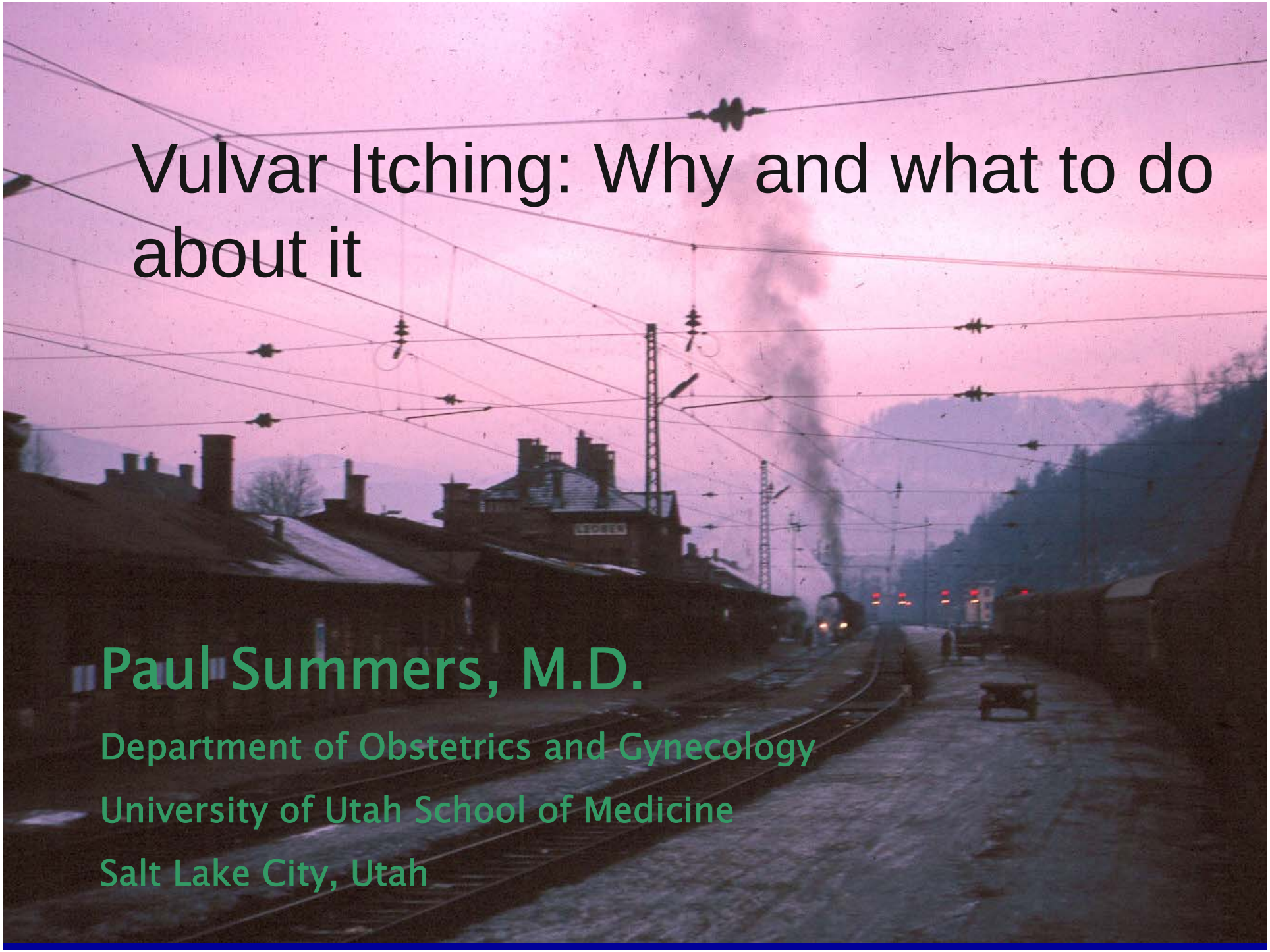


Vulvar Itching: Why and what to do about it

Paul Summers, M.D.

Department of Obstetrics and Gynecology

University of Utah School of Medicine

Salt Lake City, Utah

Degrees of Pain

Pain

Stinging

Burning

Itching

Dryness

more severe disease

What is Sensitive Skin?

- Hyper reactivity to environmental factors
- Typically no visible signs of irritation
- Symptoms of itching, burning, stinging
- Intolerance of common ingredients in topical creams or cosmetics

Berardesca, Fluhr, Maibach. Sensitive Skin Syndrome
Taylor and Francis 2006 p.1

Sensitive Skin Syndrome

sensitive — tough

Thin >0.5 mm

High friction coefficient

High transepidermal water loss

Environmental damage

Dermatitis

Superinfection

Thick 5 mm
Low friction coefficient
Low transepidermal water loss
Favorable environment
No dermatitis
No infection

Sensitive Skin Syndrome

Face

Back of the Hands

Vulvovaginal area

sensitive — tough

Thin >0.5 mm

High friction coefficient

High transepidermal water loss

Environmental damage

Dermatitis

Superinfection

Thick 5 mm
Low friction coefficient
Low transepidermal water loss
Favorable environment
No dermatitis
No infection

Sensitive Skin Syndrome

Face

Backs of the hands

Vulvovaginal area

Itching, Burning, (vulvodynia, vestibulitis)

sensitive

tough

Thin >0.5 mm

High friction coefficient

High transepidermal water loss

Environmental damage

Dermatitis

Superinfection

Thick 5 mm

Low friction coefficient

Low transepidermal water loss

Favorable environment

No dermatitis

No infection

Palms of the hands,
soles of the feet

40% of adults believe they have sensitive skin generally (hands, face) and 50% of these have no visible signs of irritation

Simion FA, Rau AH. Sensitive Skin Cosmetic Toiletries 1994;109:43

Relative Sensitivity of Vulvar Skin

- Transepidermal water loss is higher on the vulva than elsewhere Elsner, Maibach. *Acta Derm Venereol* 1990;70:141-4
- Vulvar friction coefficient is greater, making the vulva more susceptible to ***unavoidable*** mechanical damage Elsner, Maibach. *Dermatologica* 1990;181:88-91
- Hydration, occlusion, and tissue permeability heighten vulvar susceptibility to topical irritants Ferage. *Arch Gynecol Obstet* 2005;272:167-72
- Palms of the hands and soles of the feet are the only tissues designed to tolerate abrasion and irritant exposure

Normal skin only allows entry of chemicals with a molecular weight less than 500, but dermatitis allows much larger chemicals to penetrate and irritate the skin

Bos JD, Meinardi MM. The 500 Dalton rule for the skin penetration of chemical compounds and drugs. Exp Dermatol 2000;9(3):165

Harmful Ingredients in Topical agents *(high rate of irritation)*

- Benzocaine for vulvitis, cinchocaine for hemorrhoids (lidocaine is actually OK)
- Lanolin
- Propylene glycol (higher concentrations in creams than ointments)
- Fragrance in creams, toilet paper, etc (higher sensitization rate in the anal area than the vulva)

Bauer, Oehme, Geier. In Surber, Elsner, Ferage, eds. Topical Applications and the Mucosa. Karger 2011 pp.133-41

Topical agents to avoid in sensitive skin syndrome

- Yeast creams
- Vagisil
- Commercial creams
- Shaving / Brazilian wax, etc

Causes for Pain in Vulvar Sensitive Skin Syndrome

- Skin flaking compromises the skin barrier and exposes nerve fibers
- Increase in superficial nerve fibers
- Intradermal inflammation

Topics for Today

1. Dermatopathology
2. Spongiotic dermatits
3. Nerve growth factor
4. Menopausal changes

Causes for Vulvar Discomfort

Normal skin response

Laceration

Abrasion

Blister

Burn

Spongiosis

Skin disease

Lichen Sclerosus

Hailey Hailey

Pagets

Lichen Planus

Behcets

Vulvar Crohns

How is Vulvar Disease Diagnosed ?

Clinical Impression
and

A Biopsy submitted to a *dermatopathologist*

“Vulvodynia” and “Vestibulitis” show *Dermatopathology* in 2/3 of Cases

Bowen AR, et al. The role of vulvar skin biopsy in the evaluation of chronic vulvar pain *AJOG* 2008:199:467.e1-467.e6.

UNIVERSITY OF UTAH SCHOOL OF MEDICINE
DERMATOPATHOLOGY REPORT
Department of Dermatology, University of Utah Health Sciences Center
Laboratory Director: John J. Zone, M.D.

Date of Service	Submitting Service/Physician		Accession #
05-21-2007	OB/GYN	Paul Summers, MD	

Patient: W , Ja n
Sex: F
DOB: 0 80
MRN:

"nonspecific inflammation"

Clinical: Chronic vulvar "burning". History of "hay fever".

Gross: Received from Intermountain Central Laboratory, Murray, UT, at the request of Dr. Summers, are two H&E stained slides, labeled 37, A-1 and B-1, representing a biopsy from the left breast (A) and from the vulva (B), performed on 05.

DIAGNOSIS:
1. LEFT BREAST: PIGMENTED SEBORRHEIC KERATOSIS.
2. VULVA: SPONGIOTIC DERMATITIS WITH EOSINOPHILS.

Specimen #1 is a bisected shave of non-sun-damaged skin that demonstrates broad reticulated and hyperpigmented cords of bland keratinocytes around pseudo-horn cysts.

Specimen #2 demonstrates an acanthotic epithelium with overlying parakeratosis and mild spongiosis. The submucosa demonstrates interstitial and perivascular infiltrates of lymphocytes, neutrophils and occasional eosinophils.

ANNELI R. BOWEN, MD
Dermatopathologist

UNIVERSITY OF UTAH SCHOOL OF MEDICINE
DERMATOPATHOLOGY REPORT
Department of Dermatology, University of Utah Health Sciences Center
Laboratory Director: John J. Zone, M.D.

Date of Service	Submitting Service/Physician		Accession #
05-21-2007	OB/GYN	Paul Summers, MD	[illegible]

Patient: [illegible]
Sex: F
DOB: [illegible]
MRN: [illegible]

"nonspecific inflammation"

Clinical: Long history of dyspareunia.

Gross: Received from Associates of Pathology, Lakeview Hospital, Bountiful, UT, at the request of Dr. Summers, are four H&E stained slides, labeled L-[illegible], 1A-1,1A-2, 2A-1 and 2A-2, representing biopsies from the vulva performed on 04-[illegible]07.

DIAGNOSIS:
1. VULVAR LESION, WHITE: LICHENIFIED SPONGIOTIC DERMATITIS.
2. VULVAR CYST: HIDRADENOMA PAPILLIFERUM AND LICHENIFIED SPONGIOTIC DERMATITIS.

Specimen #1 is a small punch of mucosa that demonstrates epidermal acanthosis and mild spongiosis. There is hypergranulosis and compact orthohyperkeratosis. The submucosa demonstrates a mild perivascular interstitial lymphocytic infiltrate.

Specimen #2 demonstrates similar epidermal features as specimen #1, but has more interstitial neutrophils. Beneath this is a well-circumscribed collection of rounded and slit-like cystic spaces lined by columnar epithelium. There are no atypical features.

Comment: These slides were reviewed with Dr. Scott Florell, who concurs with the above interpretations.

