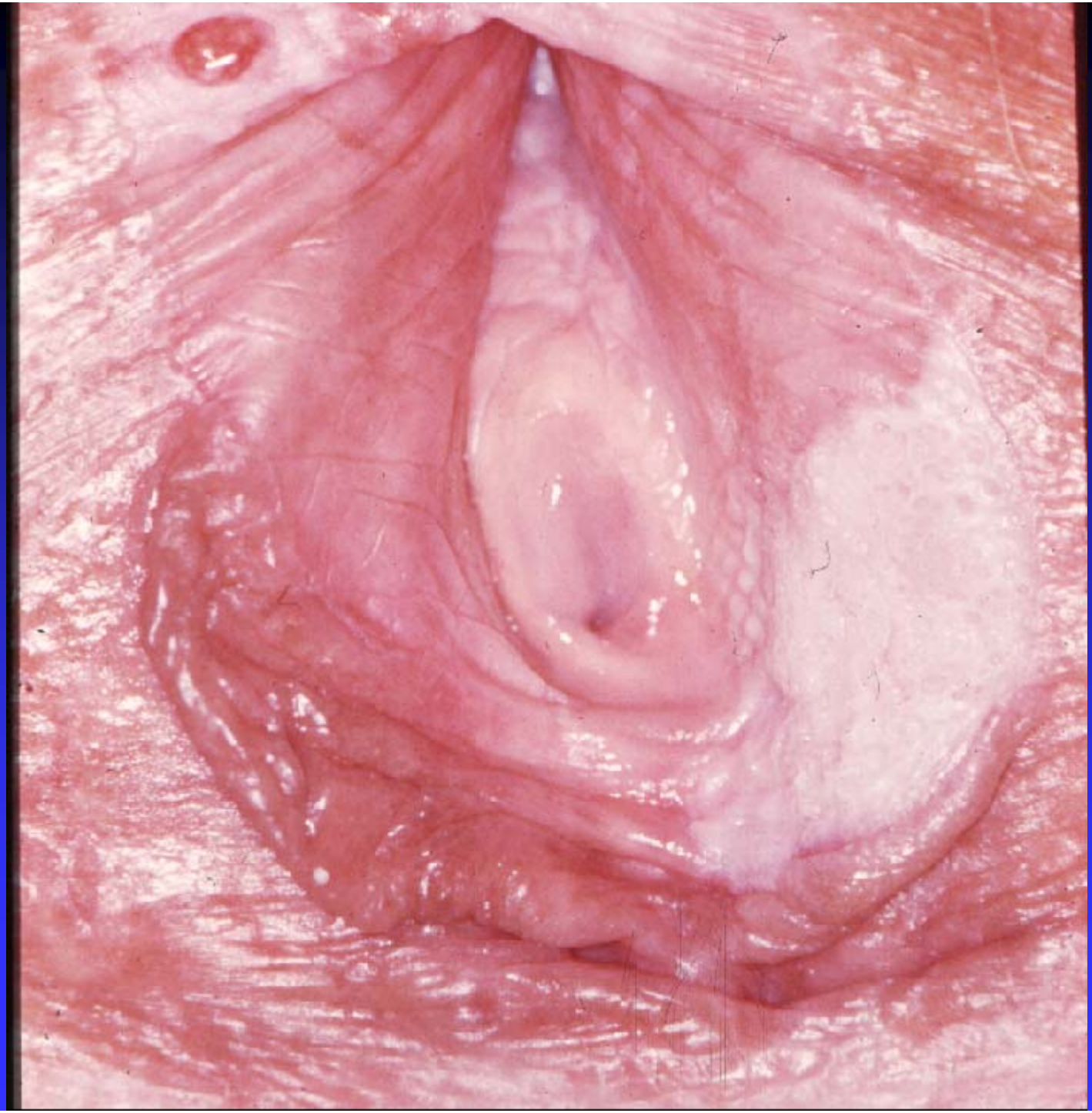
- Amount of cream
  - Squeeze correct amount of treatment sample on your own finger during office visit
- Application site
  - Some women will have never seen their vulva
  - Shade in or point to areas on a vulvar diagram to indicate correct application site
  - Have patient apply treatment during visit, using a mirror for clarity









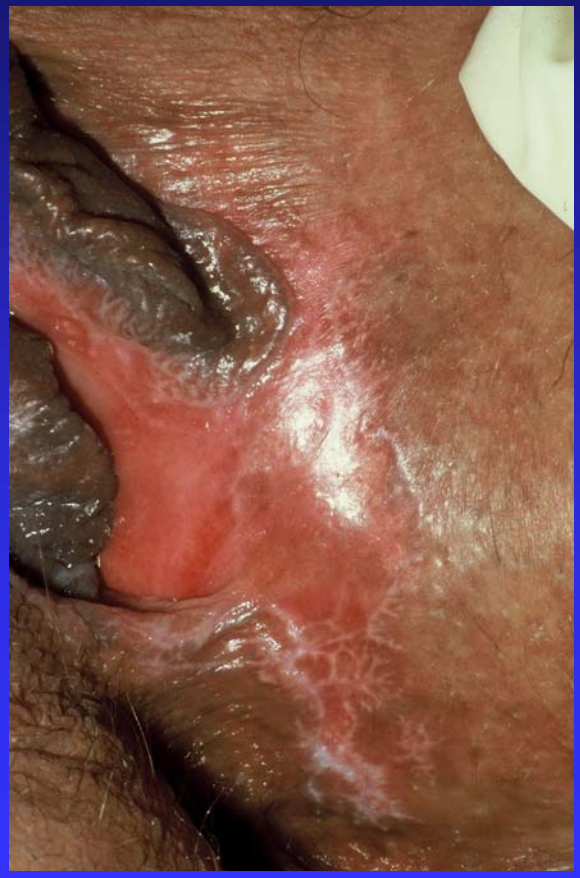


Lichen Planus (LP)

LP: Diagnosis

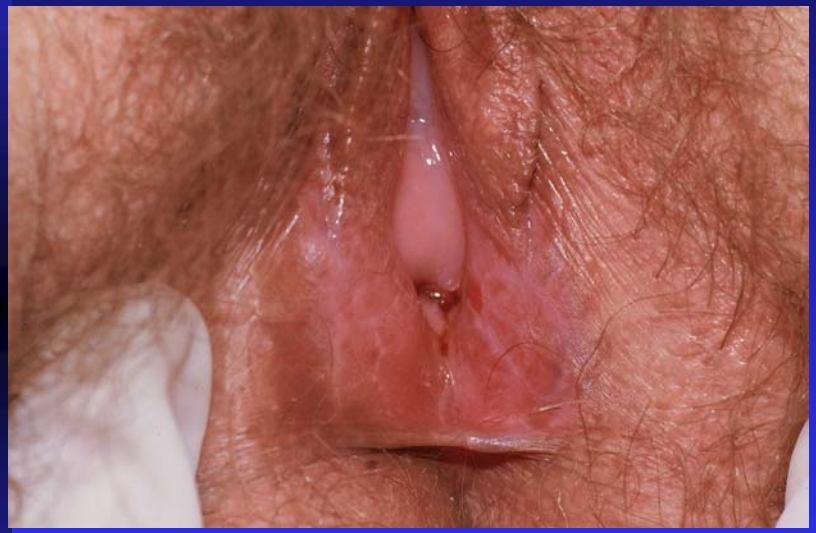
- Differentiating LS & LP can be difficult; can also co-exist
- A biopsy is helpful in diagnosing LP but histological findings are sometimes non-specific
- May be associated with slightly increased risk of cancer
- Histological findings:
  - Hallmark is a dense chronic inflammatory infiltrate hugging and obscuring the basal cell layer with occasional necrotic keratinocytes
- Classic Non-erosive Lichen Planus
  - white lacy or fern-like papules
- Erosive Lichen Planus
  - Clearly demarcated red plaques on oral and/or genital membranes with white “lacy” edges
  - Erythematous lesions in the vestibule & up into vagina
  - Burning pain; dyspareunia
  - May resemble lichen sclerosus, particularly when late agglutination of architecture occurs

LP: Classic Presentation

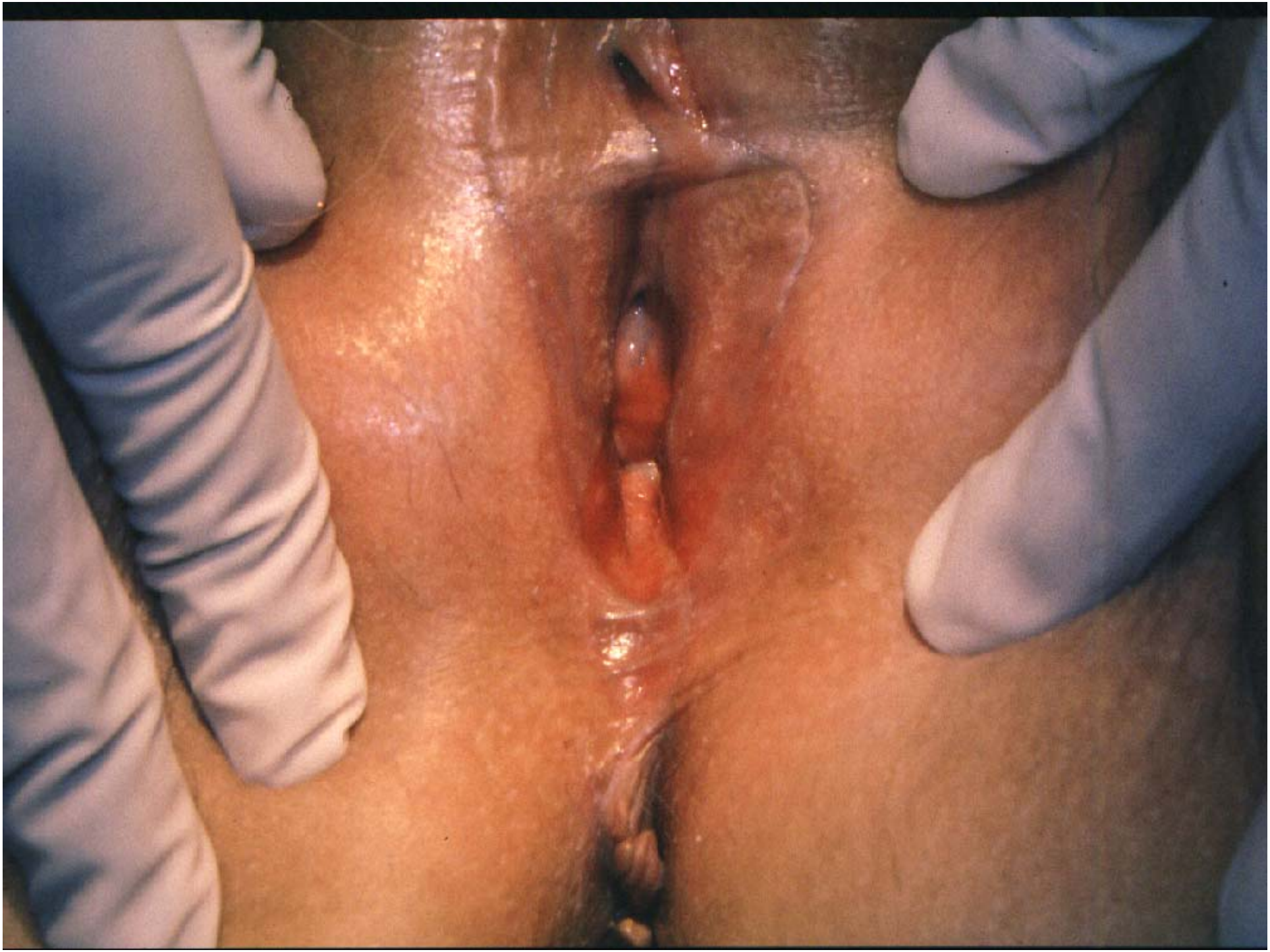


Lichen planus with irregular white lines is classic, and the deep red areas are painful erosions.

LP: Subtle Presentation



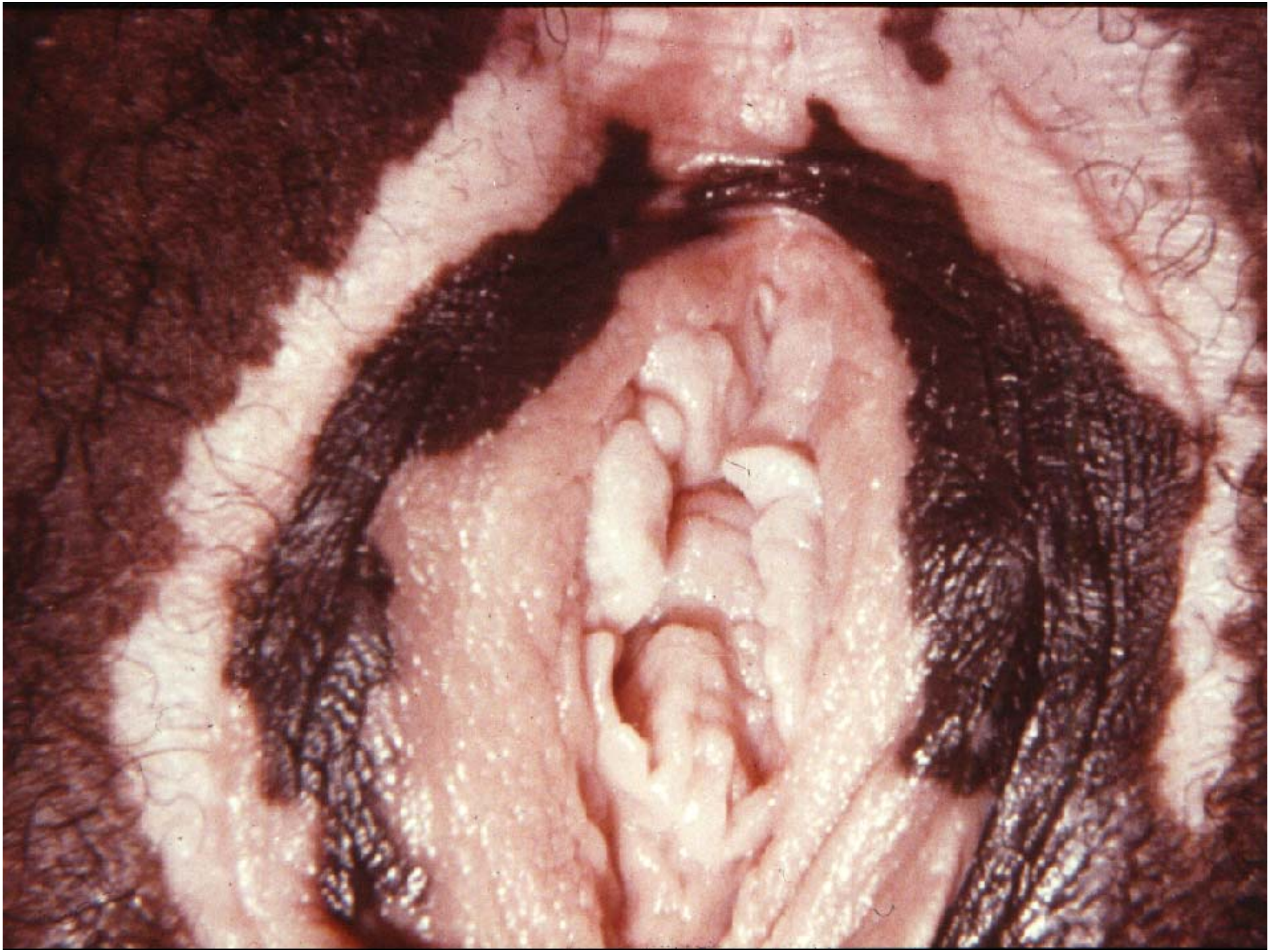
Even subtle lichen planus can hurt, as it does in this woman who has mild white streakiness towards the posterior fourchette, and small posterior vestibular erosions.

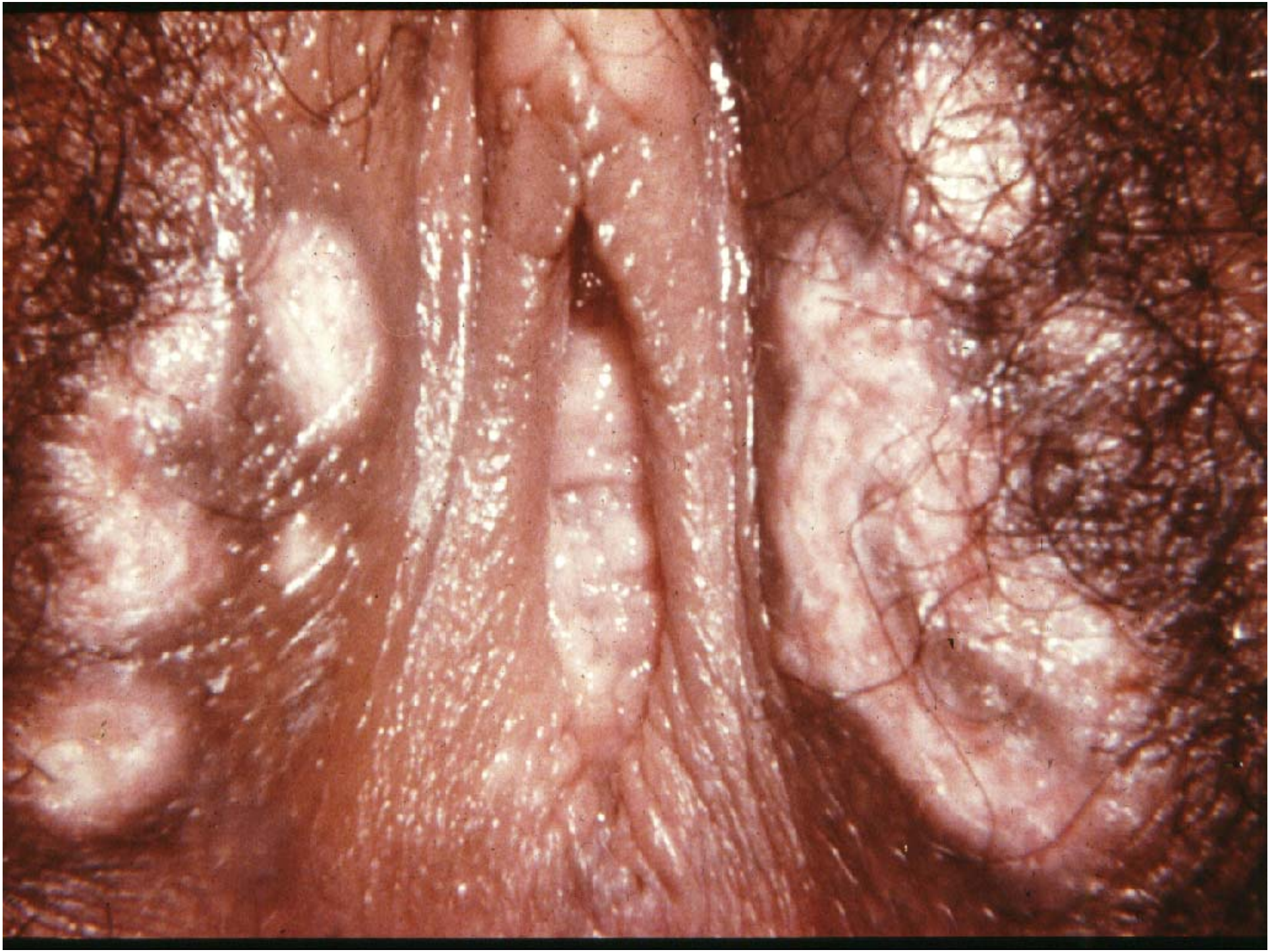


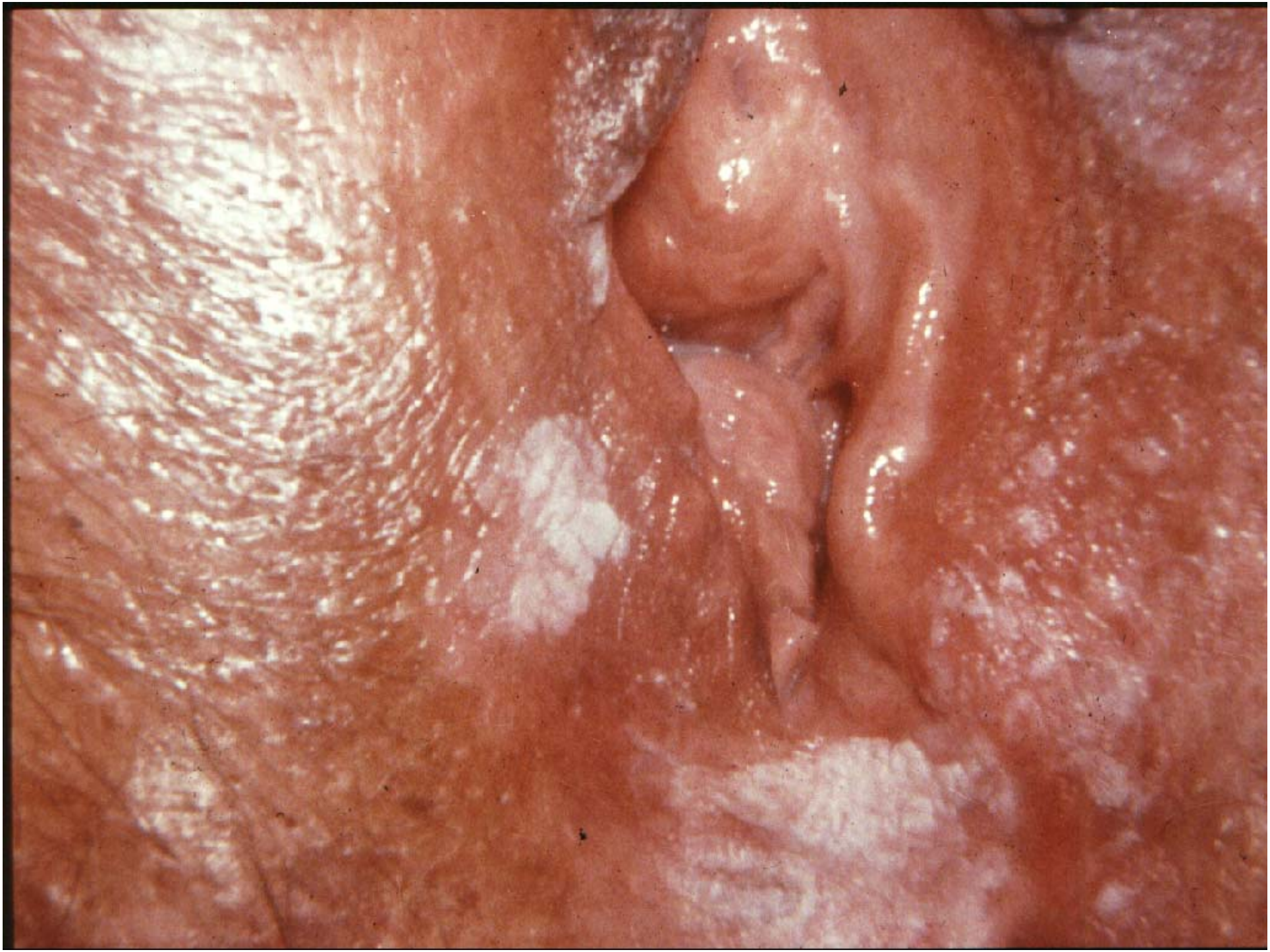
LP: Treatment

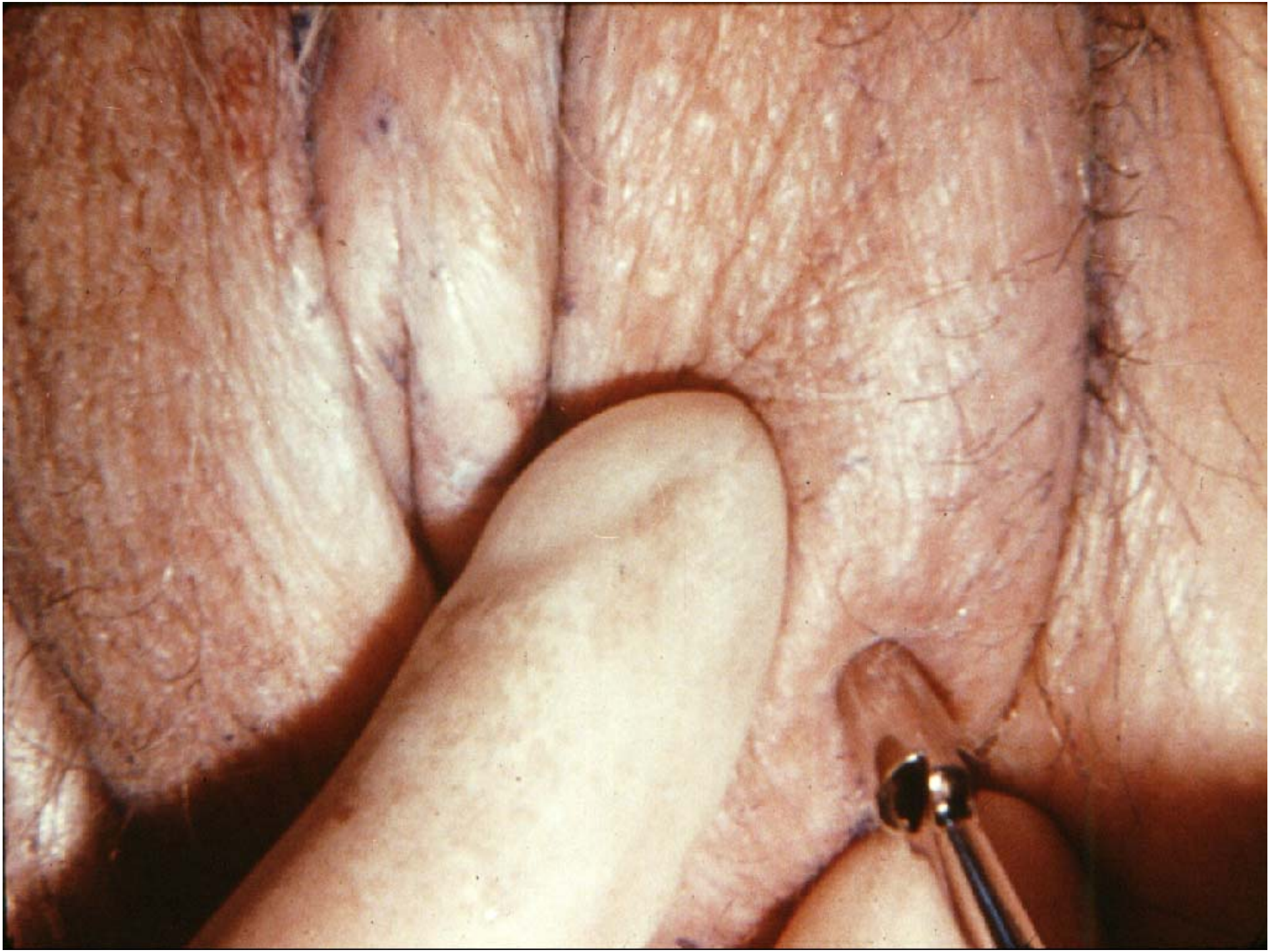
Options include:

