Genital Ulcers

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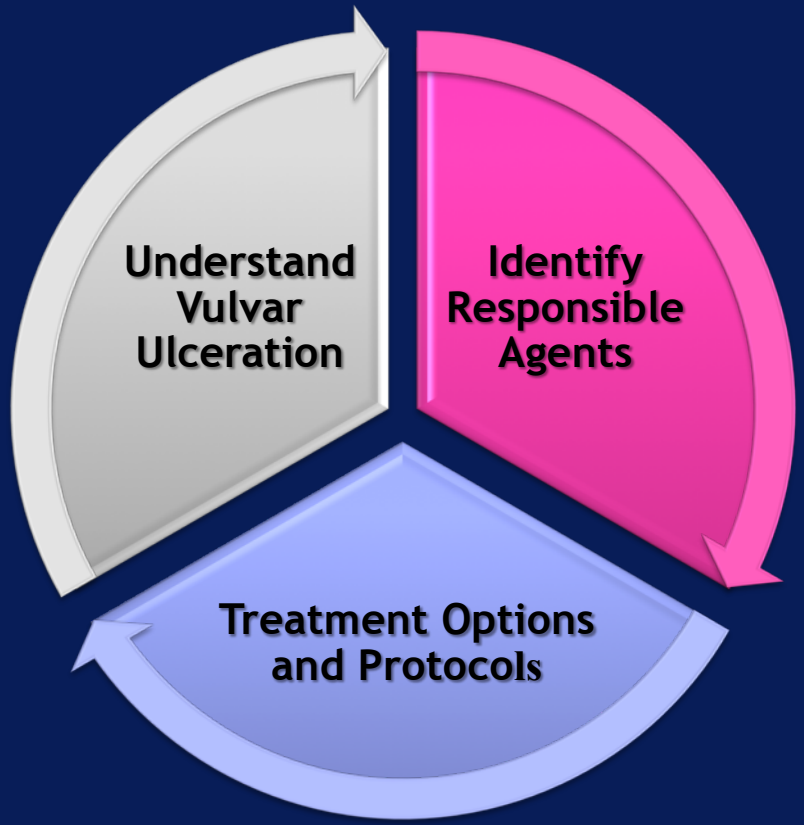
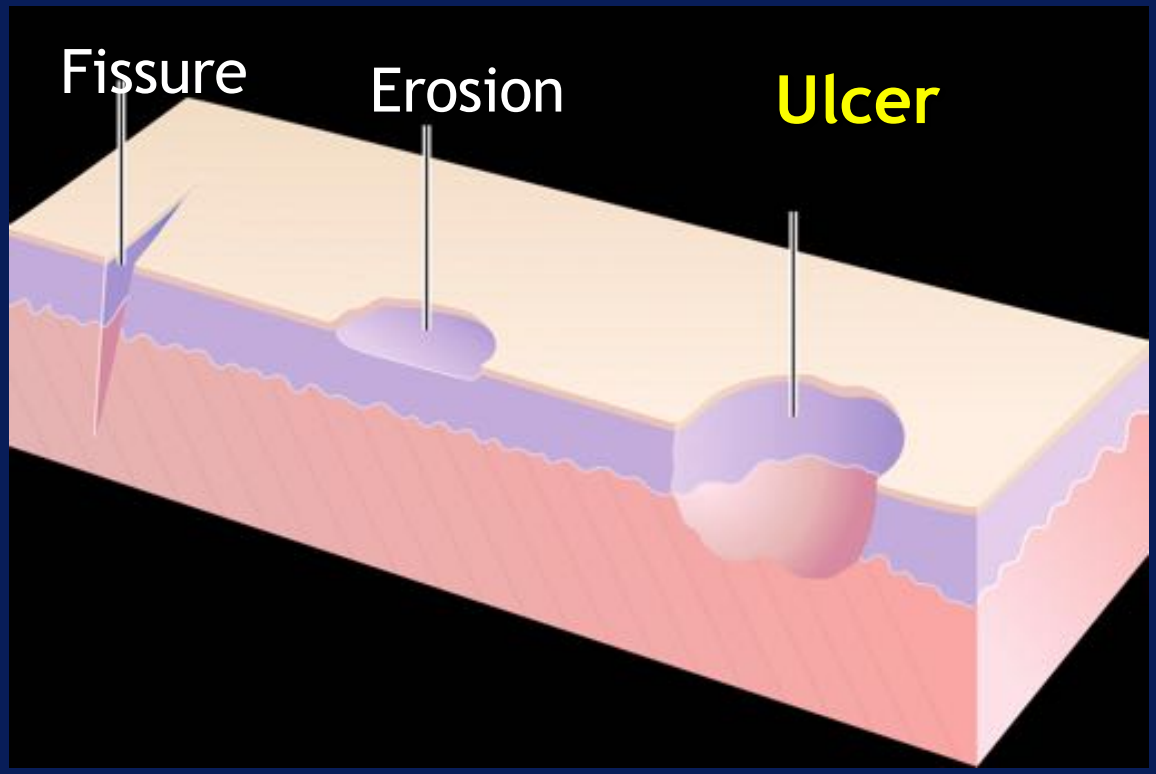
Disclosure – UpToDate author

Objectives


Understand Vulvar Ulceration
Identify Responsible Agents
Treatment Options and Protocols

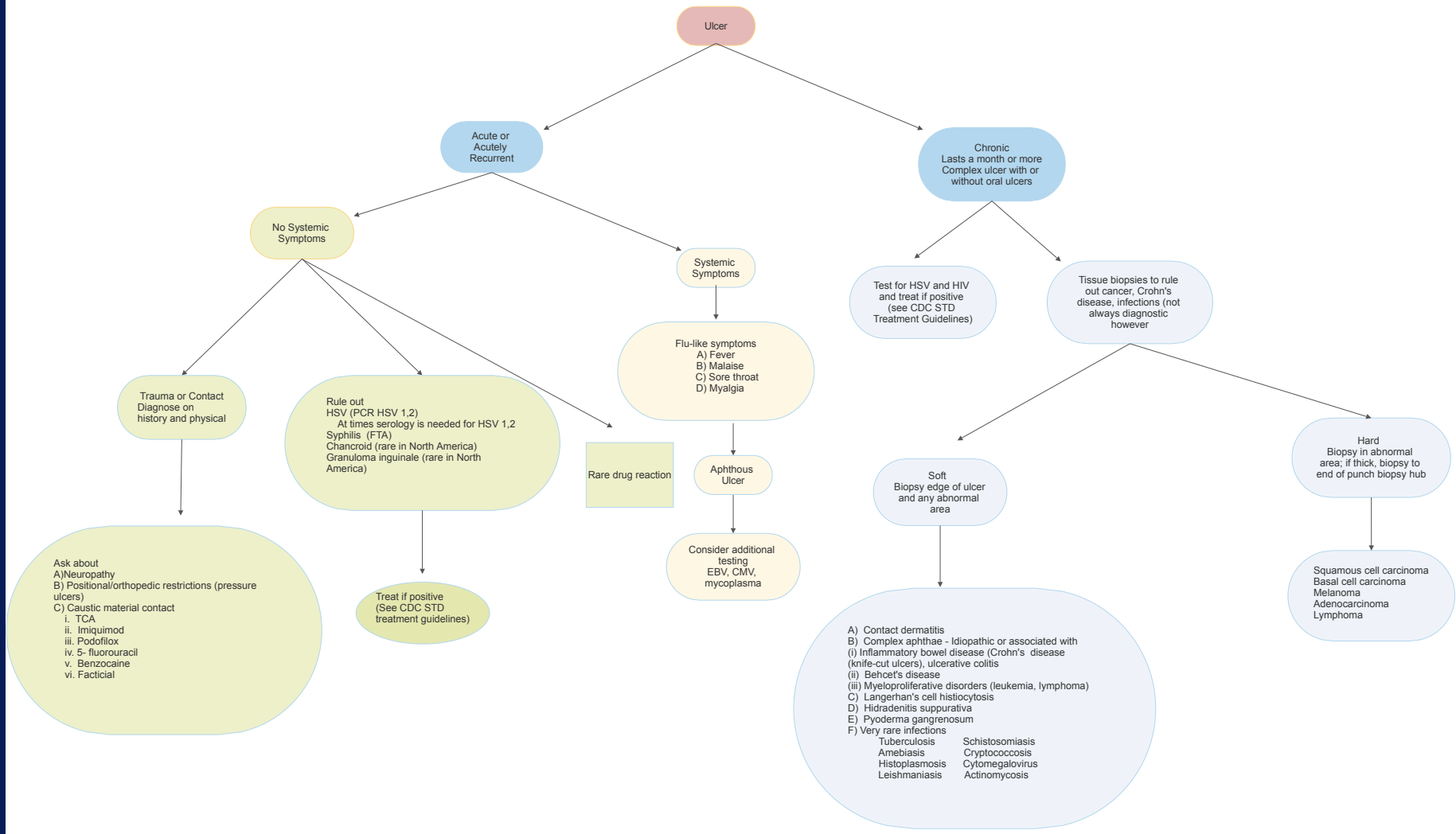
Erosions and Ulcers: Understanding the Difference

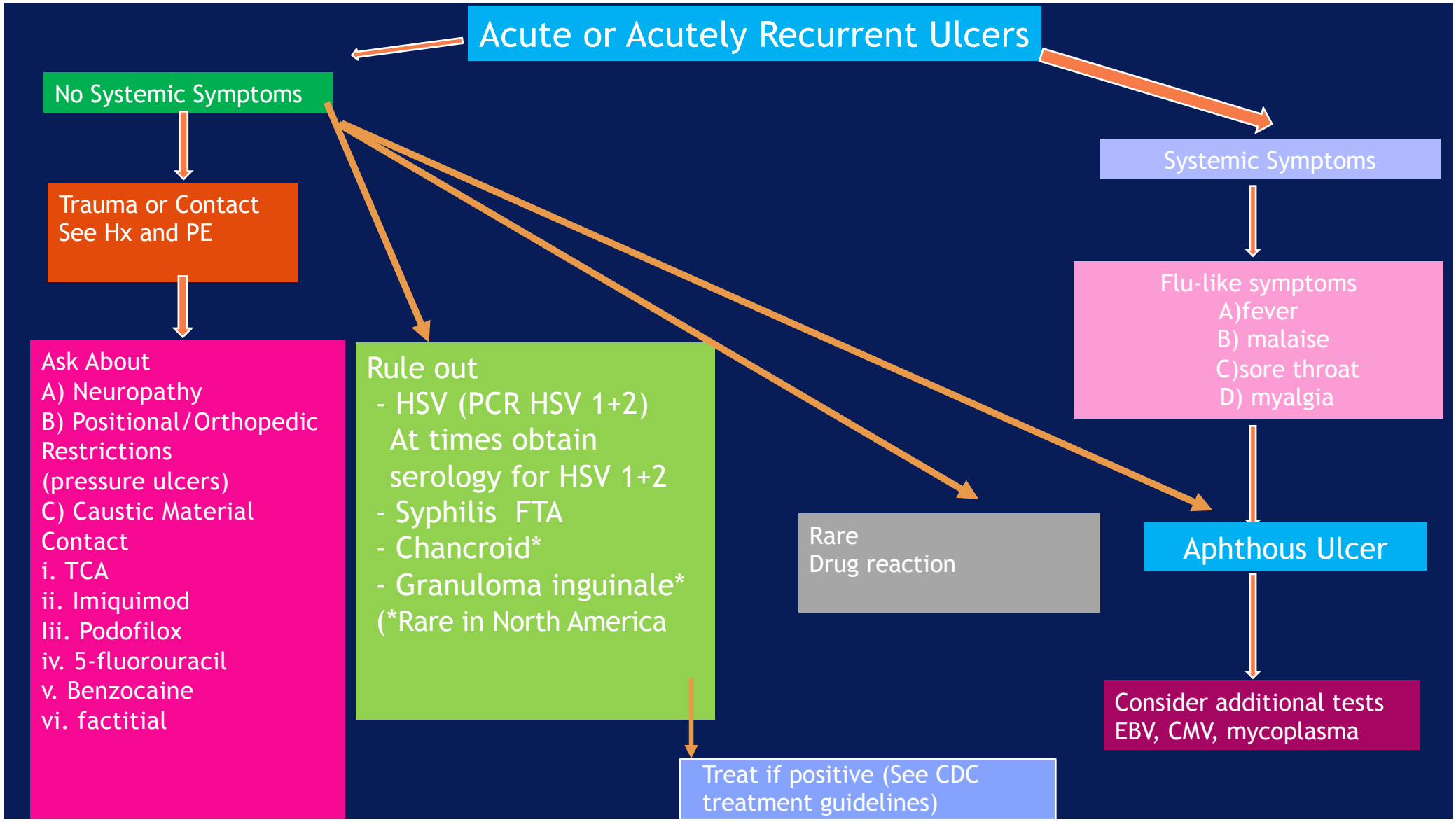


Erosions Vs. Ulcers

Ulcers are Difficult!