ANNELI R. BOWEN, MD
Dermatopathologist

Causes for Vulvar Discomfort

Normal skin response

Laceration

Abrasion

Blister

Burn

Spongiosis*

Skin disease

Lichen Sclerosus*

Hailey Hailey*

Pagets*

Lichen Planus*

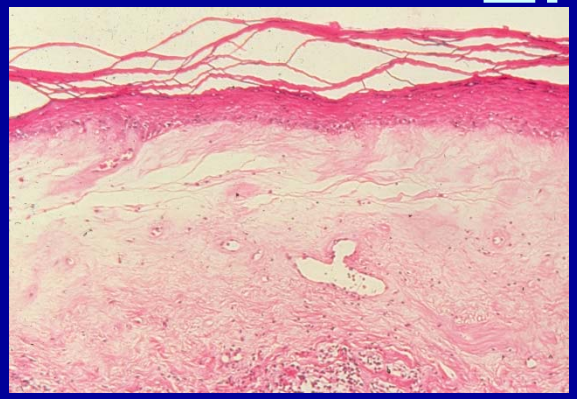
Behcets*

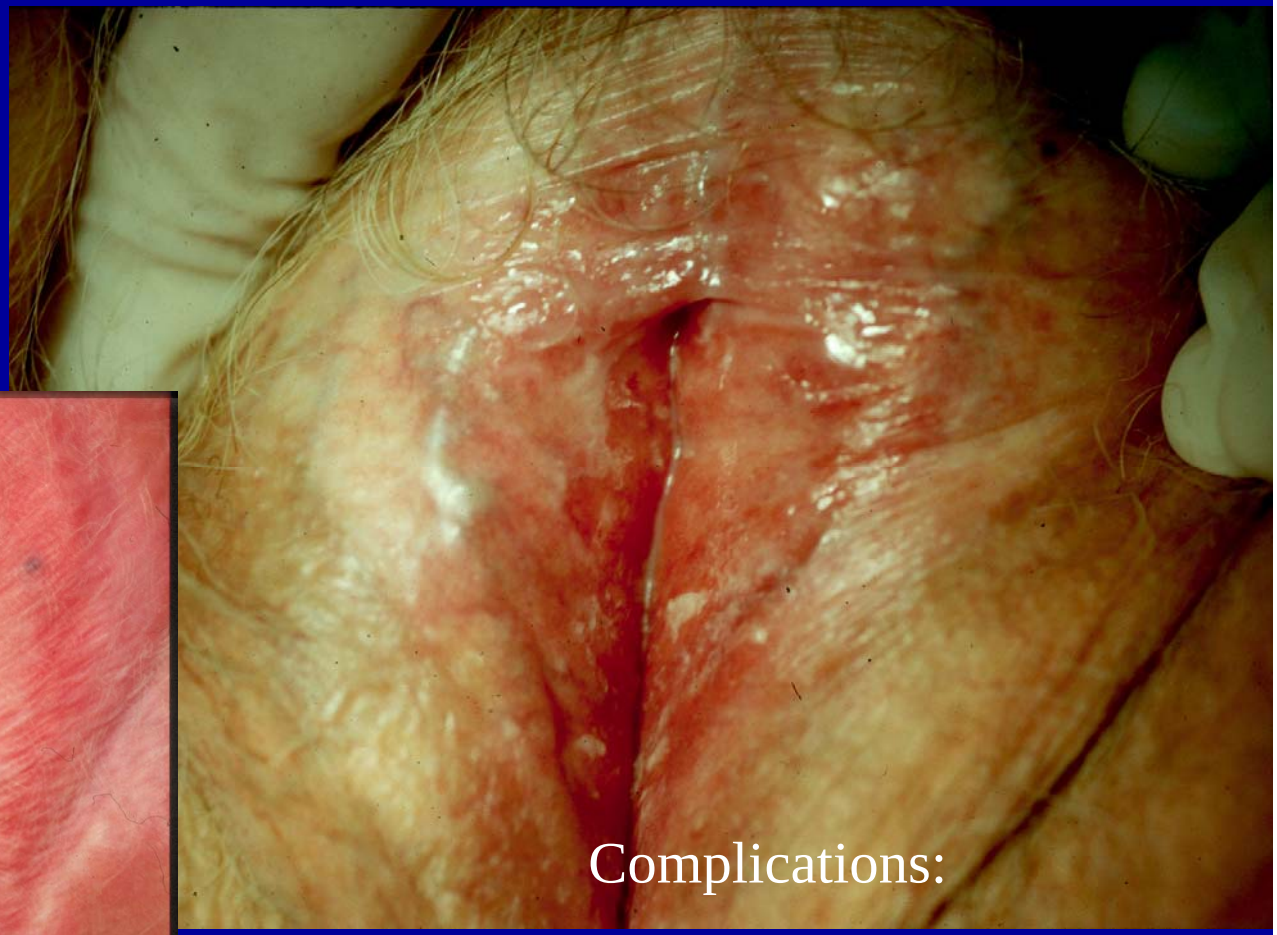
Vulvar Crohns*

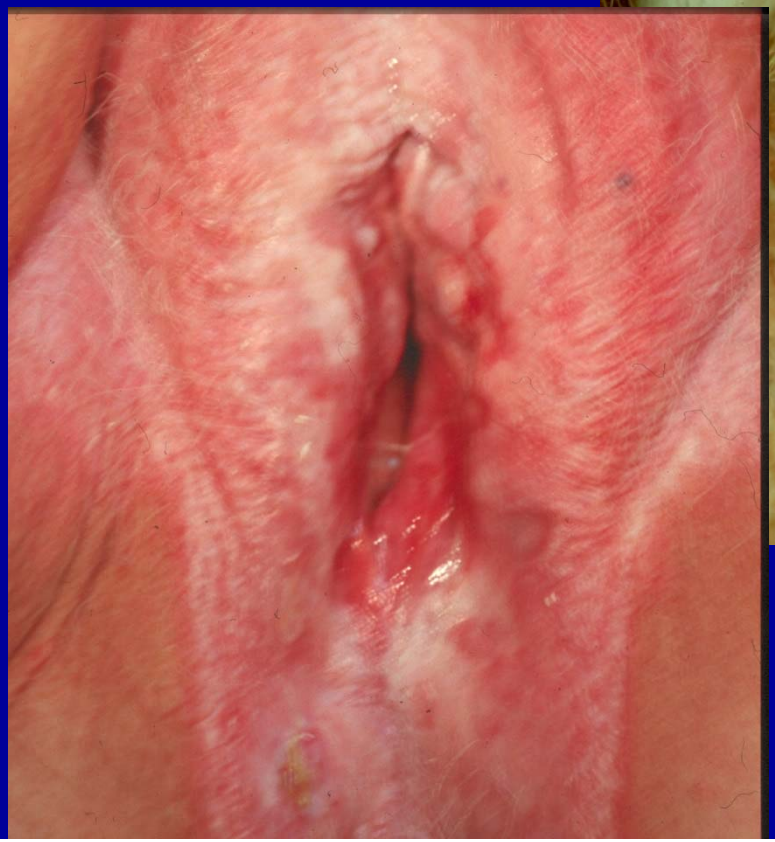
Lichen Sclerosus

- Mild lichen sclerosus is relatively common (minimal visible skin change)
- Often hour glass-shaped rash
- Any age group
- Associated with recurrent yeast infection if allergic dermatitis is superimposed (mixed vulvar dystrophy)
- Occasionally, normal flora can invade

Lichen Sclerosus



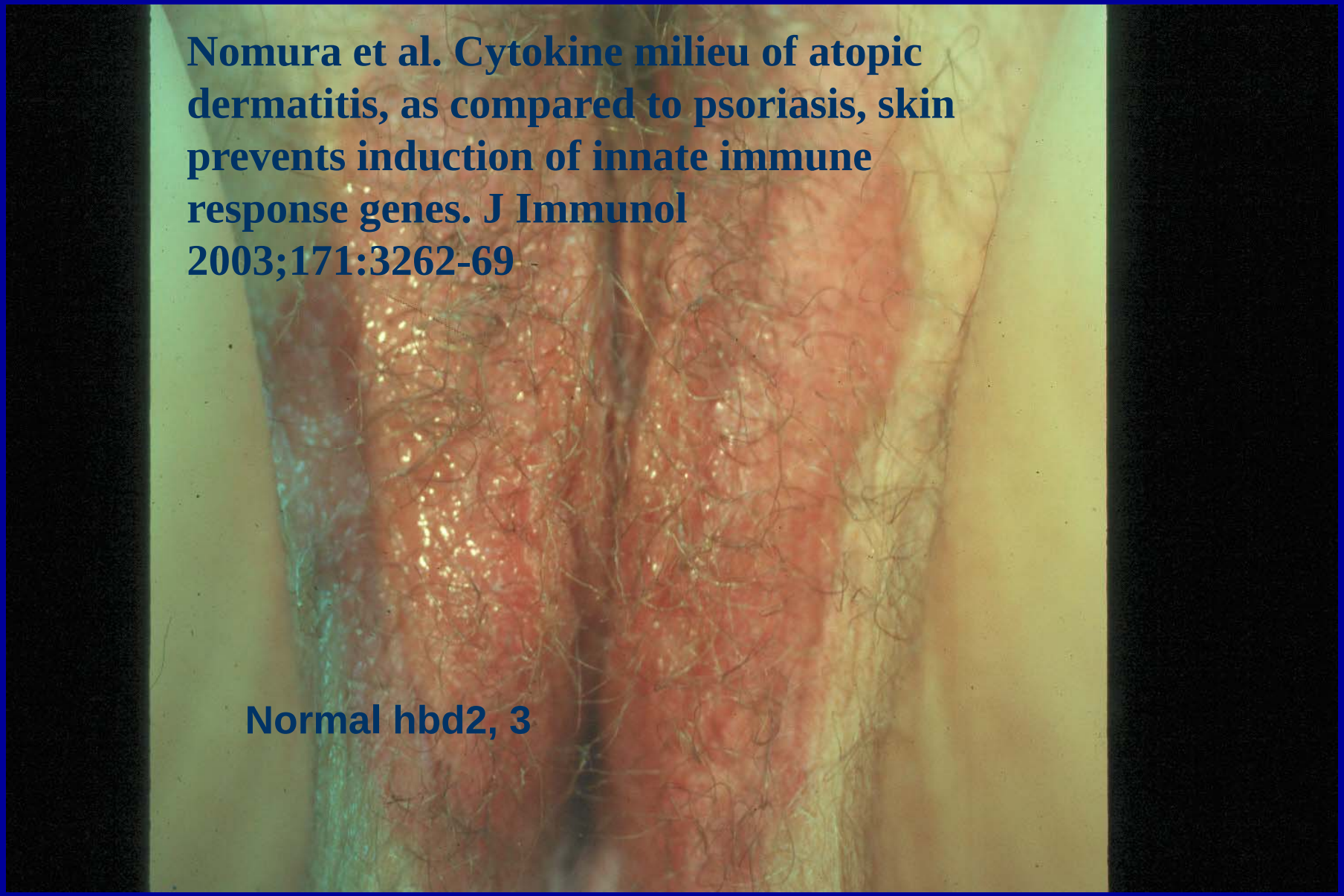




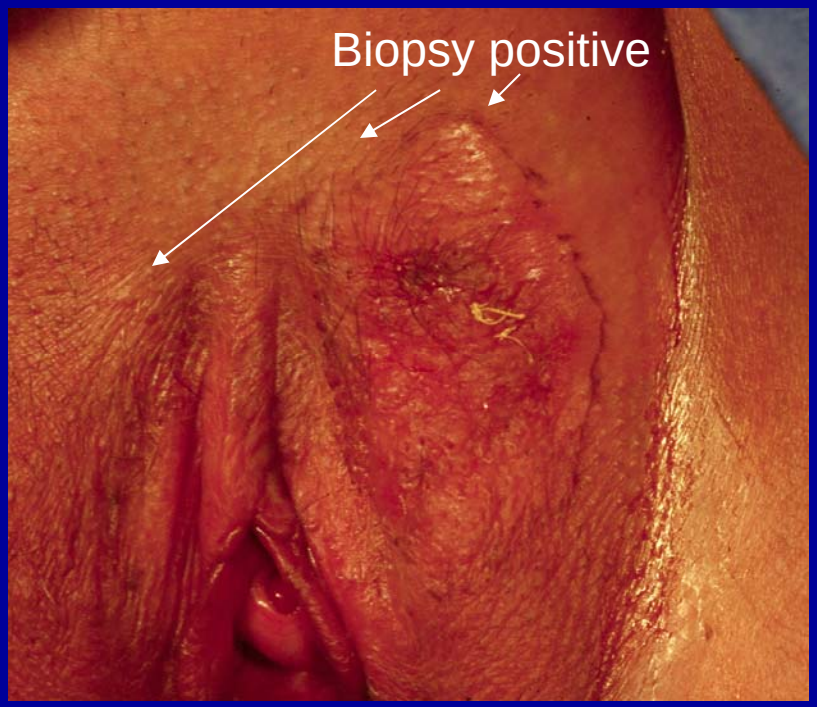
Complications:

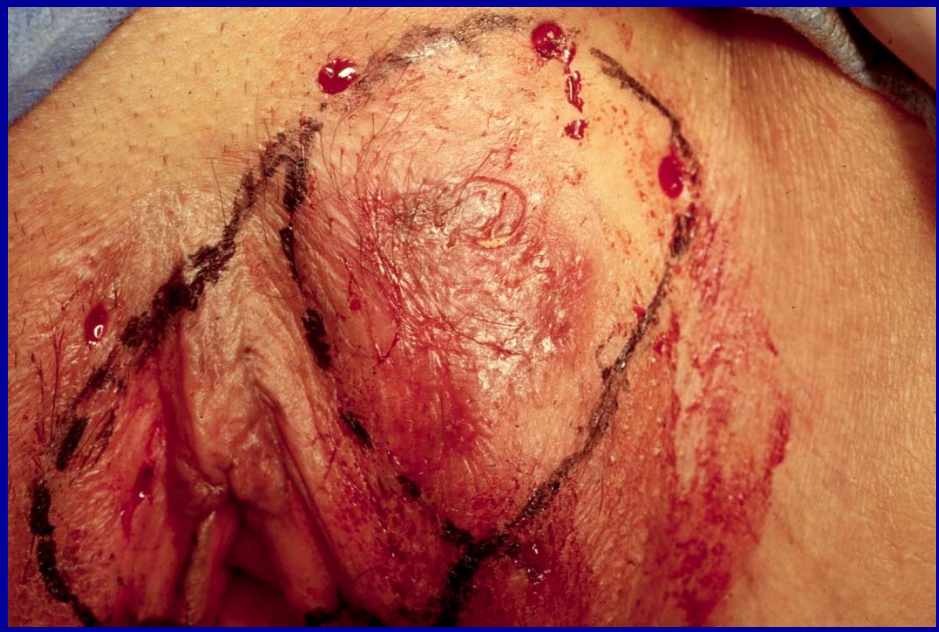
1. Irritant reaction
2. Allergy, yeast infection
3. Cancer