- Ultrapotent corticosteroids with careful follow-up for vulva; hydrocortisone foam for vagina
- Tacrolimus (be careful – absorbed from vagina)
- Hydroxychloroquine
- Anti metabolites
- Systemic retinoids
- Vaginal dilator therapy for women with introital stenosis and/or labial adhesions



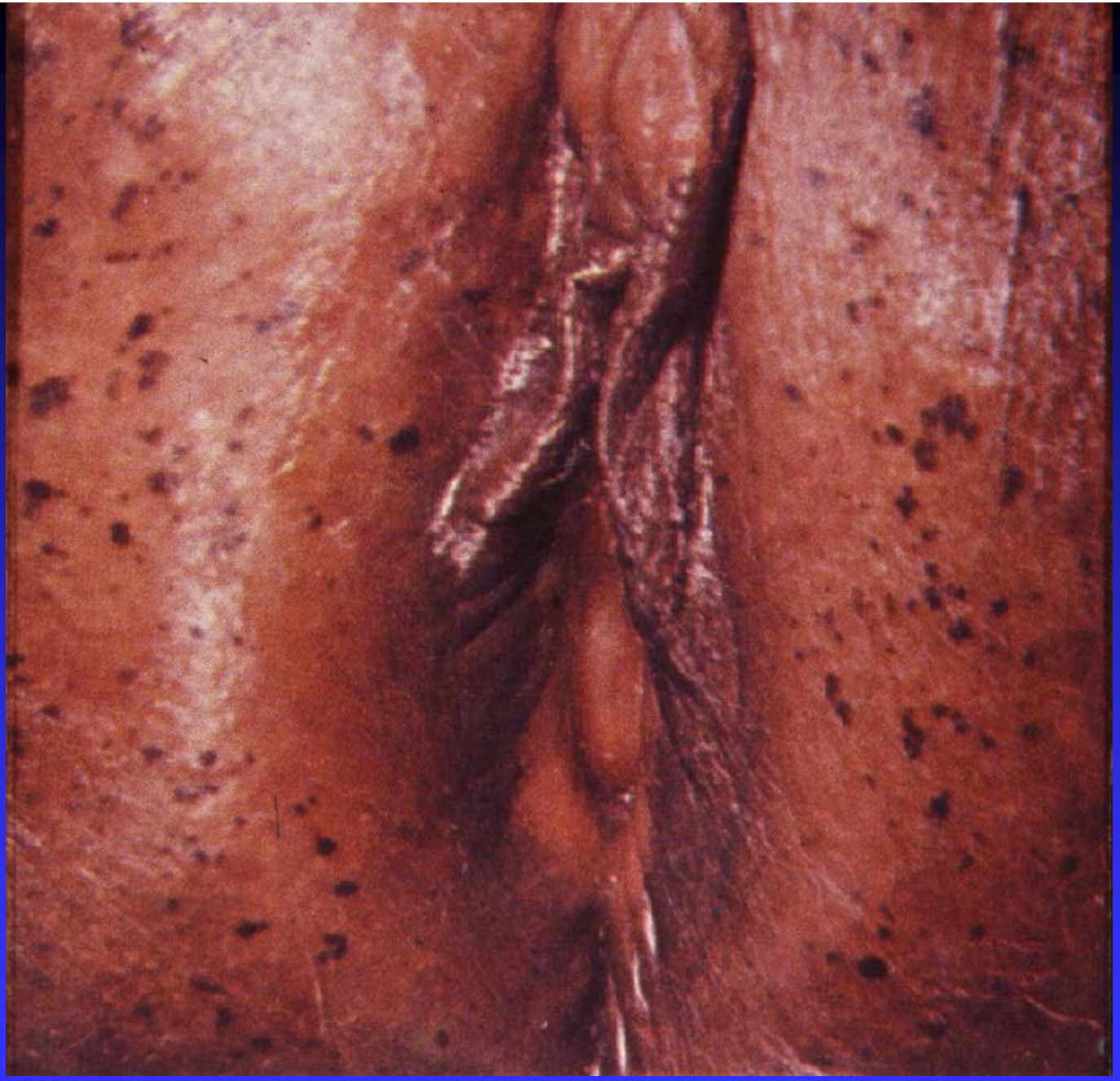




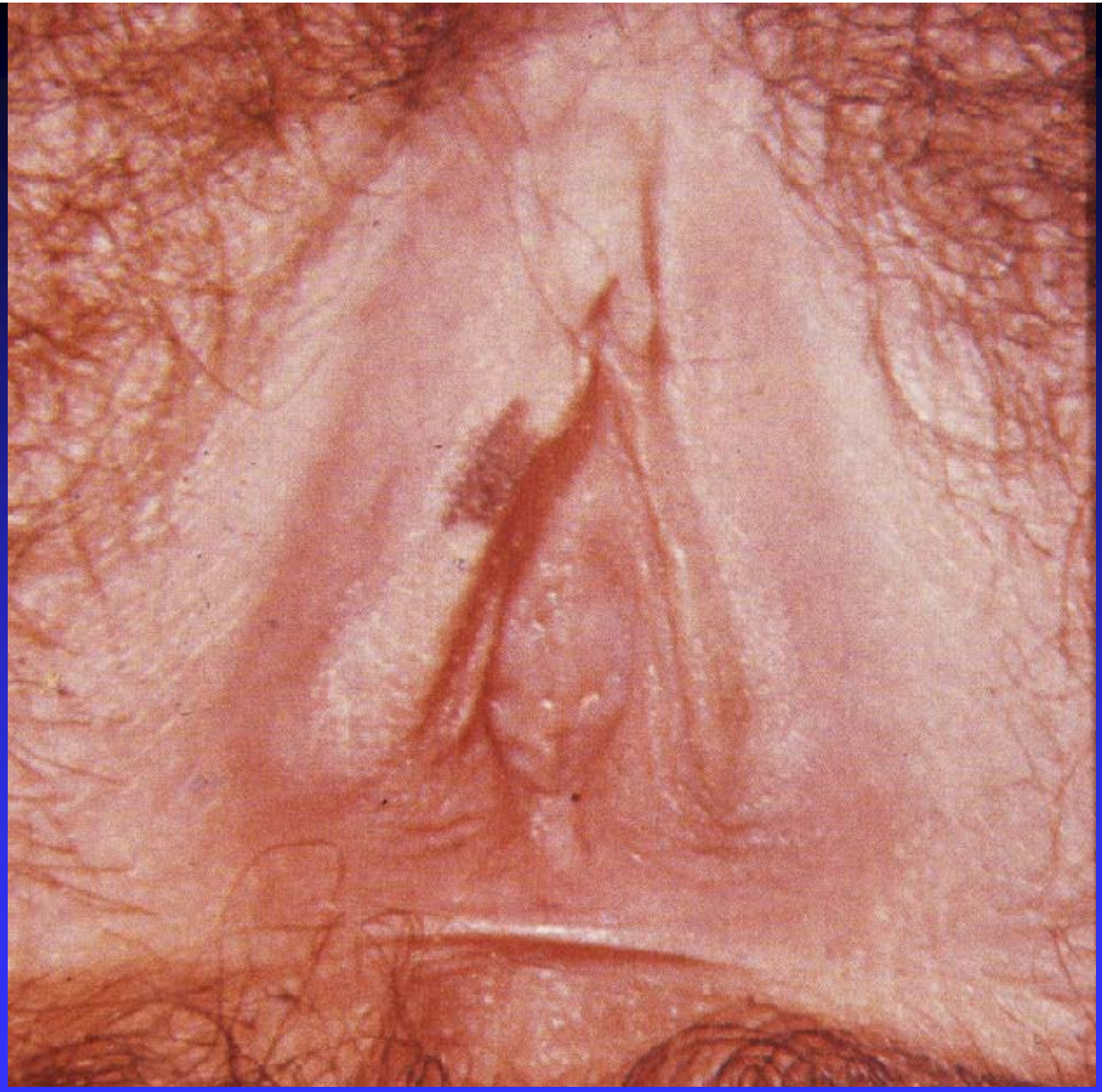


Dark Lesions

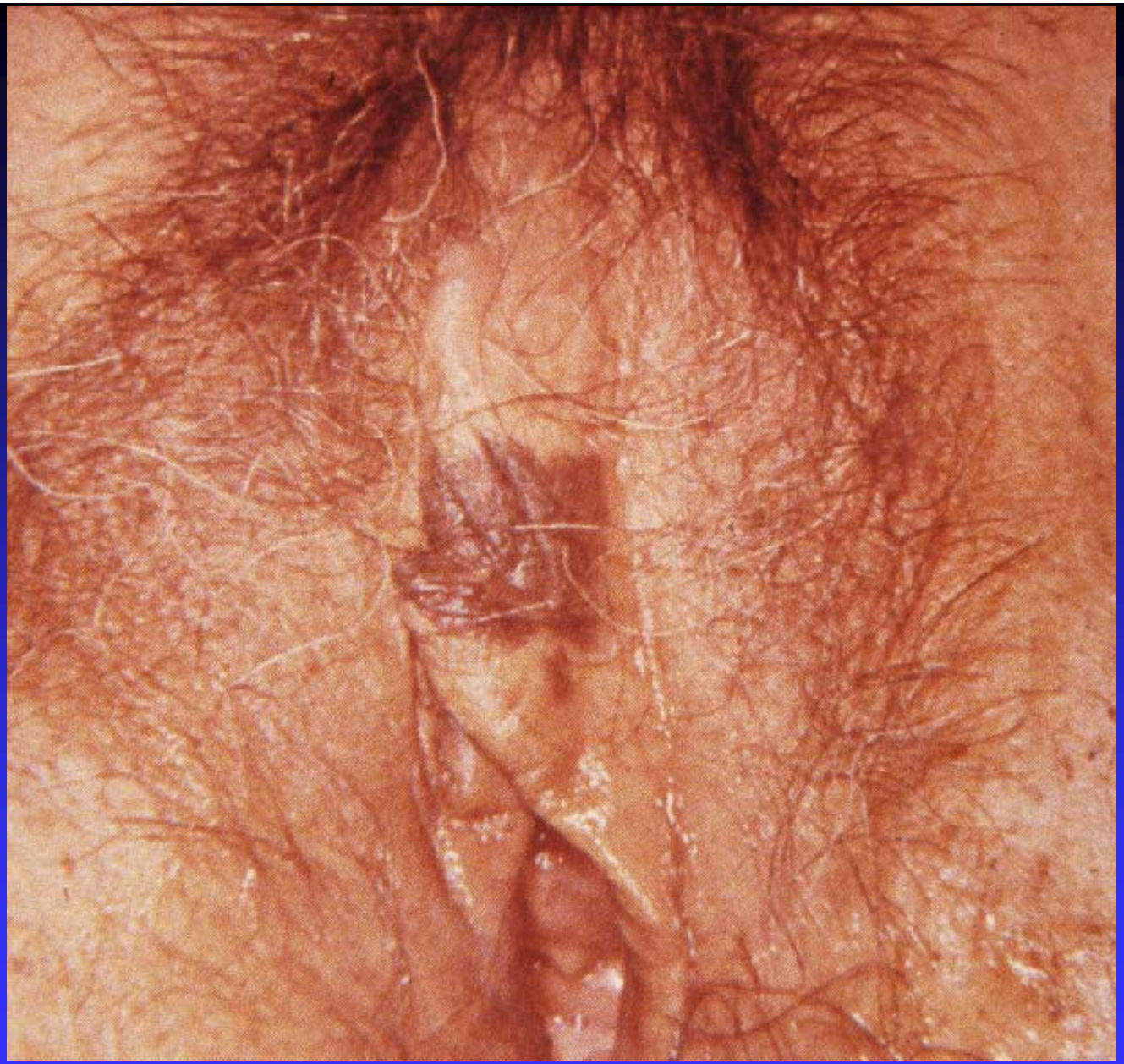
- Lentigo
- Nevi
- Melanoma
- Ca-in-situ
- Seborrheic keratosis