- Many different causes
- Vary by age, geography, ethnicity
- Often nonspecific appearance
- No overarching etiology
- Relatively rare


Ulcer
Acute or Acutely Recurrent
Chronic Lasts a month or more Complex ulcer with or without oral ulcers
No Systemic Symptoms
Systemic Symptoms
Test for HSV and HIV and treat if positive (see CDC STD Treatment Guidelines)
Tissue biopsies to rule out cancer, Crohn's disease, infections (not always diagnostic however
Trauma or Contact Diagnose on history and physical
Rule out HSV (PCR HSV 1,2) At times serology is needed for HSV 1,2 Syphilis (FTA) Chancroid (rare in North America) Granuloma inguinale (rare in North America)
Rare drug reaction
Flu-like symptoms A) Fever B) Malaise C) Sore throat D) Myalgia
Aphthous Ulcer
Soft Biopsy edge of ulcer and any abnormal area
Hard Biopsy in abnormal area; if thick, biopsy to end of punch biopsy hub
Ask about A)Neuropathy B) Positional/orthopedic restrictions (pressure ulcers) C) Caustic material contact i. TCA ii. Imiquimod iii. Podofilox iv. 5- fluorouracil v. Benzocaine vi. Factical
Treat if positive (See CDC STD treatment guidelines)
Consider additional testing EBV, CMV, mycoplasma
A) Contact dermatitis B) Complex aphthae - Idiopathic or associated with (i) Inflammatory bowel disease (Crohn's disease (knife-cut ulcers), ulcerative colitis (ii) Behcet's disease (iii) Myeloproliferative disorders (leukemia, lymphoma) C) Langerhan's cell histiocytosis D) Hidradenitis suppurativa E) Pyoderma gangrenosum F) Very rare infections Tuberculosis Amebiasis Histoplasmosis Leishmaniasis Schistosomiasis Cryptococcosis Cytomegalovirus Actinomycosis
Squamous cell carcinoma Basal cell carcinoma Melanoma Adenocarcinoma Lymphoma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At times obtain serology for HSV 1+2
- Syphilis FTA
- Chancroid*
- Granuloma inguinale*
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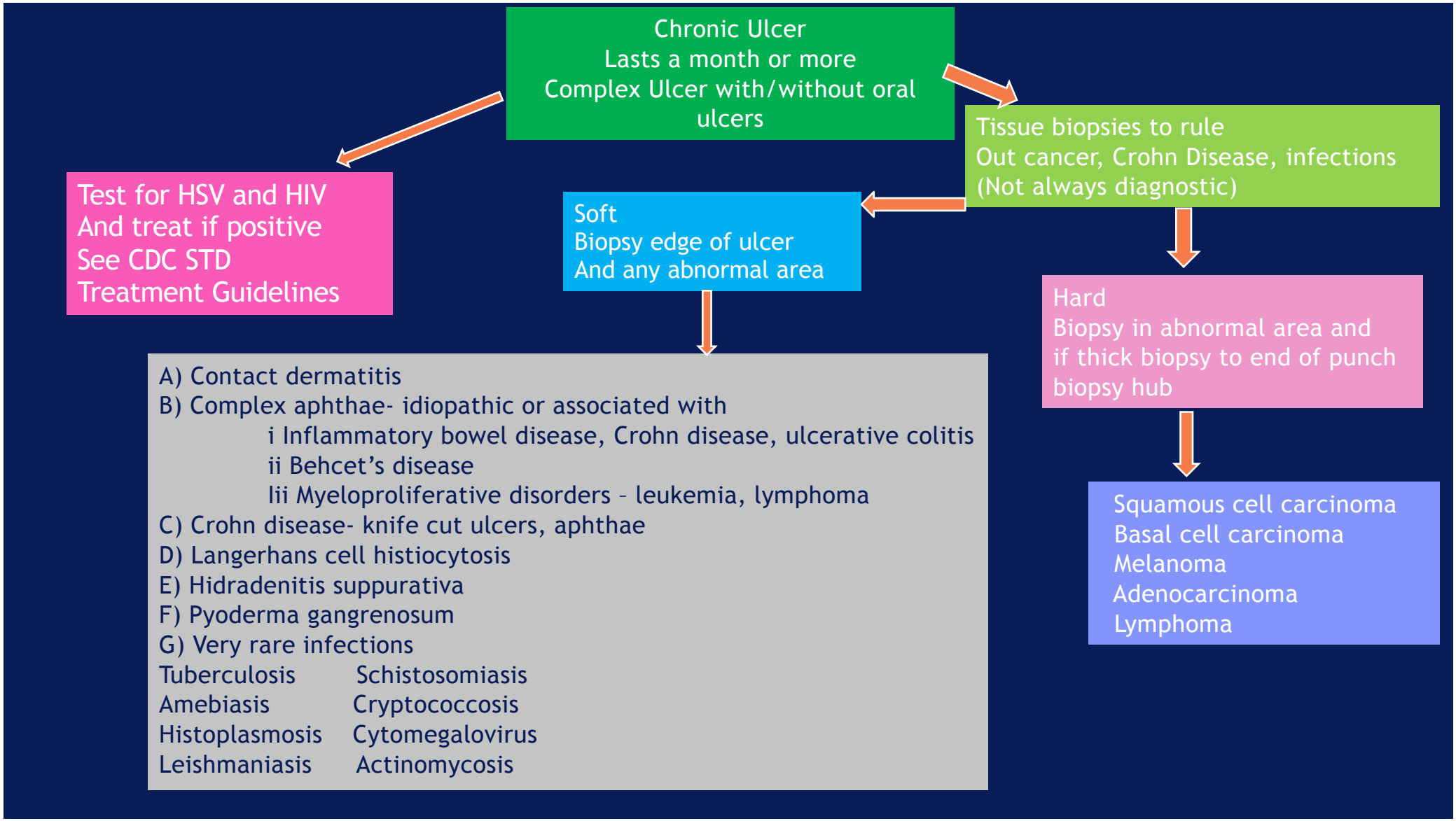
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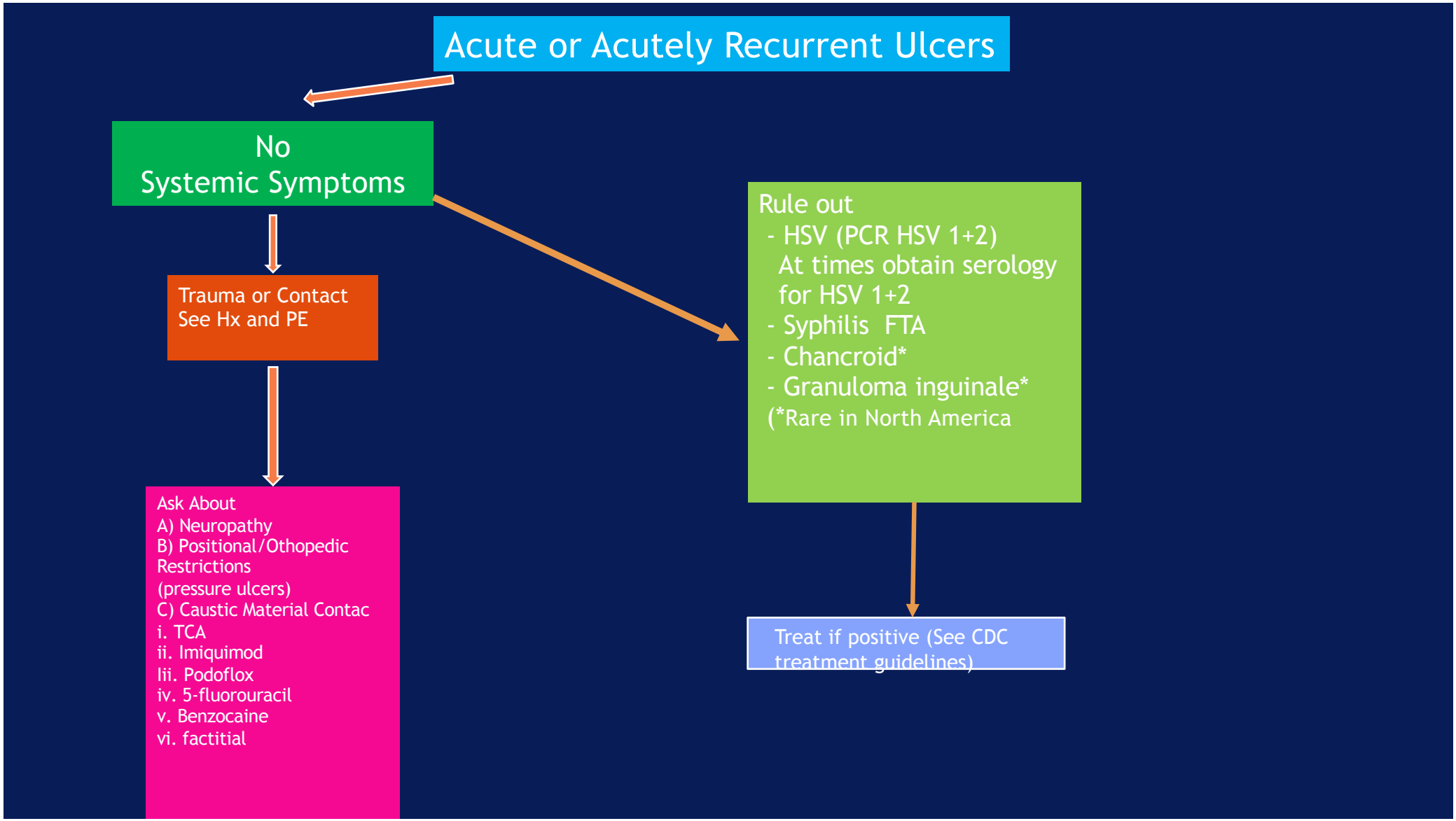
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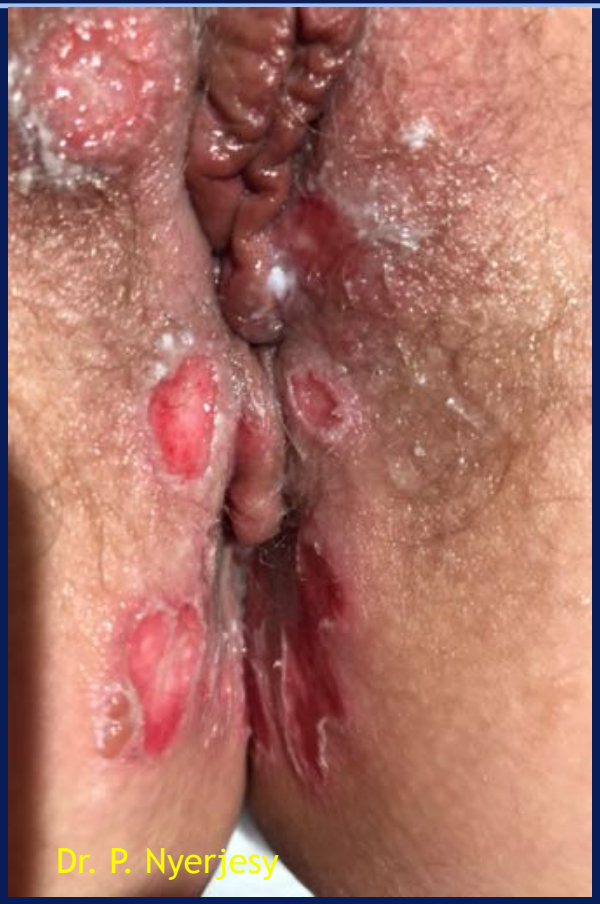
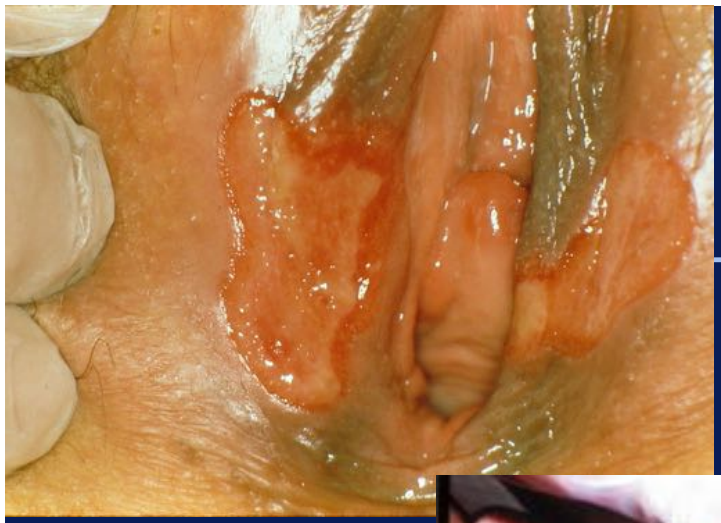
Herpes Simplex Virus (HSV) in the Immunocompromised



- Most common cause of vulvar ulcers – acute or chronic
- Typical HSV is an erosion
- If an ulcer - usually painful, non-healing, chronic ulcers
- Reactivation of pre-existing disease
- Diagnosis by – PCR , at times serology ,see CDC



Syphilis

Treponema Pallidum

Chancre: painless ulcer of Primary Syphilis

- Increasing all over the world
- 150% increase in women 2011-2017
- Related to drug use
- Multiple ulcers can be seen
- Can be painful
- Increase in congenital syphilis

- >30,000 cases in 2017(USA) an increase of 20 % in 1 year mostly in men

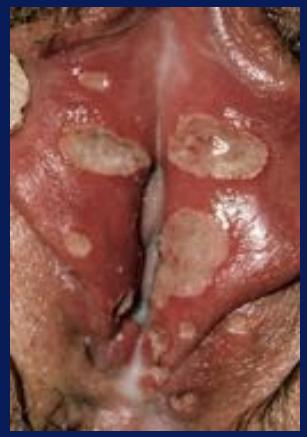
Syphilis - Diagnosis -
check testing protocol in your area

- For primary syphilis –
  Non-Treponemal tests - RPR and VDRL (prozone level) or
  Treponemal specific testing:
  - Enzyme-immunoassays (EIAs)
  - Chemiluminescence immunoassay (CIA)
  - Treponema pallidum particle agglutination (TP-PA)

- Early in the course of disease (e.g. ulcer), serologic testing and immunoassays may be negative

- If high clinical suspicion give presumptive treatment and repeat serologic testing in two to four weeks