Non-infected Vulvar Psoriasis



Paget's Disease of the Vulva





Disease is also present in adjacent normal-appearing skin

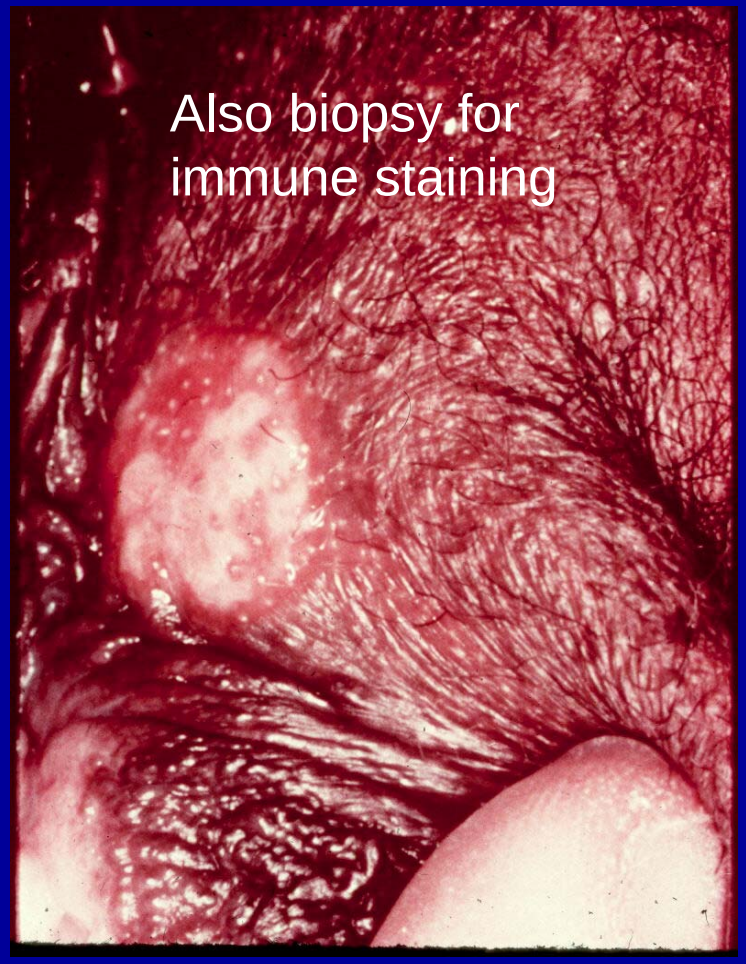
Hailey-Hailey Disorder

Autoimmune Vulvovaginitis

- Lichen Planus
- Zoon’s disorder
- Aphthous ulcer disease

Recurrent Genital Ulcer Disease

- Infectious vs autoimmune
- Painful superficial ulcers, typically burn when urine contacts the lesion
- Aphthous major vs aphthous minor
- Behcet's Disease
- Vulvar Crohn's disease

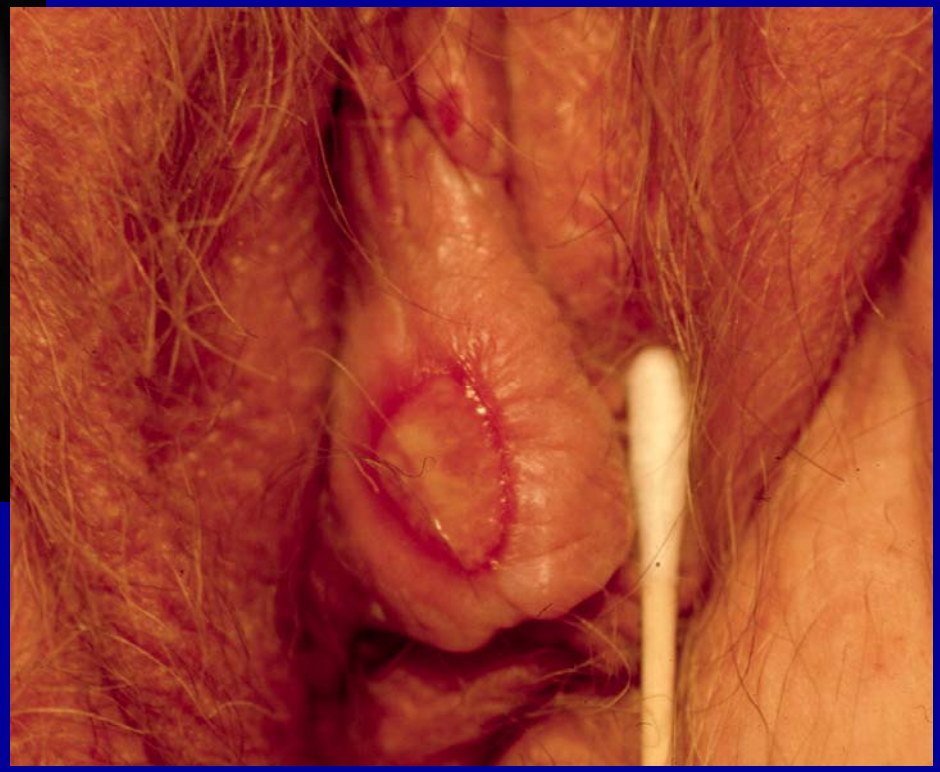


Aphthous Major vs Minor

- Distinction is greater or less than 1 cm
- Recurrent with no definitive pathology
- No systemic symptoms or findings if simply an isolated vulvar disorder

Aphthous Minor vs Aphthous Major

A spectrum of one disease?



1. Aphthous ulcer
2. Crohn's Disease
3. Behcet's Disease

Vulvar Crohn's Disease

- Recurrent painful genital aphthous major
- Associated areas of large bowel ulceration (may be asymptomatic!)

- ***Colonoscopy is important in every case of recurrent painful genital ulcers***

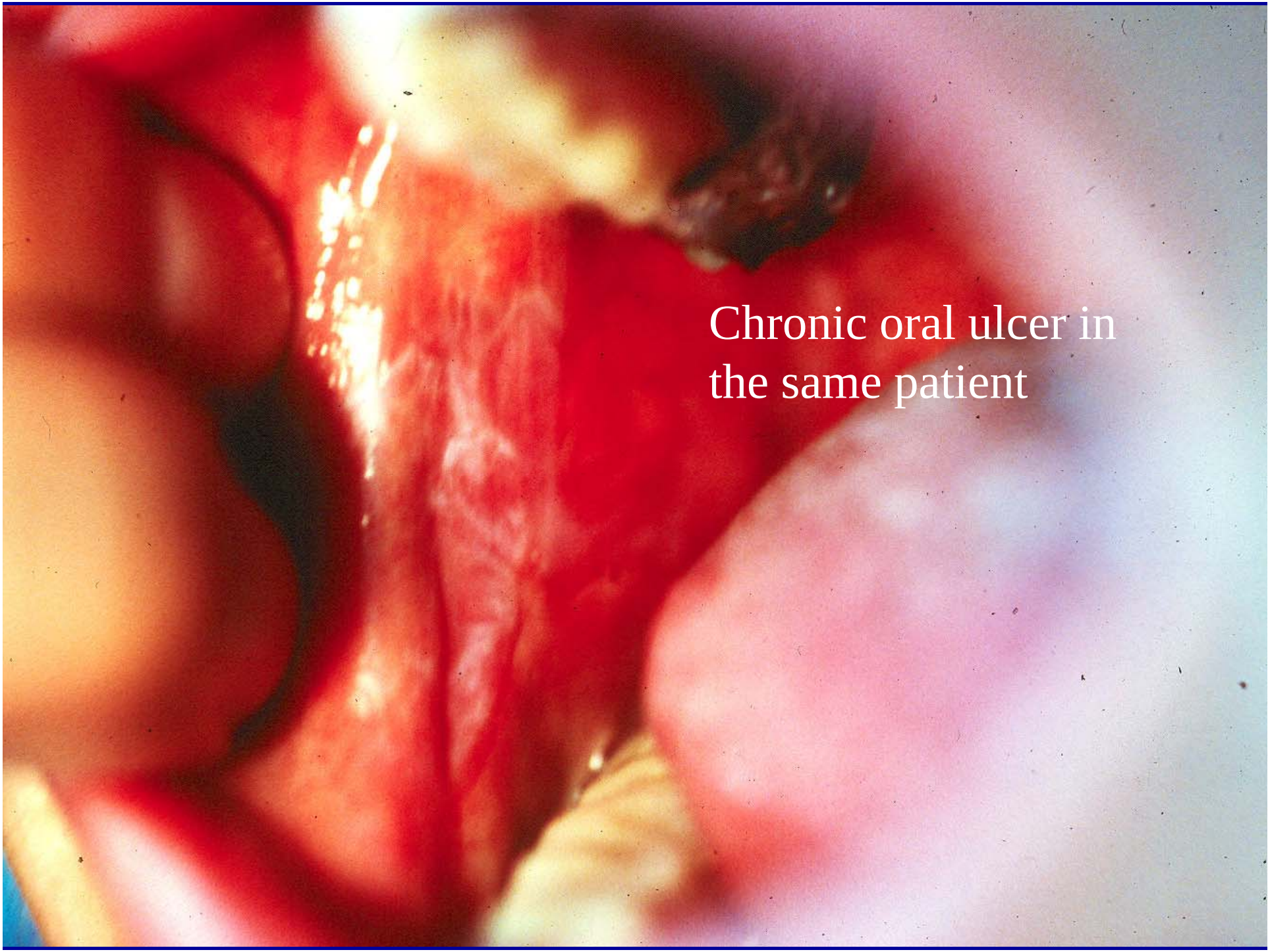
Behcet's Disease

- Common in the Middle East and Far East (a main cause for blindness)
- Recurrent oral aphthous ulcers plus ***intermittent***
  - 1. eye inflammation
  - 2. vasculitis (aortic inflammation)
  - 3. vulvar aphthous ulcers — ***may be first sign***
  - 4 . arthritis
  - 5. GI symptoms
  - 6. pathergy test

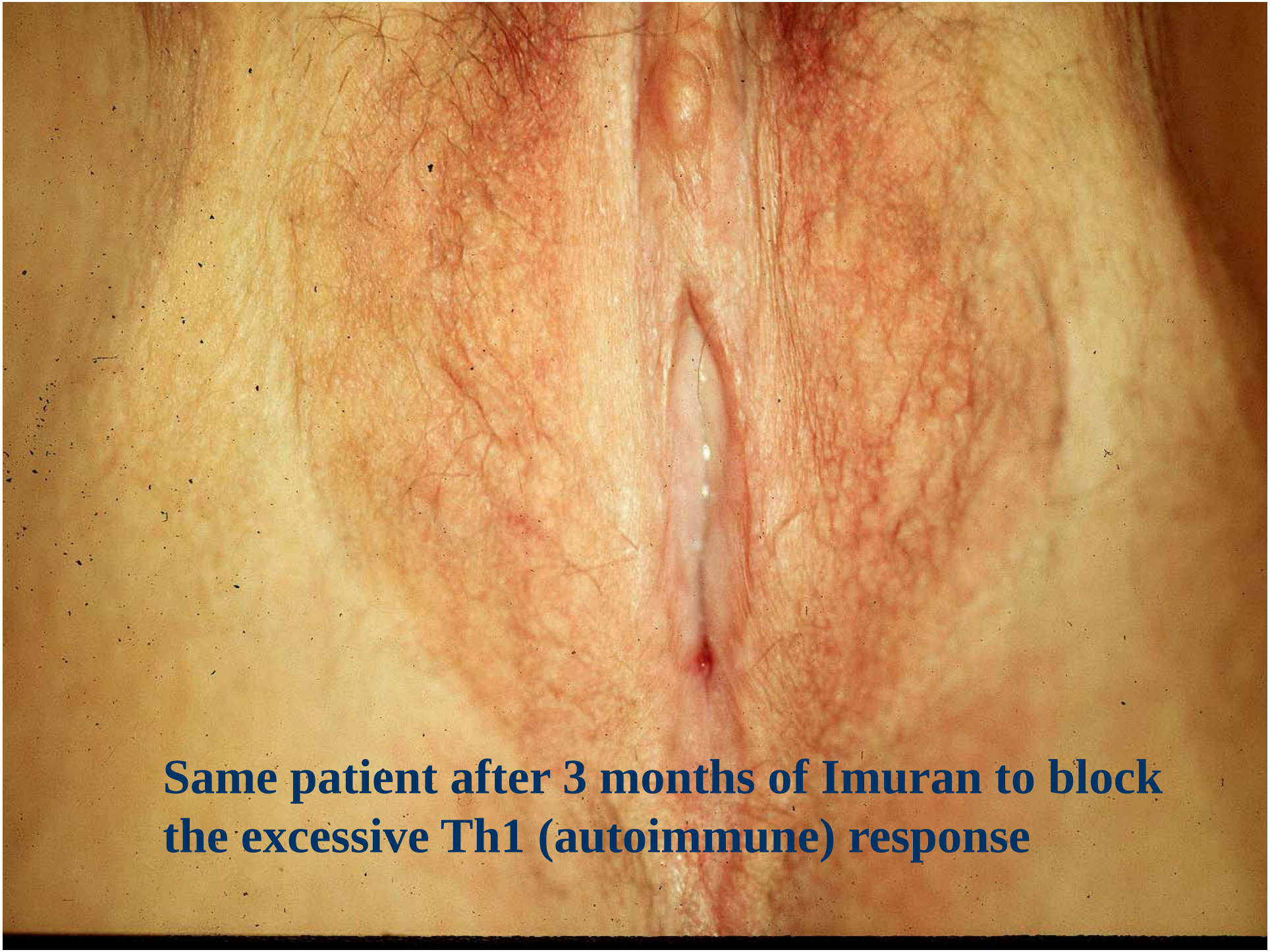
- ***Genital aphthous ulcers require an ophthalmology evaluation and observation for eye or other symptoms in the future***