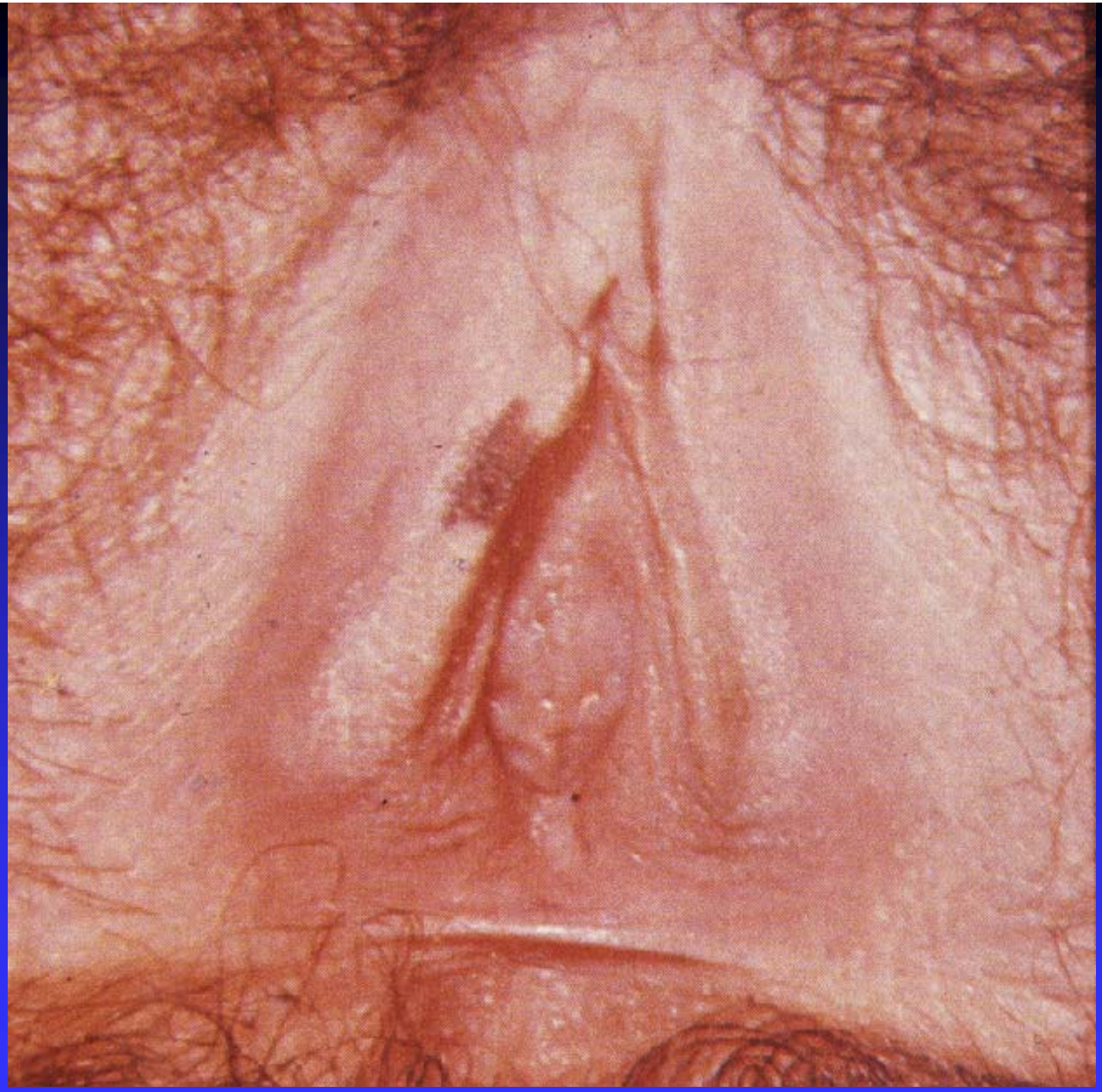
Multiple lentigines



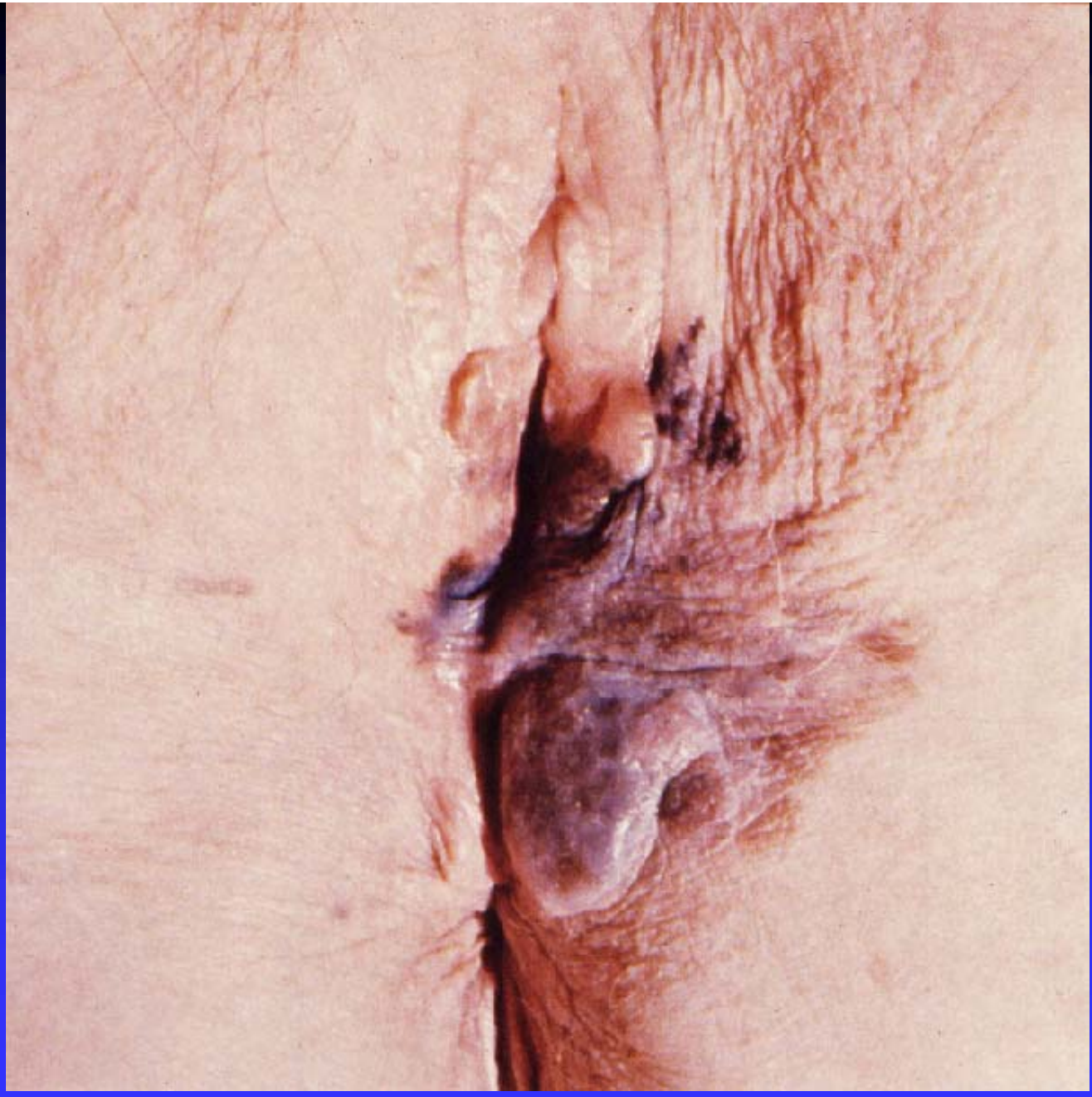
Unifocal lentigo



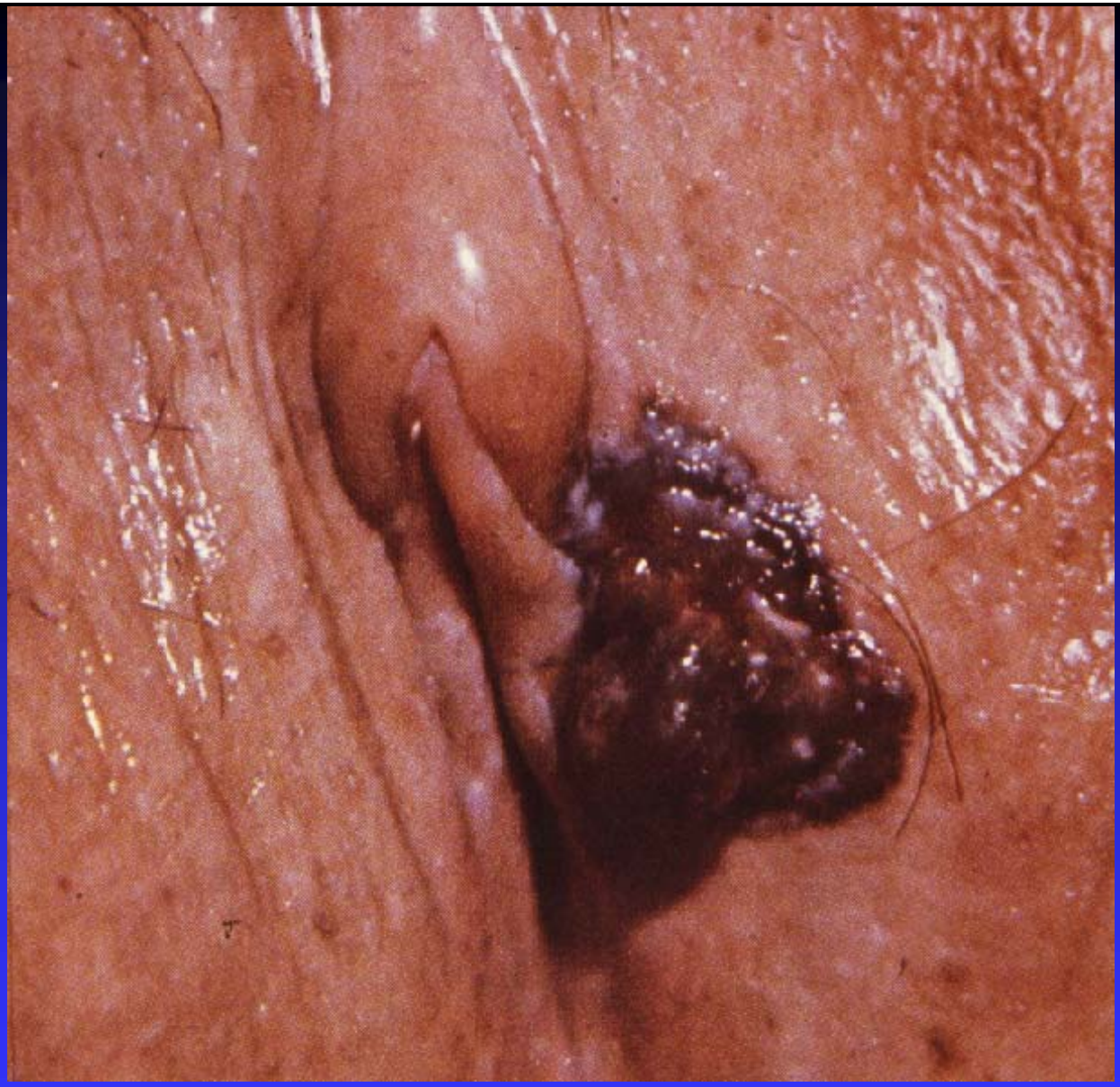
Unifocal carcinoma in situ



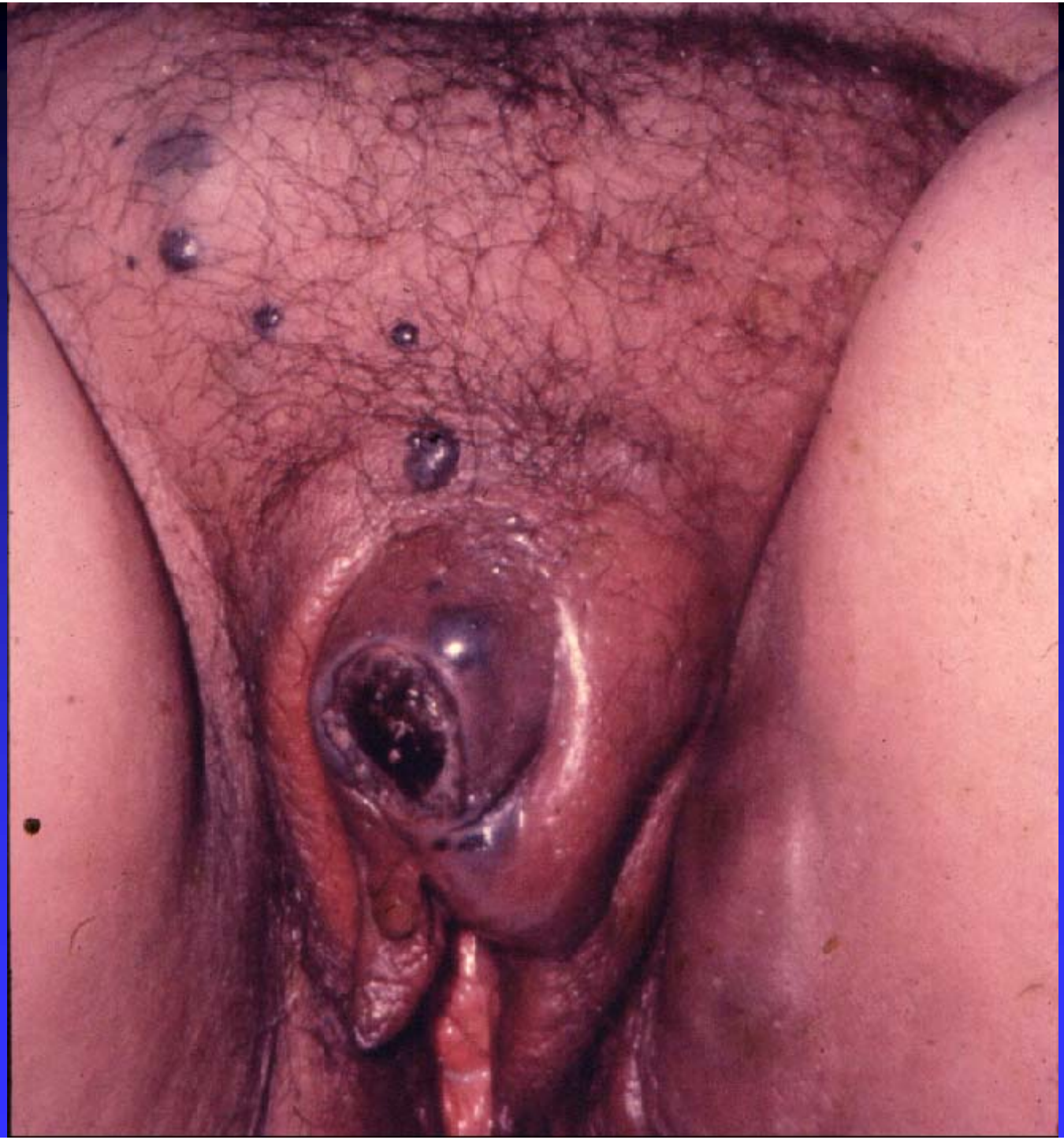
Unifocal lentigo

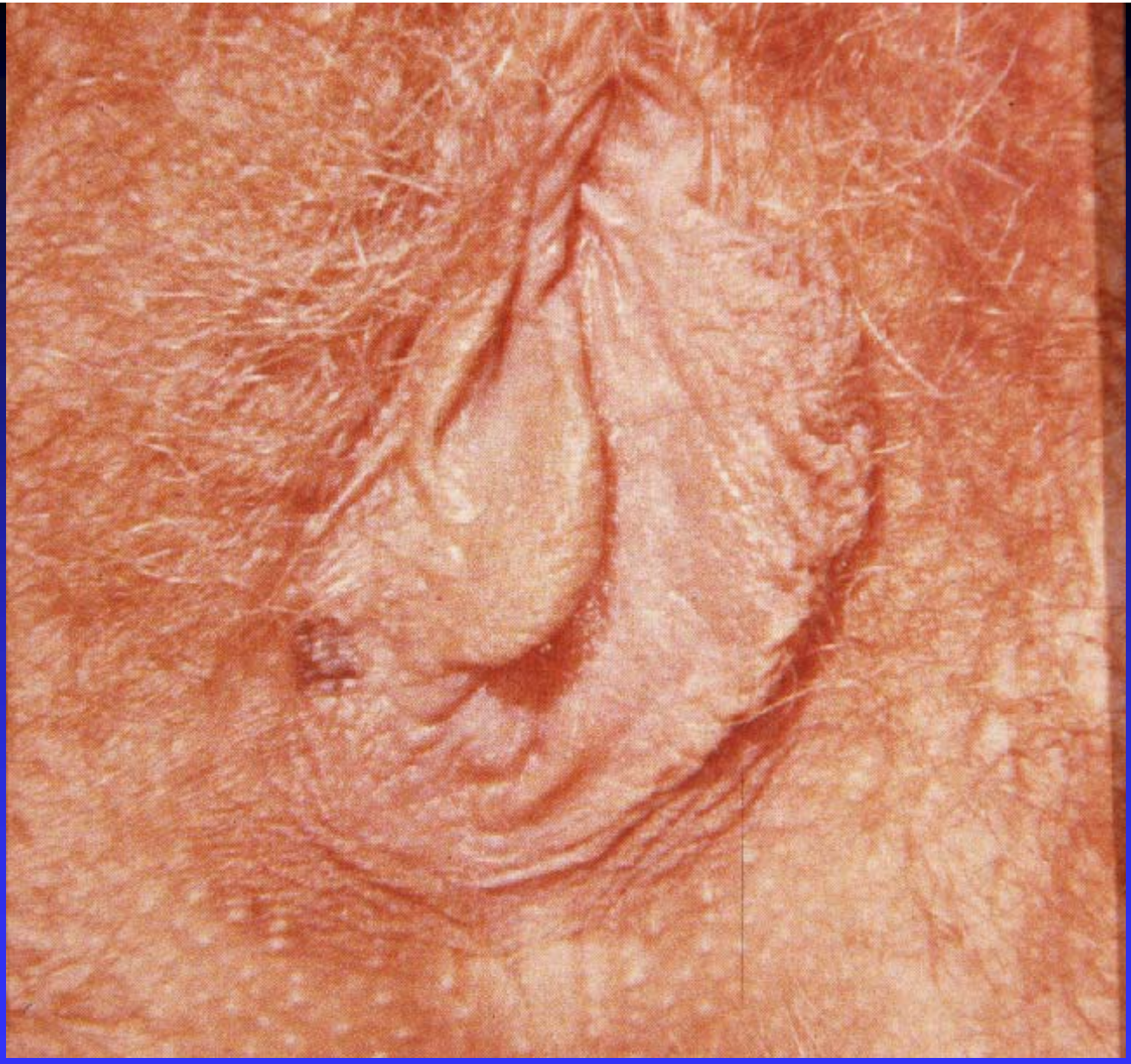


Spreading melanoma (Courtesy Dr. F.J. Fleury)

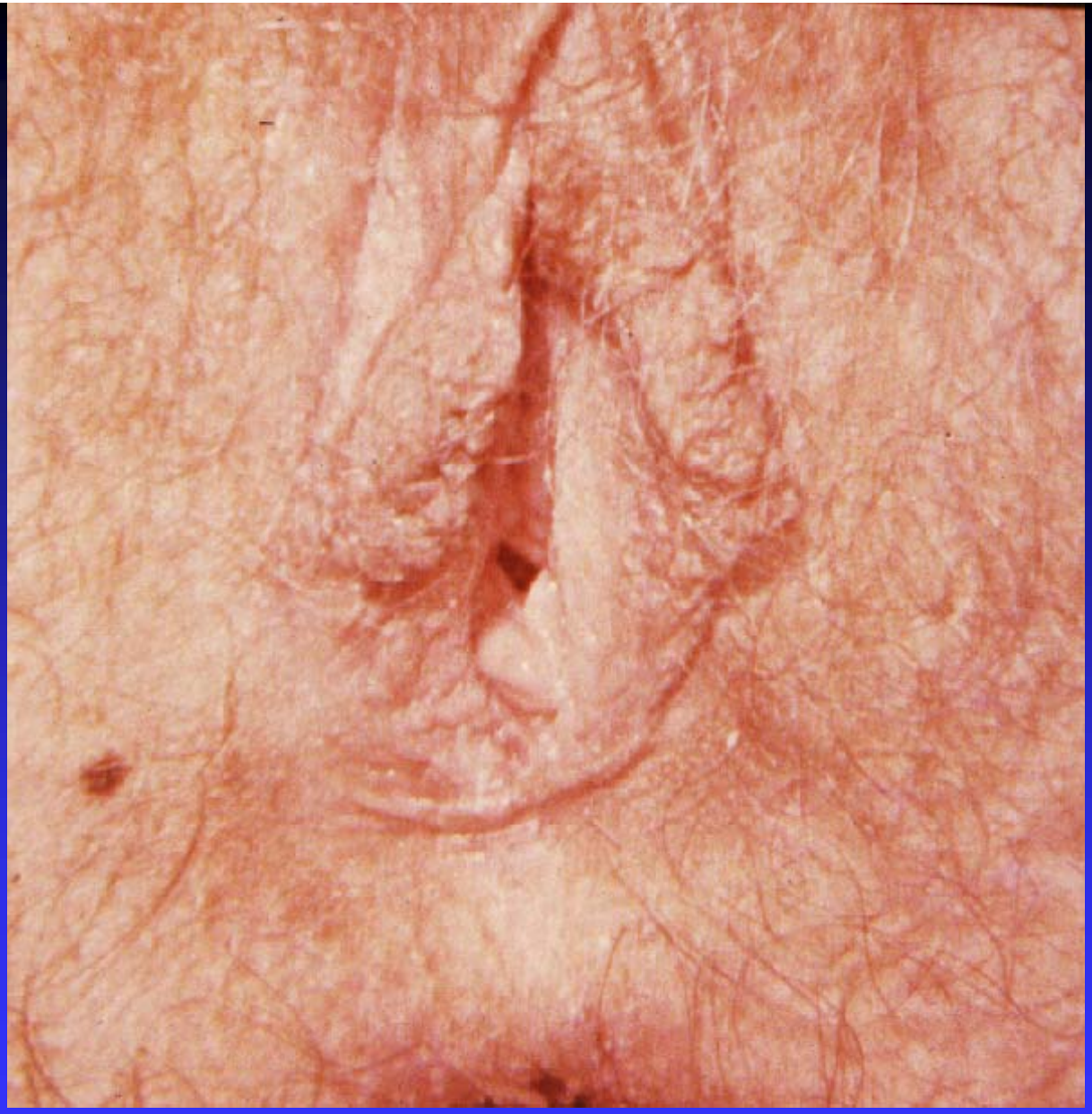


Melanoma (Courtesy Dr. W.C. Fetherston)