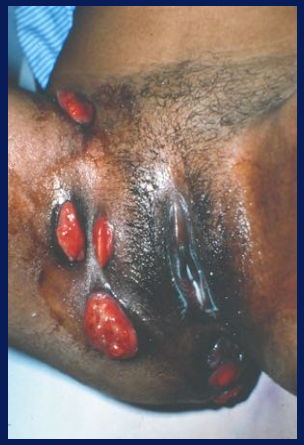
Chancroid



No cases USA

Haemophilus ducreyi

Granuloma Inguinale



-100 cases/yr males USA

-Knife-cut ulcers

Klebsiella granulomatosis

Lymphogranuloma Venereum

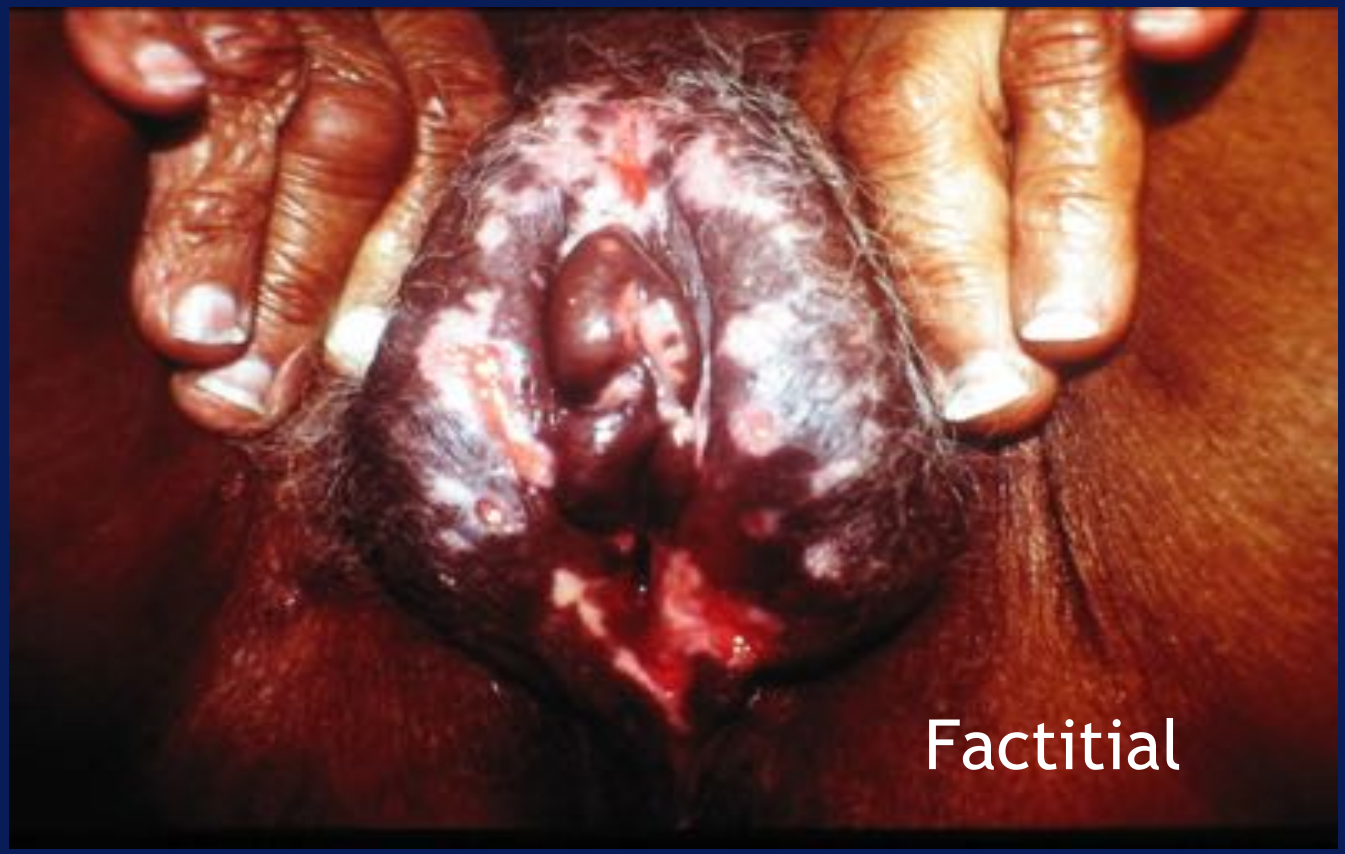
Very Rare

3 types (serovars) of Chlamydia trachomatis

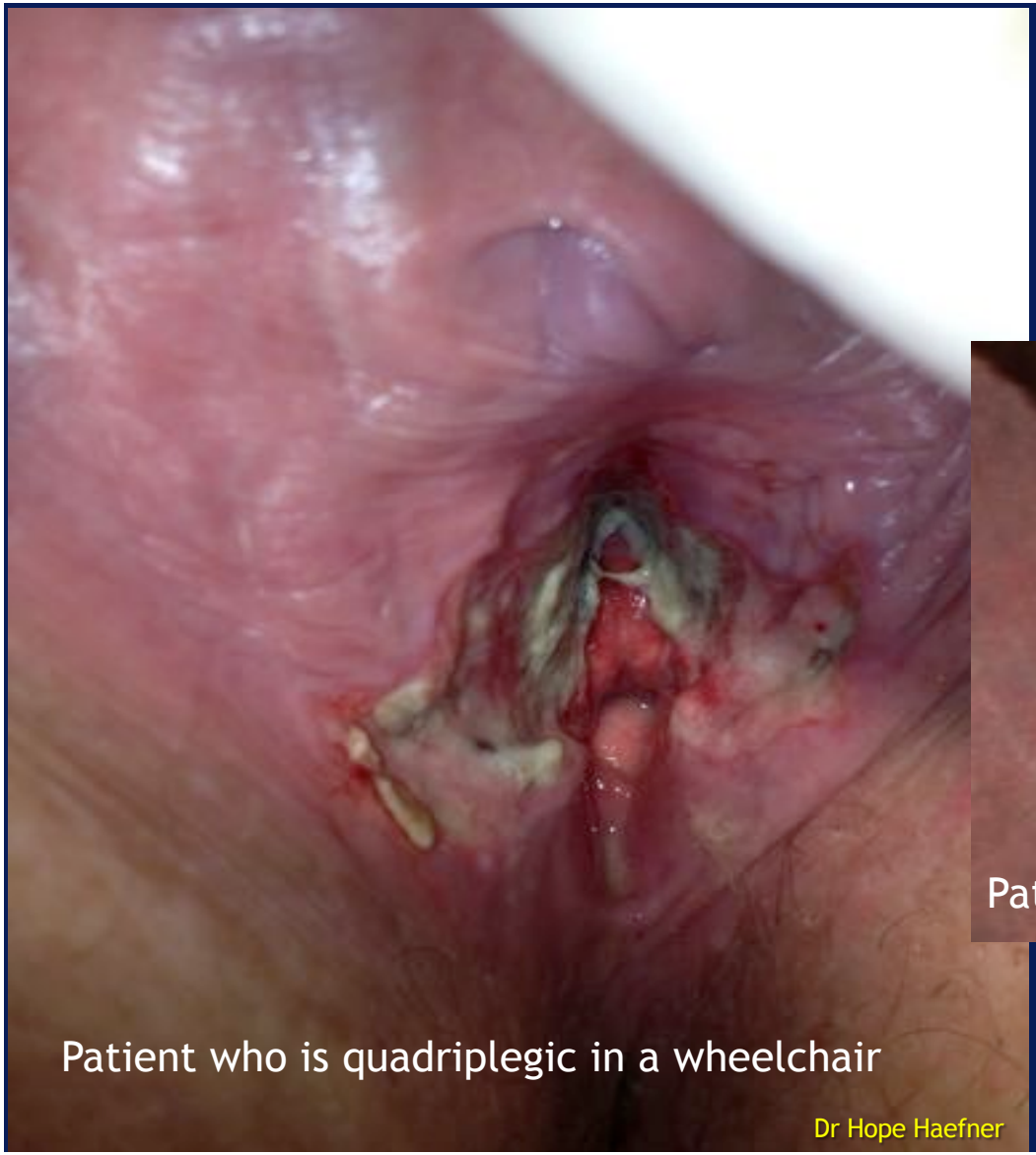
All Extremely Rare in North America

TRAUMA

Blunt / sharp
Factitial
Chemical
Mechanical
Physical heat



Pressure Ulcers:
Between clitoris and urethra



Patient who is quadriplegic in a wheelchair

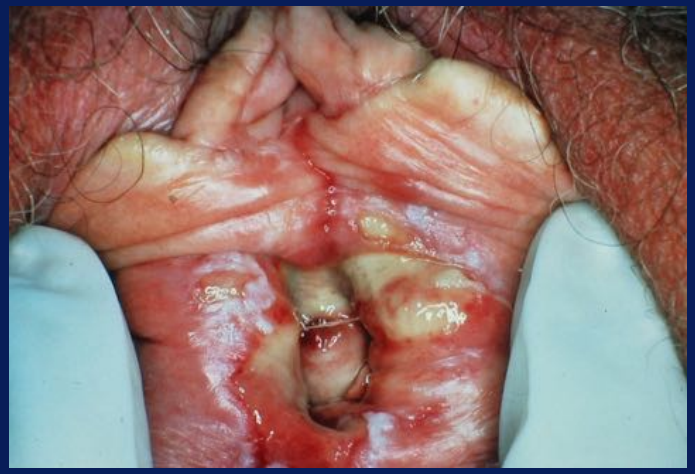
Dr Hope Haefner

Patient with Amyotrophic Lateral Sclerosis

Dr A Lev-Sagie

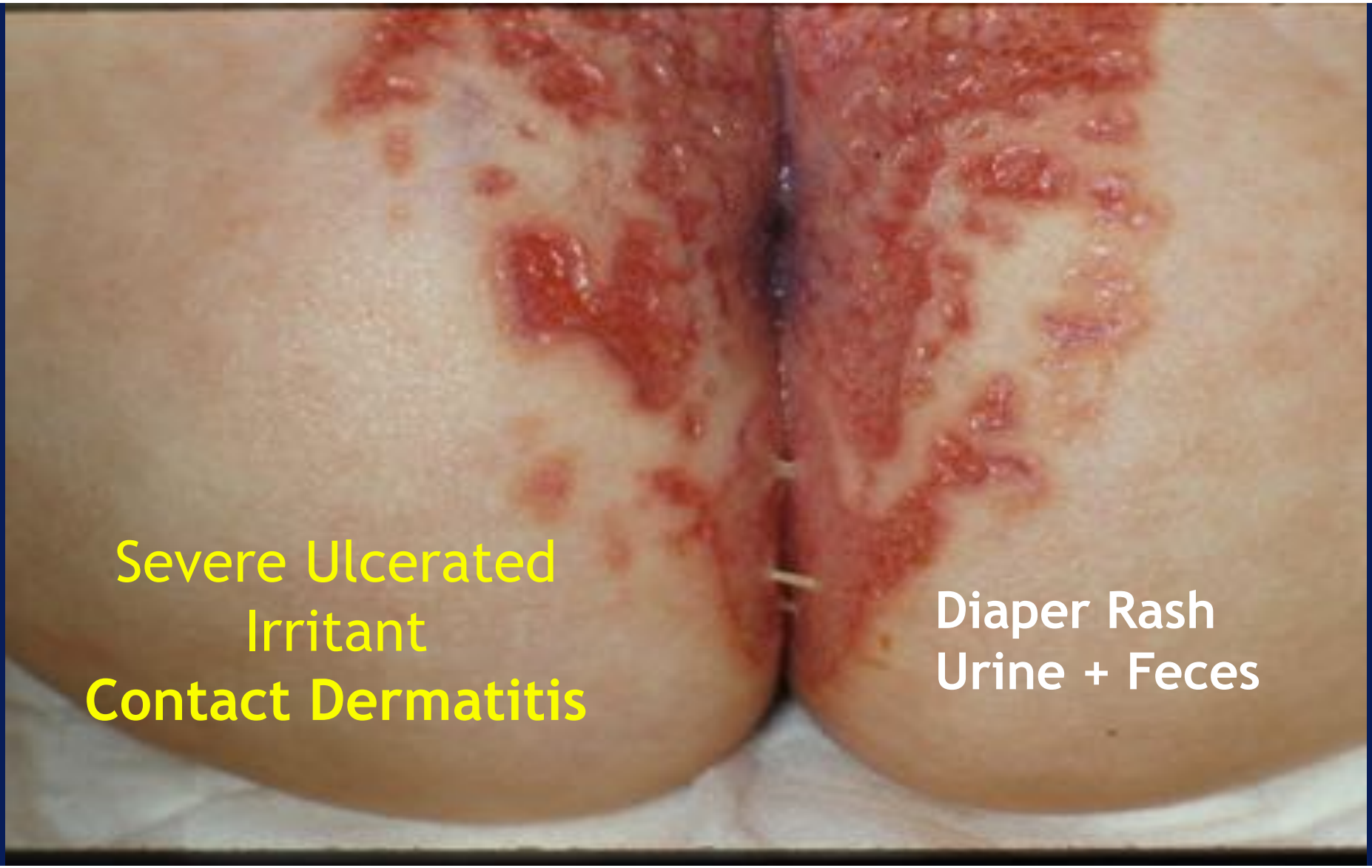
Common Erosive Vulvar Conditions Ulcerates with Trauma or Cancer

Contact Dermatitis
Lichen planus
Lichen Sclerosus



LS Sexual Trauma

Any genital lesion can ulcerate from trauma like scratching , picking or from cancer

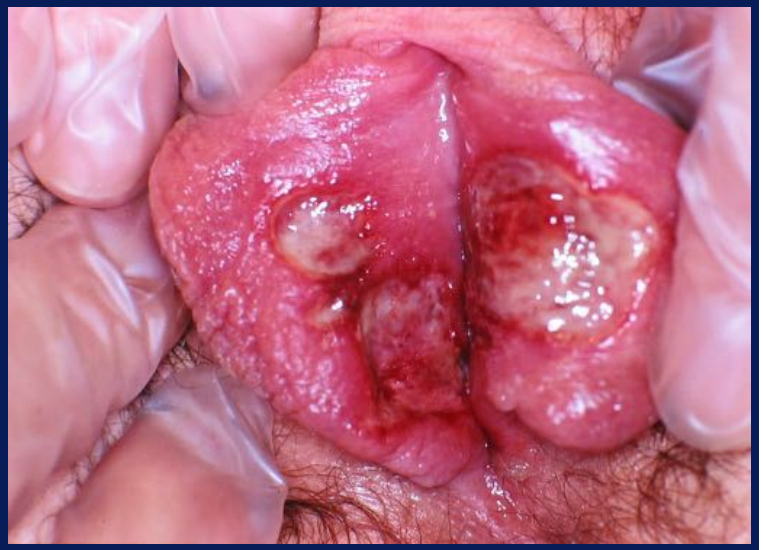

Severe Ulcerated
Irritant
Contact Dermatitis
Diaper Rash
Urine + Feces

Classification of Vulvar Aphthous Ulcers

- Simple Aphthous Ulcers – acute or recurrent
- Complex Aphthous Ulcers - recurrent, oral & vulvar ulcers
  - Idiopathic
  - Associated with –
    - Inflammatory Bowel disease: Crohn's, Ulcerative colitis
    - Behcet's disease
    - Myeloproliferative disease, neutropenia, lymphopenia, HIV

Simple Vulvar Aphthous Ulcers

- Acute, painful, reactive genital ulcers of prepubertal and adolescent girls and young women



Synonyms for acute vulvar aphthae –

Simple Aphthous Ulcers :