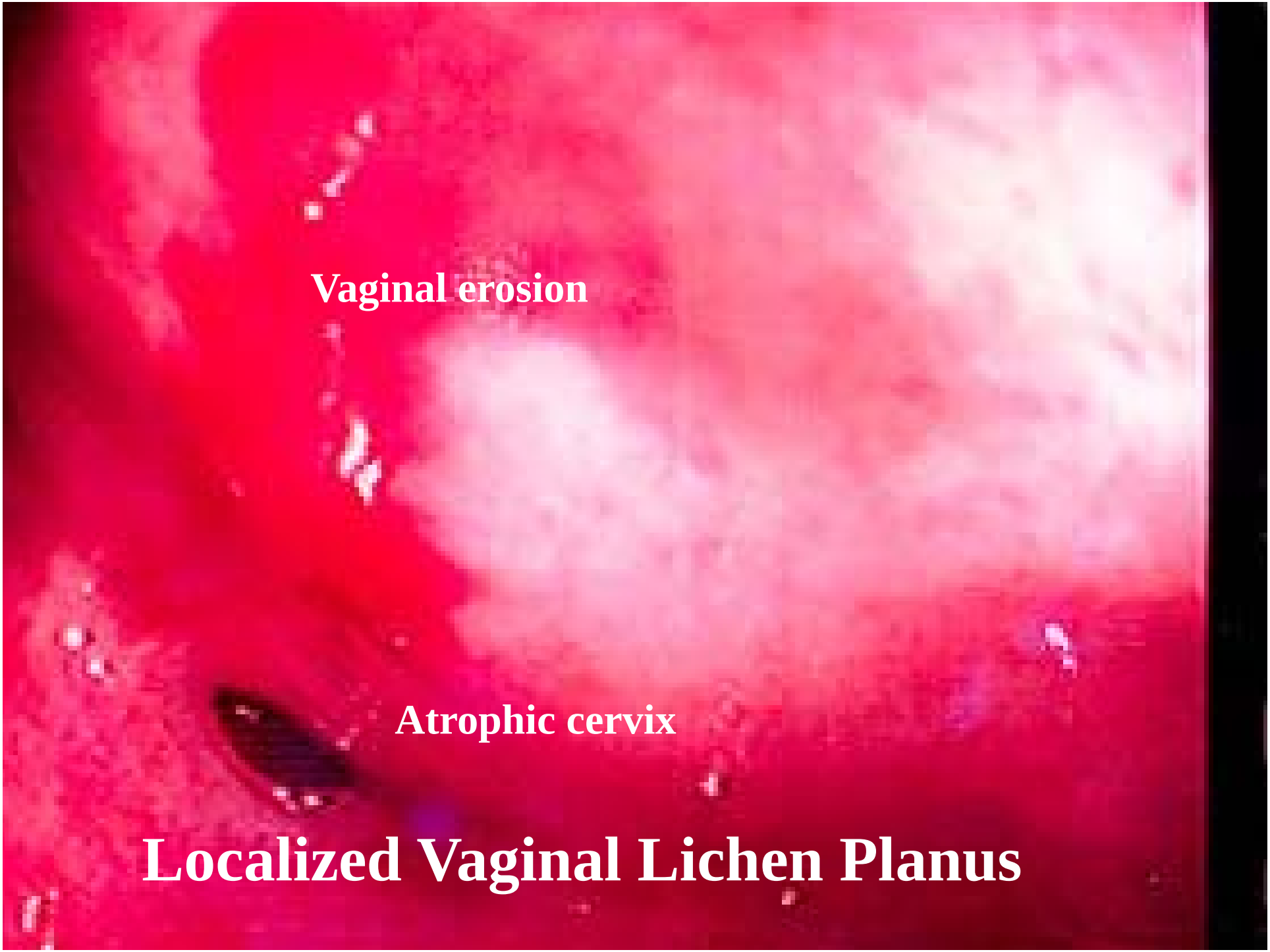
Vulva, Severe Erosive Lichen Planus

Stenosis is more often in upper vagina


Chronic oral ulcer in
the same patient


Parabasal cells
Lichen Planus, saline wet prep
White blood cells

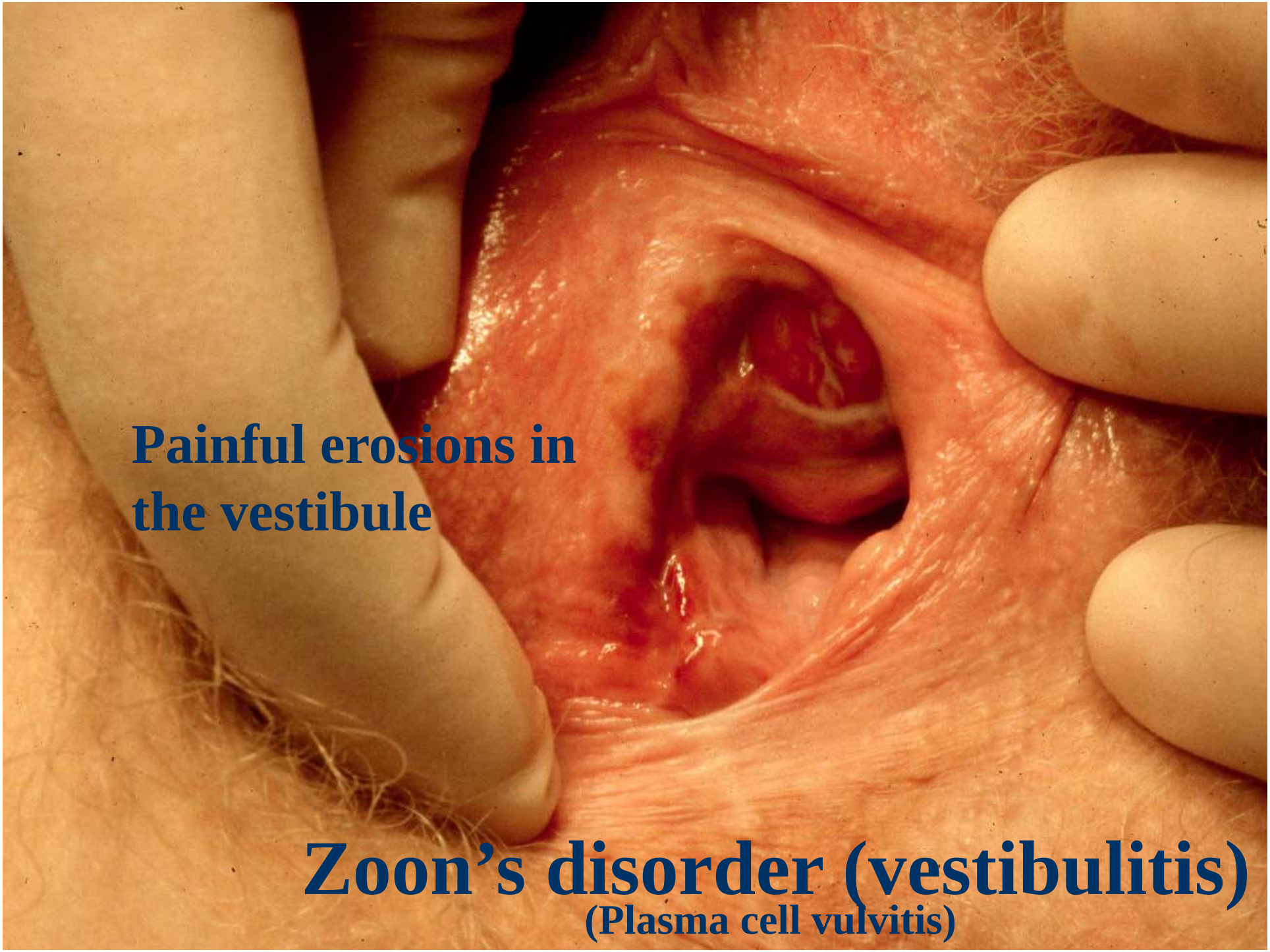

Same patient after 3 months of Imuran to block
the excessive Th1 (autoimmune) response



Localized Vaginal Lichen Planus

Therapeutic possibilities for mild Lichen Planus

- Topical steroids
- Clindamycin cream
- Oral Metronidazole 500 mg BID for 30 to 60 days (Asher V. Wahba-Yahav Ideopathic lichen planus: treatment with metronidazole. J Am Acad Dermatol 1995;33(2:1):301-2
  - Arzu Bueyuek Oral metronidazole treatment of lichen planus J Am Acad Dermatol 2000;43:260-2)

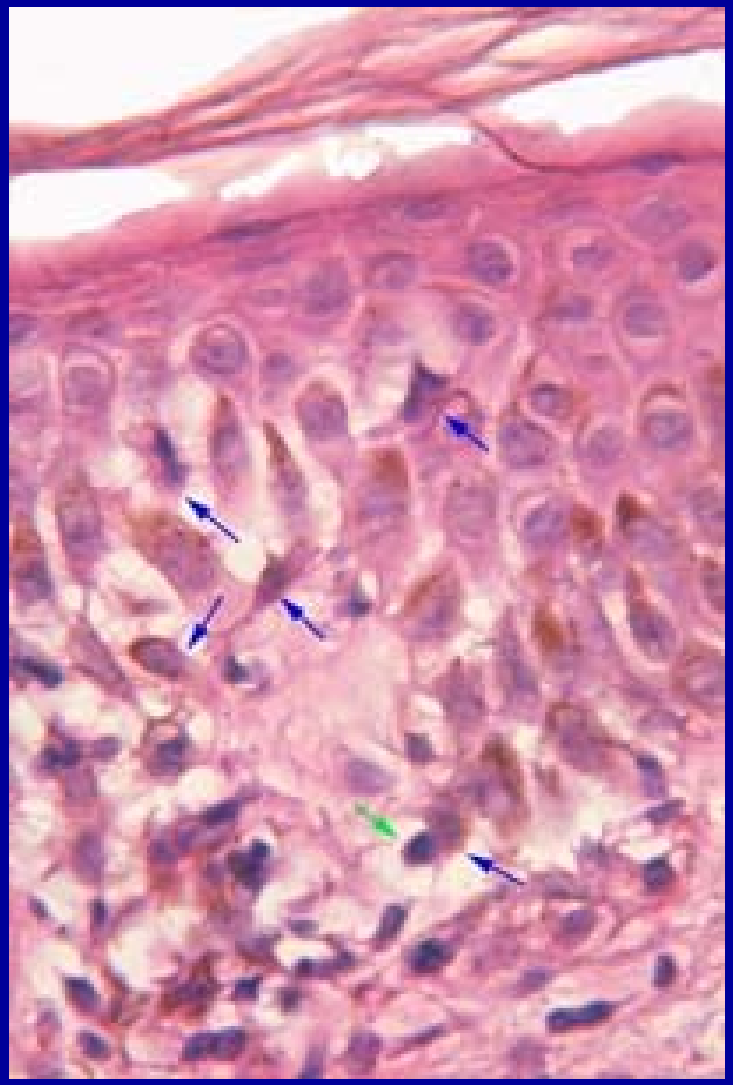


Zoon’s disorder (vestibulitis)

