

Dermatological manifestations of systemic infectious diseases

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Dienst Inwendige Ziekten - Nierziekten – Infectieziekten

AZ Sint-Jan AV, BRUGGE

1. Introduction

Diagnosis = pattern recognition

Lancet, 1997, 350, 575-80

- High fever
- Sudden onset
- Productive cough
- Crepitation right lung base

=

pneumonia

- High fever
- Conjunctivitis
- Rhinitis
- Muscle aches
- headache

=

flu

- High fever
- Sudden onset
- Diarrhea
- headache
- Just back from safari

=

malaria

- **Skin lesions** = very common in systemic infectious diseases
- **Skin lesions** = frequently + fever
- DD = often very broad, including many non-infectious diseases

Skin lesions may permit a probable diagnosis based on clinical skills only

Pathogenesis of skin lesions in ID

1. DIC/coagulopathy
2. Direct vascular invasion (bacteria/fungi)
3. Immune vasculitis/immune complex formation/other immune reactions
4. Emboli (IE)
5. Vascular effects of toxins

DIC/coagulopathy

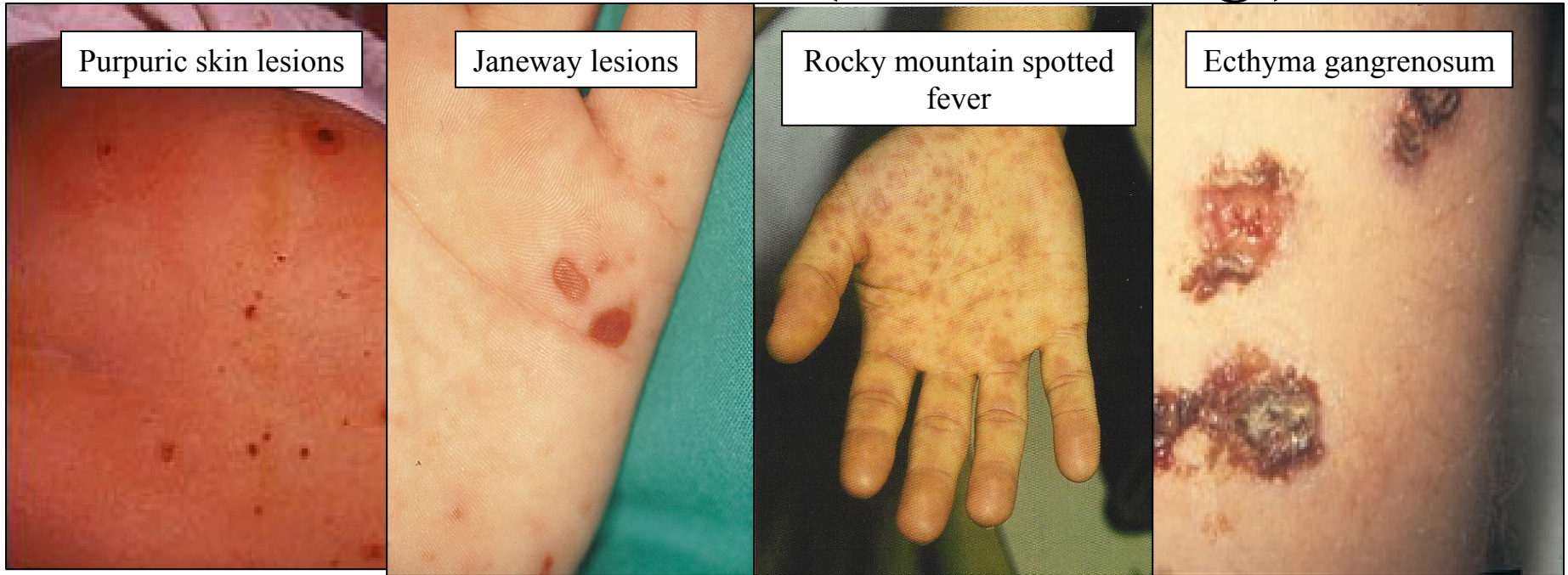


Culture = sterile

Pathology: diffuse hemorrhage, perivascular cuffing,
intravascular thrombosis

DD e.g. Cryoglobulin, ergot poisoning, ...