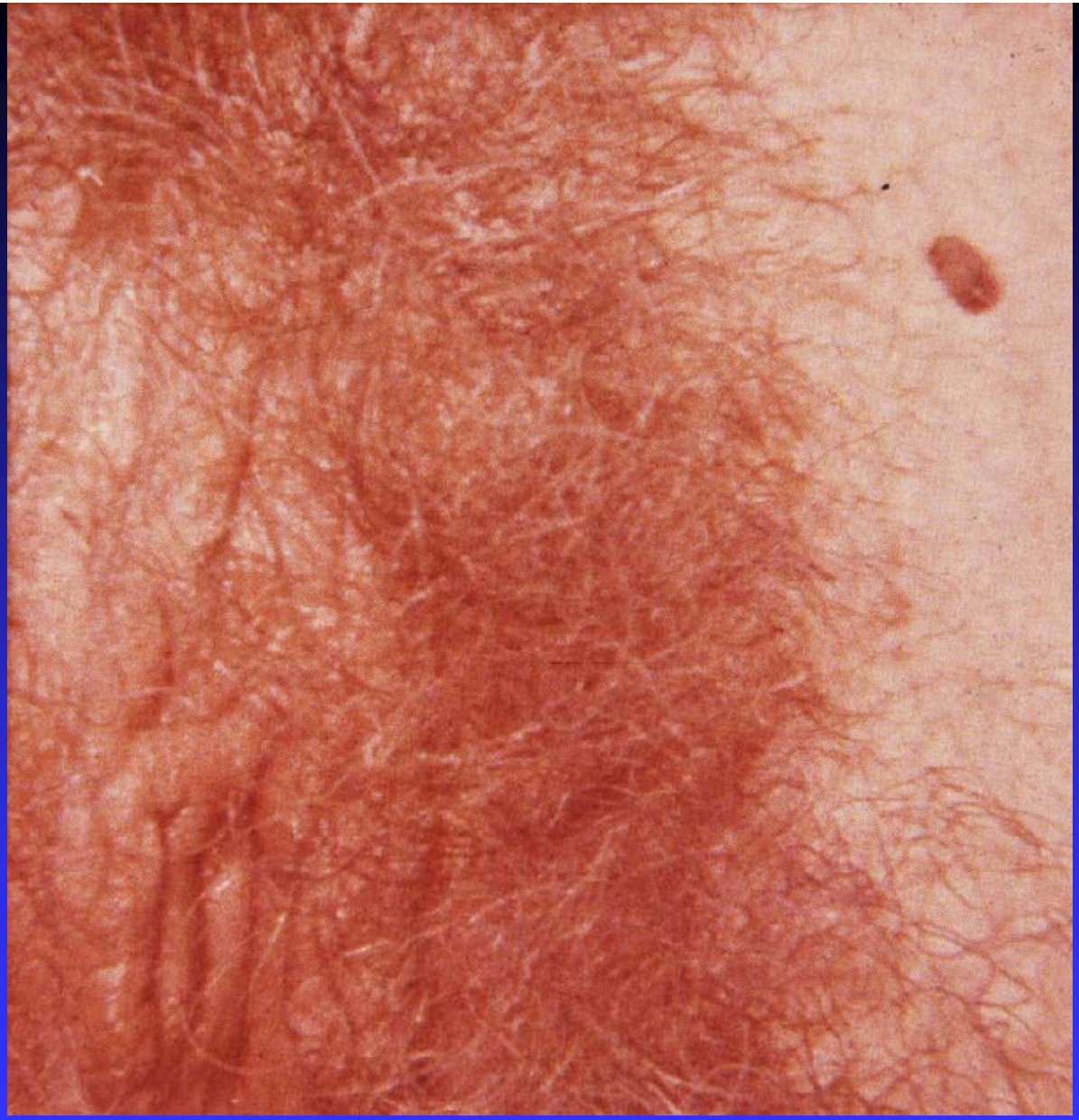




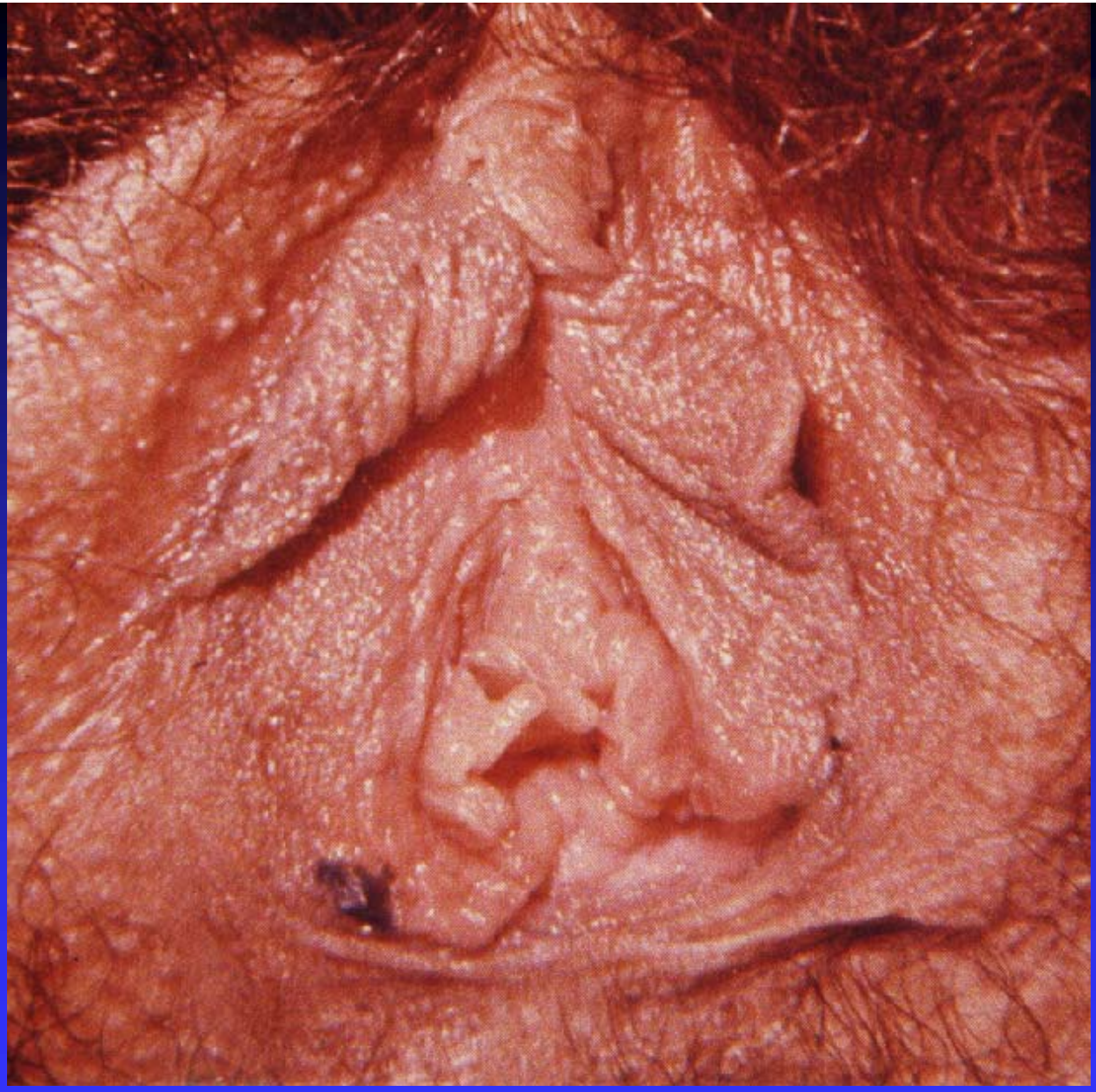
Compound nevus



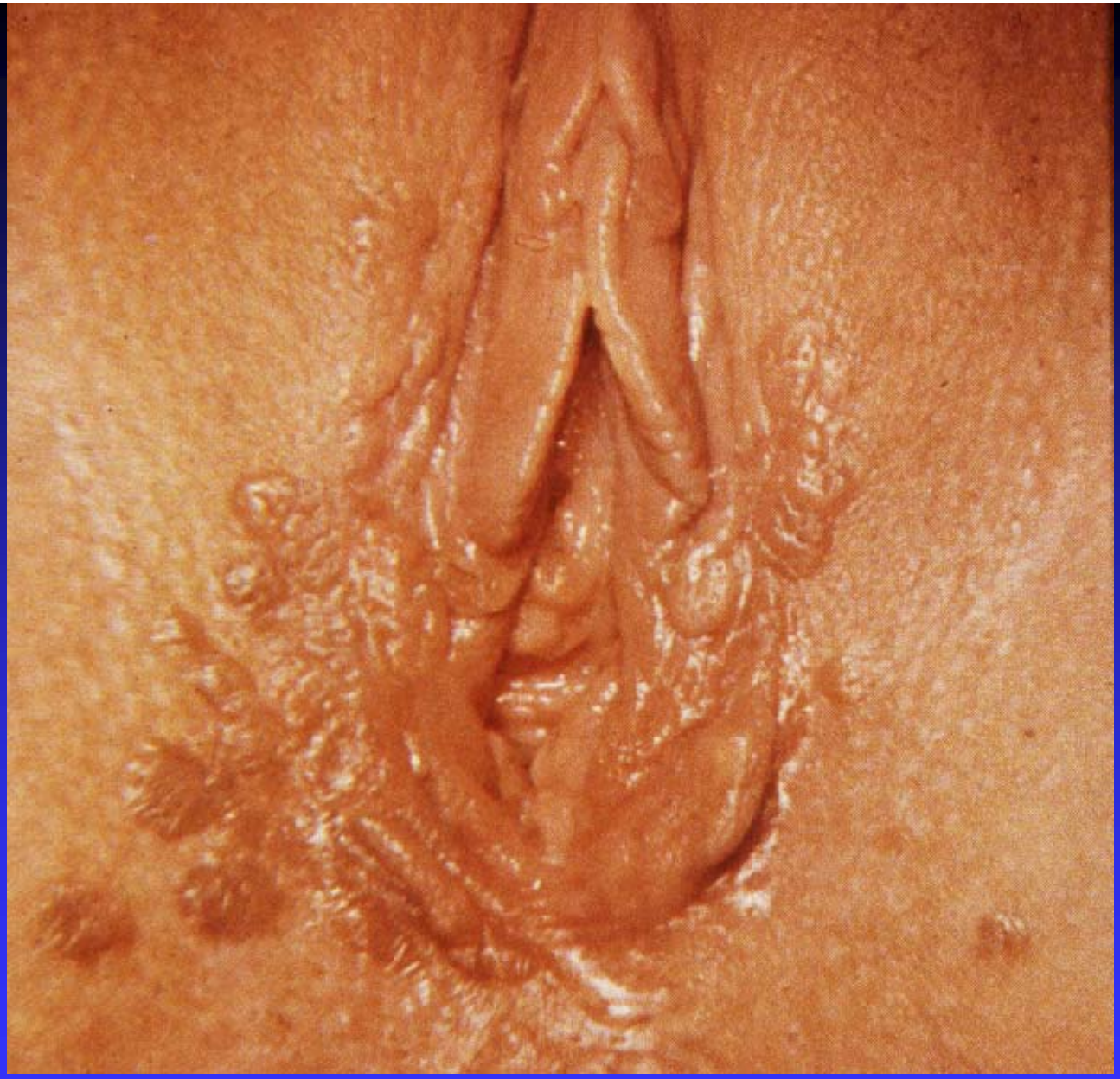
Junctional nevus



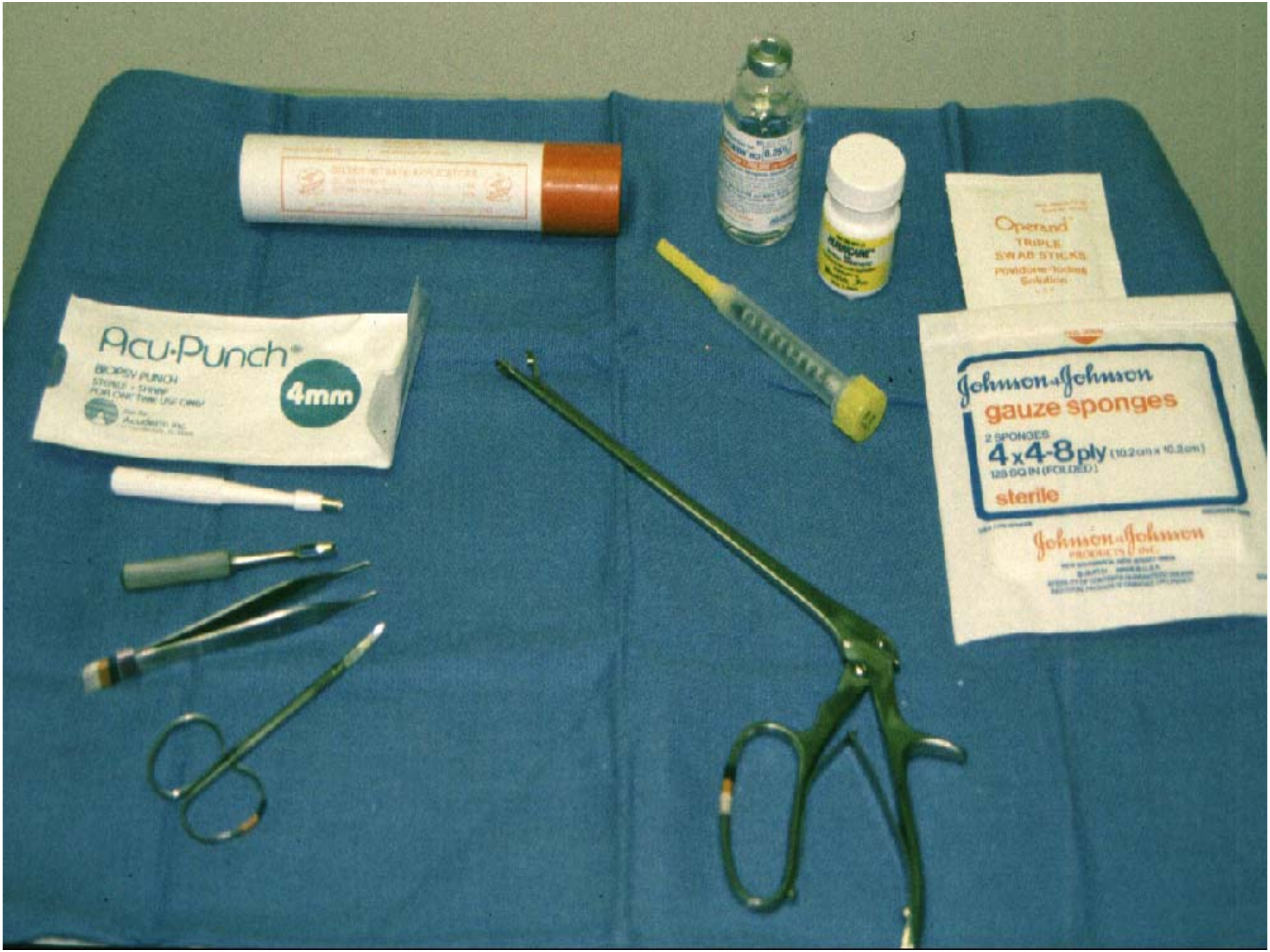
Intradermal nevus



Melanoma

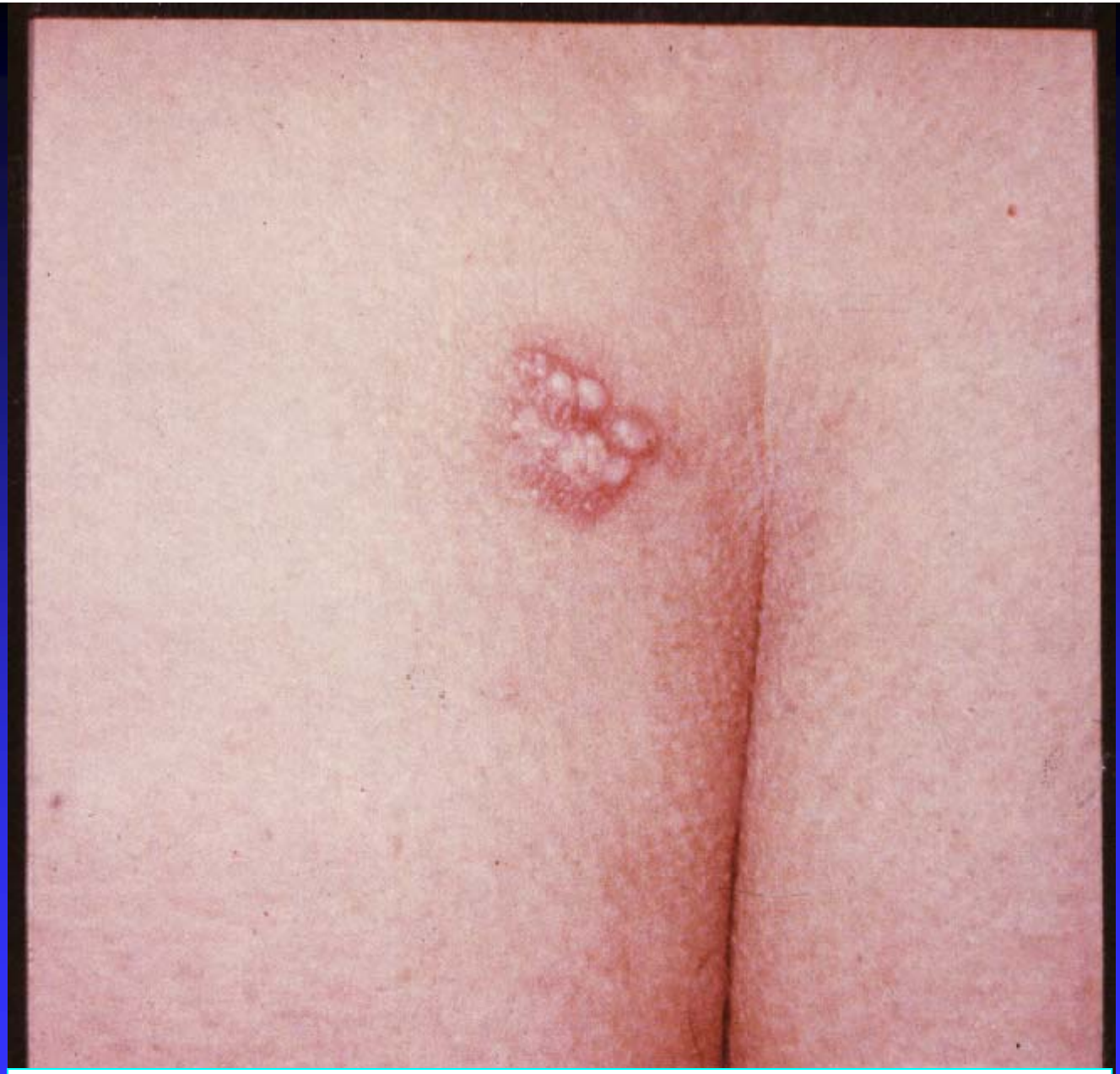


Multicentric carcinoma in situ

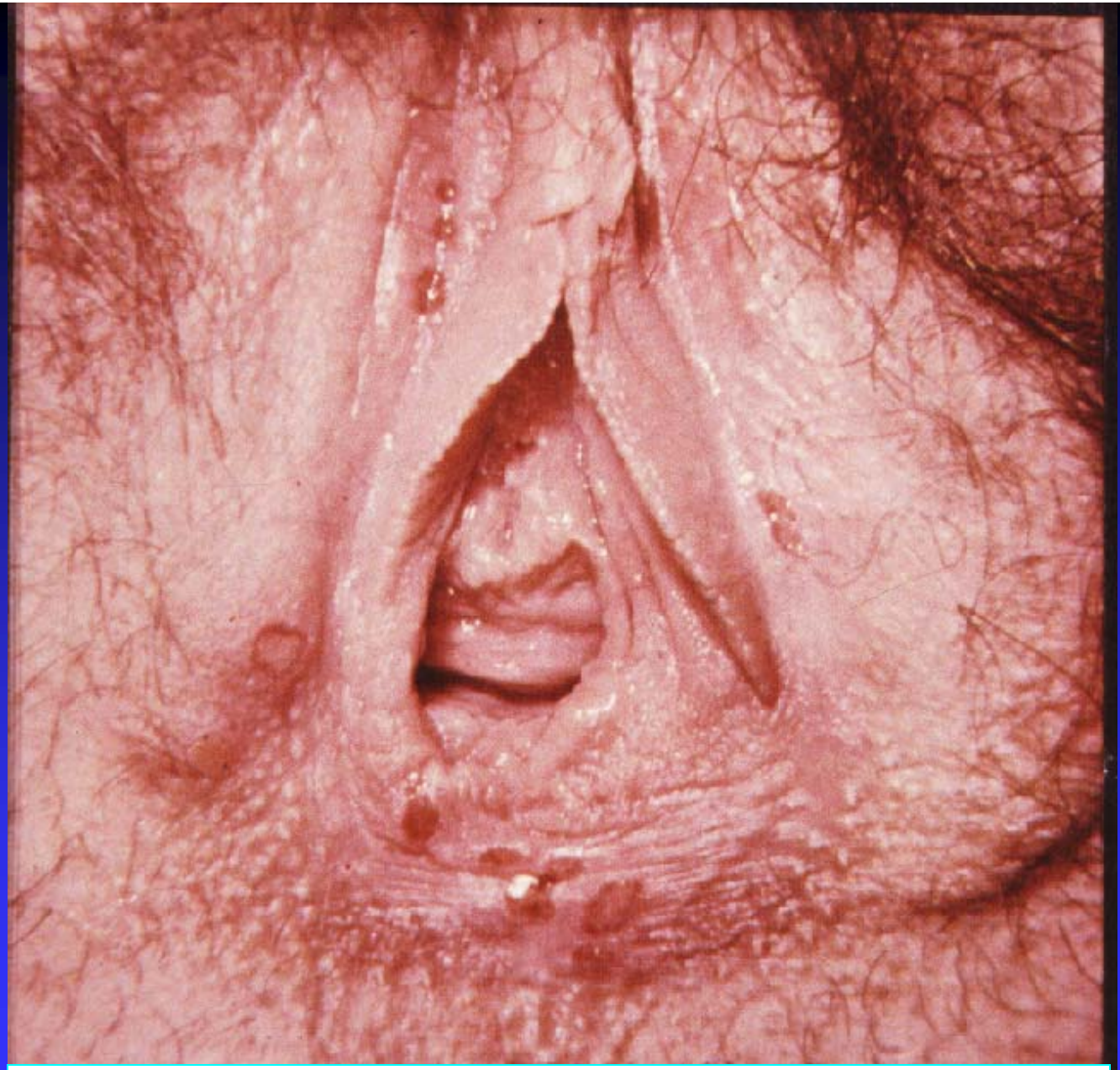

Acu-Punch
4mm
Operand
TRIPLE
SWAB STICKS
Johnson & Johnson
gauze sponges
2 SPONGES
4 x 4-8 ply
sterile
Johnson & Johnson

Ulcers

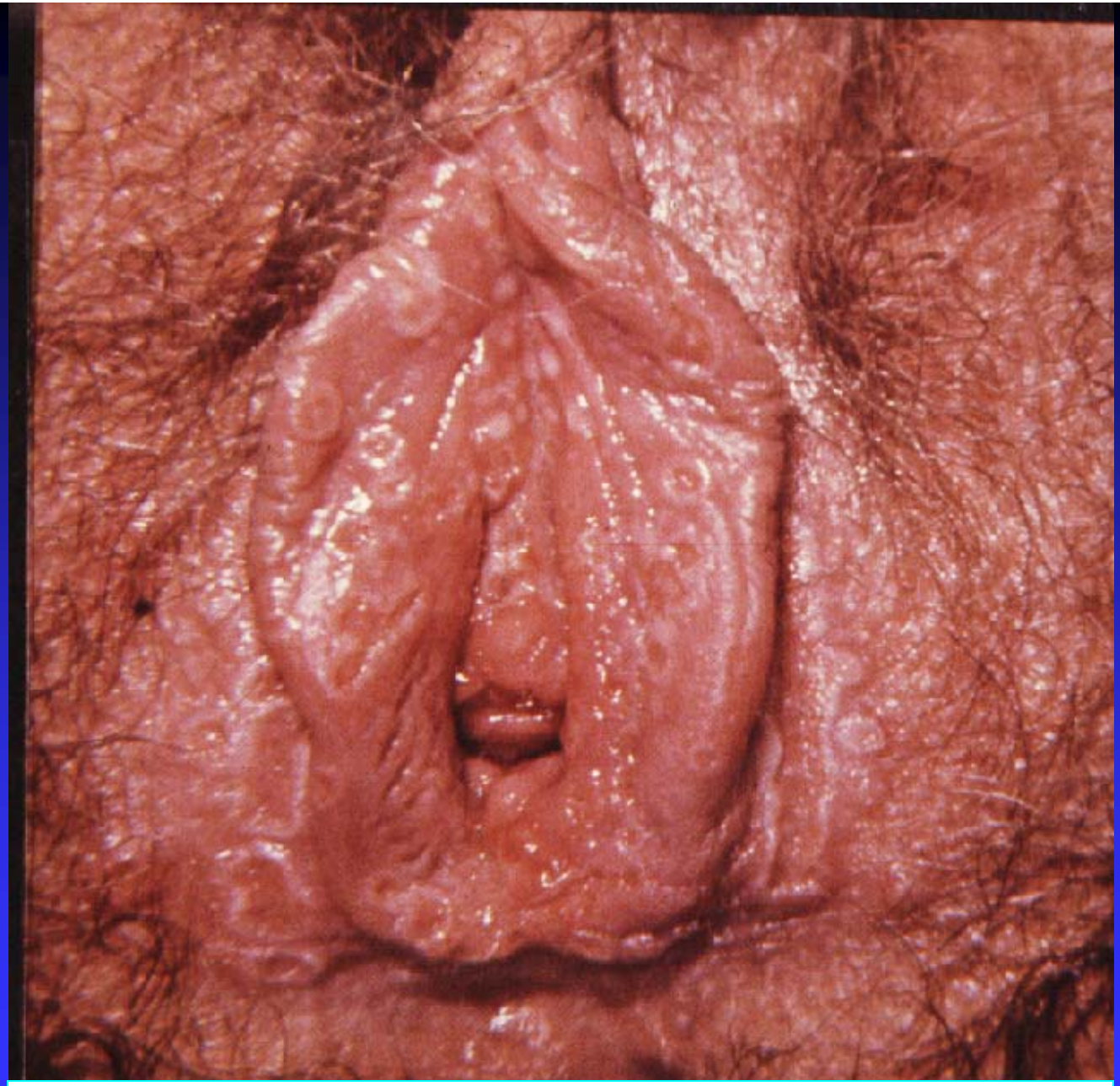
- Herpes
- Syphilis
- Behçet’s disease
- Crohn’s disease
- Hidradenitis
- Chancroid
- Granuloma inguinale
- Spider bite