(Plasma cell vulvitis)

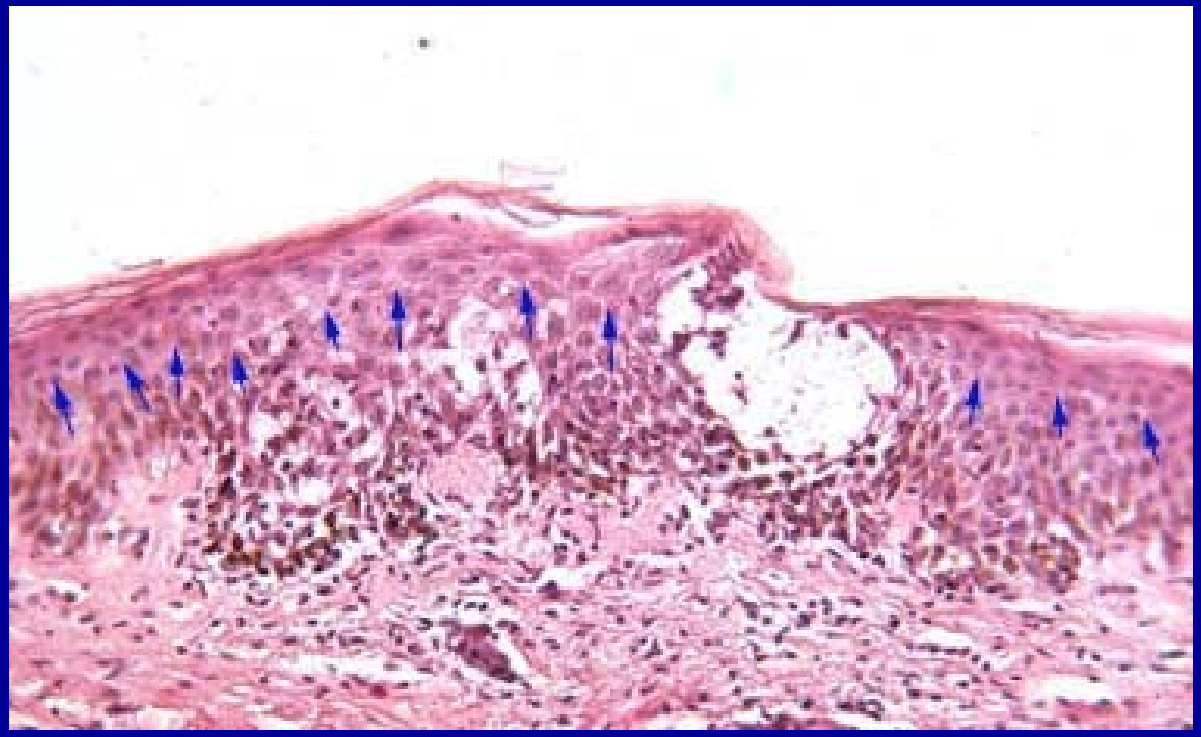
Vulvar Spongiotic Dermatitis

Spongiotic dermatitis



1. Intraepidermal edema
2. Liquifaction of dermal-epidermal interface
3. Langerhans cells—blue arrows

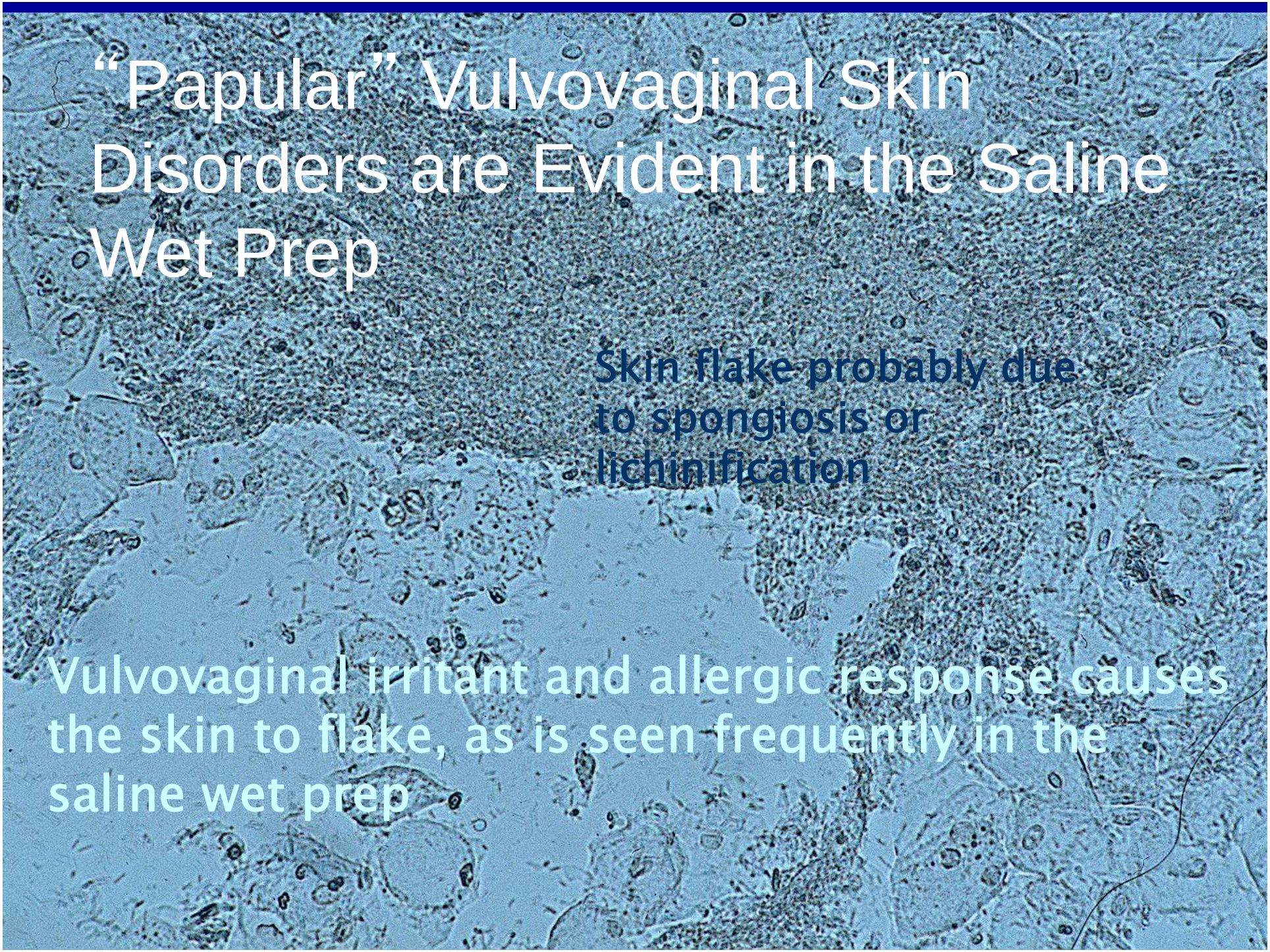
Spongiotic Dermatitis
(eczema, atopic, irritant, allergic dermatitis)



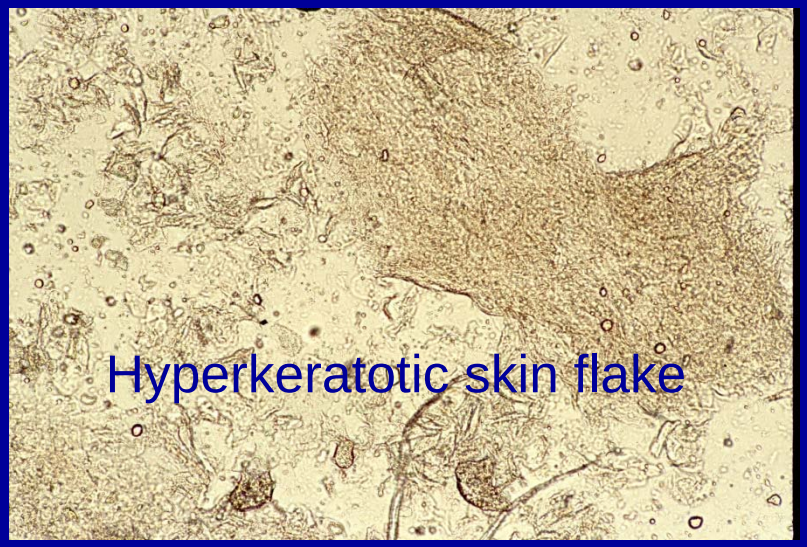
1. Hyperplastic epidermis
2. Areas of spongiosis with spongiotic vesicles
3. Blue arrows identify junction between superficial and basal parts of epidermis
4. Fluid is in the basal part

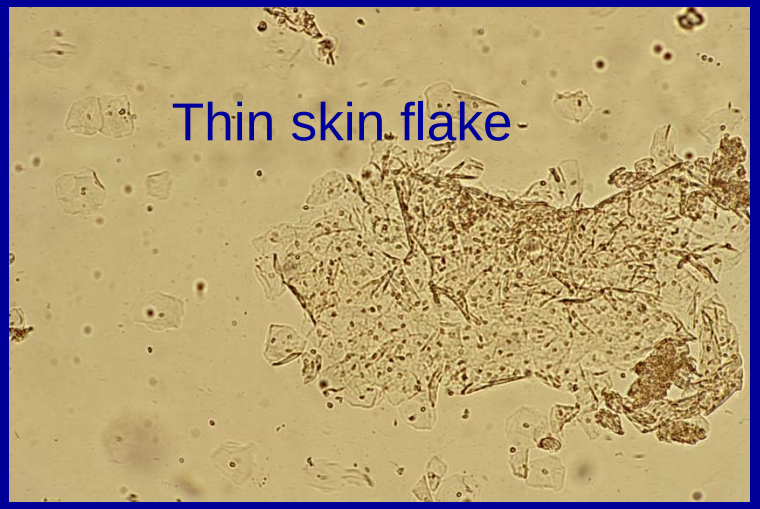
Irritants and allergens cause intradermal spongiosis leading to flakes of epithelium in the saline wet prep and “reactive change” in the pap smear

This further compromises the vulvar skin barrier


"Papular" Vulvovaginal Skin Disorders are Evident in the Saline Wet Prep
Skin flake probably due to spongiosis or lichinification
Vulvovaginal irritant and allergic response causes the skin to flake, as is seen frequently in the saline wet prep

Skin Flakes in the Wet Prep





Skin Flakes

- Normal healthy skin exfoliates individual epithelial cells
- Flaking skin is common
- Skin flakes are called “reactive change” when seen in the pap smear
- Skin flakes are found frequently in the saline wet prep
- Unfortunately, flakes are not yet listed as an element to evaluate in the saline wet prep

Skin Flakes in the Pap Smear

- Reactive, Reparative changes are reported occasionally in pap smears

- Characteristic of smears with reactive/reparative changes:

  1. cells tend to form sheets (Alexander Meisels, Carol Morin Cytopathology of the UterusASCP Press 1997:128)

  2. spongiosis is a prominent feature if the cervix is biopsied (Yao S. Fu, Pathology of the Uterine Cervix, Vagina and Vulva Saunders 2002:281)