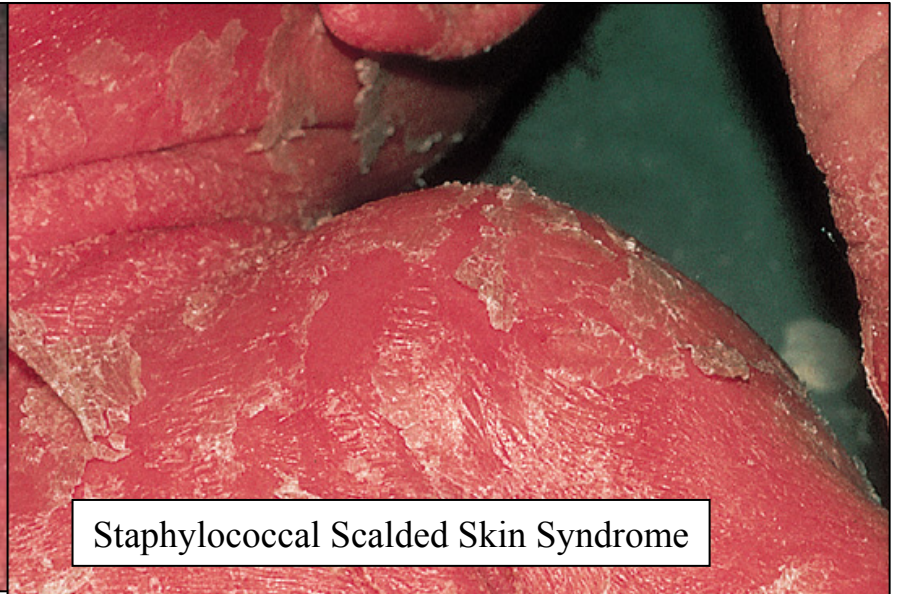
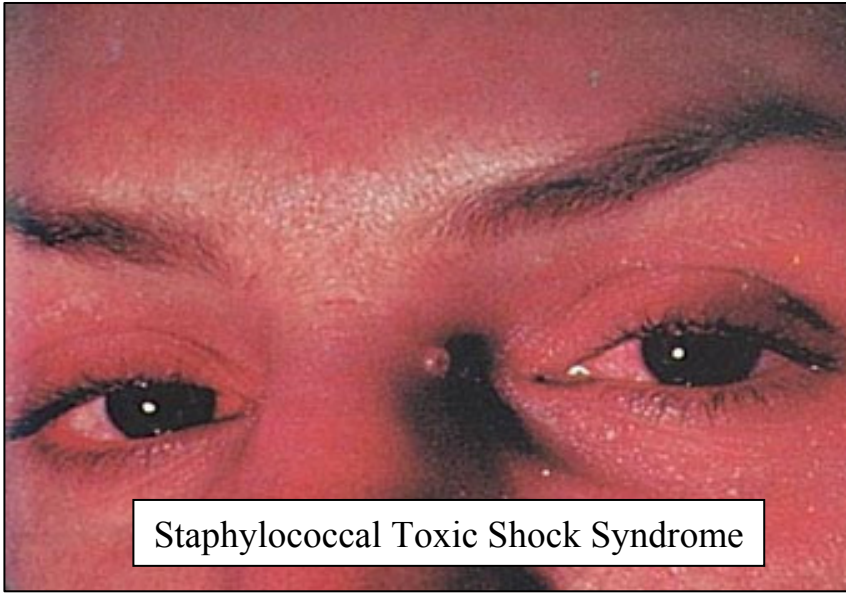
Direct vascular invasion (bacteria/fungi)



Culture = often non-sterile

Pathology: gram smear +; fibrin thrombi; extravasation of blood cells

Vascular effects of toxins



Culture = sterile

Pathology: perivascular edema, lymphatic perivascular cuffing, no immune complexes

I. Dermatological manifestations of systemic infectious diseases in immunocompetent hosts

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Skin Eruption caused by infections

Vs non-infectious skin lesions:

- Reactive conditions to underlying infections / drugs
 - Erythema multiforme
 - Erythema nodosum
 - Sweet syndrome
- Drug reactions
 - Urticaria
 - Maculopapular exanthema
 - AGEP/DRESS
 - Stevens Johnson syndrome
 - Toxic epidermal necrolysis

- Skin eruptions caused by infections

Children: viral exanthema

SPECIAL:

- Unilateral laterothoracic exanthema
- Gloves and socks
- Hand-foot-mouth disease
- Kawasaki

Adults: viral exanthema

- DD:
- EBV + ampicilline
 - Hep B
 - Secondary Syphilis
 - HIV



- Skin eruptions caused by infections
 - Parvo-virus B19
 - Erythema infectiosum
 - Gloves and Socks Syndrome



- Skin eruptions caused by infections
Hand-foot-mouth disease: Coxsackie



Ptn : Ptn: 40-year old veterinary;
high fever, rash and diarrhea



• Culture stools: positive for brucella

: Brucellosis

Ptn : Returned from South Africa

Fever, lymphadenopathies, maculopapular rash



- Clinic: 'tache noire'
- Serology: rickettsia IgM: pos 1/40

: African tick-bite fever

Lyme disease

- Clinical spectrum:
 - erythema chronicum migrans
 - lymphocytoma cutis
 - acrodermatitis atroficans