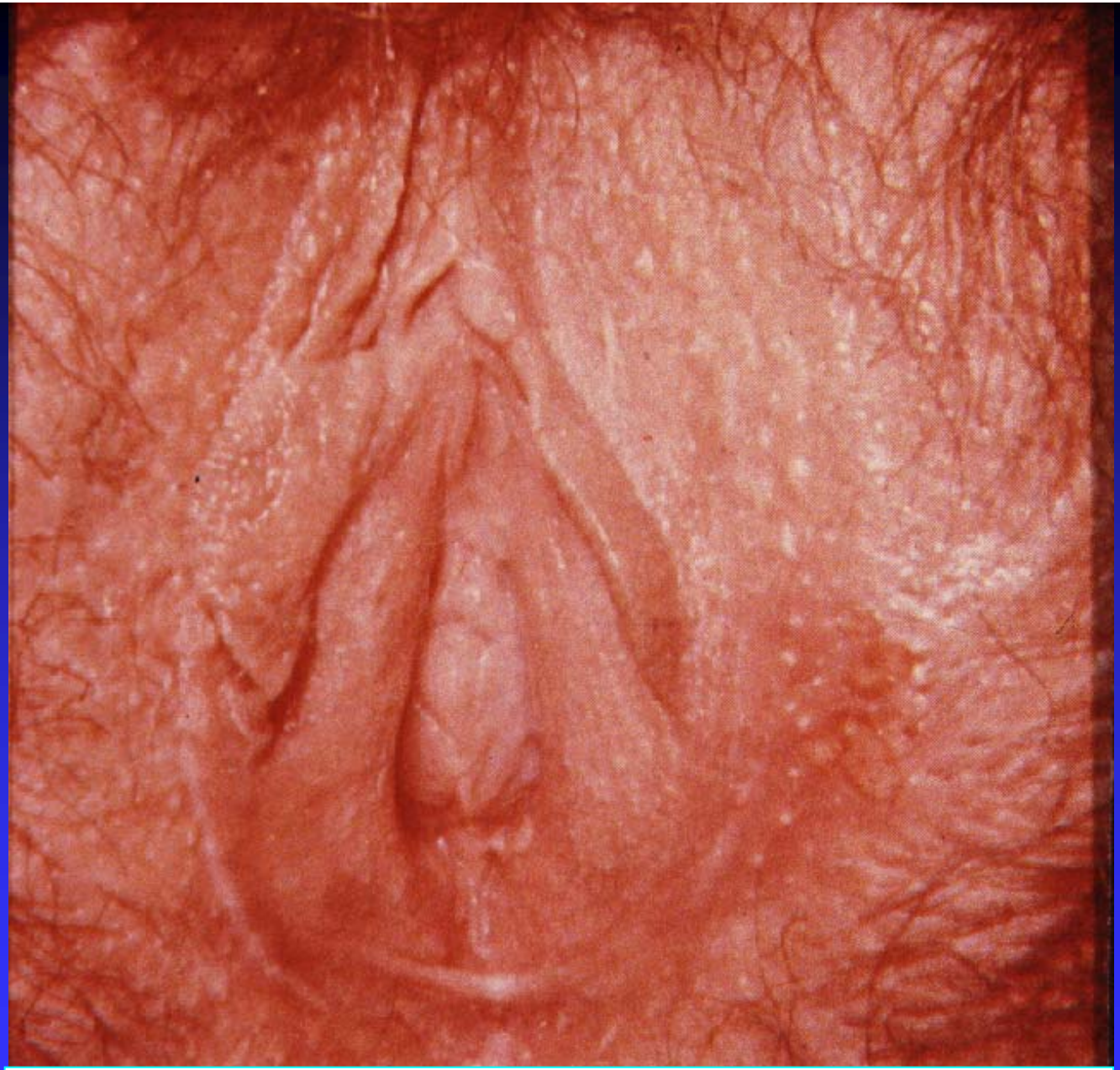
Herpetic vesicles



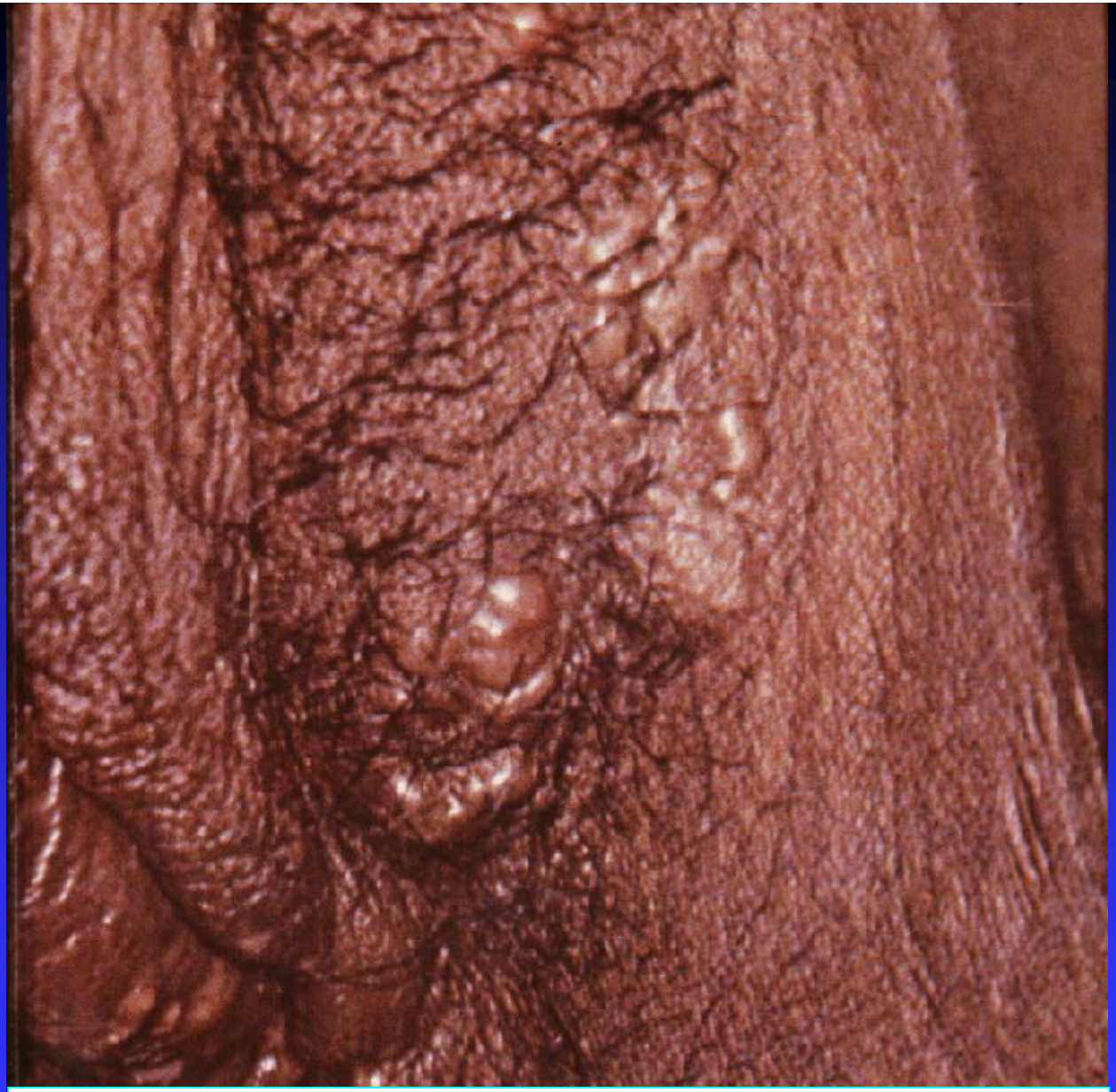
Mild herpetic ulcerations



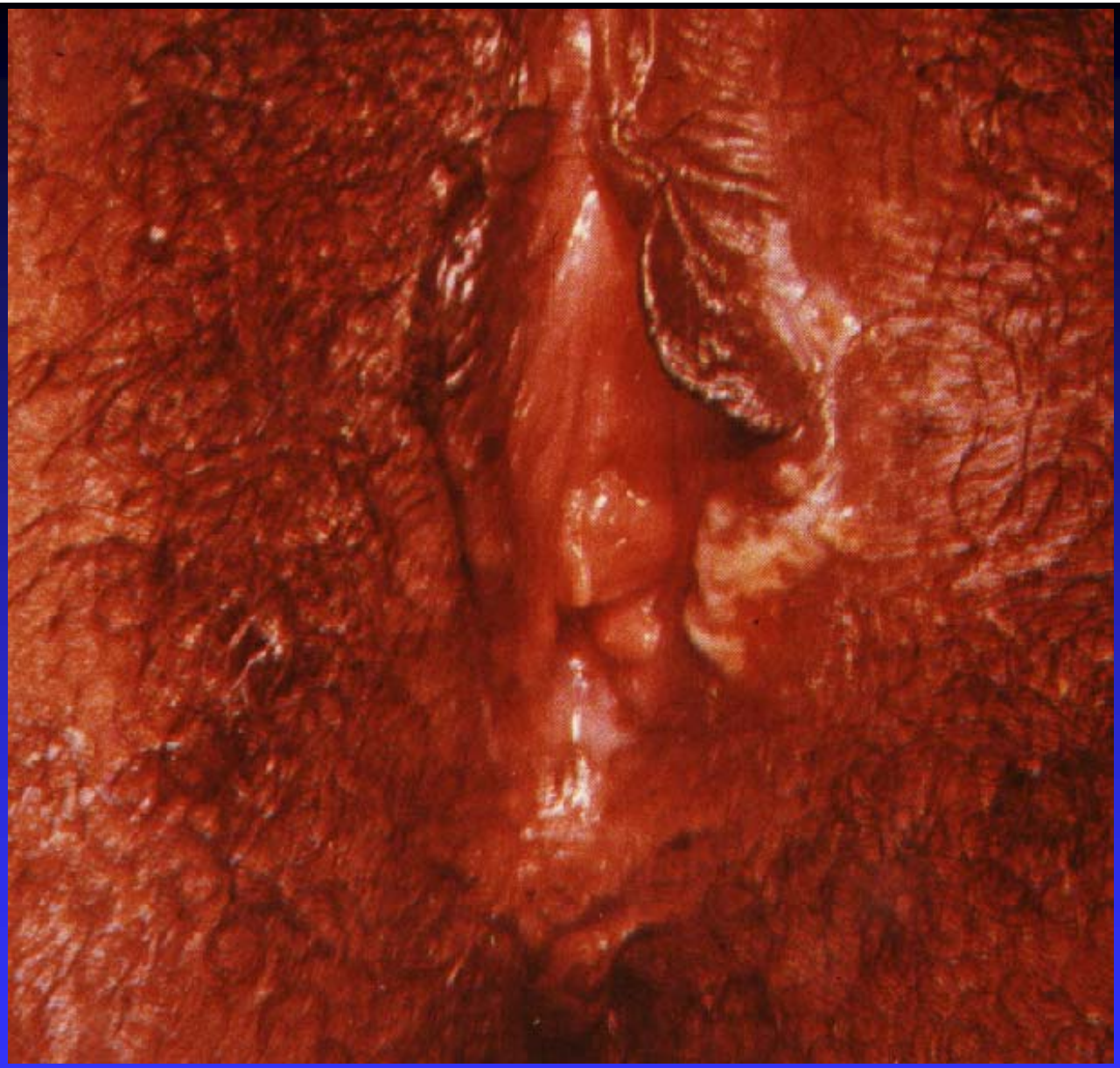
Severe herpetic vulvitis



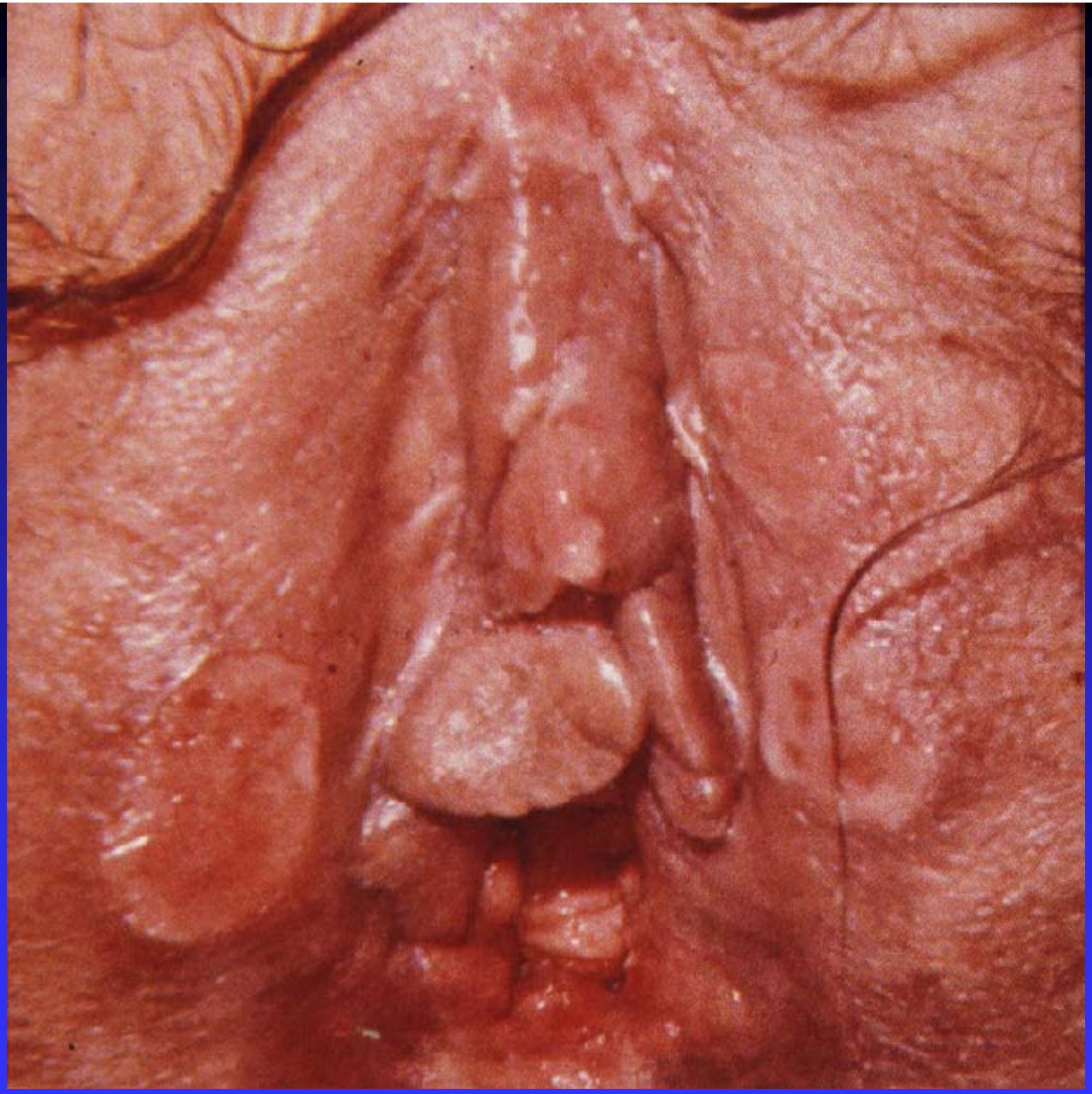
Localized recurrent herpes



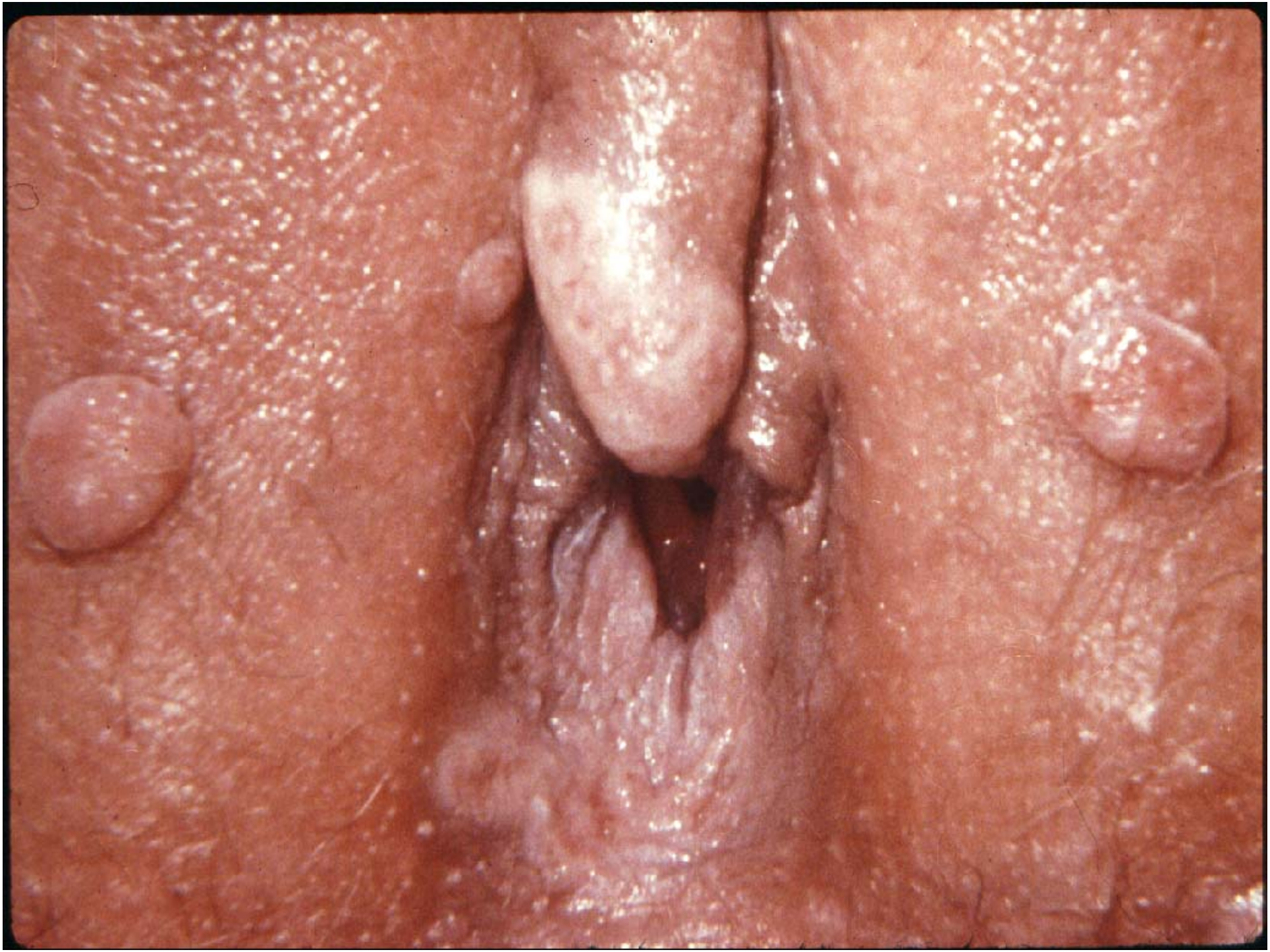
Confluent herpes vesicles

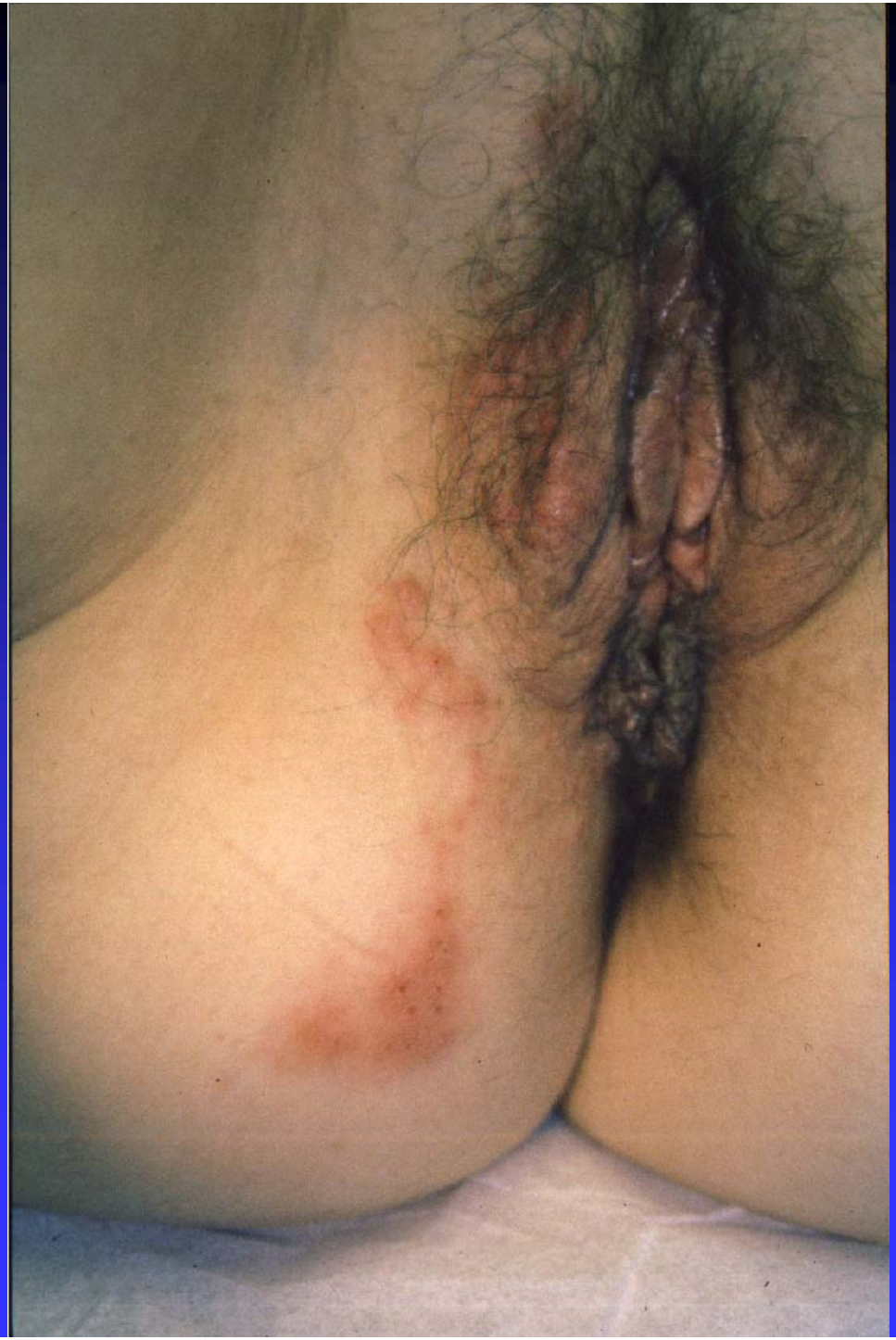


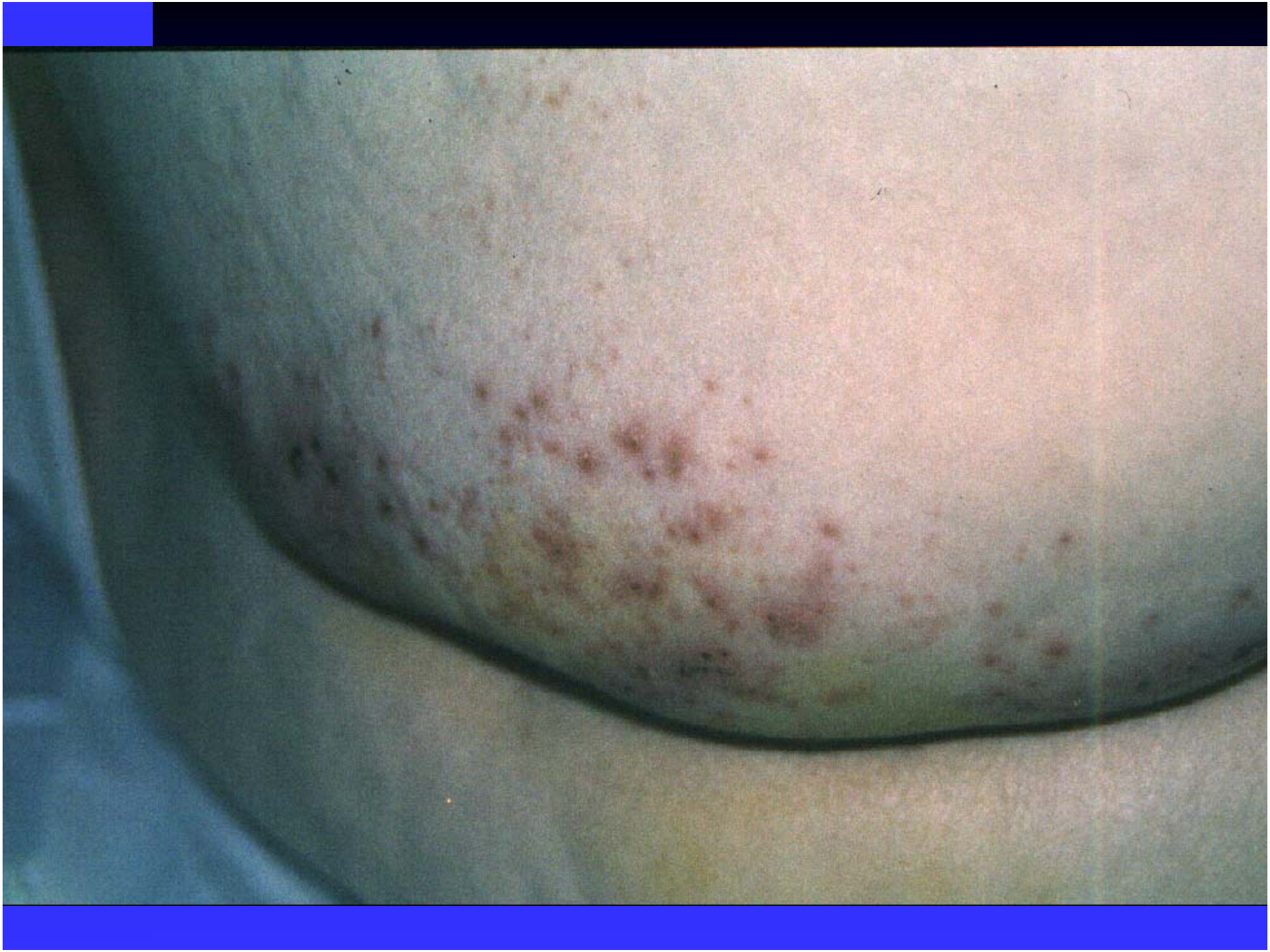
Atypical localized herpes

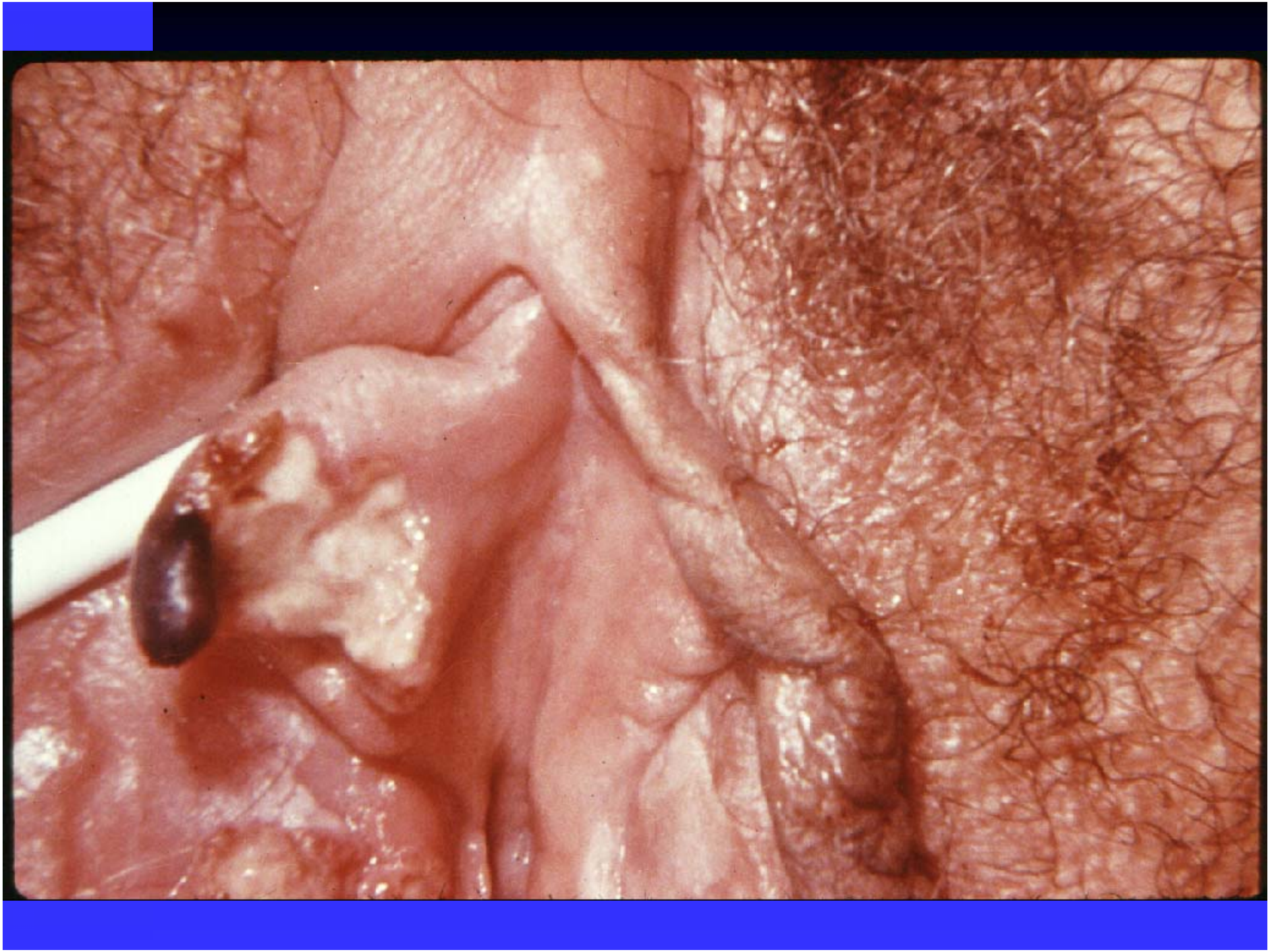


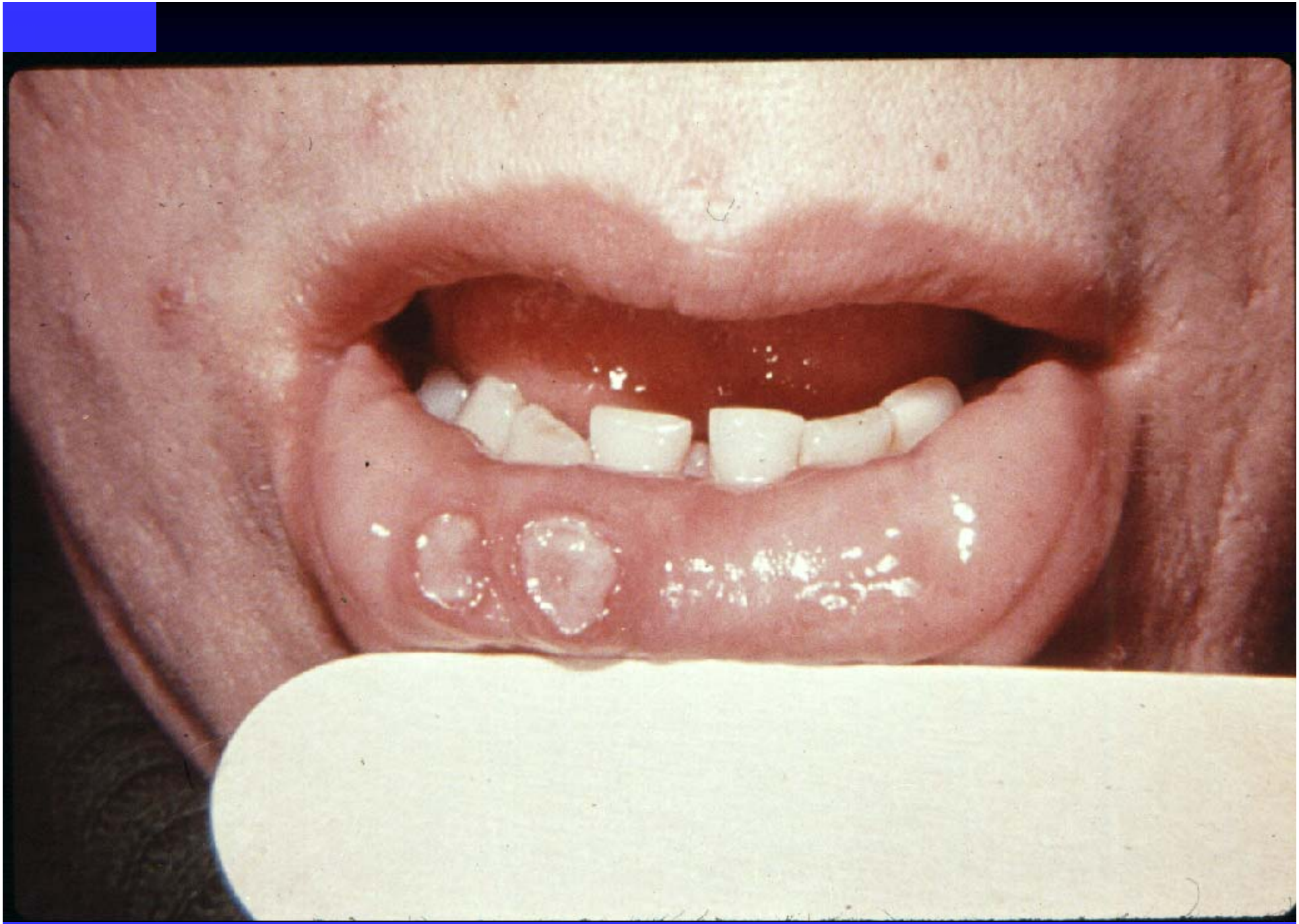