Contact Dermatitis

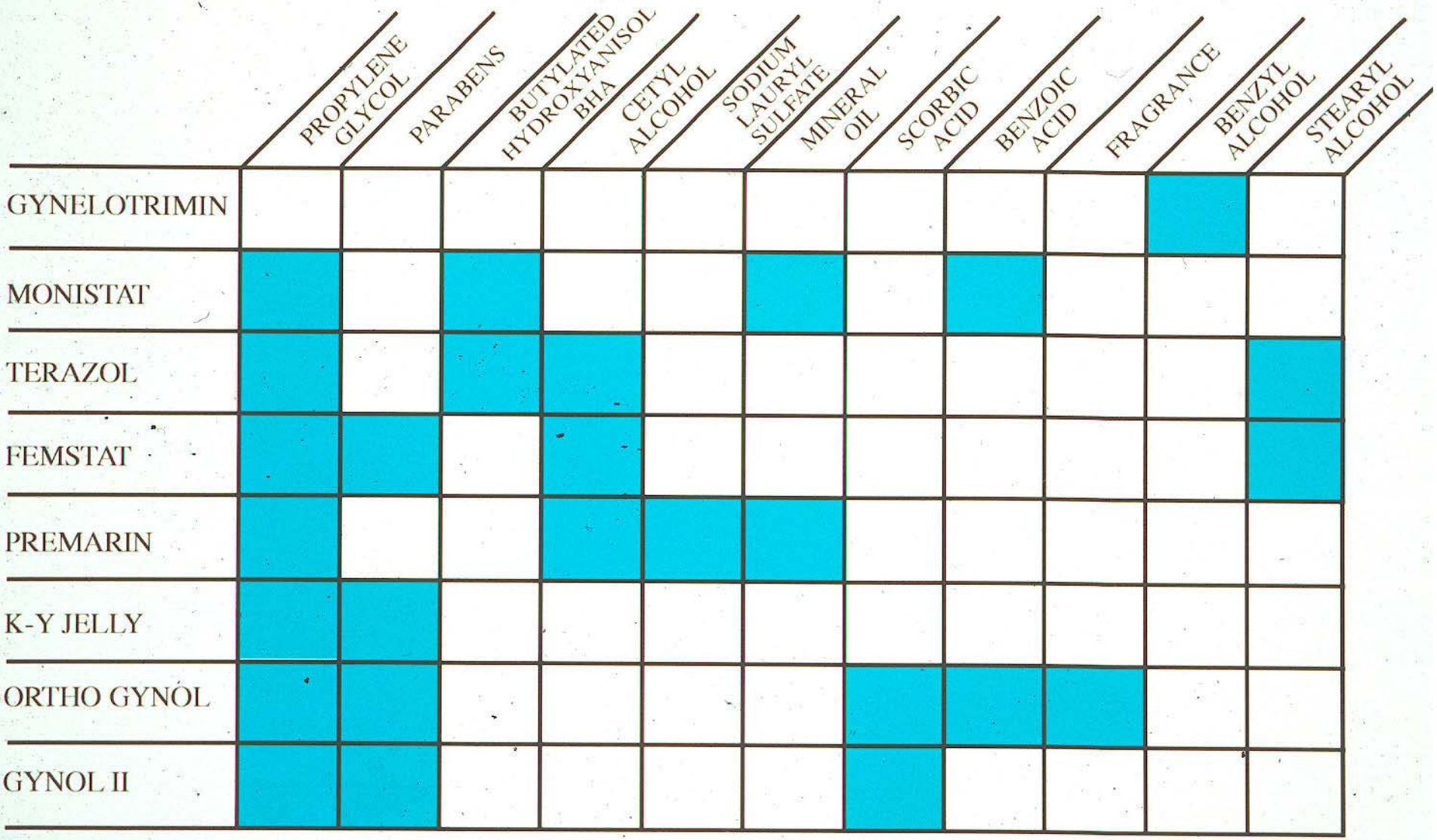
- Affects 40% of adults continuously
- All adults will have contact dermatitis at some time
- Vulva is at special risk (fragile, increased trans epidermal water loss)
- Irritants burn and have an all or none effect
- Allergy itches and has a graduated effect
- Results in ***flaking skin***, even in the vulvovaginal area
- Vulvar skin is predisposed to contact dermatitis

Irritant Dermatitis

- Irritants cause immediate or delayed burning
- Typically, there is no visible skin change
- Erythema is present in severe cases
- Microtrauma is different for each irritant
- Most commercial creams and lotions contain irritants

IRRITANTS IN COMMERCIAL PREPARATIONS

(blue squares)



Sensitivity to one environmental stimulus is not predictive of susceptibility to any other

Patch testing by a dermatologist can be helpful

Nickel sensitivity?

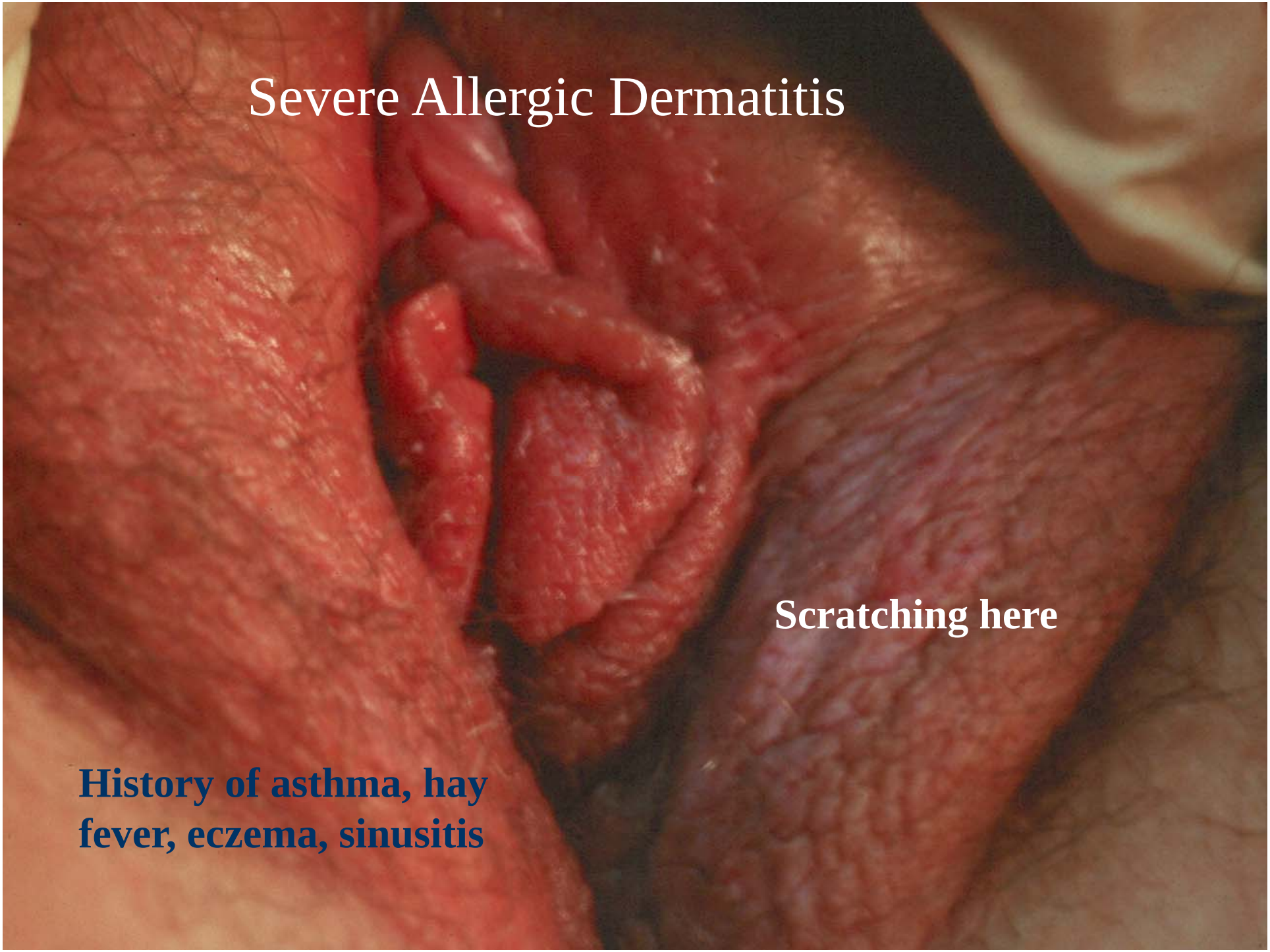
Marriott M, Holmes J, Peters L, Cooper K, Rowson M, Basketter DA. The complex problem of sensitive skin. Contact Dermatitis 2005;53:93-9

Therapy for Irritant Vulvitis

- Make the diagnosis (history of burning)
- Avoid irritants (soap, creams, urine, etc.)
- No panty liners
- Rinse with distilled water, then blot dry instead of using toilet paper (urine contains oxylate, which is irritating)
- Moisturize twice daily with non-irritating oil-based ointment

Allergic Contact Dermatitis

- Itch-scratch cycle perpetuates the disorder
- All of the patient's skin and mucosa has an atopic tendency
- Vulvar hypertrophic dystrophy or lichen simplex
- The majority also have recurrent sinusitis, asthma, hay fever, or eczema
- Diagnosis is confirmed by hyperkeratosis, spongiosis and eosinophils on biopsy


Severe Allergic Dermatitis
Scratching here
History of asthma, hay fever, eczema, sinusitis

- Vulvar contact dermatitis was the principal diagnosis in 54% of 141 patients referred to a dermatologist for chronic vulvovaginitis

Fischer GO, The Commonest Causes of Symptomatic Vulvar Disease: a Dermatologist's Perspective. *Australias J Dermatol*. 1996;37:12-18

- 38% of women with chronic vulvitis demonstrate an irritant or allergic response to vaginal creams and medications

Nardelli A, Degreff H, Goossens A. Contact Allergic Reactions of the Vulva: a 14-year Review. Dermatitis. 2004;15:131-6

Therapy for Vulvar Allergic Dermatitis

- Avoid allergens (and irritants)
- Topical corticosteroid ointment
- Moisturize with oil
- Antihistamine
- Consider the long-term risk of squamous cancer if not treated, or if no response to therapy (normal Th1 response is cancer surveillance as well)
- Oral yeast therapy for superimposed infection

Products to moisturize

- Lipocream (generic base used for compounding)
- Eletone Cream
- Epiceram
- Emulsion SB
- Cetaphil Cream
- Cerave Cream
- Vaseline
- Crisco
- Coconut oil

What helps one patient may irritate another – a highly individual response

Vulvar Contact Dermatitis Risks

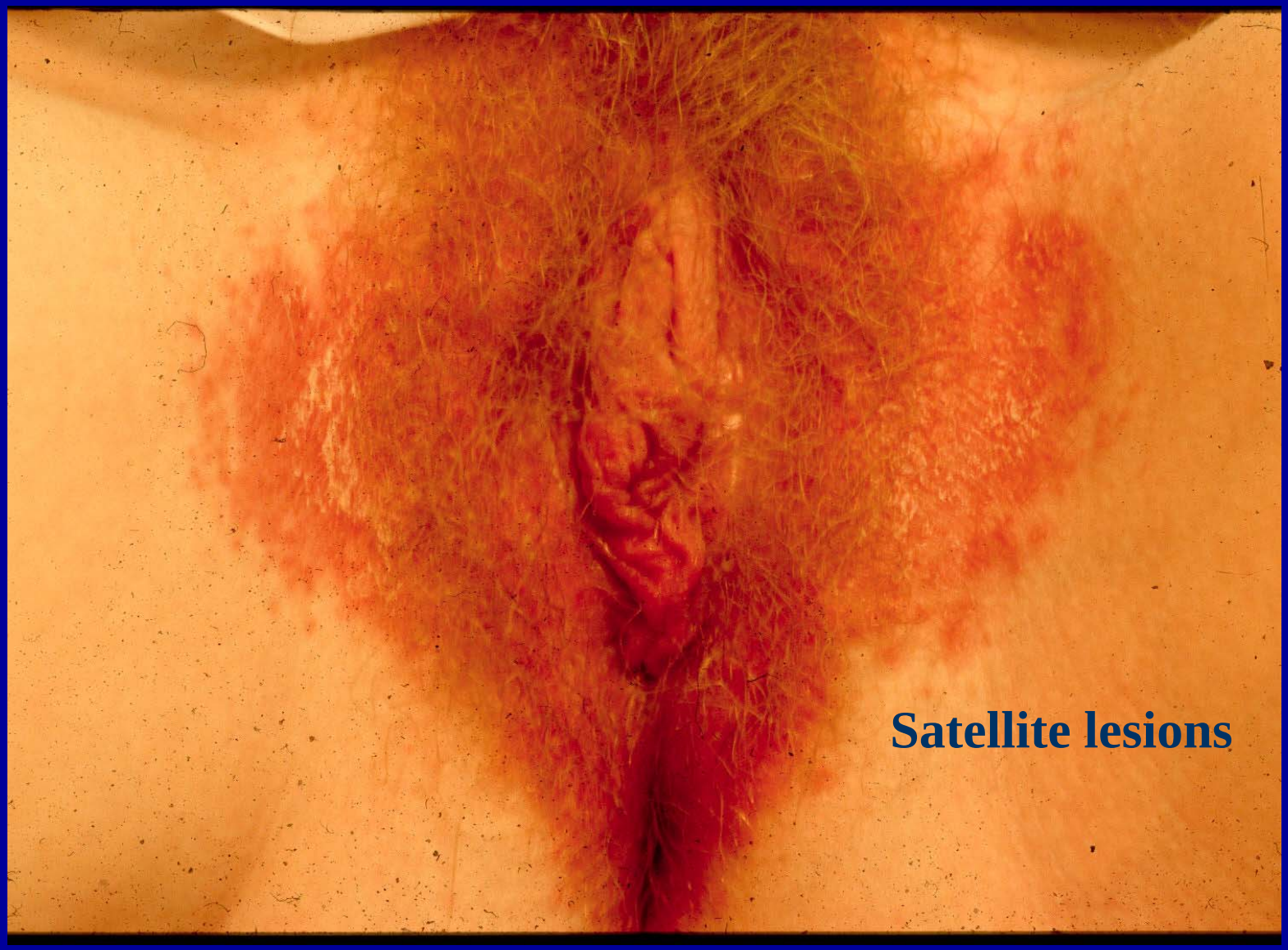
- Yeast infection
- Staph or strep infection
- Squamous cancer