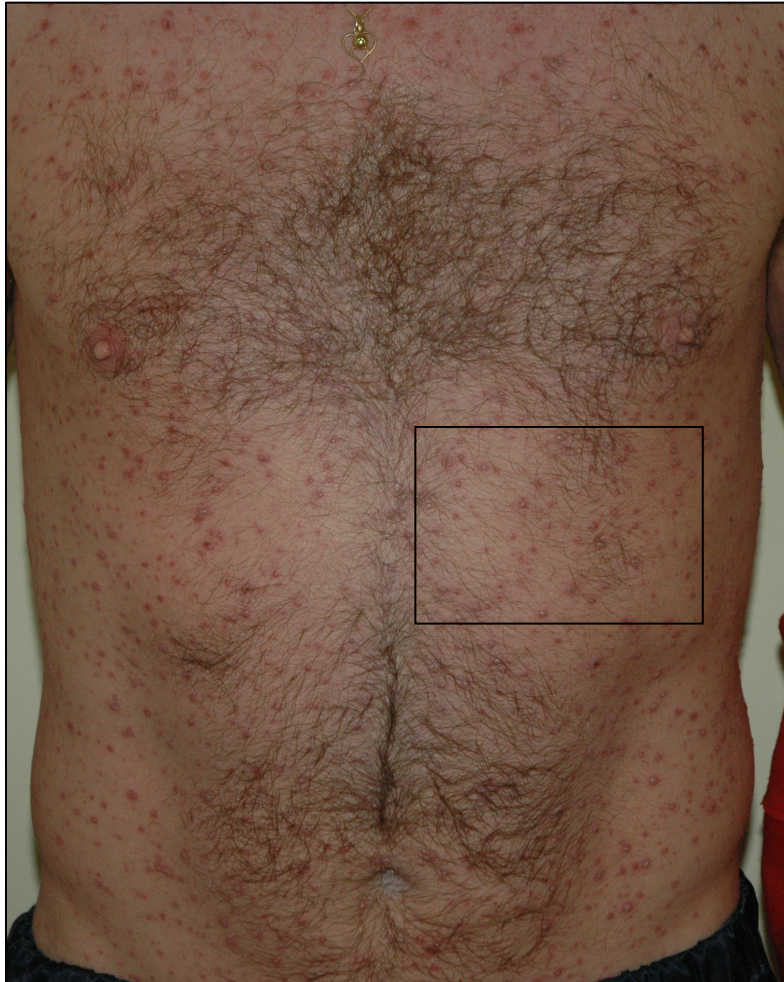


Vesicular Eruptions

- HS
- HS + EEM



Vesicular Eruptions - Varicella / Zoster



Gianotti-Crosti Syndrome

Papular acrodermatitis of childhood

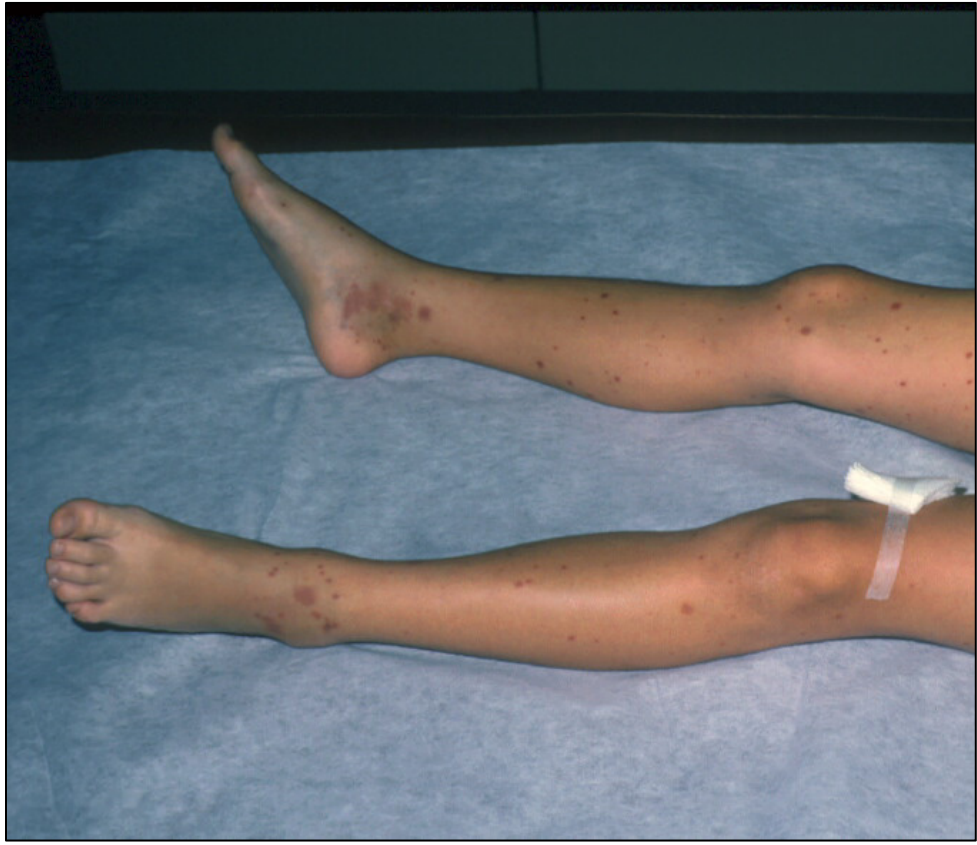


Table 81.3 Potential etiologies reported in association with Gianotti–Crosti syndrome. *Reported most commonly in Europe. §Most common cause in United States. DPT, diphtheria–pertussis–tetanus; MMR, measles–mumps–rubella.

| POTENTIAL ETIOLOGIES REPORTED IN ASSOCIATION WITH GIANOTTI–CROSTI SYNDROME |
|---|
| Viral |
| <ul style="list-style-type: none">• Hepatitis B*• Epstein–Barr virus§• Hepatitis A and C virus• Cytomegalovirus• Coxsackie virus• Respiratory syncytial virus• Adenovirus• Parainfluenza virus• Rotavirus• Parvovirus B19• Mumps virus• Human herpesvirus-6• Human immunodeficiency virus |
| Non-viral |
| <ul style="list-style-type: none">• Group A -hemolytic streptococci• <i>Mycobacterium tuberculosis</i> |
| Vaccines |
| <ul style="list-style-type: none">• Polio• DPT• MMR |