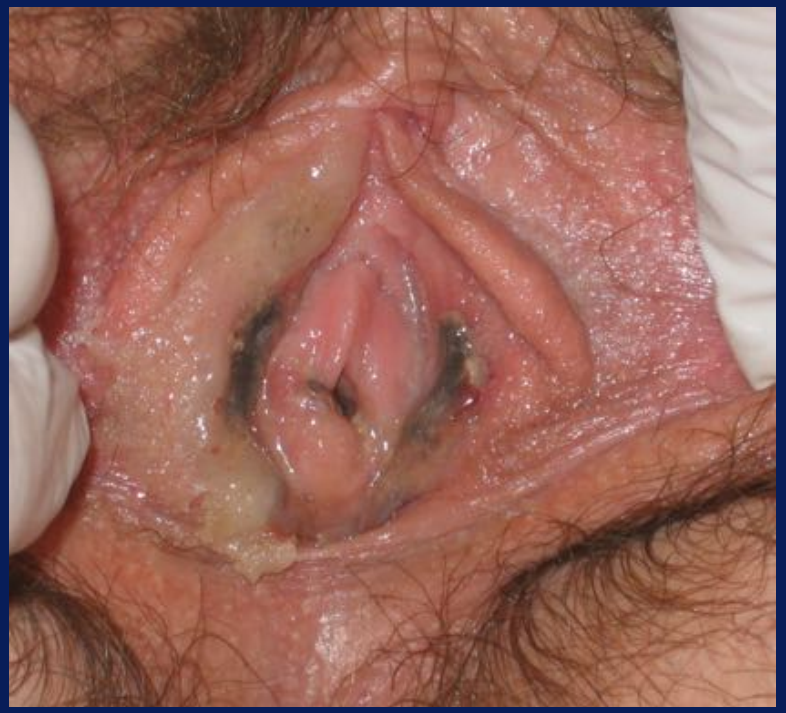
- Ulcus vulvae acutum
- Lipschütz ulcers
- Reactive nonsexually related acute genital ulcers
- Nonsexually acquired genital ulceration (NSAGU)
- Sutton's Ulcer

Aphthae from Mycoplasma pneumoniae

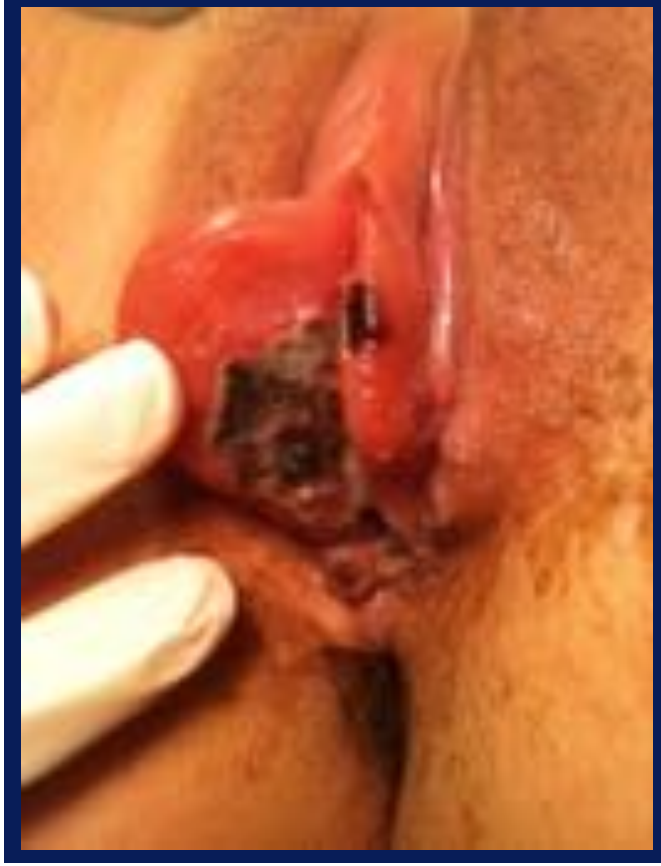
Simple Vulvar Aphthous Ulcers

- younger patients - average 29 years old
- Size – most 1-3 cm and often multiple

- Idiopathic, or in 30% cytotoxic immune response to EBV, CMV, mycoplasma pneumonia, group A strep, influenza A, parvovirus, paramyxovirus, salmonella, toxoplasma, mumps, Lyme



Simple Aphthous Ulcer Characteristics

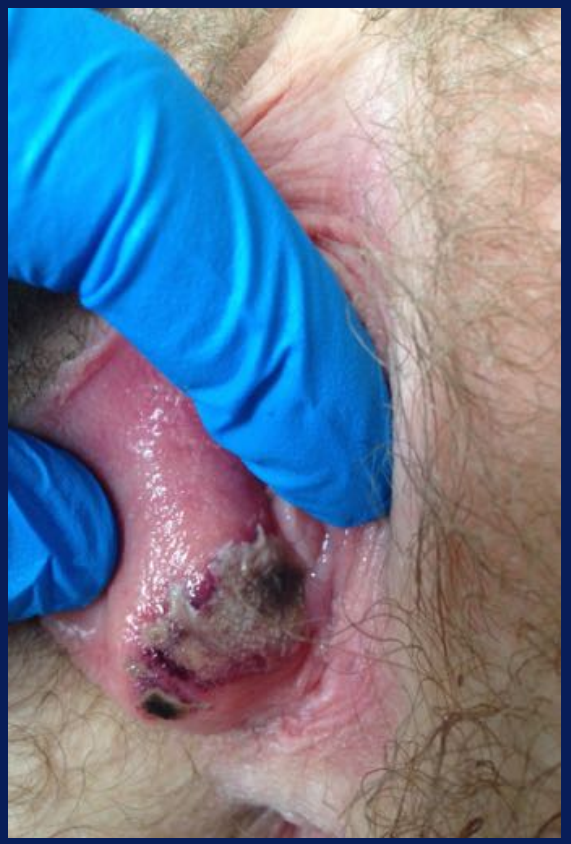


- Acute ulcers - Preceded by prodrome of fatigue, anorexia, headache, low grade fever
- Covered with pseudomembranous or necrotic eschar over white/yellow fibrinous base
- sharply demarcated ulcers with erythematous edges
- Heals within 3 weeks
- 1/3 recur

Lipschütz ulcers Vieira-Baptista P, J. Eur J Obstet Gynecol Reprod Biol. 2016 Mar;198:149-52

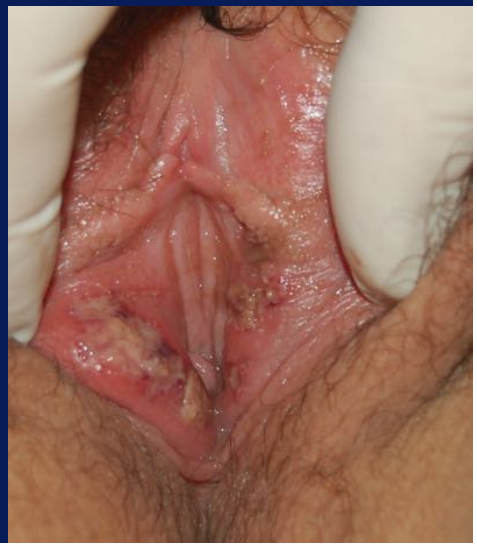
Evaluation for Simple Aphthous Ulcers

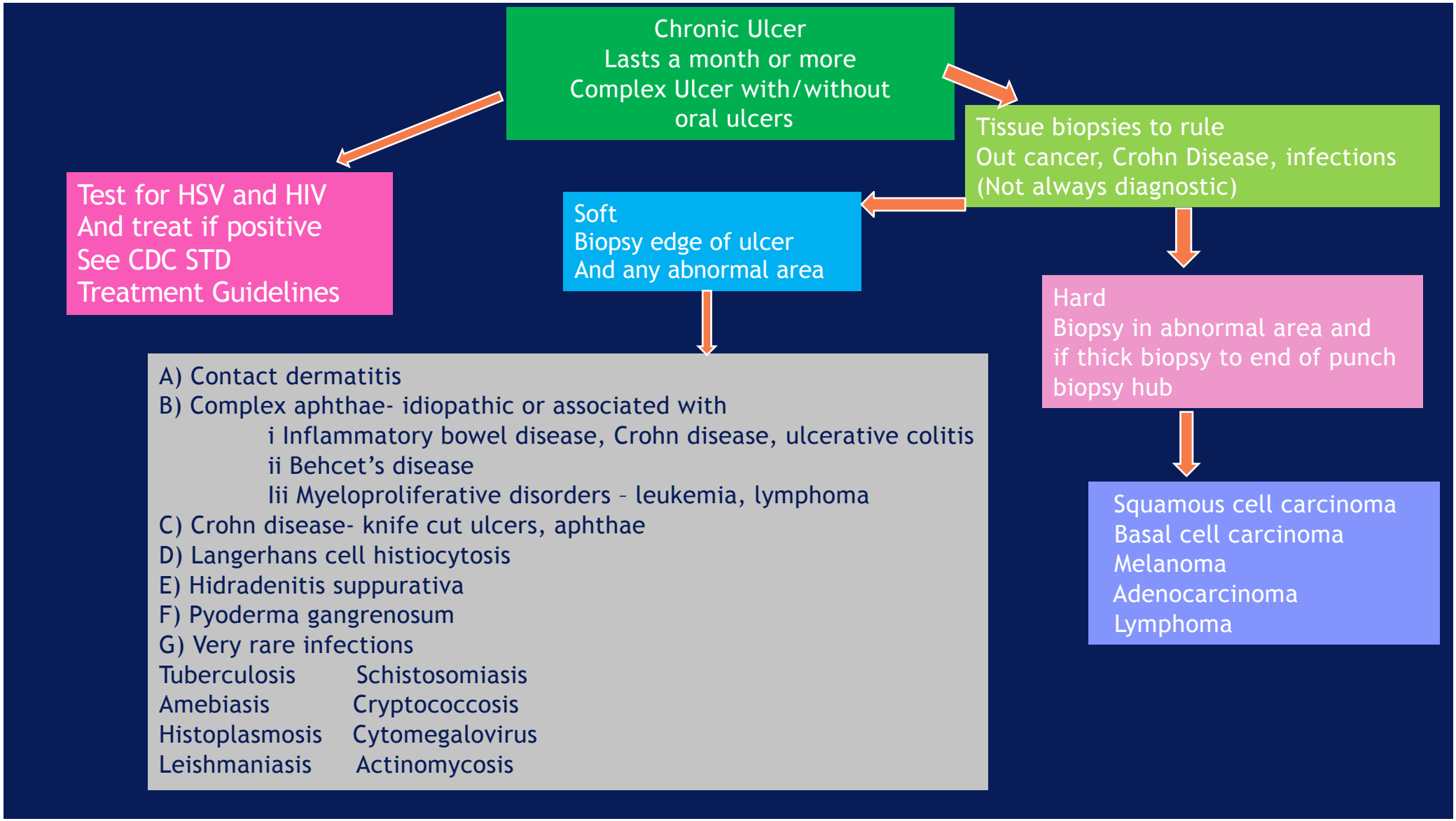
- **Diagnosis of exclusion – etiology seldom found**
- Thorough history and physical – eye, oral, genital
- Test for **HSV and SYPHILIS**
- CBC, test for infection as indicated
- No biopsy



Treatment Simple Aphthous Ulcers

- **Pain control**: local anesthetics (topical lidocaine), Acetaminophen, narcotics. Avoid NSAIDS
- **Local care**: sitz baths, whirlpool debridement
- **Oral steroids**: 40-60 mg PO prednisone daily until pain subsides (5-10 d), then ½ dose for 5-10 d.
- **Topical super-potent steroids**: clobetasol 0.05% ointment
- **Bladder drainage with catheterization** if needed
- **If persistent or recurrent -**
  - Intralesional triamcinolone 5-10 mg/ml
  - doxycycline 50-100 mg daily

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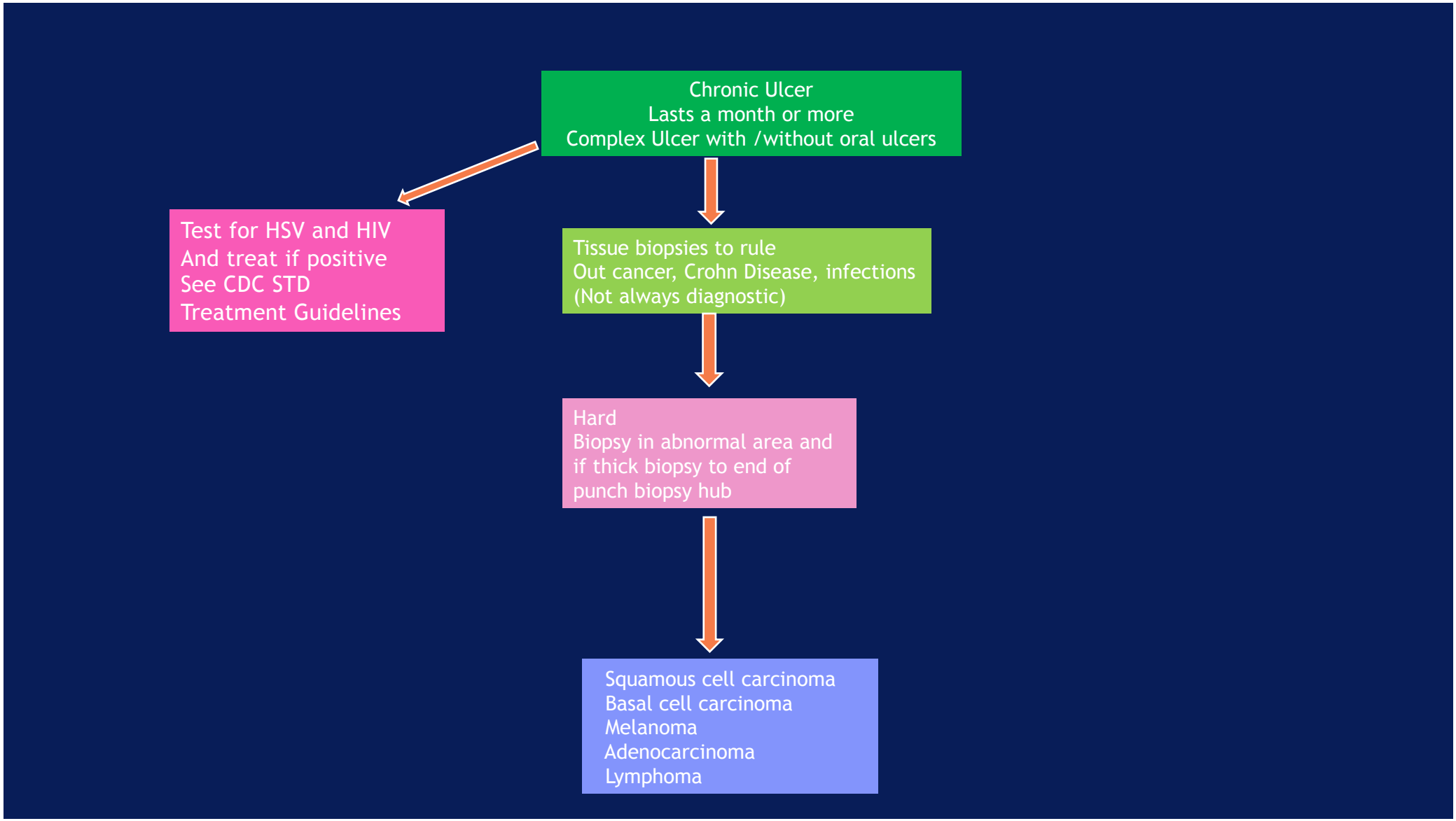
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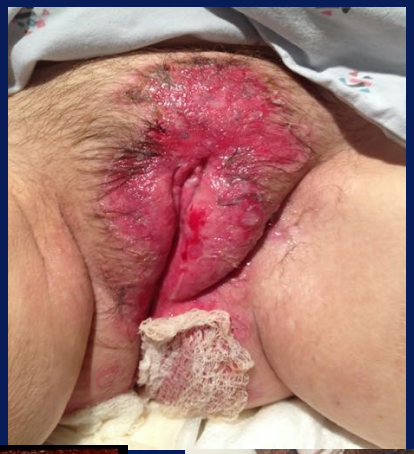
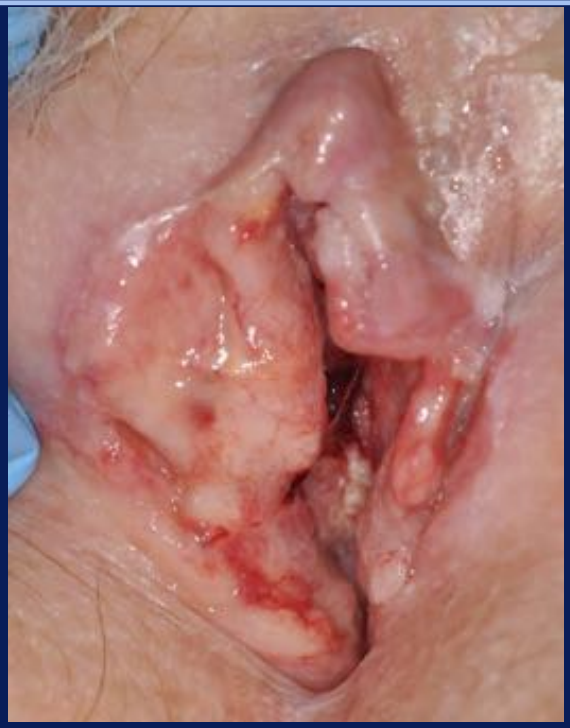
Herpes Simplex Virus (HSV) in the Immunocompromised