Atypical large herpetic ulcers

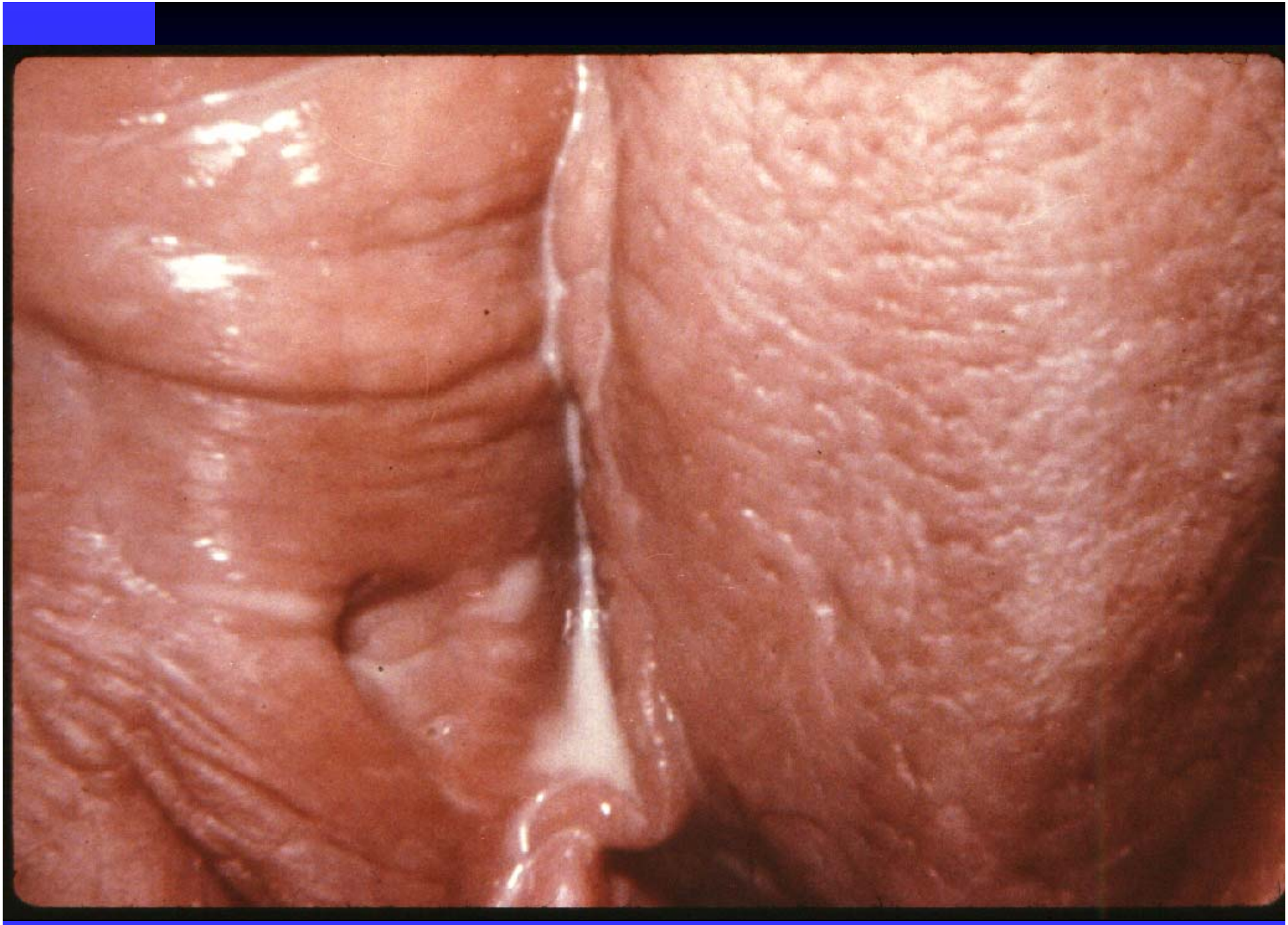


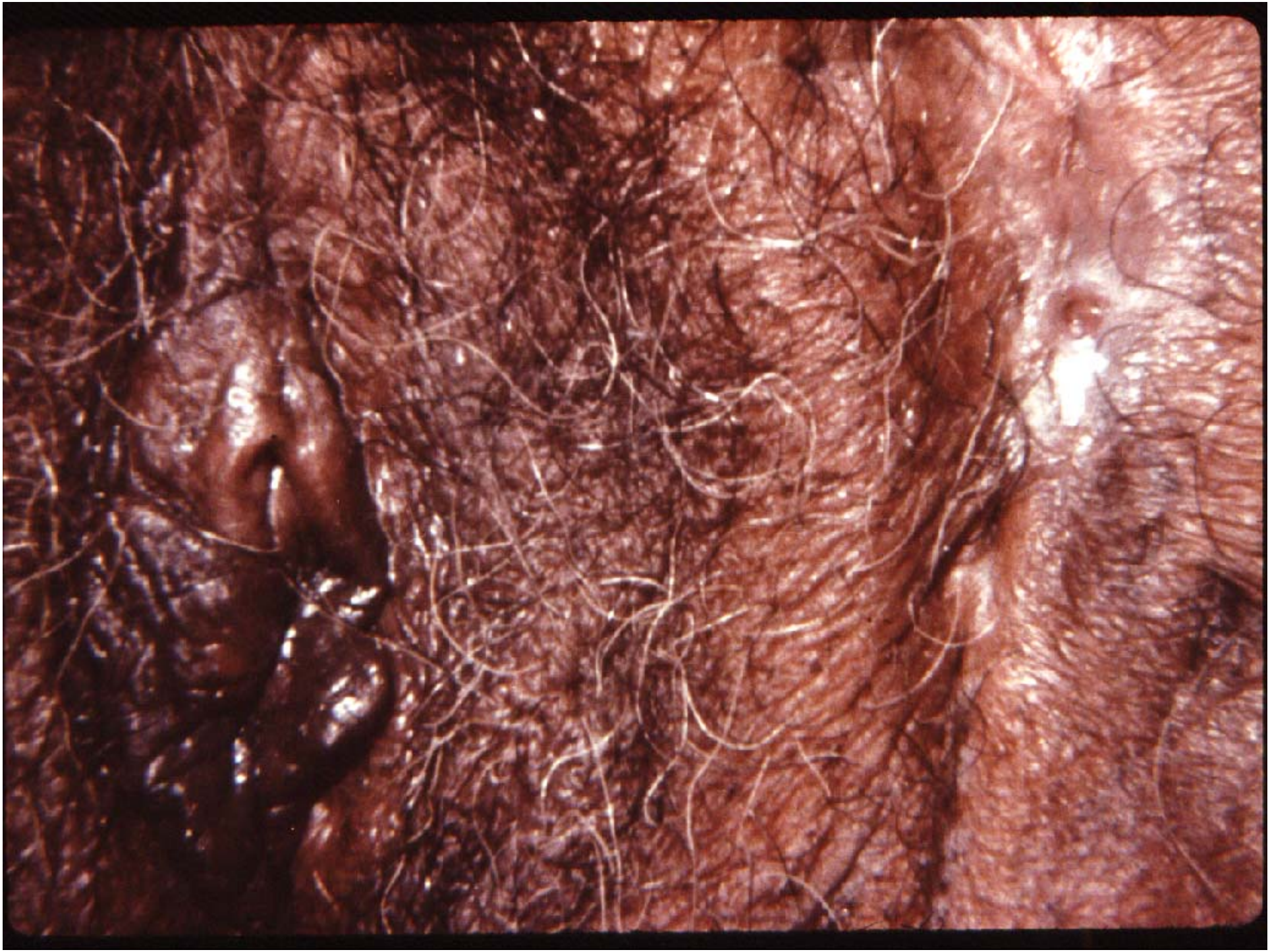


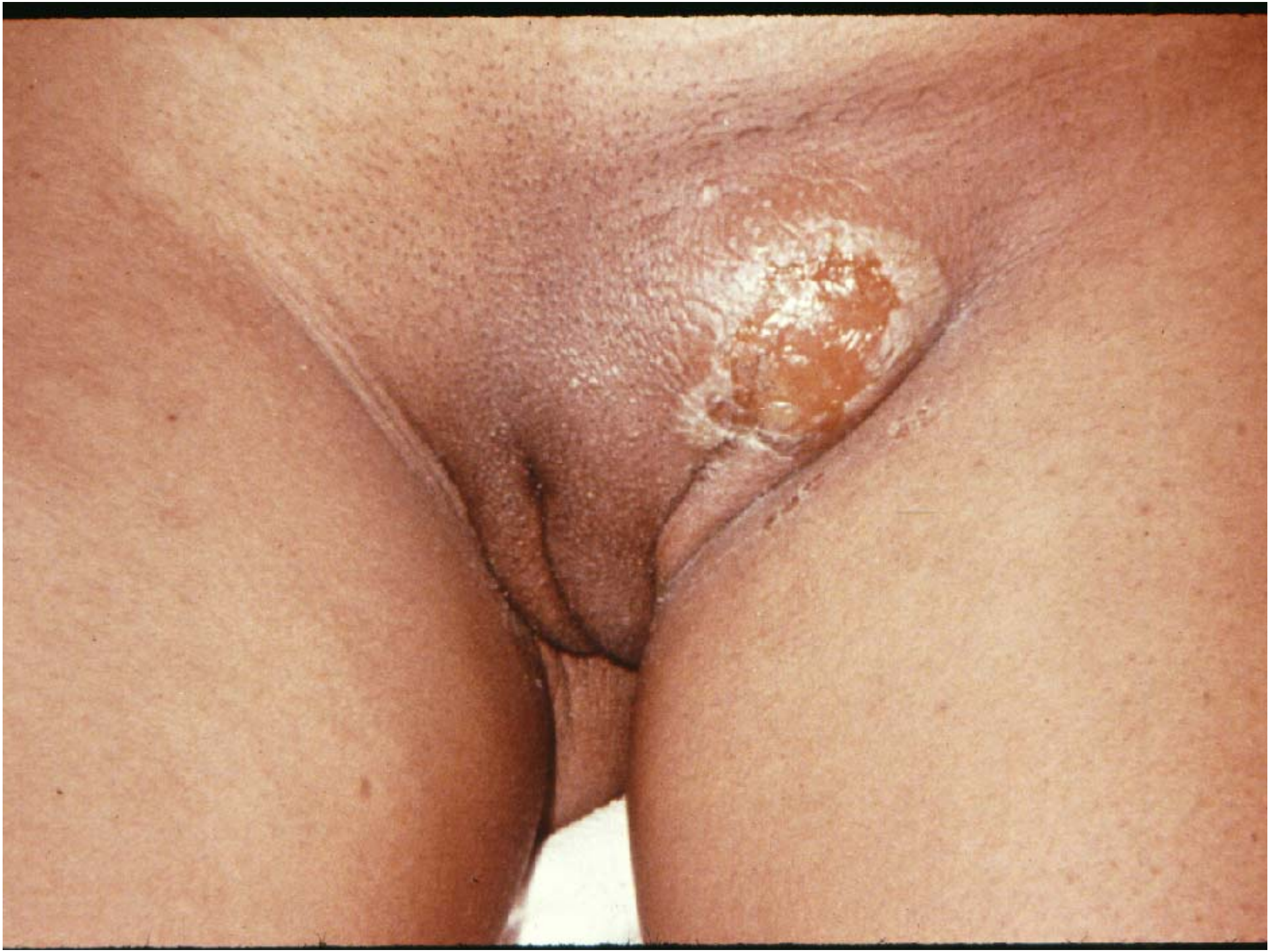


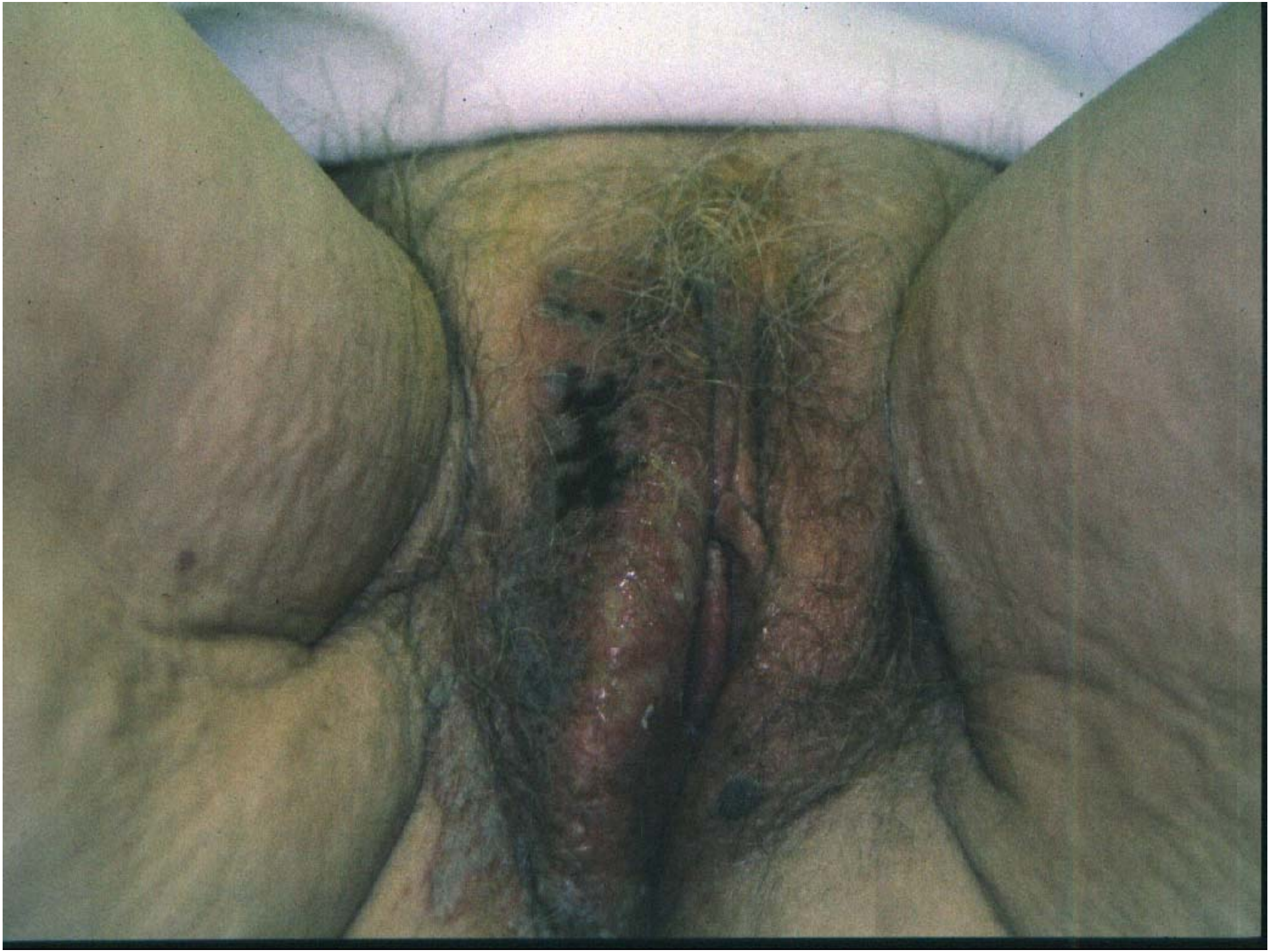






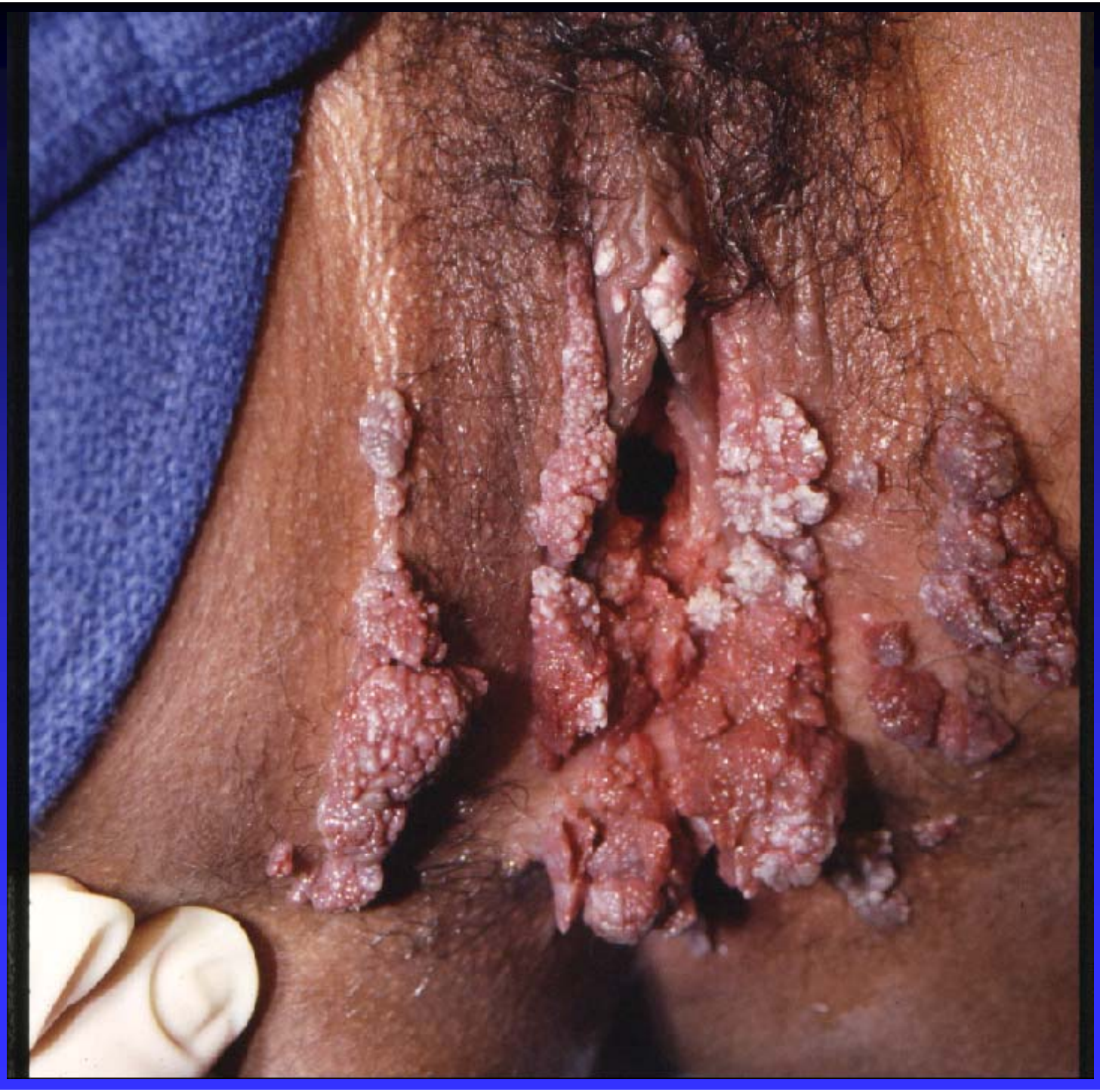


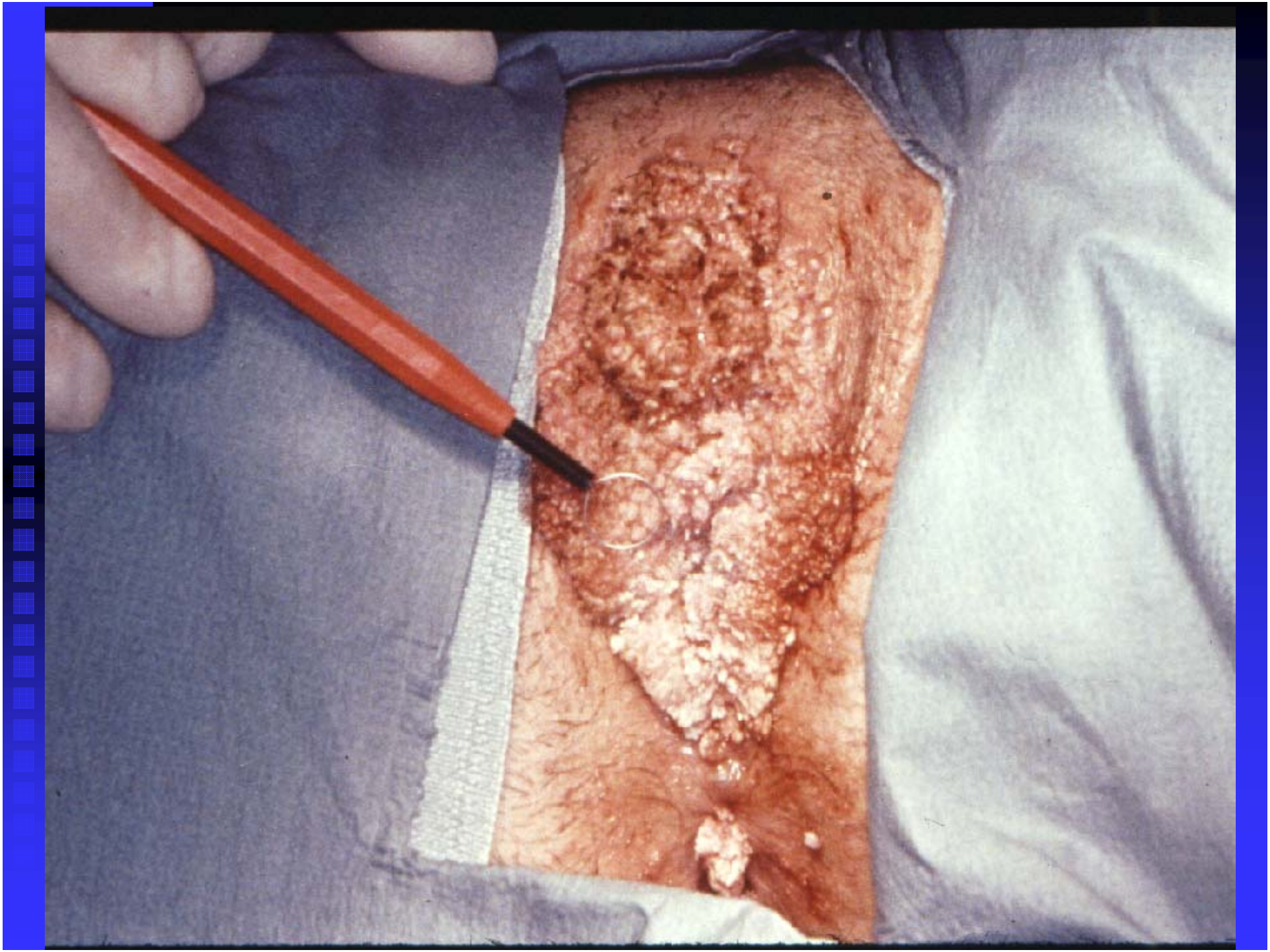


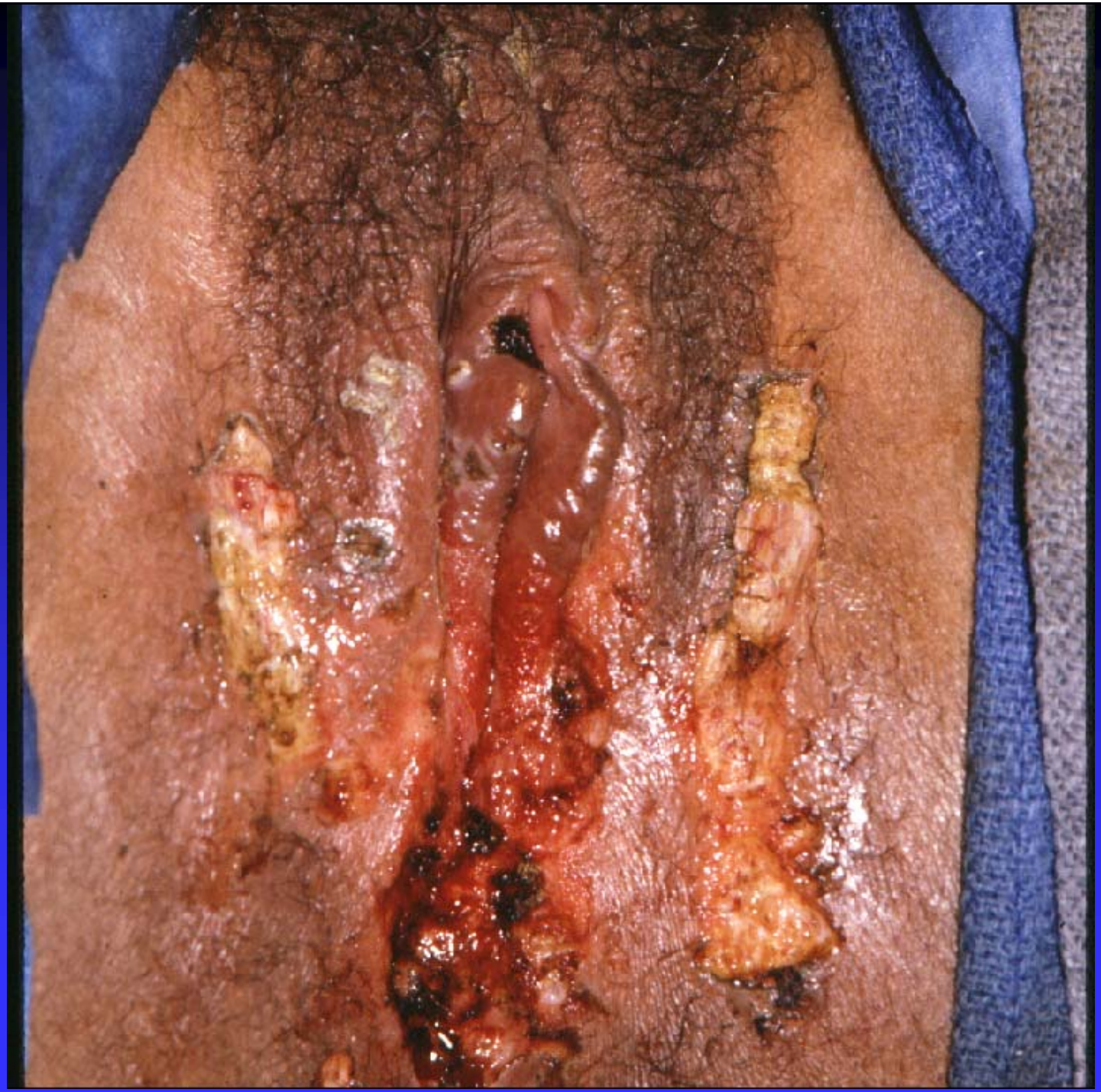


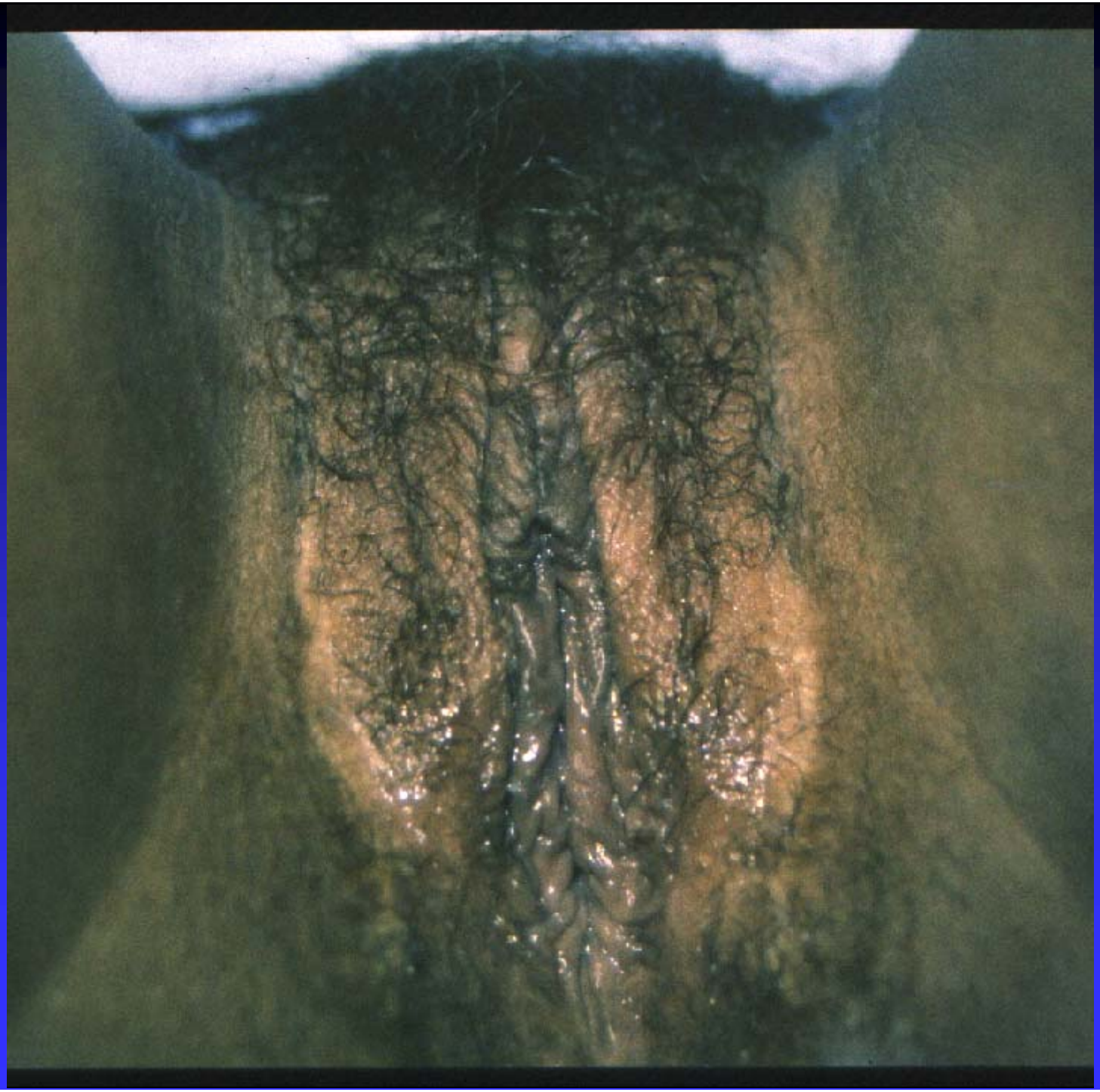
Small Tumors

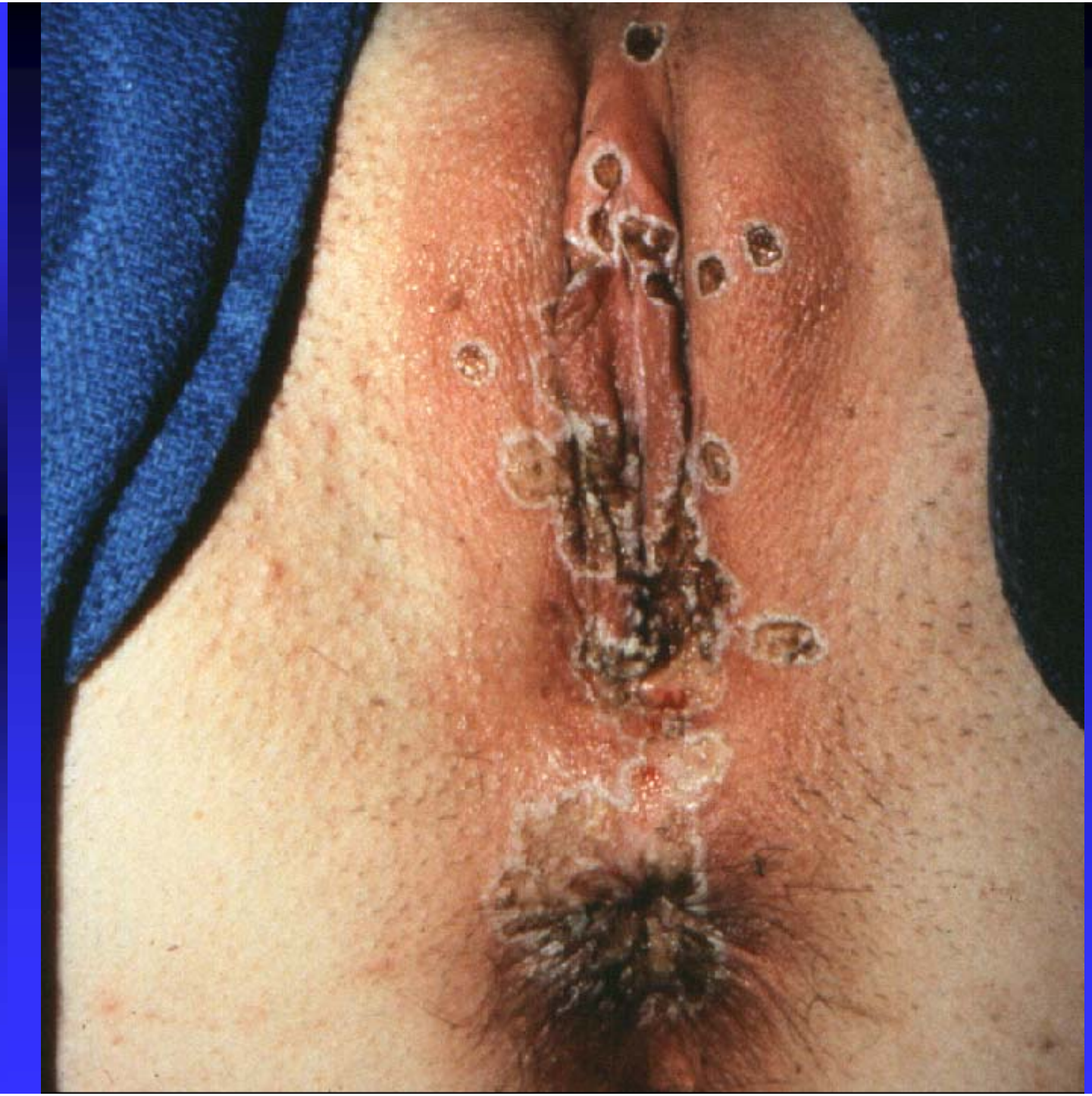
- Condylomata acuminata
- Molluscum contagiosum
- Epidermal cysts
- Angiomata
- Mucus cysts
- Acrochordon
- Hidradenoma