Purpuric Eruptions

- Septic
- Allergic/Immunologic

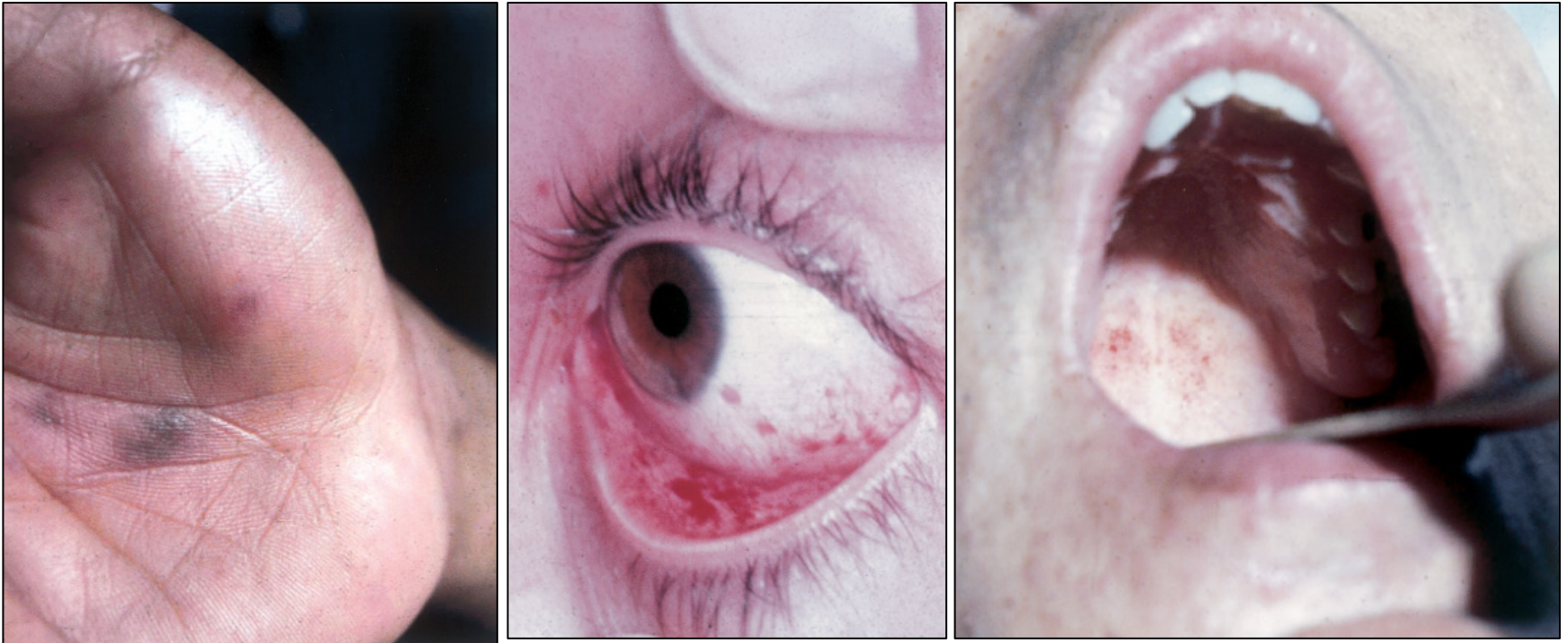


Purpuric Eruptions

- Septic
- Allergic/Immunologic



Ptn: Chills, nausea and fever since this morning

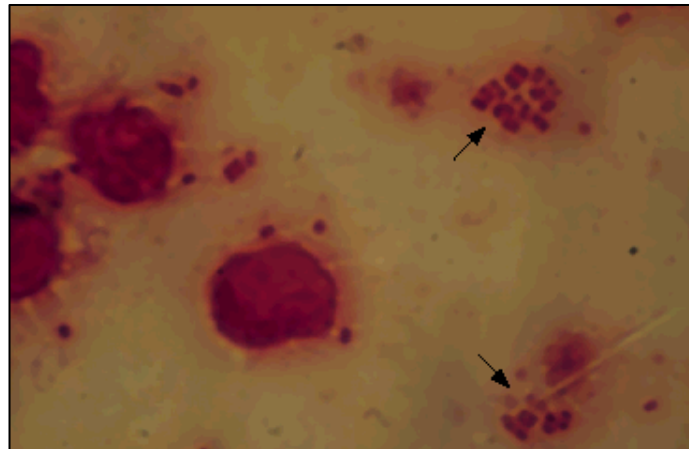


- Petechia on hand, eye and palate
- High fever, toxic patient, low blood pressure, neck stiffness

: meningococemia with bacterial meningitis

Meningococemia

- Gram- diplococcus *N. meningitidis*
- Outbreaks; CAVE predisposing factors
- Spectrum of diseases
- Rapid progression; mortality 10-25 %
- Skin lesions:
 - 75 % petechial/maculopapular lesions
 - 11 % purpuric/ecchymotic lesions
 - 14 % no skin lesions



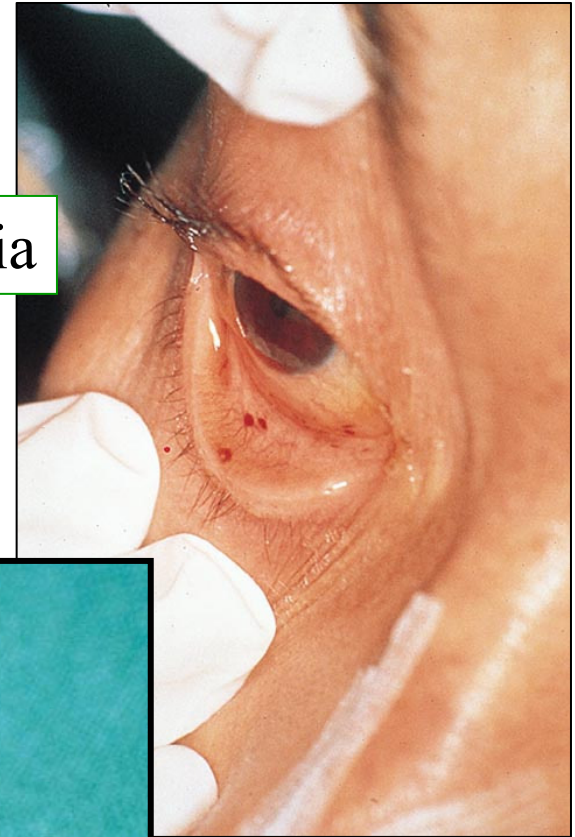
Am J Dis Child, 1974, 127, 173
Mandell, 2005, Ch 208, 2498

Ptn: Chills, nausea and fever since 3 days

Janeway lesions

Conjunctival petechia

Splinter
hemorrhaghe



- High fever, acutely sick patient, normal blood pressure, mild neck stiffness, normal heart auscultation
- Normal TEE on day 0, heart murmur on day 2 with mitral valve perforation on TTE
- 8/8 blood cultures grow gram positive cocci in cluster



: *S. aureus* acute native valve endocarditis

Endocarditis

- Spectrum of manifestations (acute, subacute, chronic)
- Mainly streptococci, staphylococci and enterococci
- Complicated by valve destruction, thrombotic complications, mycotic aneurysmata, ...
- Mortality remains high
- Skin lesions:
 - Non-specific: petechiae and splinter hemorrhages
 - Specific: Janeway lesions, Osler's nodes, Roth Spots (eye)
- Diagnosis = Modified DUKES criteria

Major criteria
Positive blood cultures for IE
Typical microorganism for infective endocarditis from two separate blood cultures in the absence of a primary focus
Viridans streptococci
Streptococcus faecalis, including nutritional variant strains
HACEK group - Haemophilus spp., Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella spp. and Kingella kingae
Community-acquired Staphylococcus aureus or enterococci
Particularly positive blood culture, defined as recovery of a microorganism consistent with IE from:
Blood cultures drawn more than 12 hours apart OR
All of three or a majority of two or more separate blood cultures, with first and last drawn at least one hour apart
Single positive blood culture for Coxiella burnetii or antiphase 1 IgG antibody titer $\geq 1:2000^*$