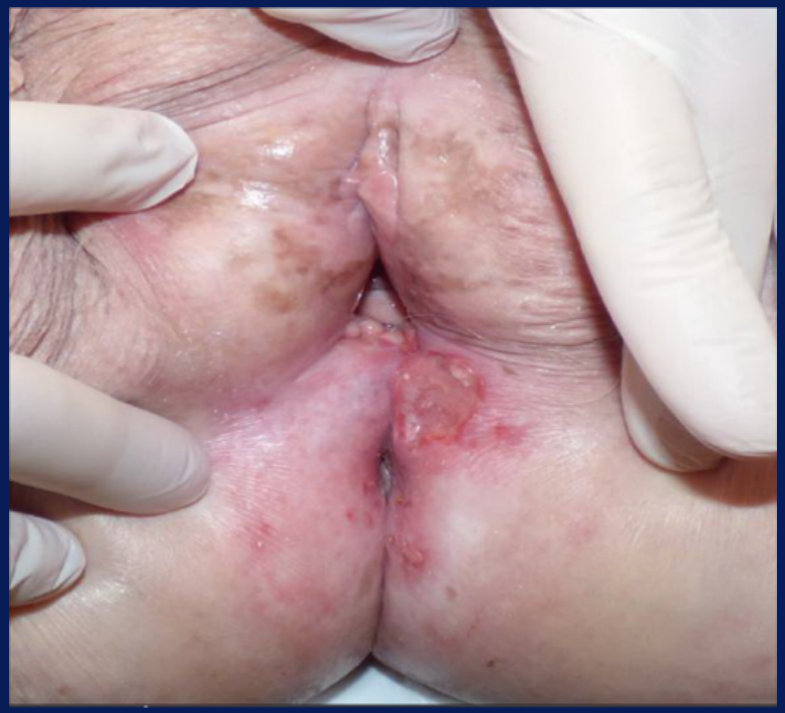


- <u>Most common cause of vulvar ulcers - chronic</u>
- Painful non-healing chronic ulcers, extending at periphery with active HSV at edges, necrotic
- Well demarcated, punched out, circular ulcers
- Reactivation of pre-existing disease
- Diagnosis – PCR, Direct immunofluorescence, biopsy

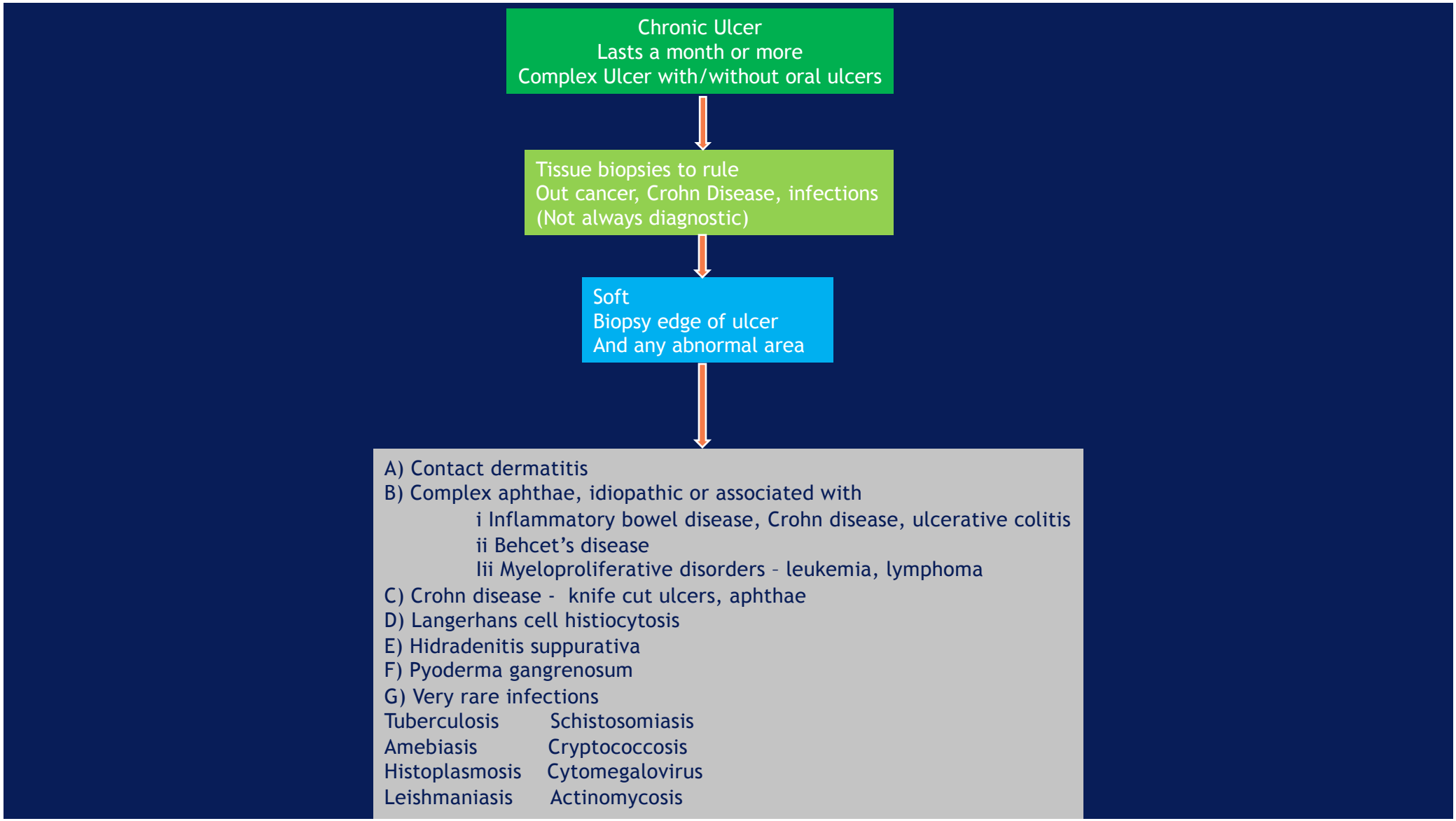
Ulcerating Vulvar Malignancies



Squamous cell CA in Lichen Planus



Squamous cell CA in Lichen Sclerosus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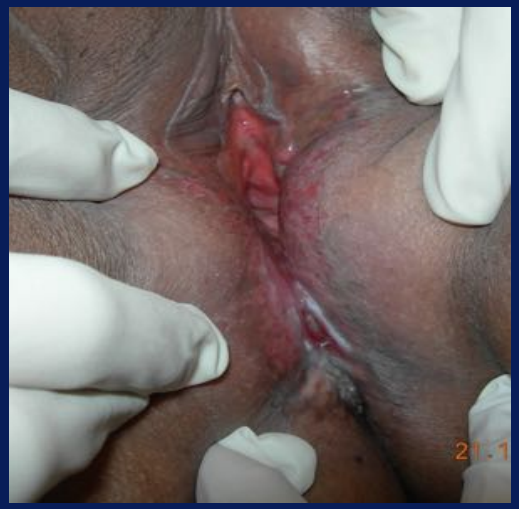
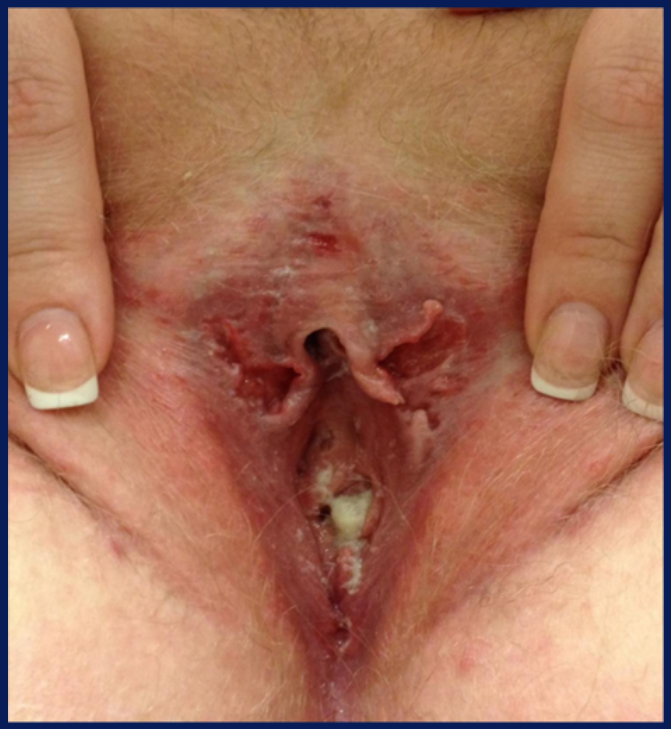
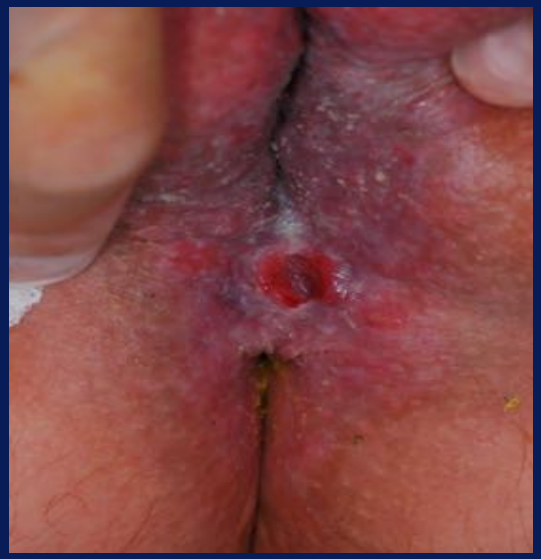
Tumors







Vulvar Langerhan's Cell Histiocytosis

Severe Chronic Irritant Contact Dermatitis

B) Complex aphthae, idiopathic or associated with
- i Inflammatory bowel disease, Crohn disease, ulcerative colitis
- ii Behcet's disease
- Iii Myeloproliferative disorders – leukemia, lymphoma

C) Crohn disease - knife cut ulcers, aphthae

R/O Inflammatory Bowel Disease, Behcet's, Myeloproliferative Disorders and Crohn Disease

Complicated / Complex Aphthous Ulcers

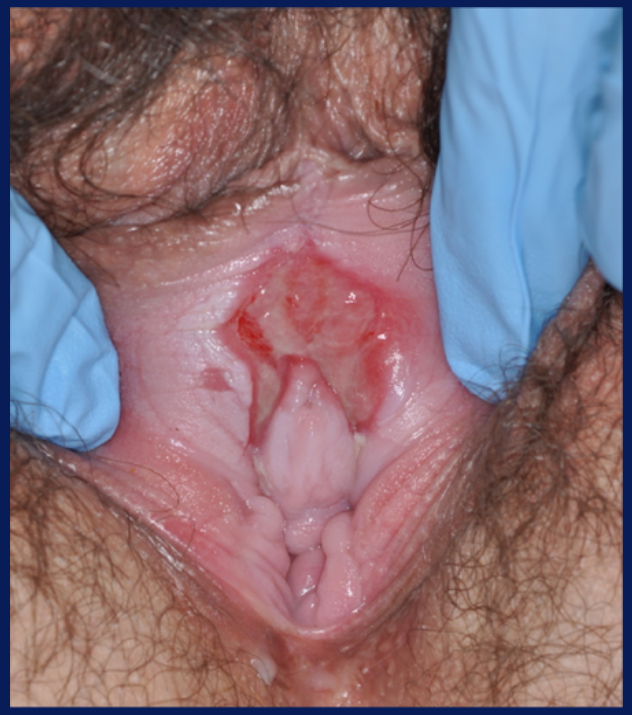
Definition:

Recurrent or chronic vulvar +/_ oral aphthae*

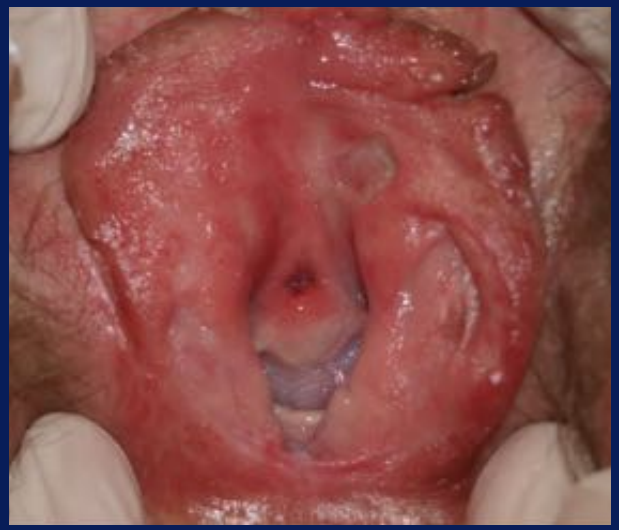
(**oral and vulvar aphthae may or may not be concurrent*)

Idiopathic or Associated conditions:

- Inflammatory Bowel disease: Crohn's, Ulcerative colitis
- Bechet's Disease
- Myeloproliferative disease, cyclic neutropenia, lymphopenia. HIV



Complex Aphthous Ulcer Characteristics



- Less common and ulcers almost constant with one or more or recurrent ones, possibly with oral ulcers (not concomitant).
- Size: most < 1cm; can be 1-3 cm
- No Prodrome, except for Behcet's
- The ulcer base(s) then have a fibrinous base evolving into a deep punched out ulcer with variable swelling and pain. These can heal with scarring.
- Usually multiple ulcers seen
- Duration weeks but can last for months.