Allergic Vulvar Dermatitis with Recurrent Yeast Infection

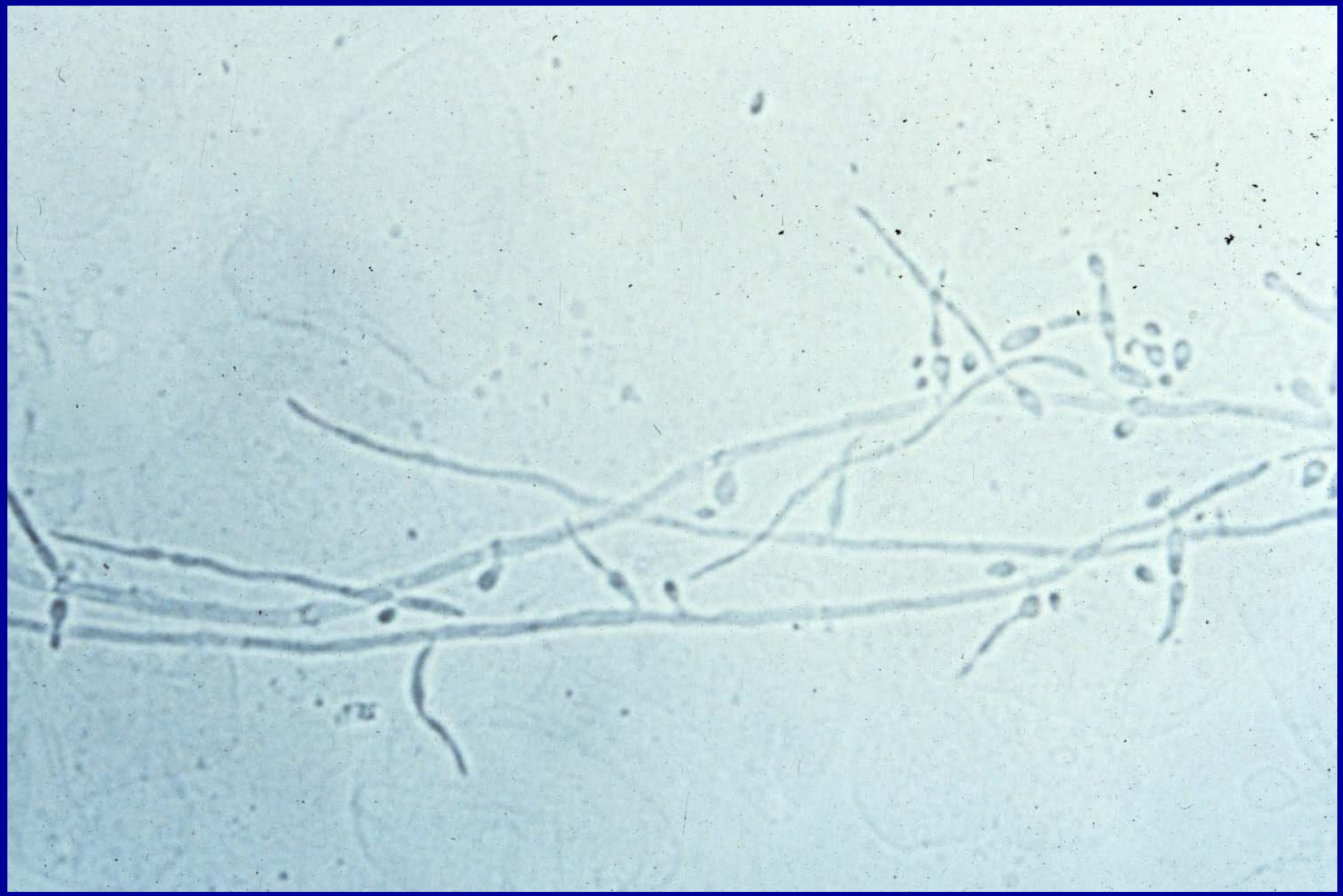
Yeast organisms in the skin release acid protease that further promotes the Spongiotic change

- Perpetuates the infection
- Contributes to an environment that favors re-infection after anti-yeast therapy