Evidence of endocardial involvement
Positive echocardiogram for IE
TEE recommended in patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE (see criteria above); TEE as first test in other patients
Definition of positive echocardiogram
Oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jet, or on implanted material, in the absence of an alternative anatomic explanation OR
Abscess OR
New partial dehiscence of prosthetic valve

New valvular regurgitation
Increase in or change in preexisting murmur not sufficient

Minor criteria
Predisposition - predisposing heart condition or intravenous drug use
Fever - $\geq 38.0^{\circ}\text{C}$ (100.4°F)
Vascular phenomena - major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
Immunologic phenomena - Osler nodes, Roth spots, rheumatoid factor
Microbiologic evidence - positive blood culture but not meeting major or minor as noted previously
Including single positive culture for coagulase negative staphylococci and organisms that do not cause endocarditis OR serologic evidence of active infection with organism consistent with IE
Etiologic agent major criteria not met

Definite IE
Pathologic criteria
Microorganism demonstrated by culture or histology in a vegetation, or in a vegetation that has embolized, or in an intracardiac abscess OR
Pathologic lesions - vegetation or intracardiac abscess, confirmed by histology showing active endocarditis

Clinical criteria - using specific definitions listed in Table B:
2 major criteria OR
1 major and 3 minor criteria OR
5 minor criteria

Possible IE*
1 major criterion and 1 minor criterion OR 3 minor criteria

Rejected IE
IE in alternate diagnosis for manifestations of endocarditis OR
Resolution of manifestations of endocarditis, with antibiotic therapy for four days or less OR
No pathologic evidence of infective endocarditis at surgery or autopsy after antibiotic therapy for four days or less
Does not meet criteria for possible infective endocarditis, as above

Clin Infect Dis, 2000, 30, 633
Mandell, 2005, Ch 74, 975

Ptn: chills, myalgia, diarrhea and weakness since this morning



- Conjunctival injection, erythematous maculopapular eruption
- toxic patient, low blood pressure, headache

: staphylococcal toxic shock syndrome

Staphylococcal toxic shock syndrome

- TSST-1, enterotoxin A, B, C, D, E and H
→ superantigen → massive T cell activation
- Rapidly evolutive with multi-system involvement (renal, hepatic, neurological, ...)
- Mortality 10-50 %

Case definition - Staphylococcal toxic shock syndrome

1. **Fever:** > 38,9 °C
 2. **Hypotension:** systolic BP ≤ 90; orthostatic drop diastolic BP ≥ 15 mmHg, orthostatic syncope or dizziness
 3. **Rash:** diffuse macular erythema
 4. **Desquamation:** 1-2 weeks after onset, particularly palms and soles
 5. **Multisystem involvement (≥ 3 organ systems):**
 1. GI: vomiting or diarrhea
 2. Muscular: severe myalgia or CK > 2 x ULN
 3. Mucous membranes: vaginal, oropharyngeal, conjunctival hyperemia
 4. Renal: BUN or creat > 2 x ULN or pyuria (> 5 WBC/hpf)
 5. Hepatic: Bili or transaminases 2 x ULN
 6. Hematological: platelets < 100.000/μl
 7. CNS: desorientation, altered consciousness without focal neural signs and in the absence of high fever or hypotension
 6. **Negative tests for:**
 1. Blood, CNS and throat cultures (except blood cultures for *S. aureus*)
 2. Serology for Rocky Mountain spotted fever, leptospirosis, measles
- **Confirmed case = 6 criteria; probable case = 5 criteria**

MMWR, 1990, 39(RR-13):1

Clin Microbiol
Rev 1997 Jul;10(3):505-20
Mandell, 2005, Ch 192, 2321

Staphylococcal Scalded Skin Syndrome



Drug eruptions

- Urticaria
- Morbiliform/ Maculopapular exanthema
- AGEP: acute generalized exanthemic pustulosis
- DRESS: drug reaction, eosinophilia, systemic symptoms
- Stevens Johnson syndrome
- Toxic Epidermal Necrolysis /Lyel' syndrome

- Urticaria
- Acute hemorrhagic edema (Finkelstein)



Erythema Exudativum Multiforme

= Mostly associated with infections

Stevens Johnson Syndrome

= Mostly associated with drugs



Stevens Johnson Syndrome (BSA < 10%)



Toxic Epidermal Necrolysis (BSA > 30%)