Treatment Complex Aphthous Ulcers

- Intralesional triamcinolone 5-10 mg/ml
- doxycycline 50-100 mg daily
- colchicine 0.6 mg bid-tid if tolerated
- dapsone 50-150 mg per day
- dapsone + colchicine
- pentoxifylline 400 mg tid
- cyclosporine 100 mg 1-3/d
- apremilast 30 mg bid
- TNFα inhibitors (adalimumab, infliximab)

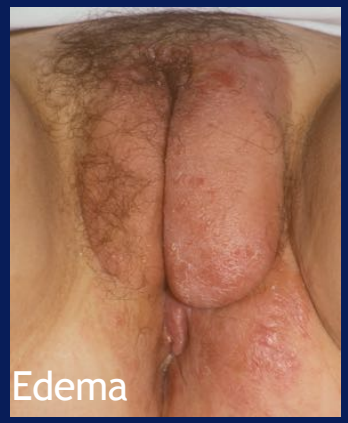
Dixit S, Bradford J, Fischer G. J Am Acad Dermatol. 2013

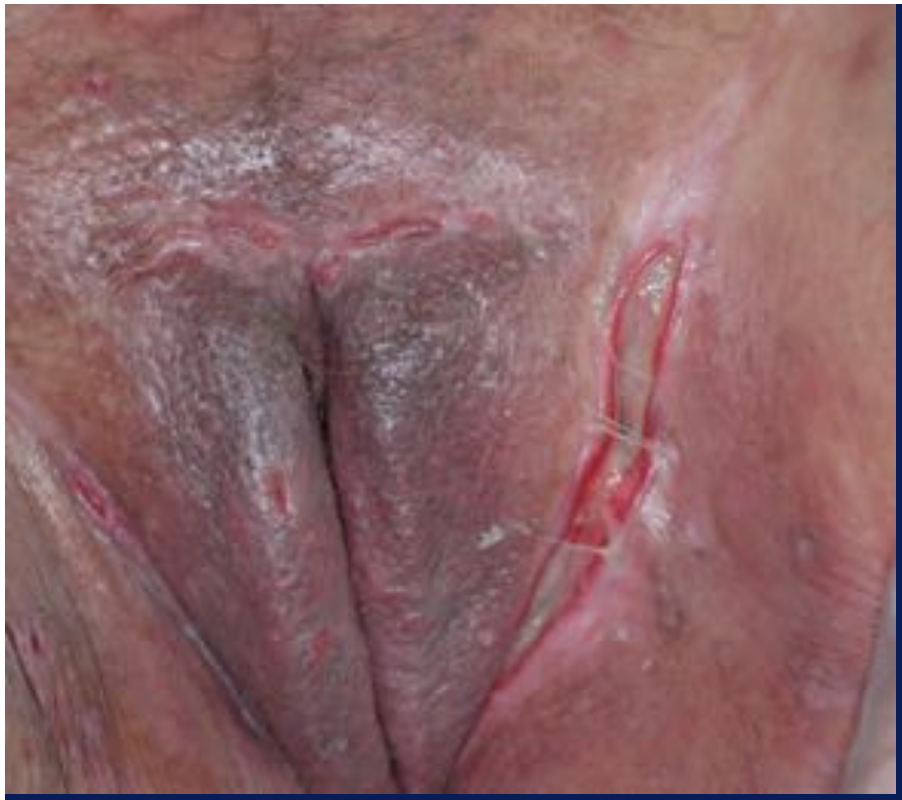
Metastatic Vulvar Crohn Disease

- Inflammatory bowel disease with mucocutaneous vulvar and perianal involvement in 25-30%
- "Rare:" about 300 vulvar CD cases reported since 1965
  - Under diagnosed and underreported
- Vulvar CD can **precede** GI Crohn's in 25% by 3-4 years
- Average age of onset 30 years

Consider Vulvar Crohn Disease as Diagnosis

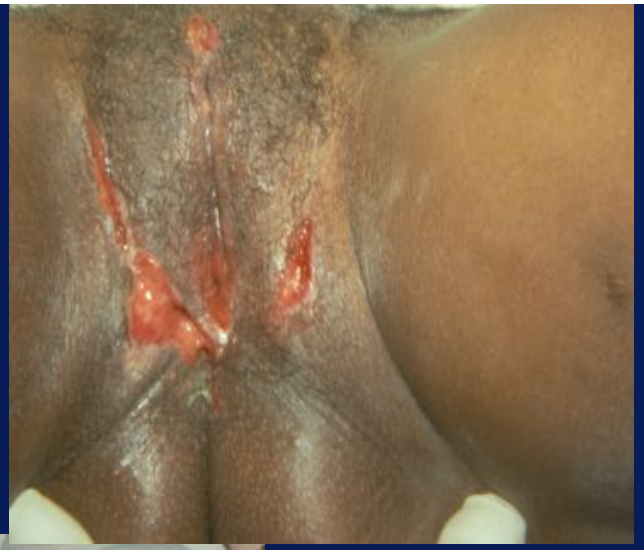
- Vulvar Swelling – 60% -
  Edema, diffuse swelling, lymphedema,
  lymphangiectasia, hypertrophic labia with pseudocondylomata
- Vulvar ulcers – 35% - "Knife cut" ulcers, aphthous ulcers
  Aphthous ulcers can precede GI disease for years
- Suppuration with hidradenitis suppurativa
- Perianal disease – perianal tags, swelling, fissures
- Fistulae
- Inflammatory vaginitis - Desquamative Inflammatory Vaginitis (personal experience)