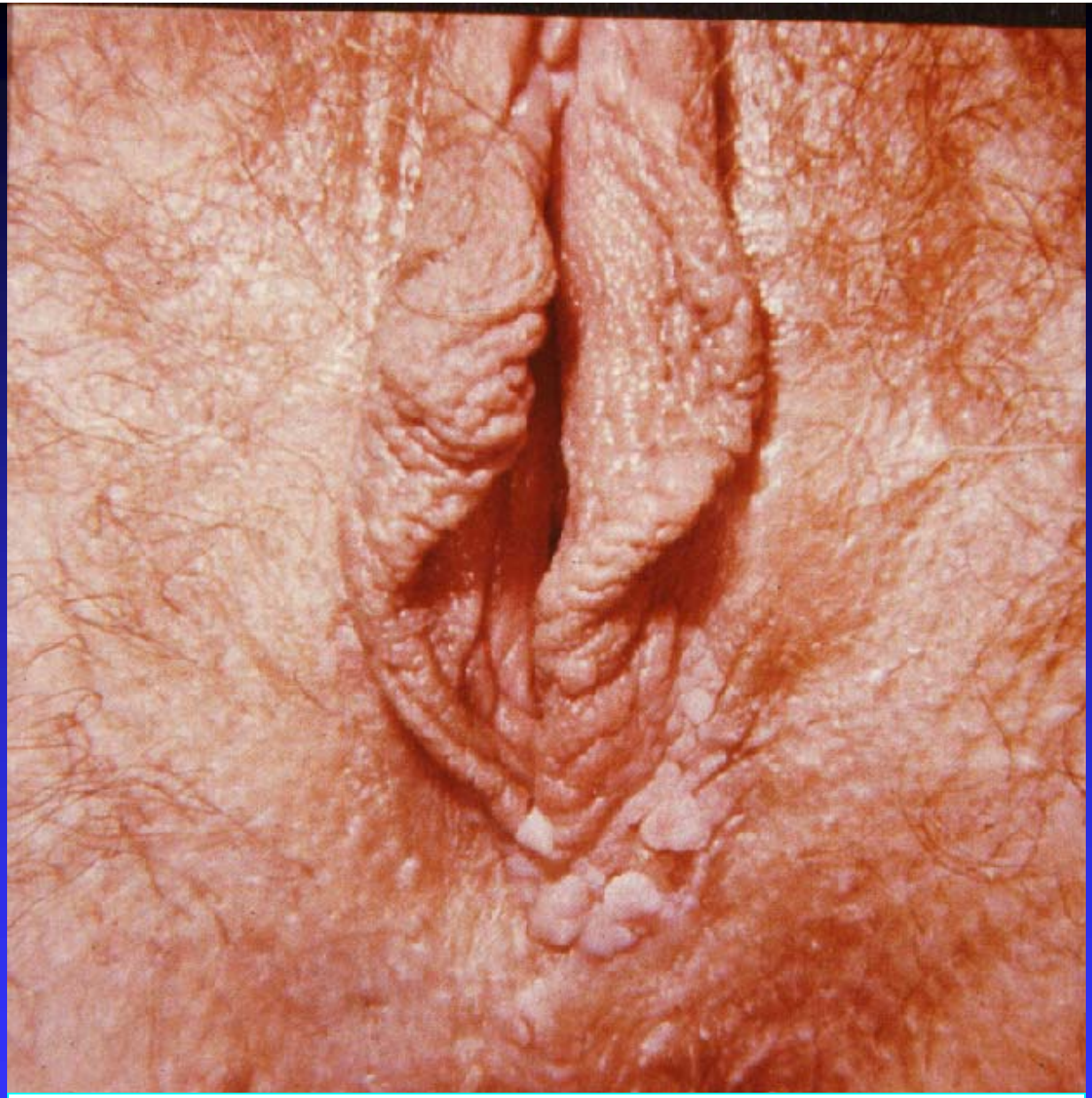




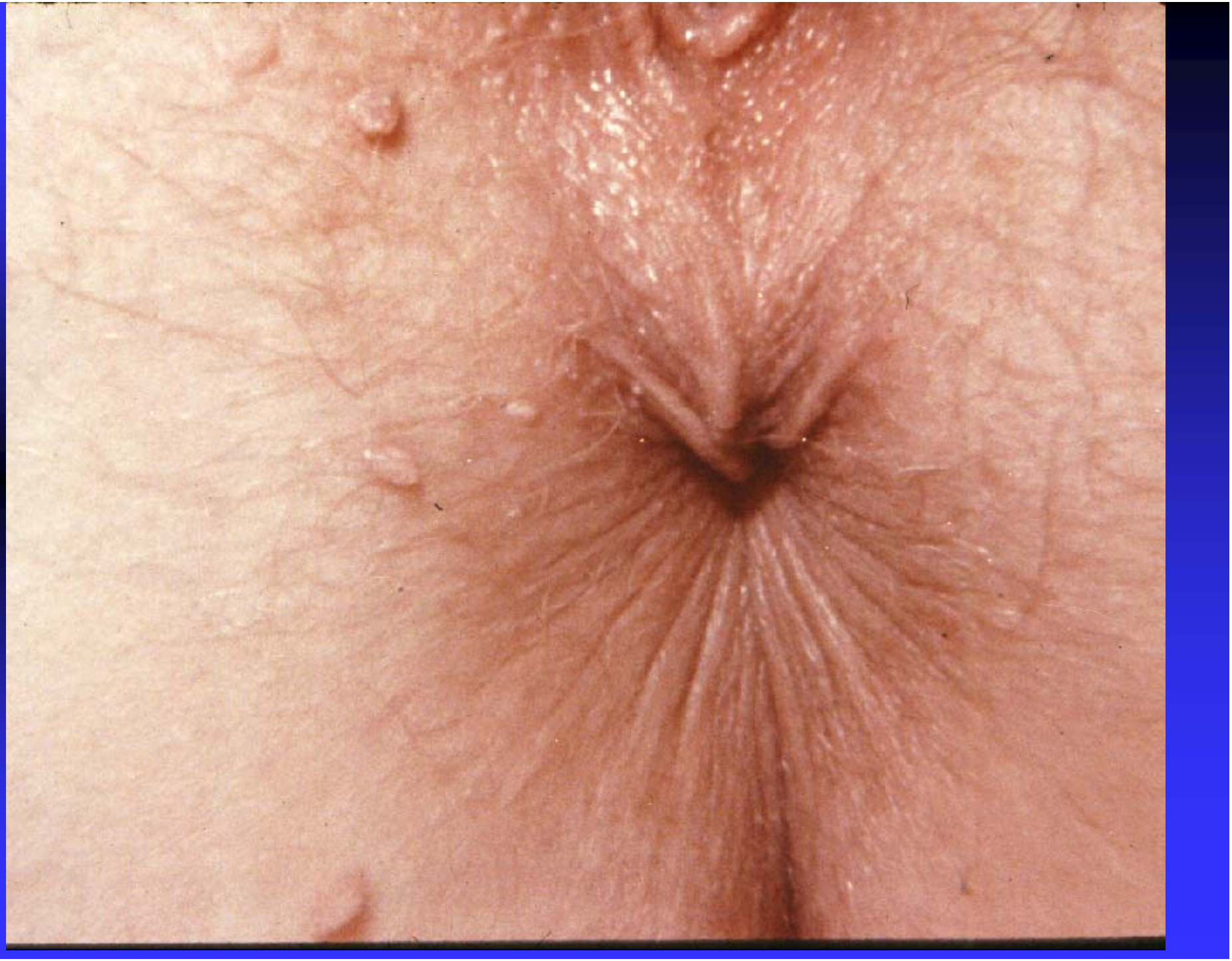


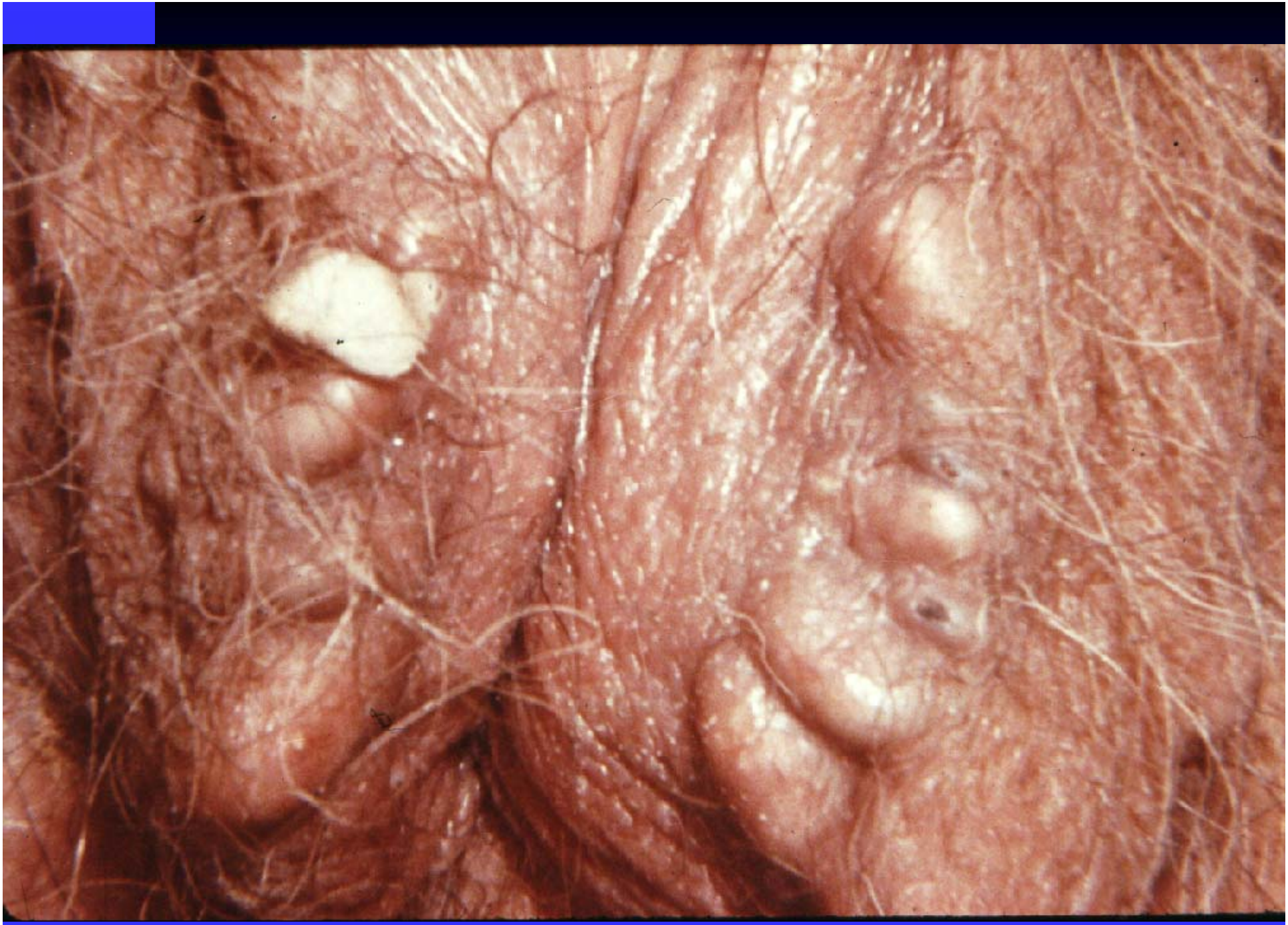


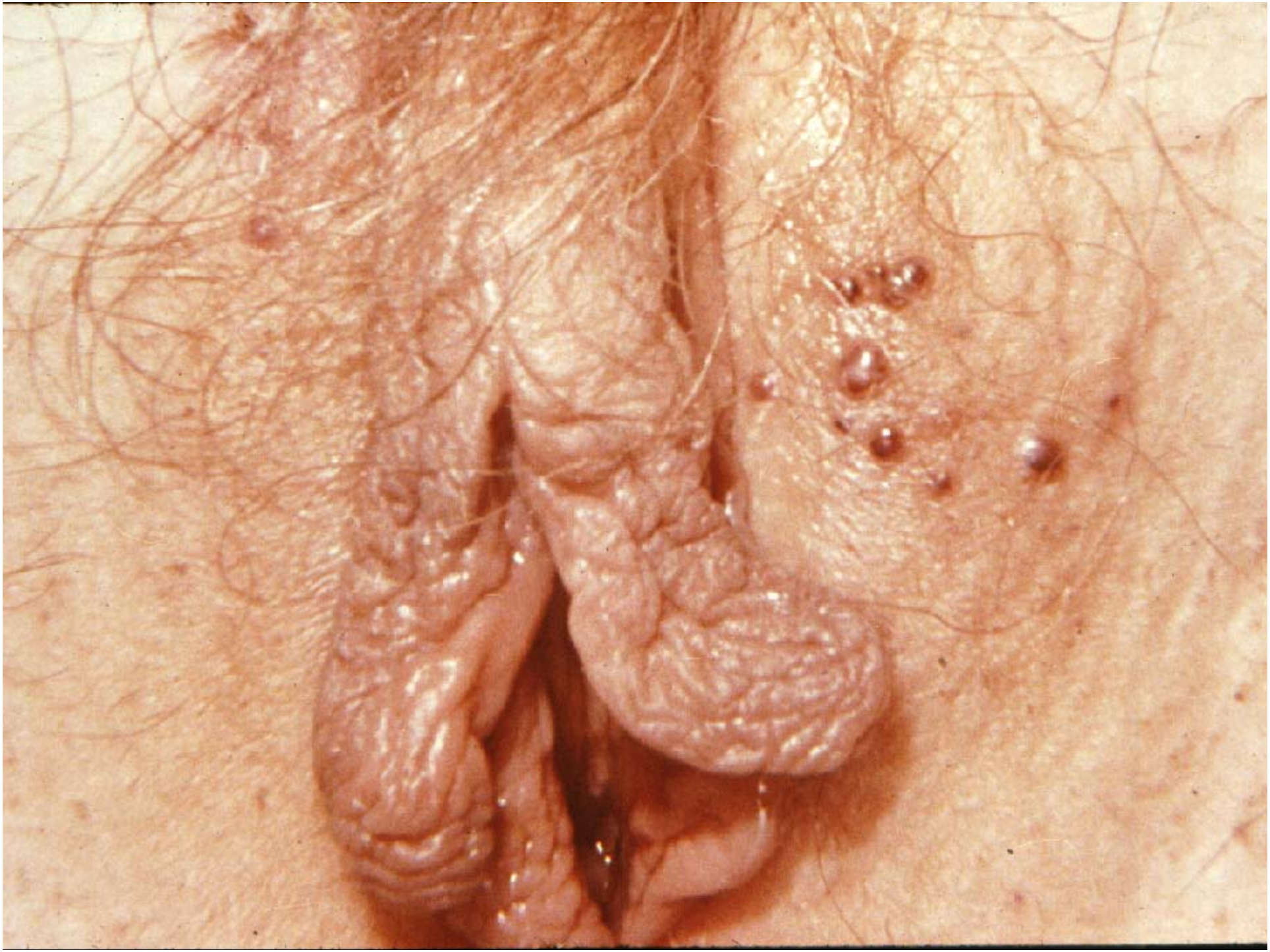


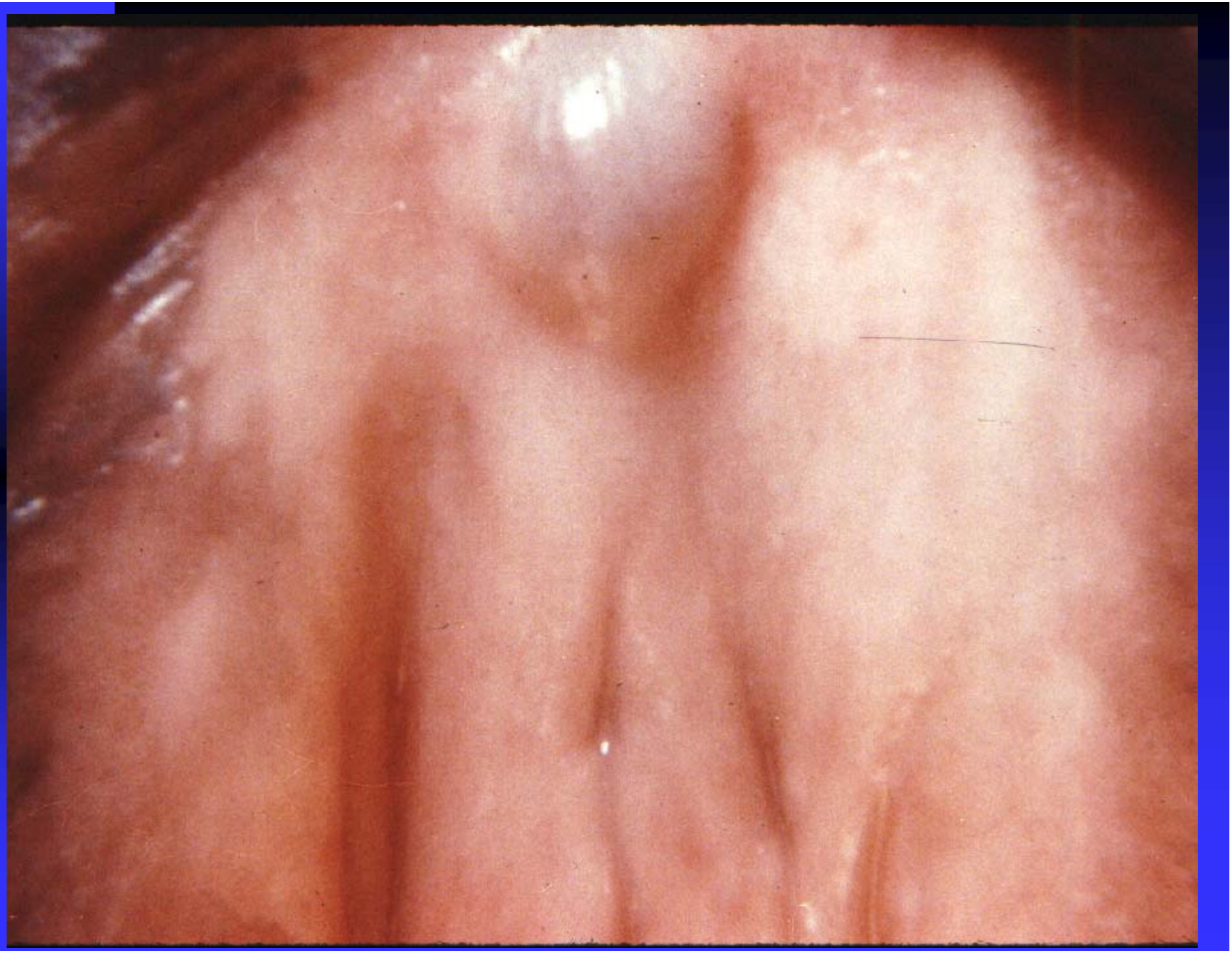


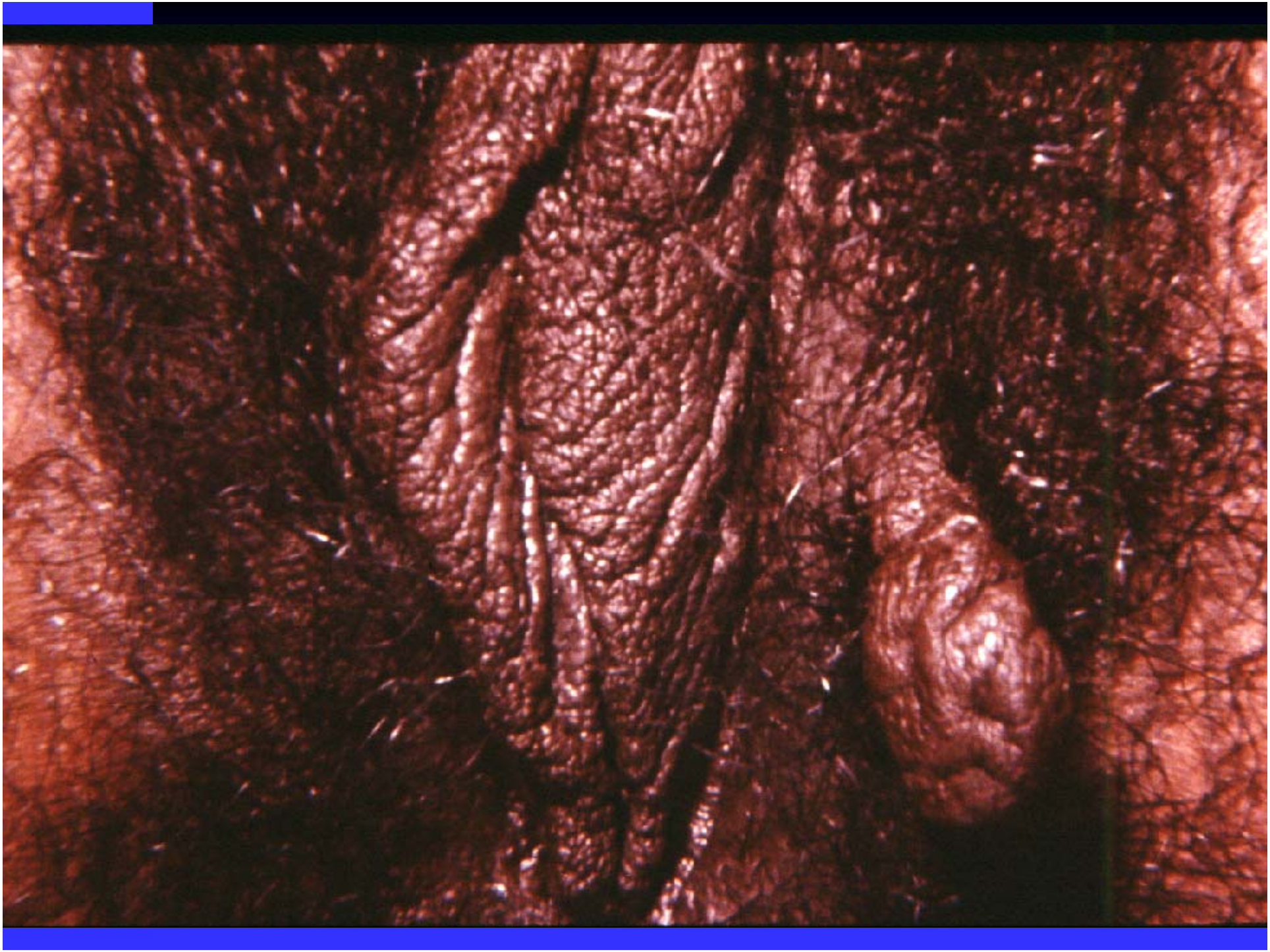
Carcinoma in situ

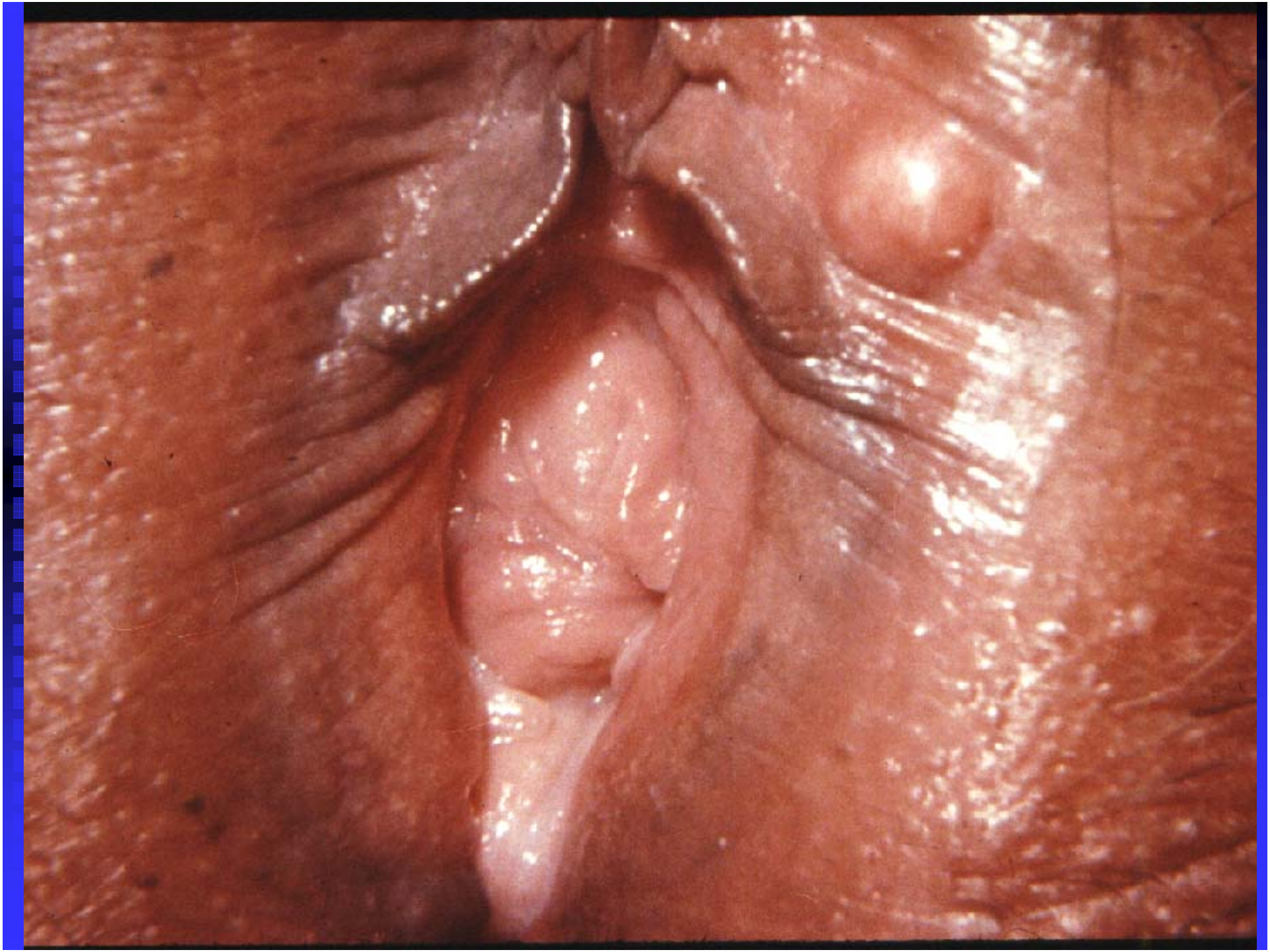






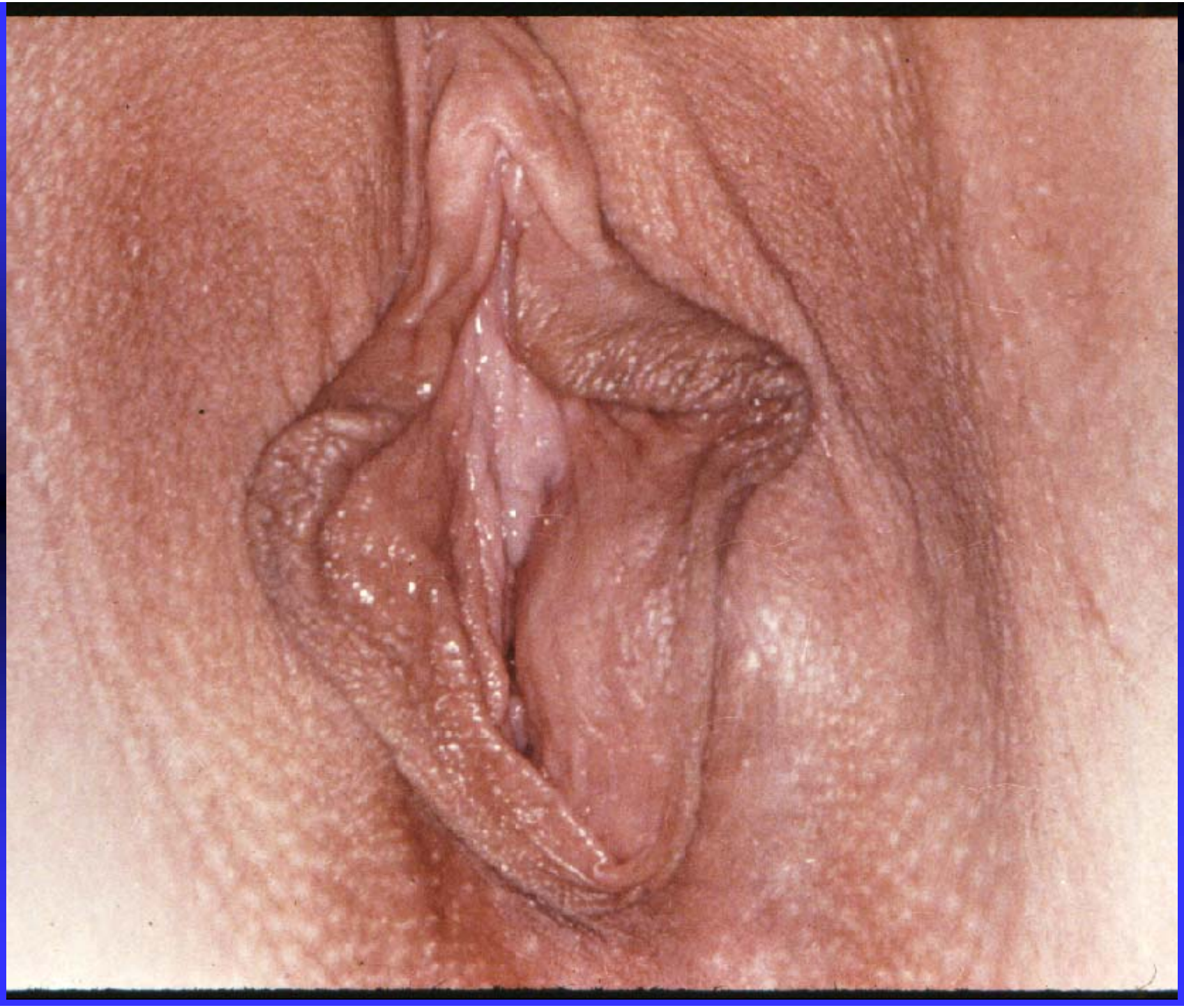


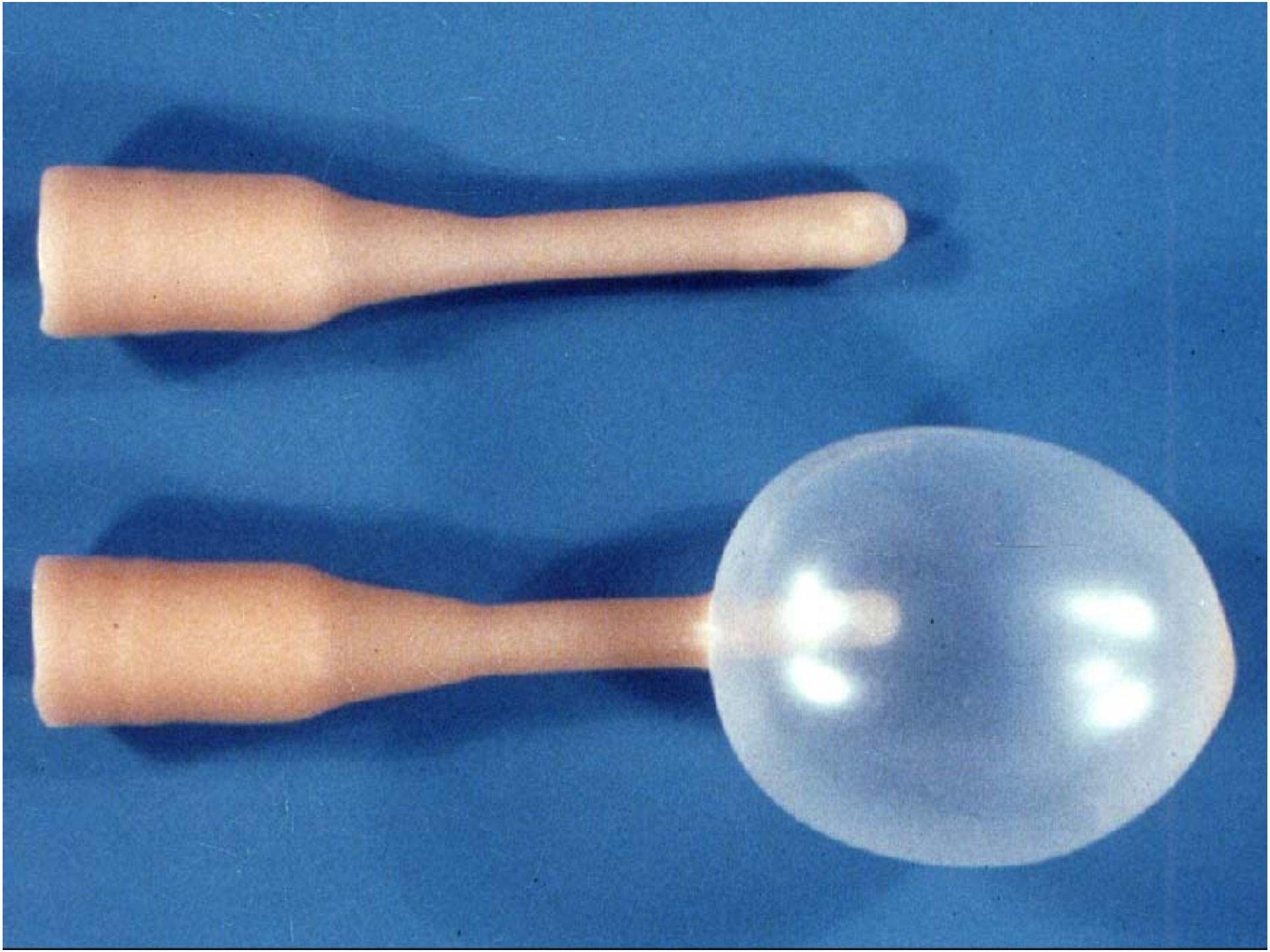


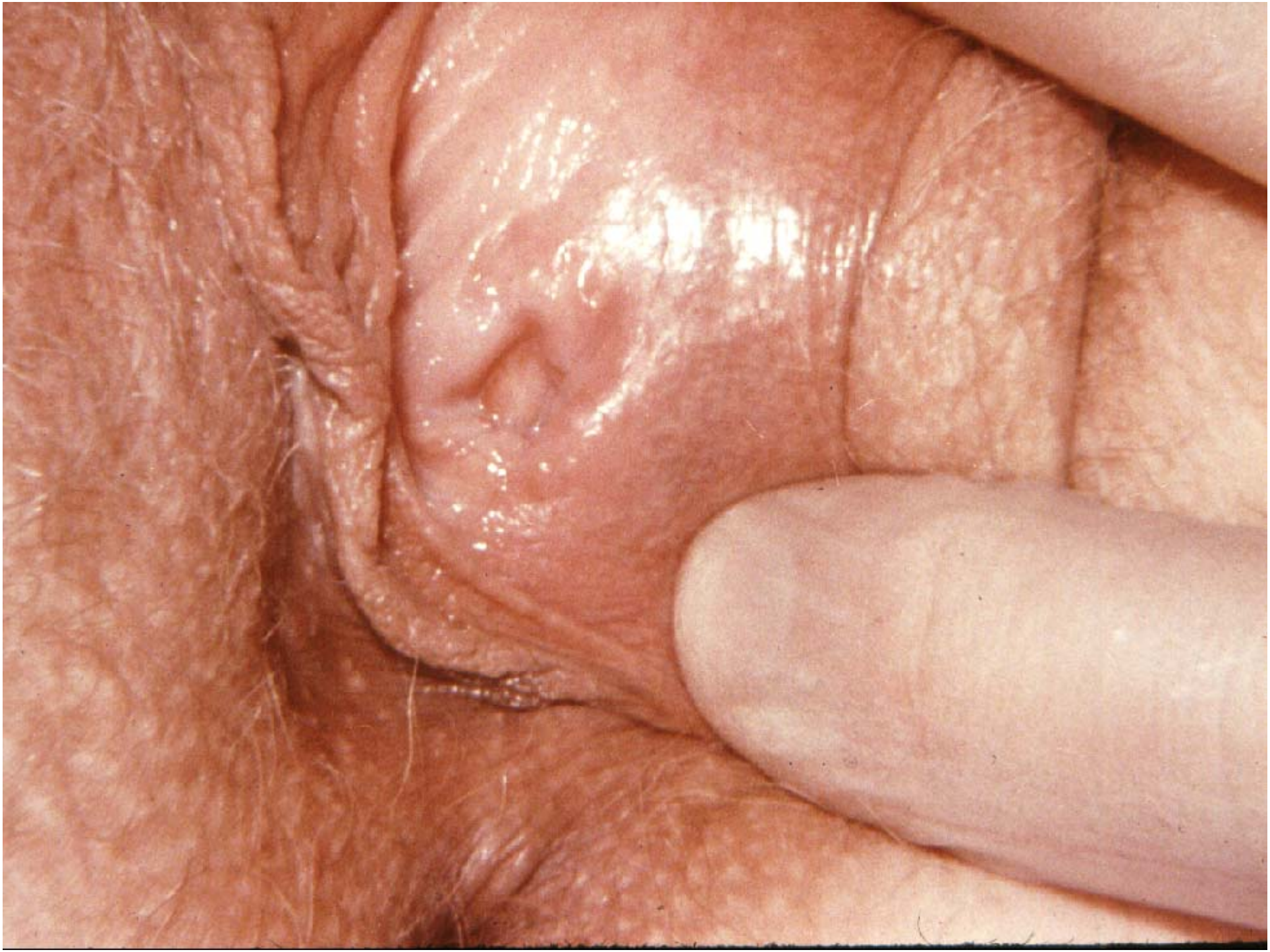