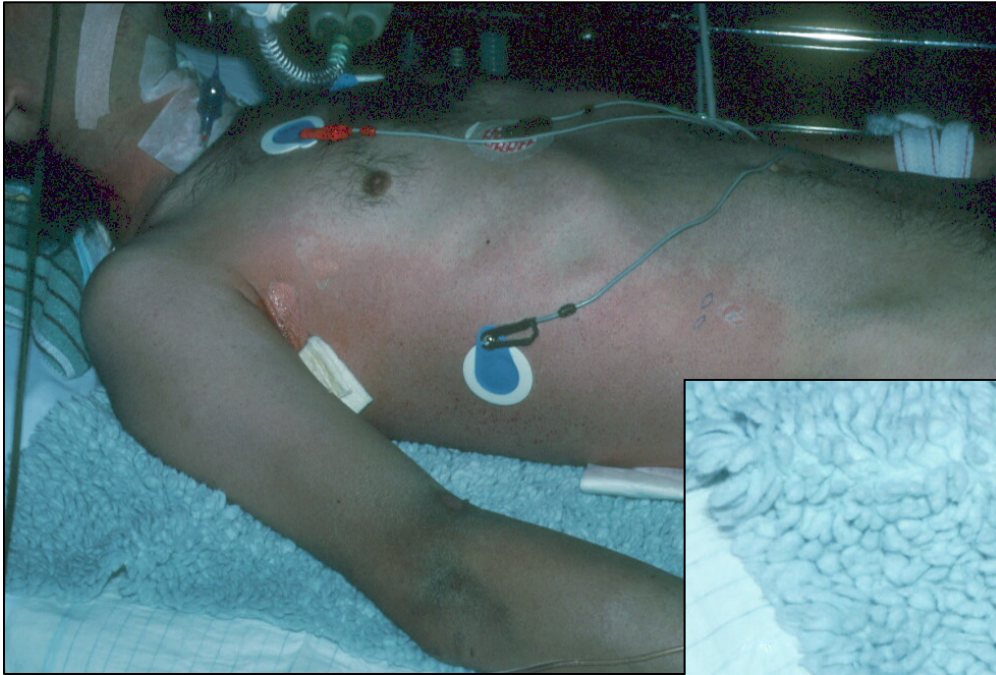


Table 21.2 Precipitating factors in Stevens–Johnson syndrome.

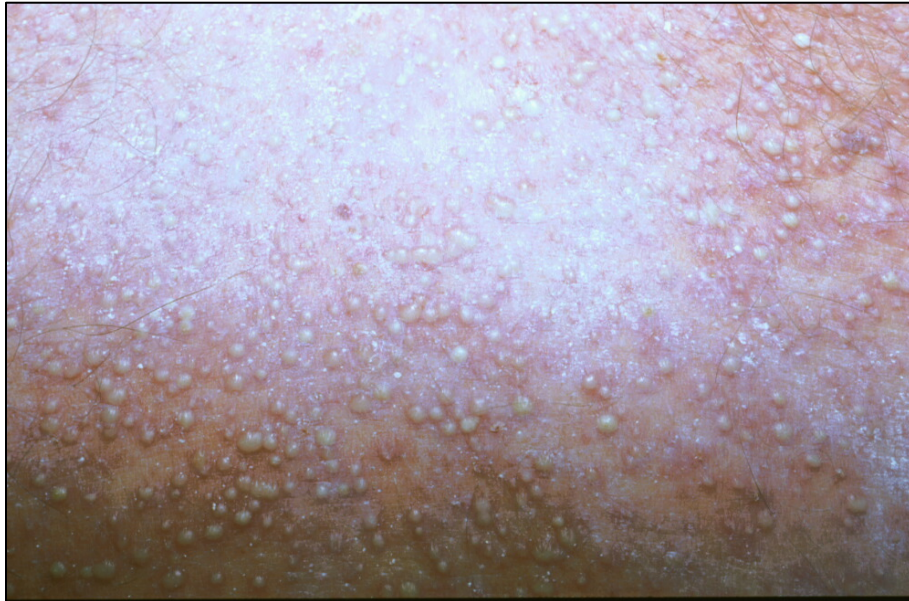
| PRECIPITATING FACTORS IN STEVENS–JOHNSON SYNDROME | |
|---|---|
| Drugs | NSAIDs, especially ibuprofen and naproxen Sulfonamides Anticonvulsants (see Table 21.3) Penicillins, doxycycline, tetracyclines Others |
| Bacterial infections | <i>Mycoplasma pneumoniae</i> <i>Yersinia</i> <i>Mycobacterium tuberculosis</i> <i>Treponema pallidum</i> <i>Chlamydia</i> Others (<i>Streptococcus</i> , <i>Salmonella typhi</i> , <i>Pneumococcus</i> , Enterobacteria) |
| Fungal infections | Coccidioidomycosis Histoplasmosis |
| Viral infections | Enteroviruses Adenoviruses Measles Mumps Influenza Others |
| X-irradiation | |
| Inflammatory bowel disease | |
| Vaccines BCG | |

Table 22.3 SCORTEN severity-of-illness score.

| SCORTEN SEVERITY-OF-ILLNESS SCORE | | | |
|--|------------------|------------------------------------|-------------------------|
| SCORTEN Parameter | Individual score | SCORTEN (sum of individual scores) | Predicted mortality (%) |
| Age > 40 years | Yes=1, No=0 | 0-1 | 3.2 |
| Malignancy | Yes=1, No=0 | 2 | 12.1 |
| Tachycardia (>120/min) | Yes=1, No=0 | 3 | 35.8 |
| Initial surface of epidermal detachment >10% | Yes=1, No=0 | 4 | 58.3 |
| Serum urea >10 mmol/l | Yes=1, No=0 | ≥5 | 90 |
| Serum glucose >14 mmol/l | Yes=1, No=0 | | |
| Bicarbonate <20 mmol/l | Yes=1, No=0 | | |

Acute Generalized Exanthematous Pustulosis:

AGEP



DRESS: Drug Reaction Eosinophilia and Systemic Symptoms

- Lymphadenopathies
- PBO: eosinophilia
- LFT ↑
- Lung infiltrate



Table 23.5 Characteristics of major drug-induced eruptions. *Also referred to as hypersensitivity syndrome. **Nonpigmenting.

| CHARACTERISTICS OF MAJOR DRUG-INDUCED ERUPTIONS | | | | |
|--|--------------------------------------|------------------|---------------|--|
| Clinical presentation | Percentage that are drug-induced (%) | Time interval | Mortality (%) | Responsible drugs |
| Exanthematous eruption | Child: 10–20 Adult: 50–70 | 4–14 days | 0 | Aminopenicillins Sulfonamides Cephalosporins Anticonvulsants Allopurinol |
| Urticaria Anaphylaxis 30 | <10 | Minutes Hours | 0 5 | Penicillins Cephalosporins NSAIDs Monoclonal antibodies Contrast media |
| Fixed drug eruption | 100 | <48 hours | 0 | TMP-SMX NSAIDs Tetracyclines Pseudoephedrine** |
| Acute generalized exanthematous pustulosis (AGEP) | 70–90 | <4 days | 1–2 | -Lactam antibiotics Macrolides Calcium channel blockers |
| Drug reaction with eosinophilia and systemic symptoms (DRESS)* | 70–90 | 15–40 days | 5–10 | Anticonvulsants Sulfonamides Allopurinol Minocycline |
| Stevens-Johnson syndrome (SJS) Toxic epidermal necrolysis | 70–90 | 7–21 days | 5 30 | Sulfonamides Anticonvulsants NSAIDs Allopurinol |

Diagnosis of drug reaction

Anamnesis: chronology

Clinical characteristics

- itch or pain

- mucous membrane involvement

- systemic symptoms (fever, adenopathies)

Histology

LAB: RAST

Patch testing / Photopatch testing

When you suspect a serious cutaneous drug reaction:
Stop the suspected drug!!!