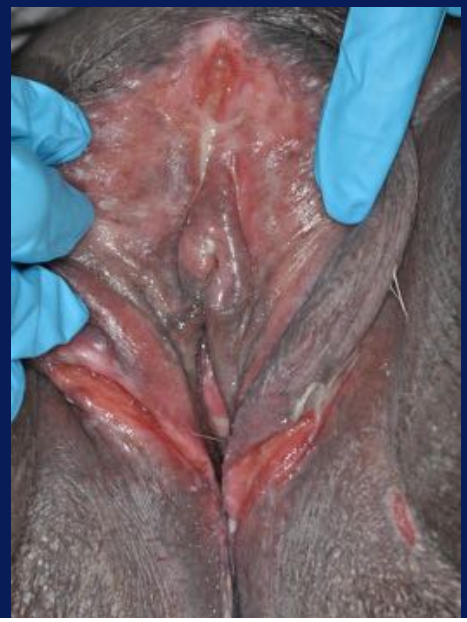

Edema

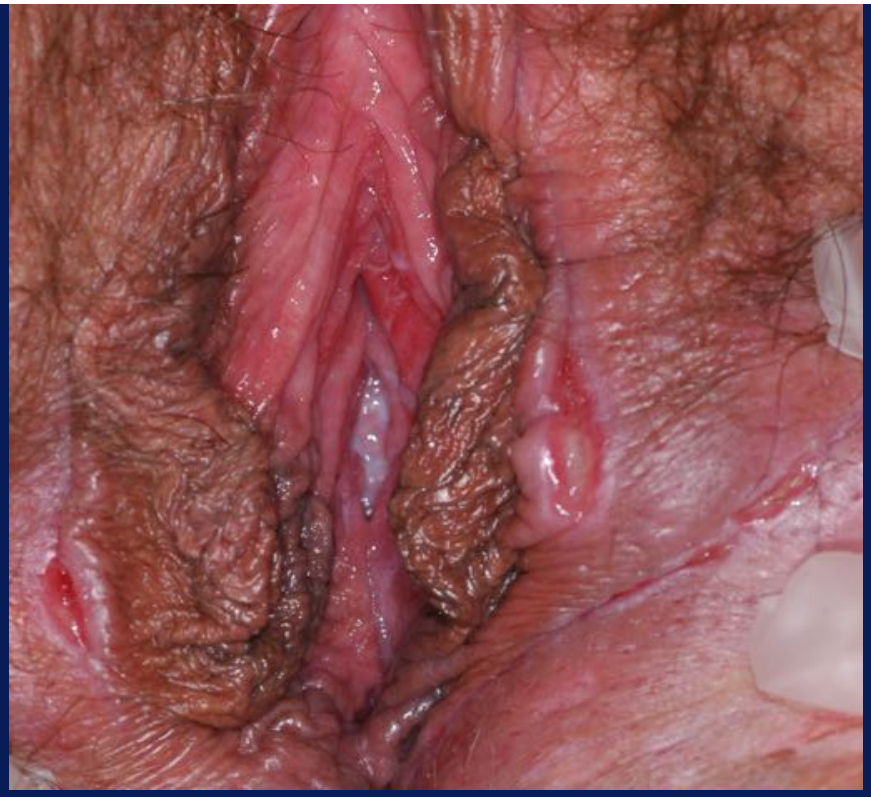


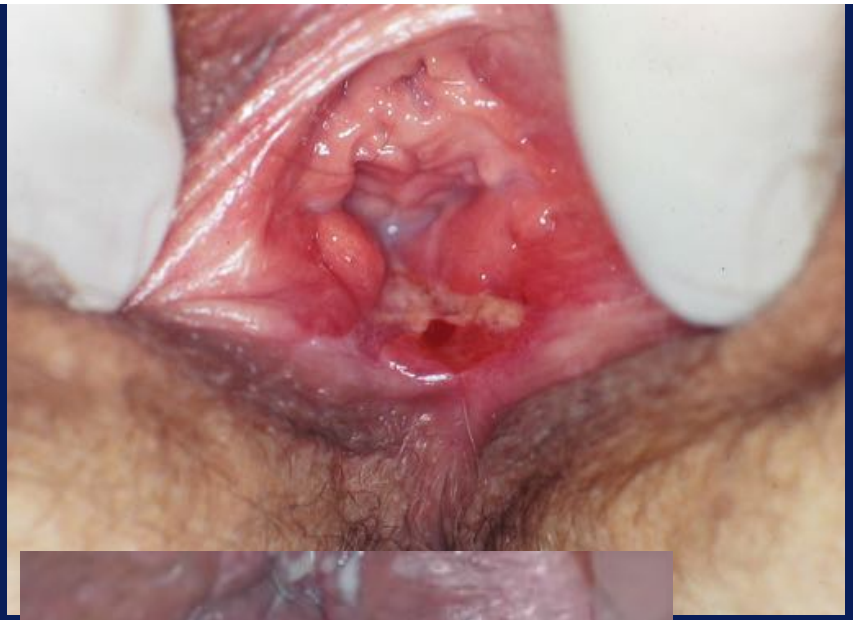
Crohn

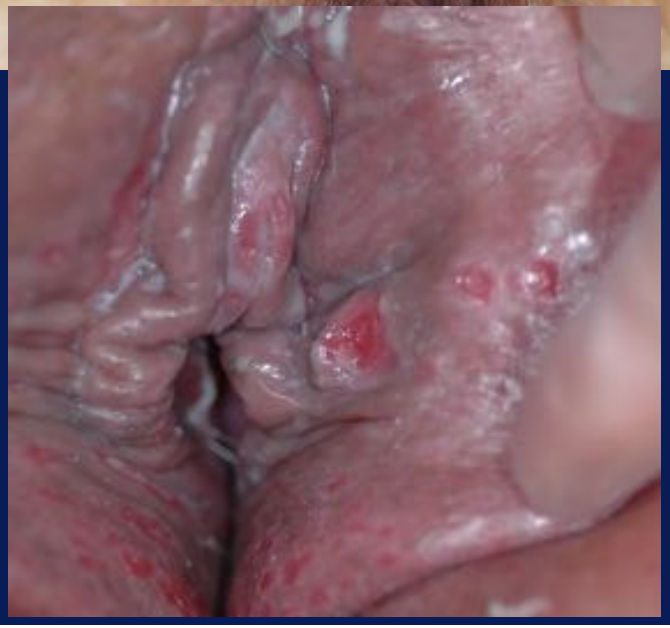
"Knife Cut" Ulcers











Aphthous Ulcers in Crohn Disease

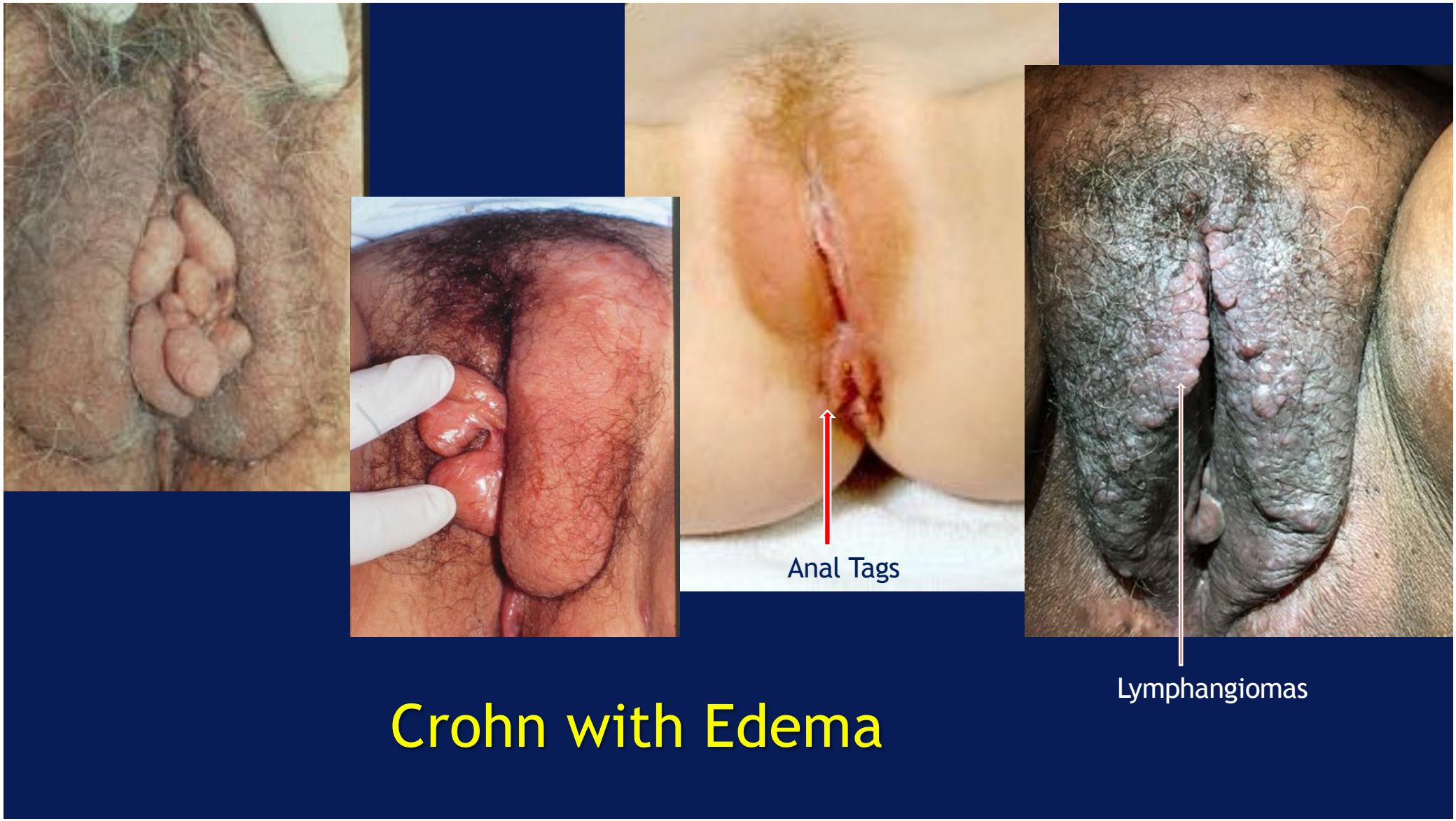
Vulvar Crohn Disease

Commonly missed

Diagnosis: BIOPSY of GI tract or Skin

- May show diffuse lymphohistiocytic infiltrate and loose non-caseating granulomas
  (biopsy positive in 50% - 60% of cases)

- Often a clinical diagnosis



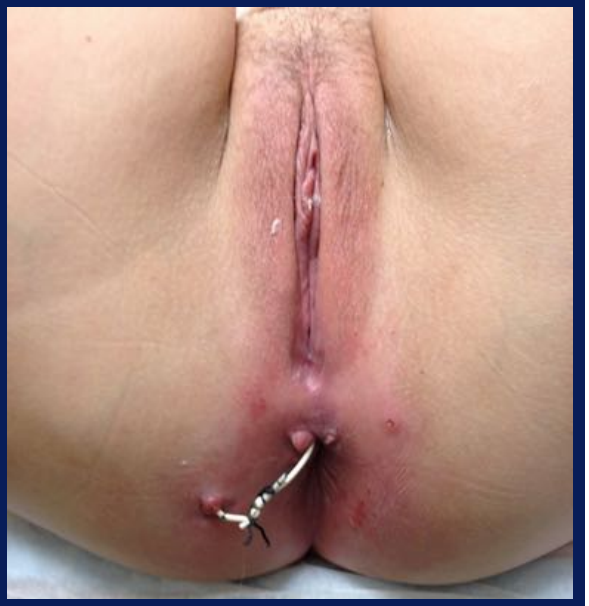
Crohn with Edema

Treatment of Vulvar Crohn Disease

Control of bowel disease vital for anogential disease control

Systemic treatment:

Metronidazole,
prednisone, azathioprine,
6-mercaptopurine,
TNF alpha inhibitors – infliximab, adalimumab,
certolizumab pegol, natalizumab, ustekinumab



Topical treatment:

- Topical super potent corticosteroids
- Calcineurin inhibitors (tacrolimus)

Intralesional: triamcinolone 3.3-10 mg/ml

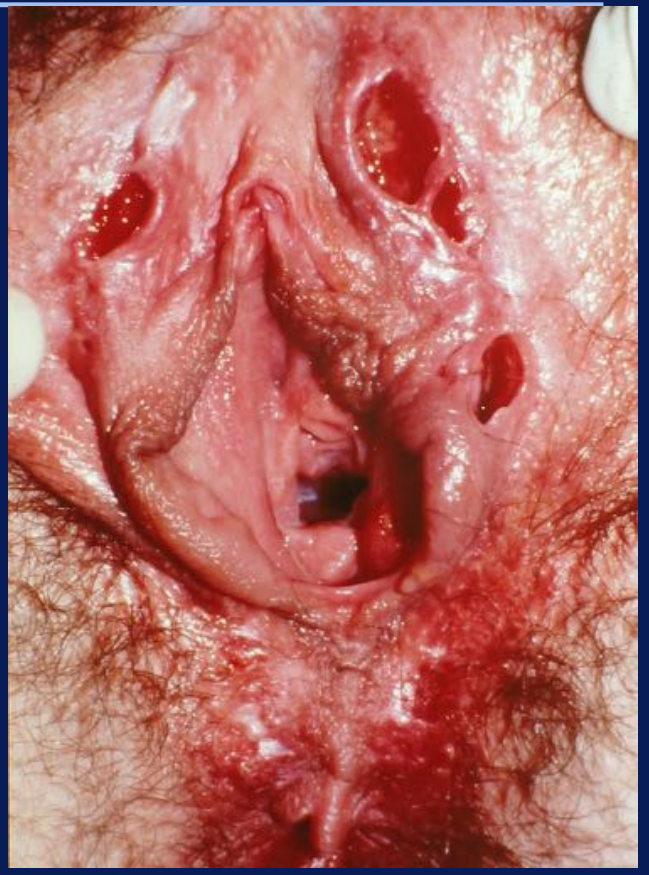
Surgery – avoid as heal poorly

Treatment of Vulvar Crohn Disease Reality

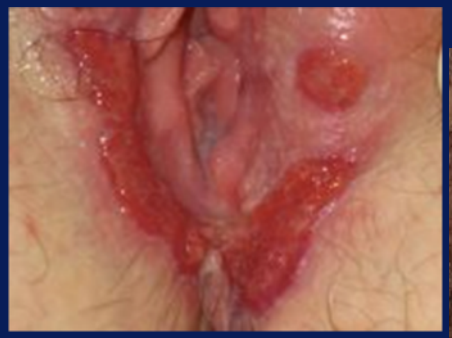
- No consensus on treatment
- Need multidisciplinary approach –usually not available
- Vulvar Crohn's in younger patients associated with poorer prognosis
- Topicals – superpotent corticosteroids and, less effective, safer, calcineurin inhibitors (tacrolimus 0.1% oint)
- Metronidazole + prednisone - response, not remission, 88%
- Azathioprine - response 57%
- TNF-alpha meds - remission 53% partial 33%
- Compression garments helpful

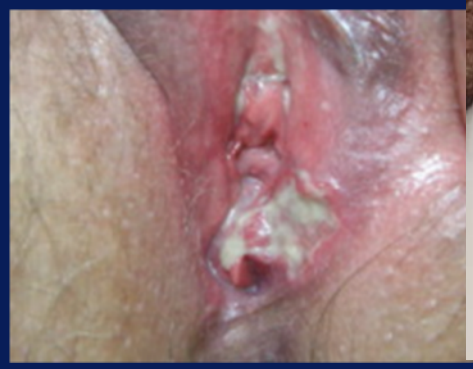
Behcet's Disease: Oculo-Oro-Genital Syndrome RARE

- Chronic relapsing systemic T-Cell mediated vasculitis
  - Oral aphthae
  - Genital aphthae
  - Ocular lesions (uveitis)
  - Visceral or cutaneous lesions
  - Positive pathergy test
  - defined by a triad, oral ulcers, genital ulcers and uveitis and has specific criteria
- Rare in US and Europe

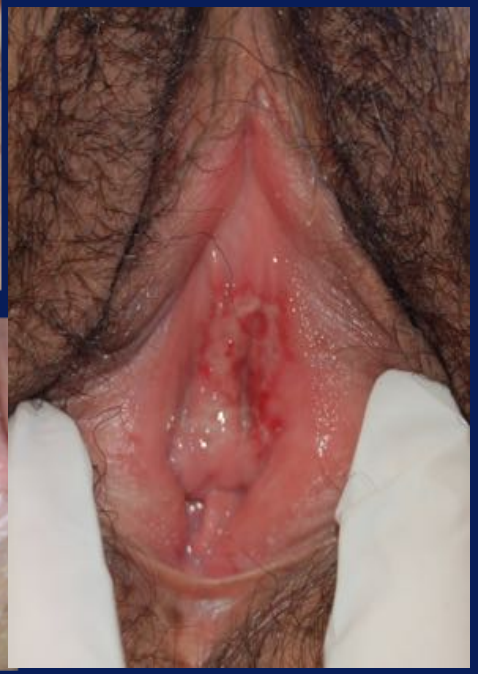


Behcet's Ulcers





Photos courtesy of DermNet NZ



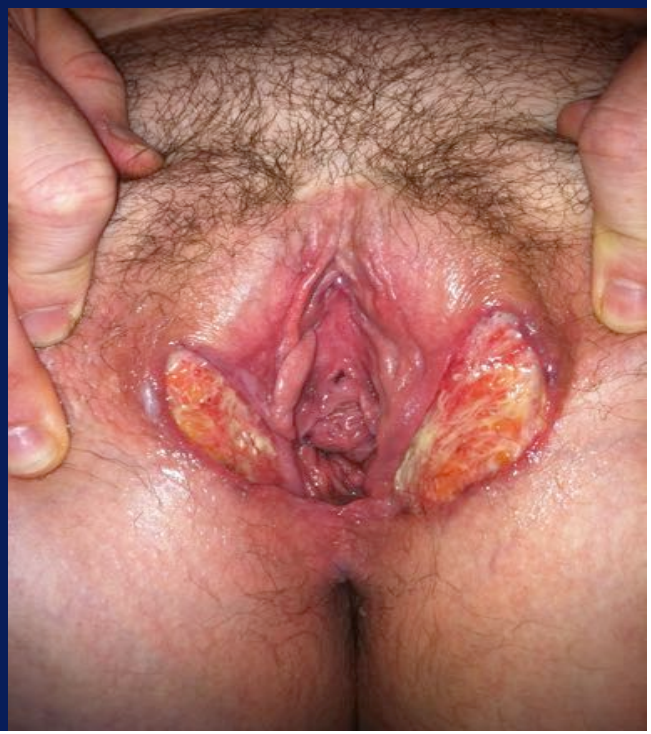
Ahinoam Lev-Sedgie

- Prodrome: tender nodule
- Oval or round, well-demarcated ulcers with grayish yellow necrotic base, erythematous rim, heals with scarring
- Cervical, vaginal, labial, perineal, perianal
- Can cause labial destruction, urethral or bladder fistulas
- Treatment depends on organ system involved – treat ulcres as complex aphthae

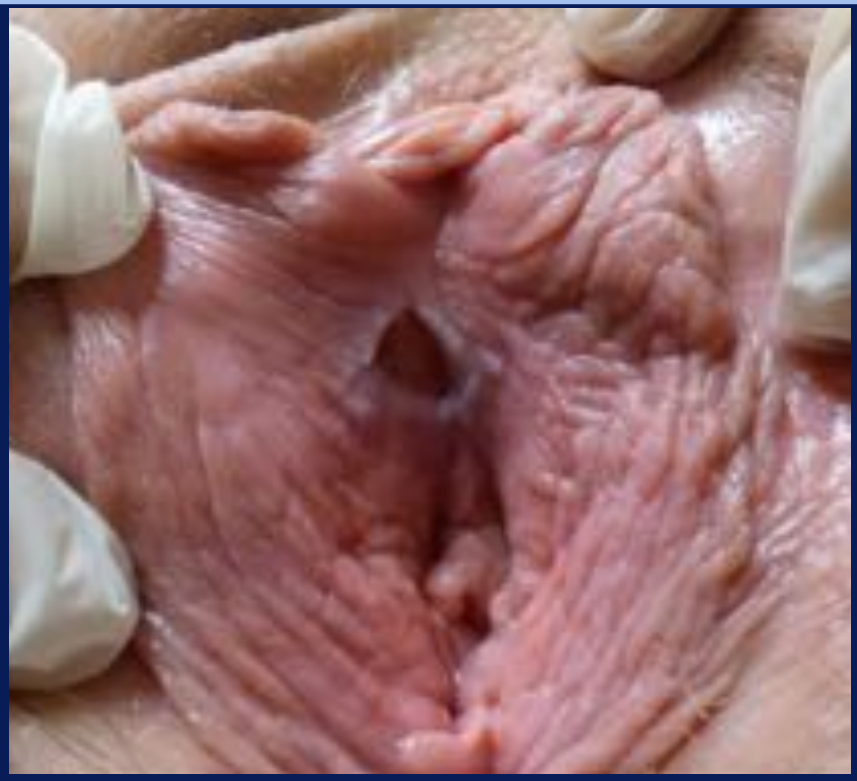
Pyoderma Gangrenosum

- An uncommon, neutrophilic dermatosis causing very painful skin ulcers at injury sites - legs, peristomal, rare on genital area
- > 50 years age
- A skin reaction to an internal disease or condition:
  - inflammatory bowel diseases,
  rheumatoid arthritis, blood dyscrasias,
  chronic hepatitis – 40% - 50% unknown cause
- a very painful ulcer with a purple edge that
  undermined as it enlarges and cribriform scar(s).
- Treat with topical, intralesional or
  systemic steroids, cyclosporine, infliximab, etc