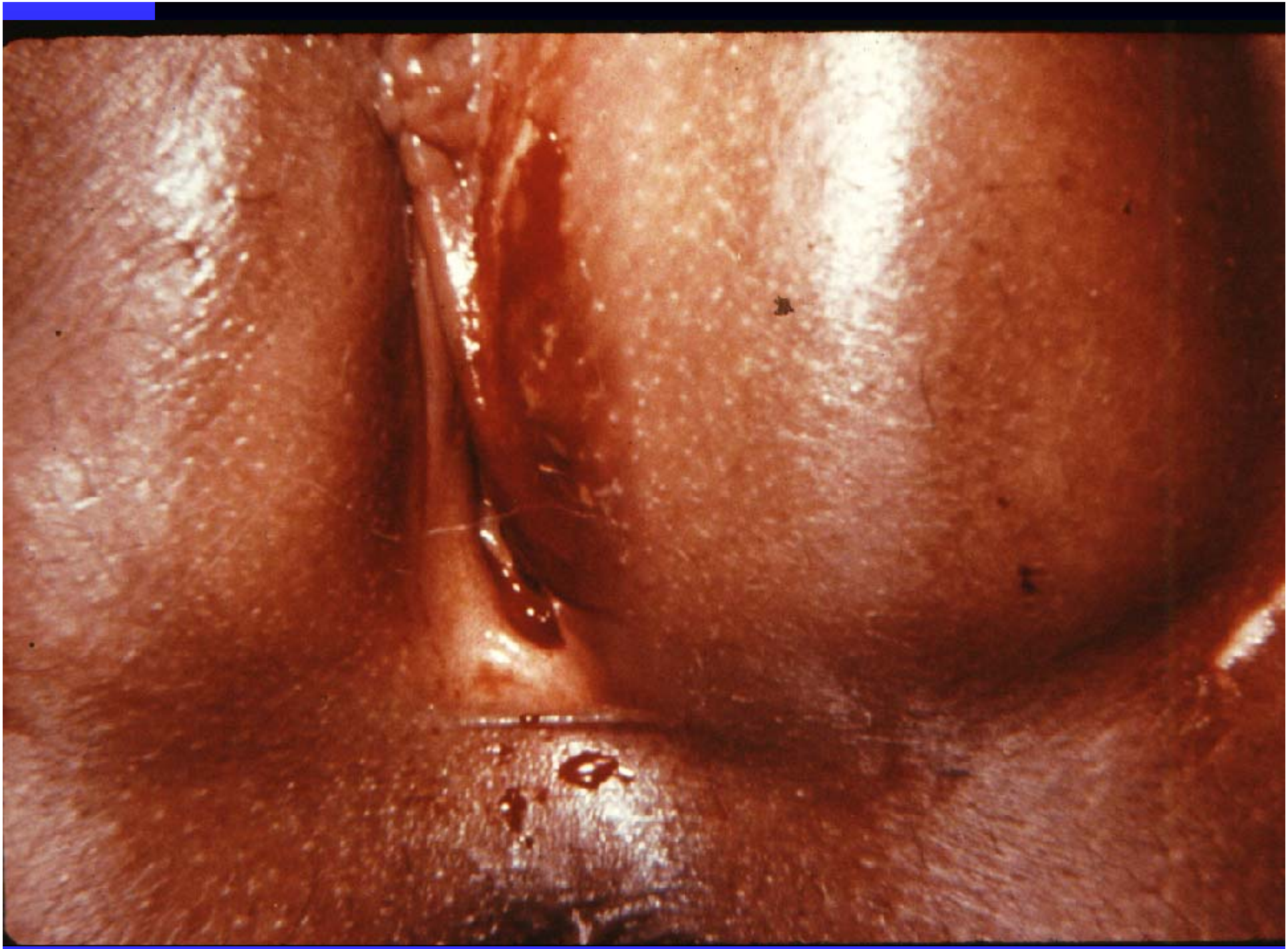
Large Tumors

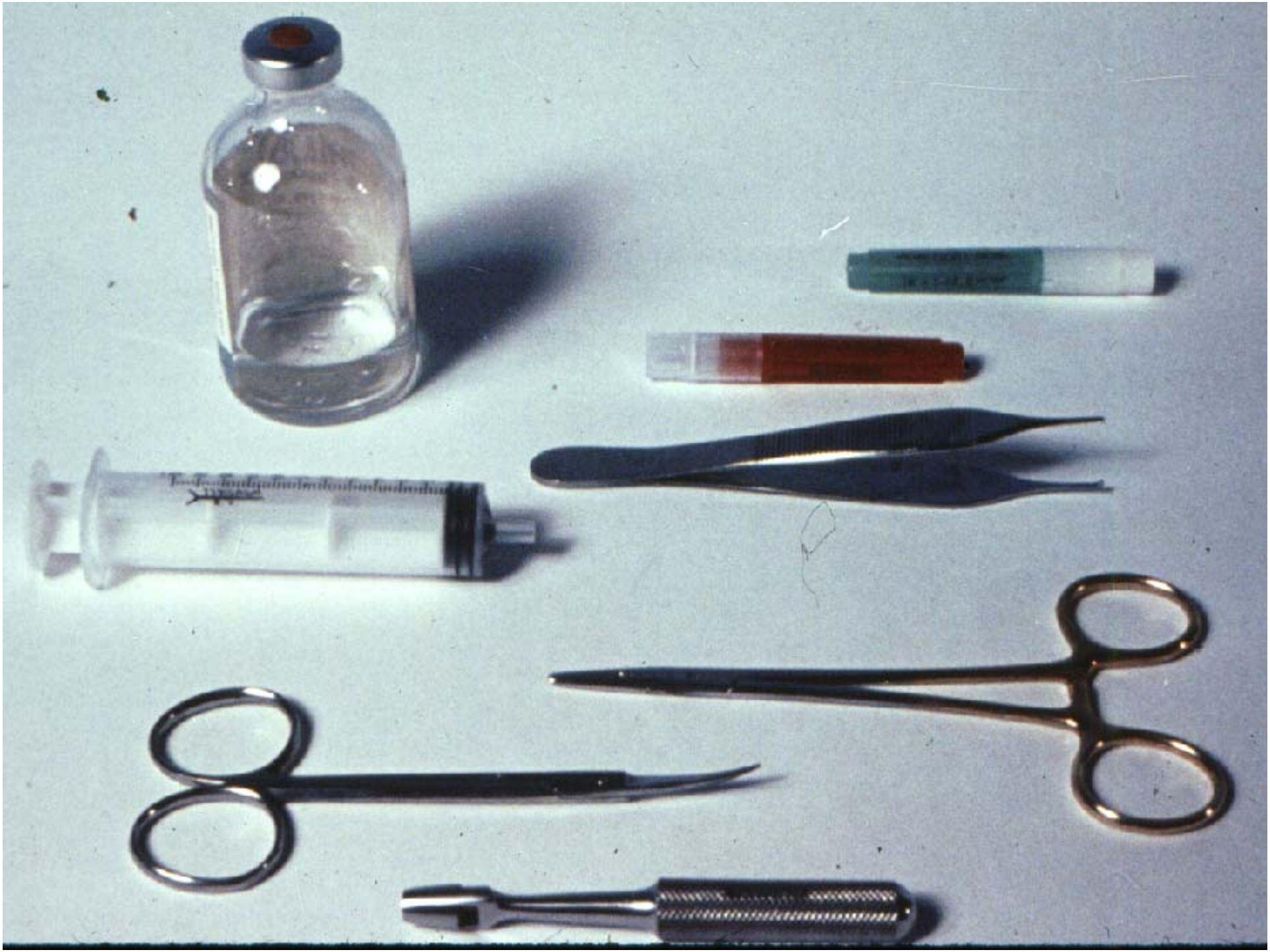
- Bartholin duct obstruction
- Trauma
- Lymphogranuloma venereum
- Squamous cell carcinoma

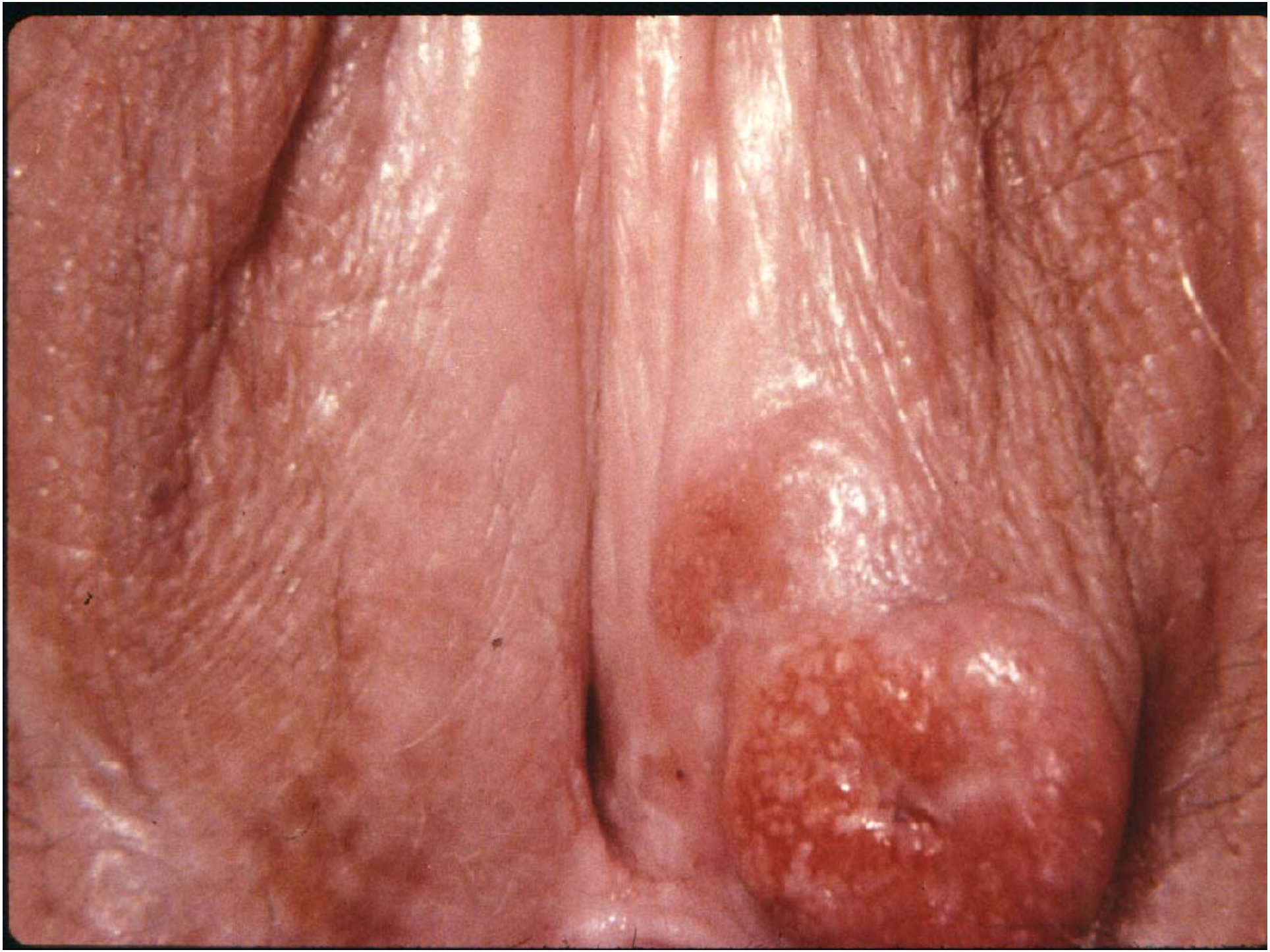


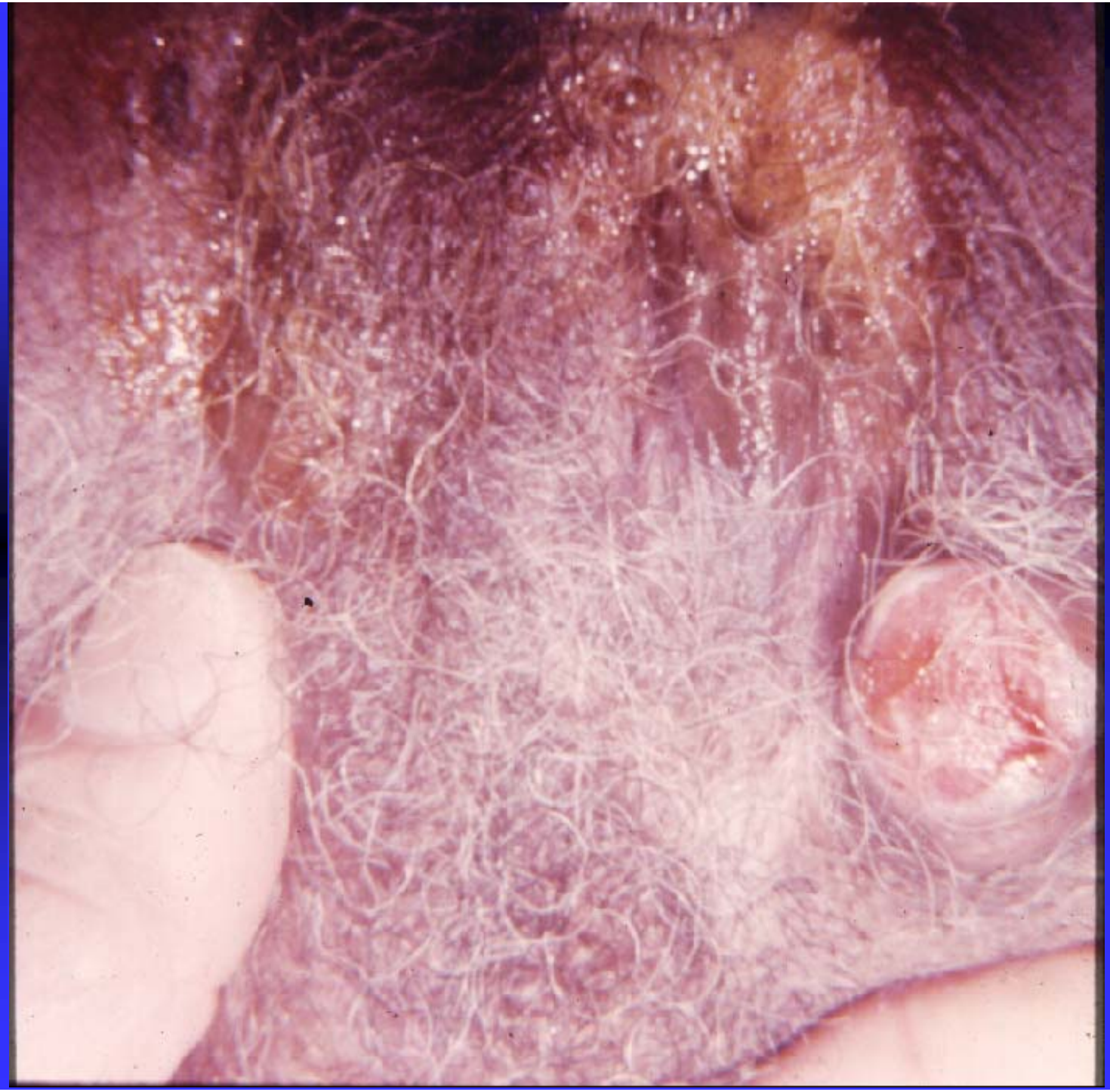


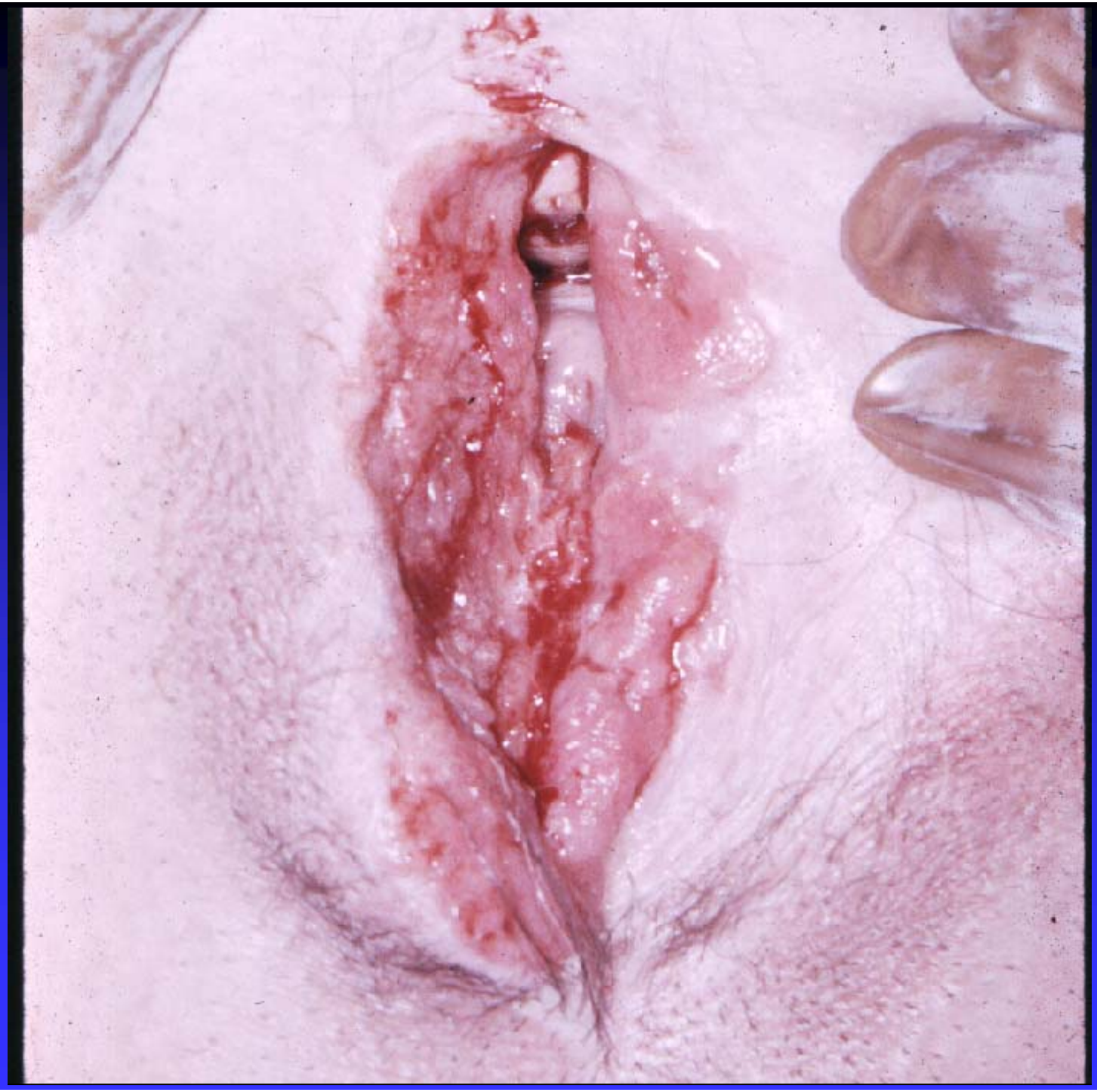












Resources

- Benign Diseases of the Vulva & Vagina
  – Kaufman, Friedrich, Gardner
- Genital Dermatology – Lynch & Edwards
- Vulvar Disease – E. Friedrich