Pleva



Psoriasis Erythroderma



Erythema Nodosum



CAUSES OF ERYTHEMA NODOSUM

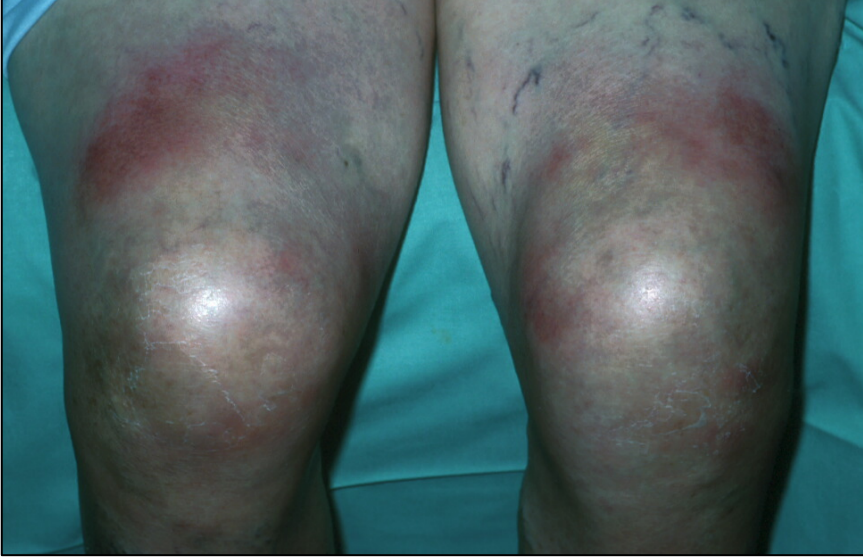
| Incidence | Cause | Comments |
|-------------------------|---|--|
| Most common | Idiopathic | Still the largest single category, ranging from 35 to 55% of cases |
| | Streptococcal infections, especially upper respiratory tract | The largest single infectious cause |
| | Some other infections (e.g. upper respiratory tract viruses, <i>Mycoplasma</i> , tuberculosis) | Infection in general may account for 1/3 or more of cases |
| | Drugs | Especially estrogens and birth control pills, also sulfonamides, penicillin, bromides, iodides |
| | Sarcoidosis | 11–22% of cases in some series |
| | Inflammatory bowel disease | Crohn's disease has a stronger association with erythema nodosum than does ulcerative colitis |
| | Coccidioidomycosis | Erythema nodosum appears to have a protective effect, with lower incidence of disseminated disease |
| Uncommon | Uncommon infectious associations: <i>Yersinia</i> , hepatitis B Behçet's disease Sweet's syndrome Pregnancy | |
| Rare or newly described | Rare infectious associations: Brucellosis Meningococcosis Gonococcus <i>Escherichia coli</i> Pertussis Syphilis Leprosy Cat scratch disease <i>Chlamydia</i> Blastomycosis Histoplasmosis HIV infection | Erythema nodosum leprosum is really a different disease with leukocytoclastic vasculitis |

Sweet Syndrome

- Fever
- PBC: neutrophilia
- Hist: Neutroph. Infiltr.



Erythema Nodosum + Sweet Syndrome



Ptn : Fever, rash, rhinitis.