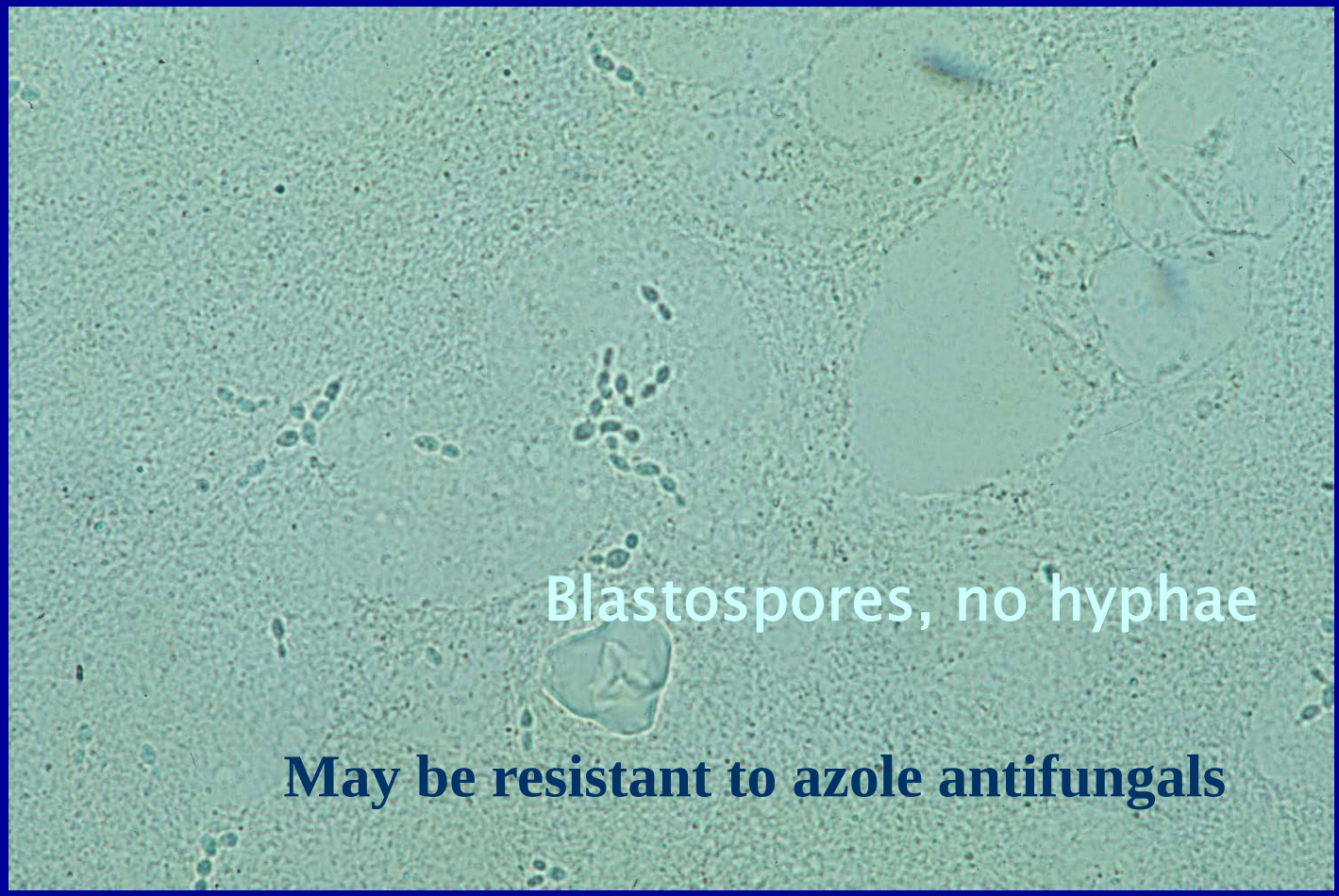
Severe Yeast

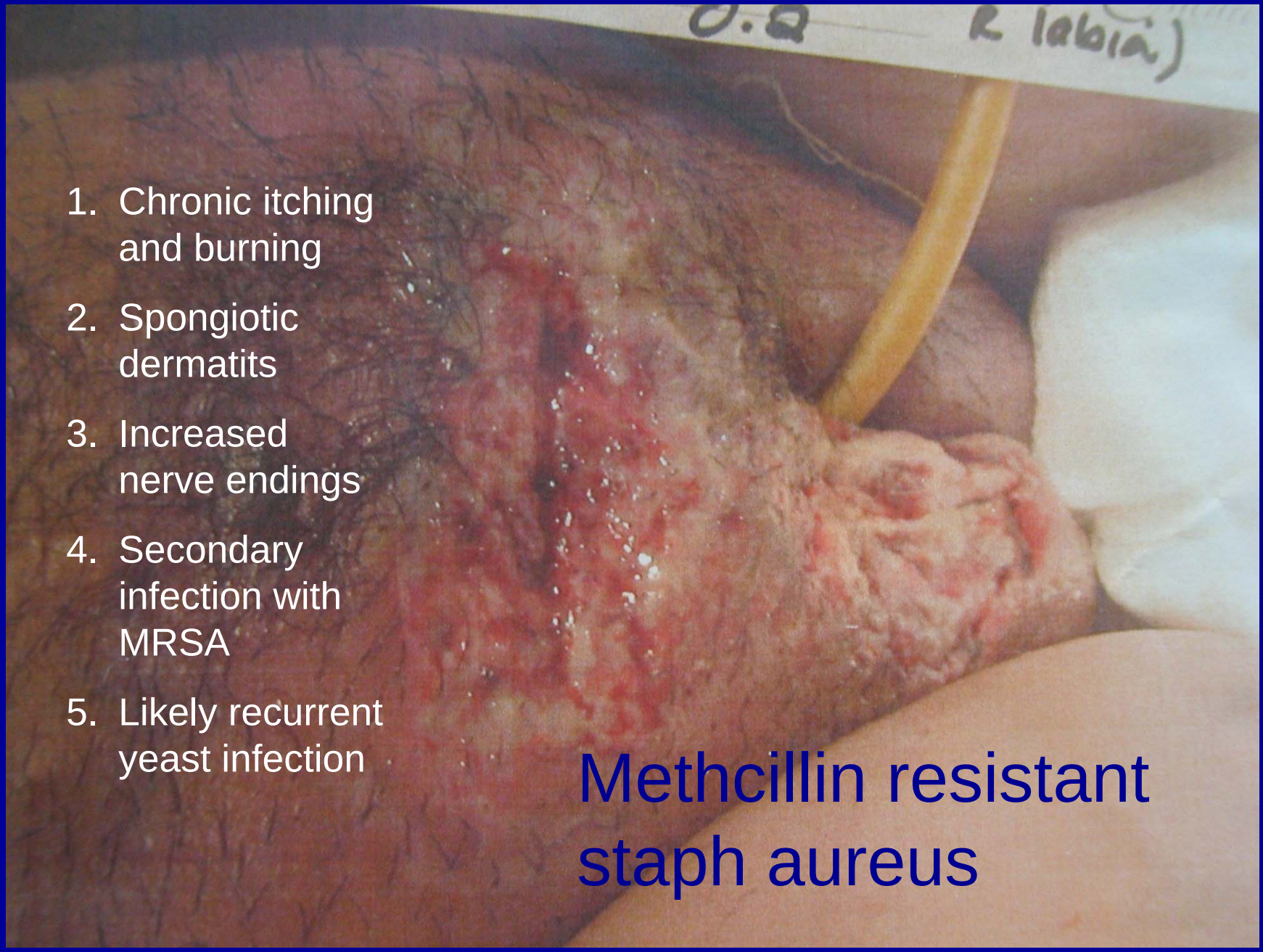


Candida albicans



Non-albicans Yeast

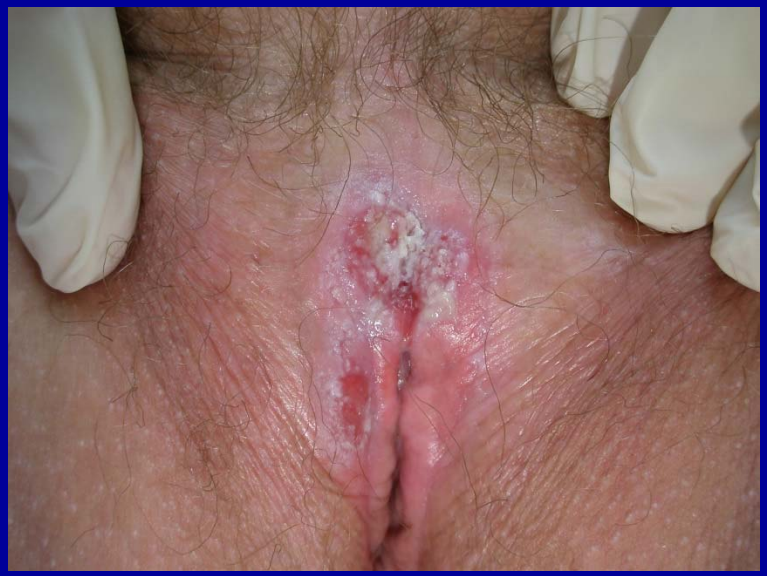


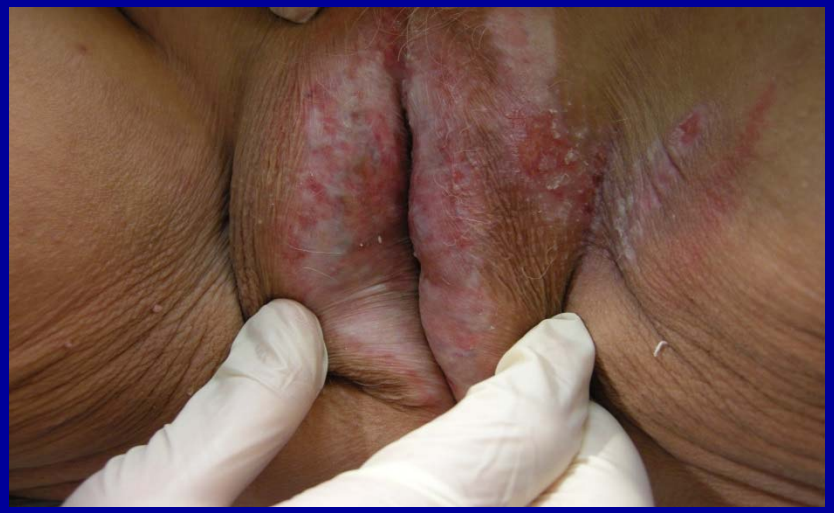


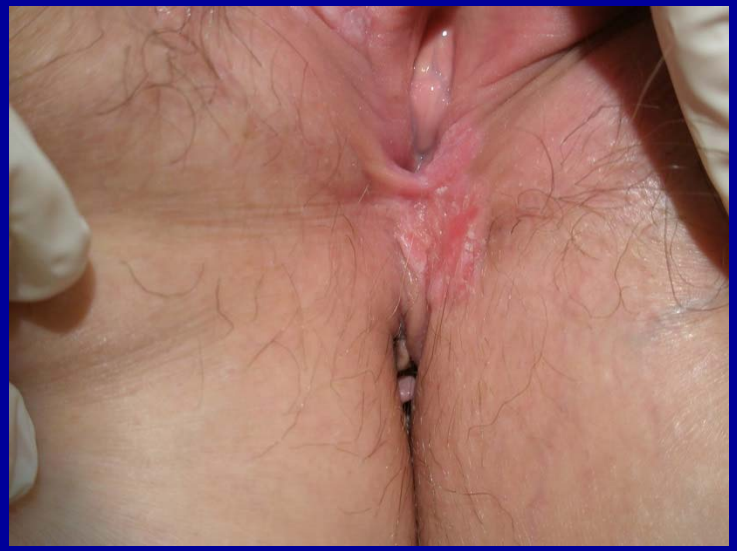
1. Chronic itching and burning
2. Spongiotic dermatits
3. Increased nerve endings
4. Secondary infection with MRSA
5. Likely recurrent yeast infection

Methcillin resistant staph aureus

Vulvar Carcinoma







Nerve Growth Factor

Nerve Growth Factor

- Discovered in 1950's by Levi-Montalcini and Cohen at Washington University in St. Louis
- Nobel Prize in Medicine / Physiology in 1986
- Present in seminal fluid and stimulates ovulation in some animals
- Main role is to maintain nerves fibers and to regenerate damaged nerves
- May be found to have a therapeutic role in neuro-degenerative disorders
- Induced by prostaglandins
- Unfortunately causes new nerve endings to sprout if inflammation is chronic, such as in endometriosis
- This leads to progressively more sensitive skin in cases of chronic vulvitis

Nerve proliferation with chronic Inflammation

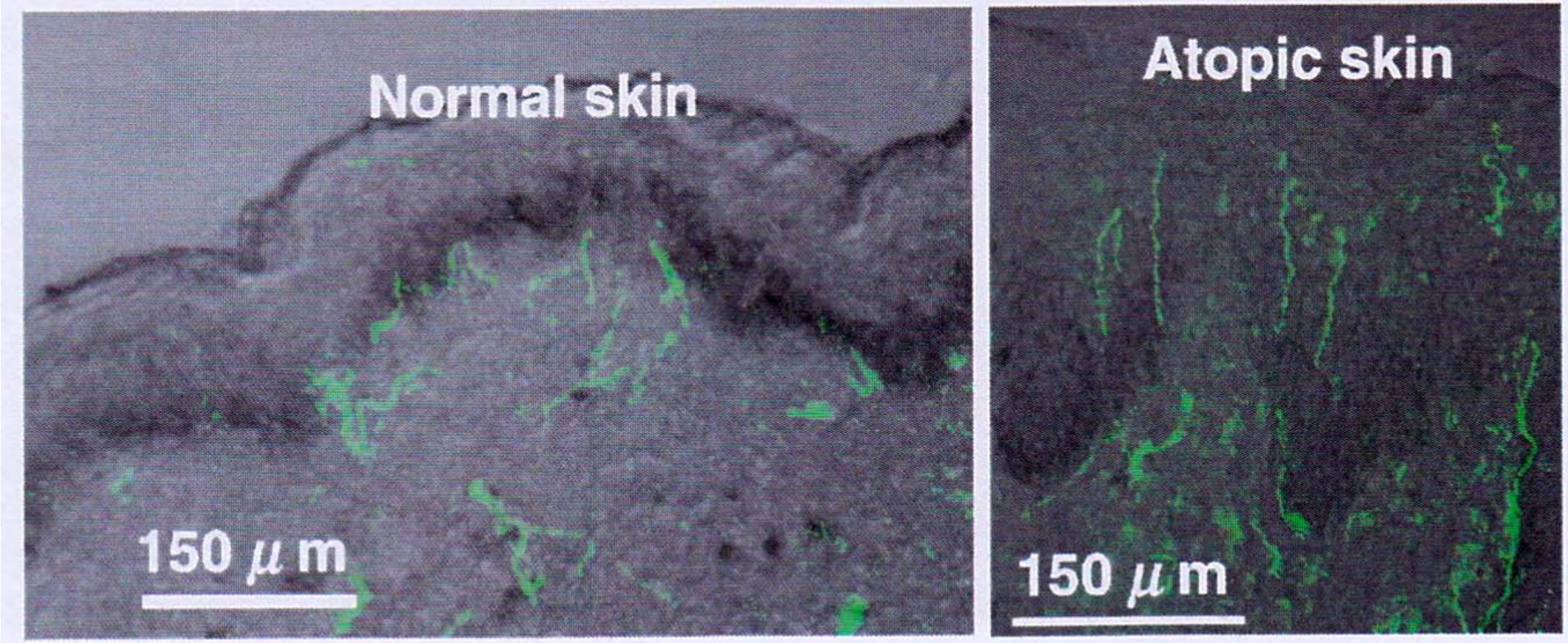


Figure from Misery, Staender. Pruritus Springer 2010 p. 4

Proliferation of nerve endings causes ***progressively*** increased skin sensitivity in spongiotic dermatitis (eczema)

a common vulvar problem

Bentley FR. Non-specific irritant reactions in eczematous subjects. Br J Dermatol 1964;76:116

Nerve Proliferation in "Vulvar Vestibulitis"

- Bohm-Starke N, Hilliges M, Falconer C, Rylander E. **Increased intraepithelial innervation in Women with vulvar vestibulitis syndrome**. *Gynecol Obstet Invest* 1998;46:256-60

- Westrom LV, Willen R. **Vestibular nerve fiber proliferation in vulvar vestibulitis syndrome**. *Obstet gynecol* 1998;91:572-6

- Bohm-Starke N, Hilliges M, Falconer C, Rylander E. **Neurochemical characterization of the vestibular nerves in women with vulvar vestibulitis syndrome**. *Gynecol Obstet Invest* 1999;48:270-5

Menopause and Vulvar Tissue

- Atrophy—loss of normal thickness
- Rise in vulvovaginal skin surface pH
- Decline in metabolism
- Slower healing
- Loss of intercellular lipids
- Decline in immune competence
- Decline in barrier function

- Decline in spongiotic dermatitis unless estrogen is administered

What Persists after Menopause

- High transepidermal water loss, poor barrier function
- High friction coefficient related to high moisture content of the skin
- Constant irritant, allergen, and mechanical abrasion exposure
- Any dermatologic disease like lichen sclerosus

Vulvar Treatment Concepts

- Moisturize and avoid irritants to correct barrier compromise
- Neurontin and analgesics for hypersensitive nerve reception
- Anti-inflammatory steroids for intradermal inflammation

Itching and Burning Summary

- The vulvovaginal area is normally a high risk location
- Secondary infection or a skin disorder further compromises the skin barrier
- Chronicity amplifies the problem through continued release of Nerve Growth Factor

Itching and Burning Summary

- Consider a biopsy to be sent to Dermatopathology
- Consider secondary yeast or bacterial infection
- Irritant avoidance, and compound anti-inflammatories, anti-infectives rather than commercial products

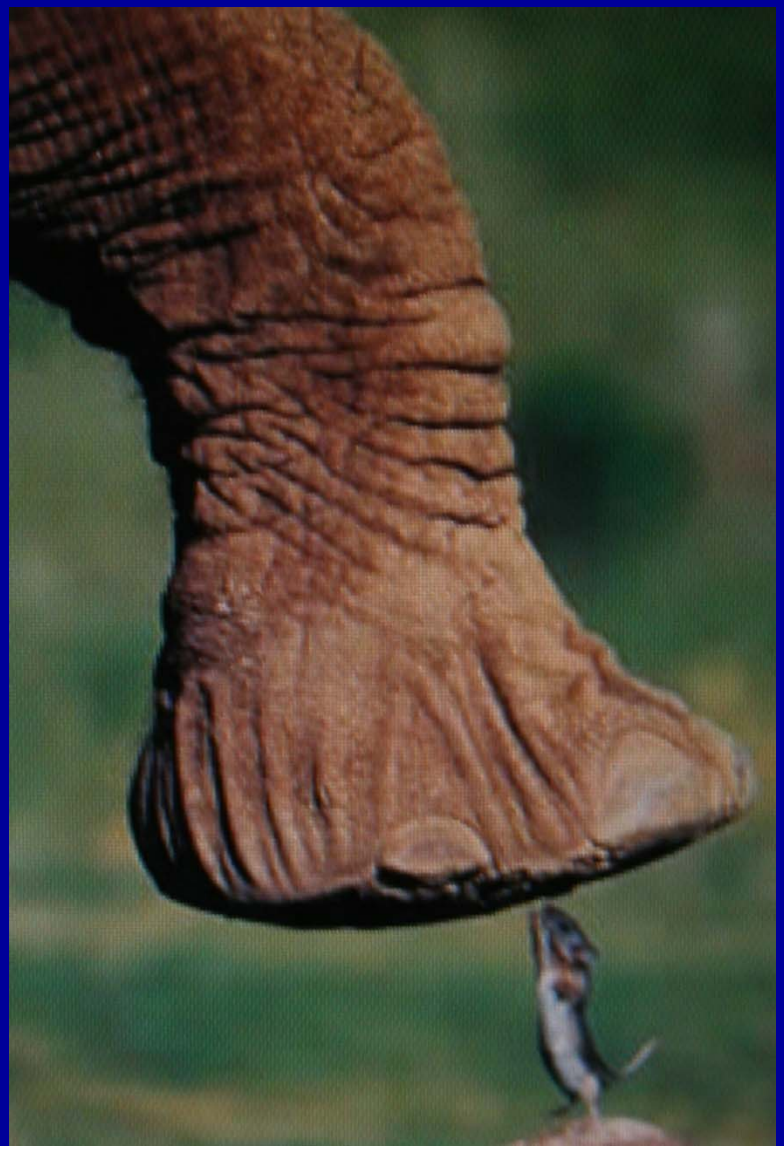
Chronic Vulvovaginitis: Several Levels of Possible Investigation

- 1. Symptoms, Clinical findings
- 2. Wet Prep, Culture for Microbes

******Clinical interest generally stops here******

- 3. Known dermatology (history and exam)
- ***4. Patch testing by a dermatologist***
- 5. Biopsy ***(dermatopathology)***
- ***6. Colposcopy, contact microscopy***
- 7. Molecular markers, cytokines, immunology
- 8. Genetic markers, alleles

The Skin Physiology vs. the Microbe



The End