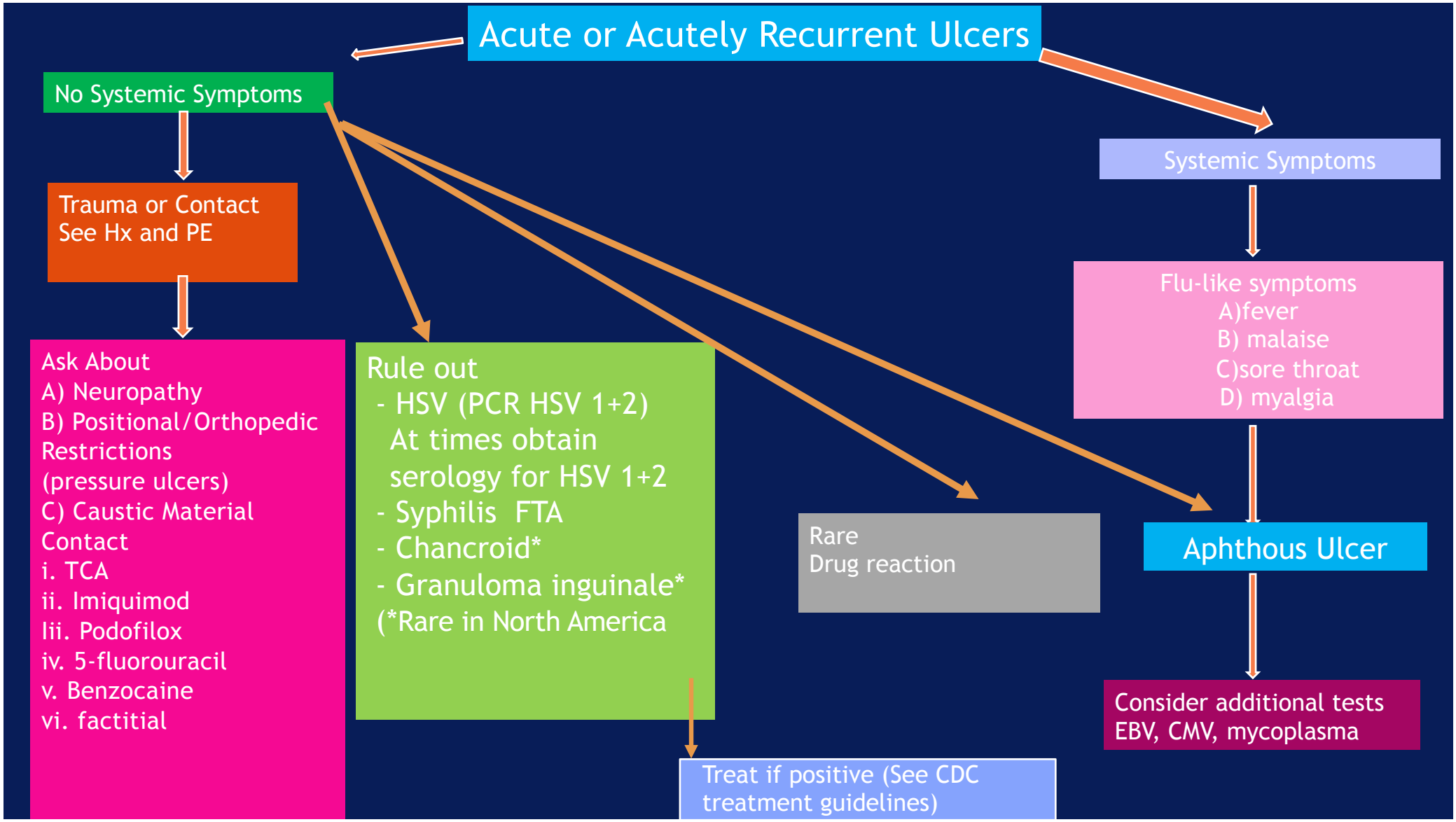
VERY RARE

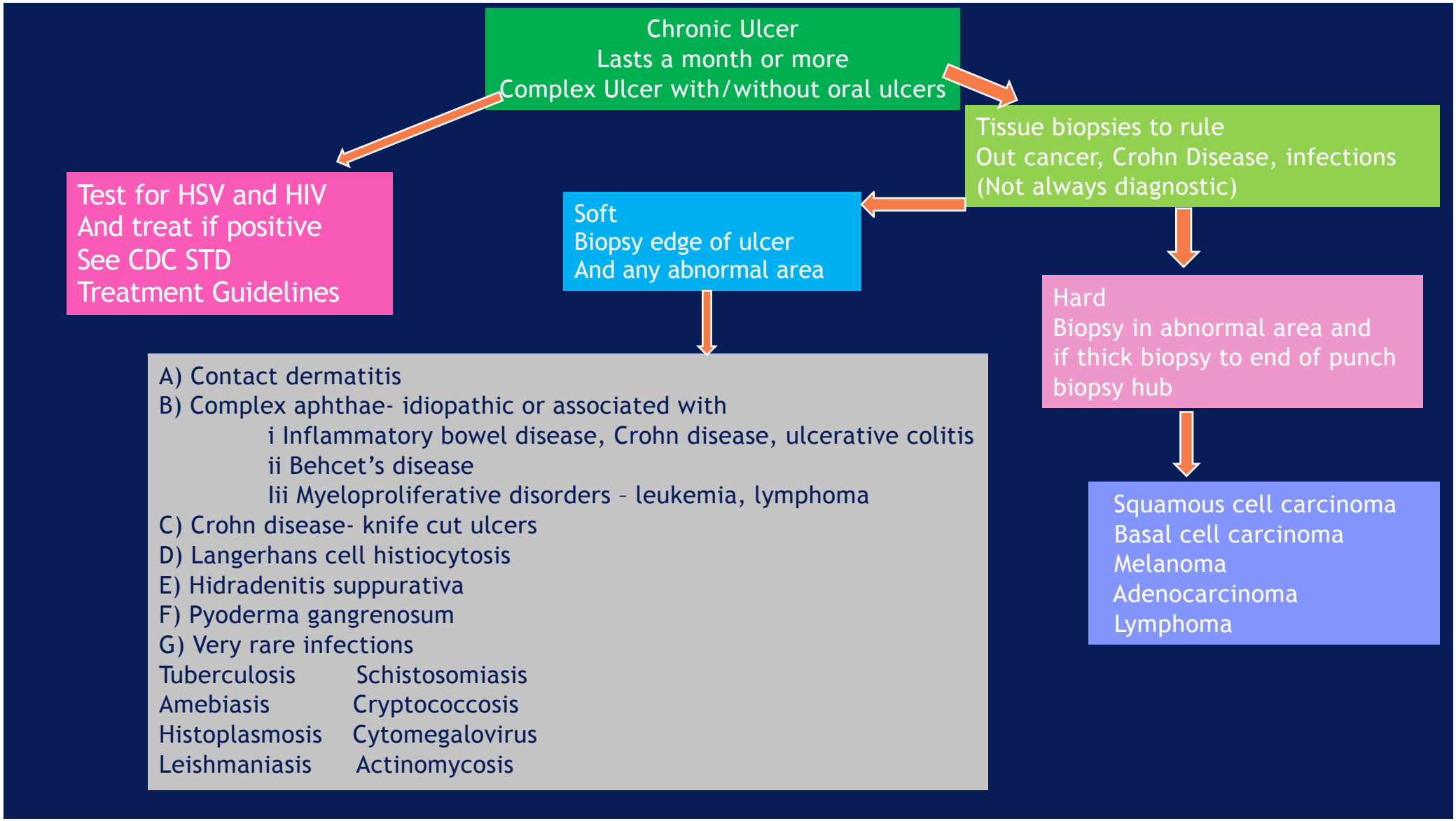


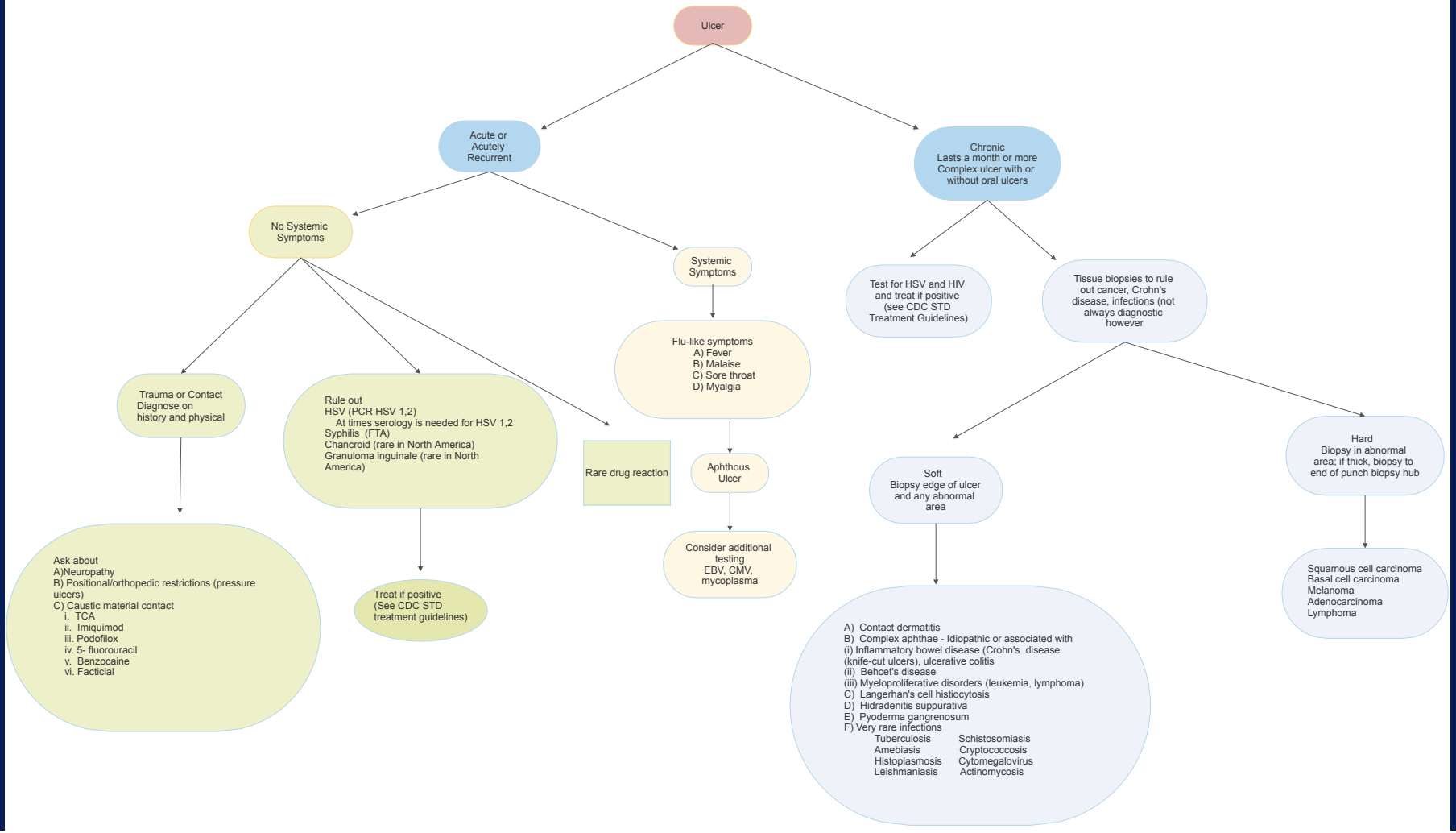
Idiopathic Ulcers



Rx Surgery


Acute or Acutely Recurrent Ulcers
No Systemic Symptoms
Trauma or Contact
See Hx and PE
Ask About
A) Neuropathy
B) Positional/Orthopedic Restrictions
(pressure ulcers)
C) Caustic Material Contact
i. TCA
ii. Imiquimod
Iii. Podofilox
iv. 5-fluorouracil
v. Benzocaine
vi. factitial
Rule out
- HSV (PCR HSV 1+2)
At times obtain serology for HSV 1+2
- Syphilis FTA
- Chancroid*
- Granuloma inguinale*
(*Rare in North America
Treat if positive (See CDC treatment guidelines)
Rare
Drug reaction
Systemic Symptoms
Flu-like symptoms
A)fever
B) malaise
C)sore throat
D) myalgia
Aphthous Ulcer
Consider additional tests
EBV, CMV, mycoplasma


Chronic Ulcer
Lasts a month or more
Complex Ulcer with/without oral ulcers
Test for HSV and HIV
And treat if positive
See CDC STD
Treatment Guidelines
Tissue biopsies to rule
Out cancer, Crohn Disease, infections
(Not always diagnostic)
Soft
Biopsy edge of ulcer
And any abnormal area
Hard
Biopsy in abnormal area and
if thick biopsy to end of punch
biopsy hub
A) Contact dermatitis
B) Complex aphthae- idiopathic or associated with
i Inflammatory bowel disease, Crohn disease, ulcerative colitis
ii Behcet's disease
Iii Myeloproliferative disorders – leukemia, lymphoma
C) Crohn disease- knife cut ulcers
D) Langerhans cell histiocytosis
E) Hidradenitis suppurativa
F) Pyoderma gangrenosum
G) Very rare infections
Tuberculosis
Amebiasis
Histoplasmosis
Leishmaniasis
Schistosomiasis
Cryptococcosis
Cytomegalovirus
Actinomycosis
Squamous cell carcinoma
Basal cell carcinoma
Melanoma
Adenocarcinoma
Lymphoma


Ulcer
Acute or Acutely Recurrent
Chronic
Lasts a month or more
Complex ulcer with or without oral ulcers
No Systemic Symptoms
Systemic Symptoms
Test for HSV and HIV and treat if positive (see CDC STD Treatment Guidelines)
Tissue biopsies to rule out cancer, Crohn's disease, infections (not always diagnostic however
Trauma or Contact
Diagnose on history and physical
Rule out
HSV (PCR HSV 1,2)
At times serology is needed for HSV 1,2
Syphilis (FTA)
Chancroid (rare in North America)
Granuloma inguinale (rare in North America)
Rare drug reaction
Flu-like symptoms
A) Fever
B) Malaise
C) Sore throat
D) Myalgia
Aphthous Ulcer
Soft
Biopsy edge of ulcer and any abnormal area
Hard
Biopsy in abnormal area; if thick, biopsy to end of punch biopsy hub
Ask about
A)Neuropathy
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