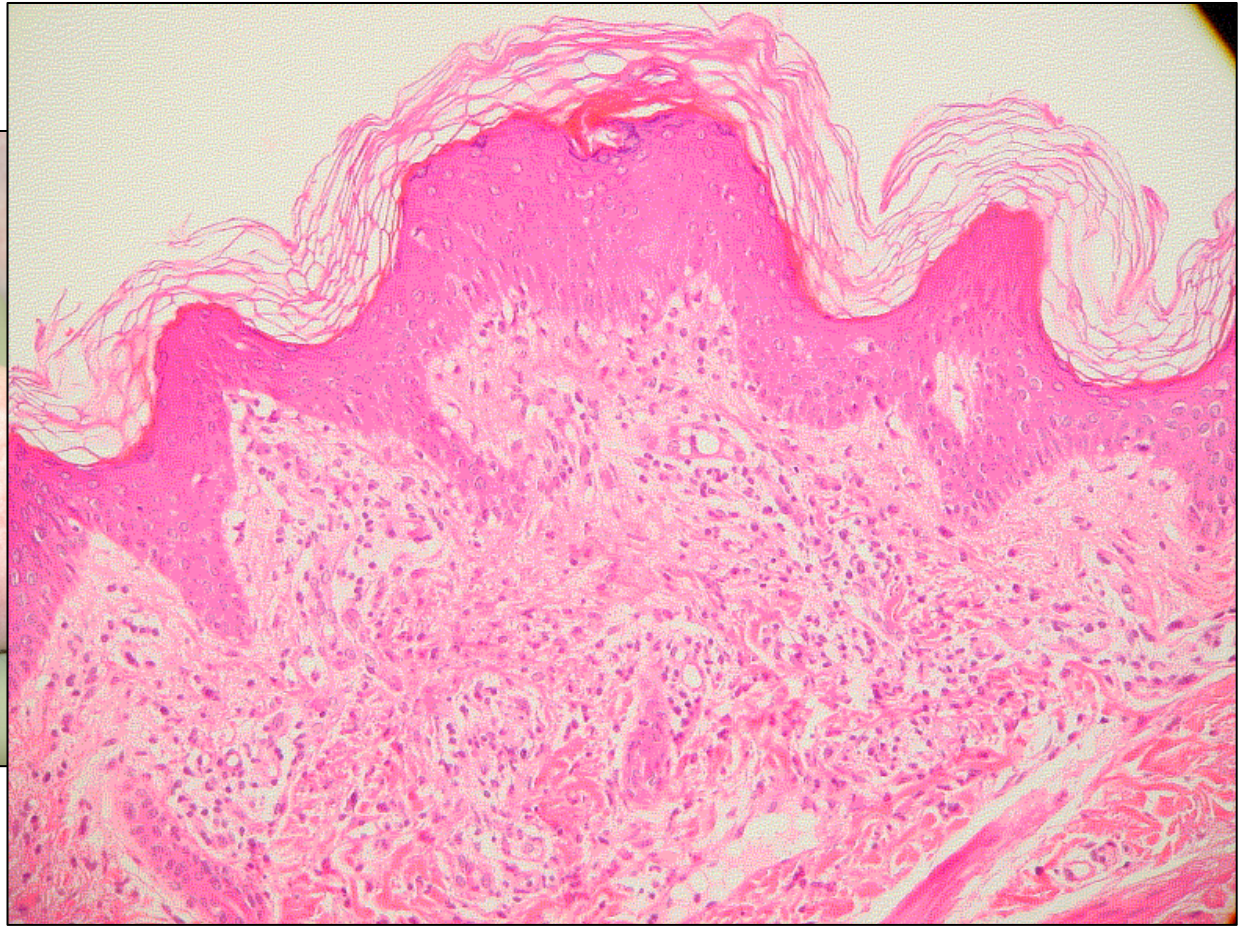
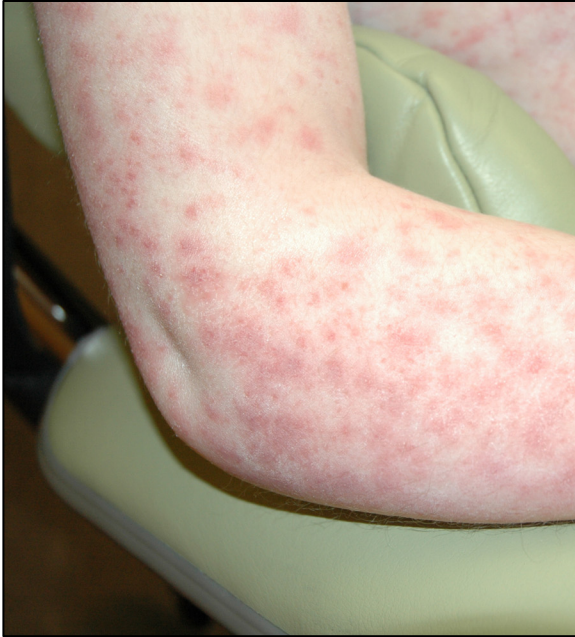


- PBC : eosinophilia
- History: epilepsy R/lamotrigine

: Viral infection or DRESS



Ptn : Fever, rash, rhinitis.



- Serology: coxsackie IgM: positive

: coxsackie infection

II. Dermatological manifestations of systemic infectious diseases in immunocompromised hosts

S.J. Vandecasteele, MD, PhD

Dienst Inwendige Ziekten - Nierziekten – Infectieziekten

C. De Cuyper, MD

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AZ Sint-Jan AV, BRUGGE

1. Introduction

- > 20 % of immunocompromised patients will develop skin lesions, often with fever

Infect Dis Clin North Am 1996, 10:129-48.

- Occasionally, these lesions reflect disseminated infection

Medicine, 1985, 64: 115-33.

- These lesions are of significant importance: they permit early recognition and treatment of disseminated infection (“early warning”)

Medicine, 1985, 64: 115-33.
Clin Infect Dis, 2006, 42:296-297
Rev Infect Dis, 1986, 8:1-11

Different kinds of defects in host defence:

1. Neutropenia/neutrophil dysfunction disorders
2. Humoral dysfunction disorders
3. Cell mediated immune dysfunction disorders
4. Diseases associated with immune dysfunction
 - Cirrhosis
 - Diabetes
 - SLE
 - Uremia/dialysis

2. Neutropenia or neutrophil dysfunction

- Prolonged or profound neutropenia
- Increased risk for infection with gram - and gram + bacteria, anaerobic bacteria and fungi
- Causes:
 - Chemotherapeutic agents (cancer/leukemia)
 - Myeloproliferative, myelodysplastic disorders, aplastic anemia
 - Congenital/cyclic neutropenia
 - Felty syndrome, overwhelming sepsis, some drugs

- BACTERIAL INFECTIONS

- *Pseudomonas aeruginosa*
- *Stenotrophomonas maltophilia*
- *Aeromonas hydrophila*
- *Streptococcus viridans*
- *Clostridium spc*

- FUNGAL INFECTIONS

- *Candidiasis*
- *Aspergillus spc*
- *Trichosporon beigelii*
- *Fusarium spc*



Ptn: Treatment for AML, neutropenic for 15 days

- New episod of fever with dyspnea and several painful erythematous papels on the thrunk
- Papels rapidly evolve → bullae → hemorrhagic bullae → gangrenous ulcer + halo



: Ecthyma gangrenosum (*Pseudomonas spc*)

Ecthyma gangrenosum

- Perivascular invasion veins/arteria + secondary ischemic necrosis
- Mainly caused *Pseudomonas spc*, also described with staphylococci, streptococci, numerous gram- bacteria, fungi and HSV
- Septic form and non-septic form (local inoculation)
- Located on gluteal or perineal region (57%), extremities (30%), trunk (6%), and face (6%)
- High mortality, lower in non-septic form
- Importance of skin biopsy (culture and pathology) in diagnosis

Ptn: Patient with CLL and pneumonia; receiving steroids and antibiotics for 14 days

- Low grade fever, anorexia and CRP 12 mg/dl since a few days

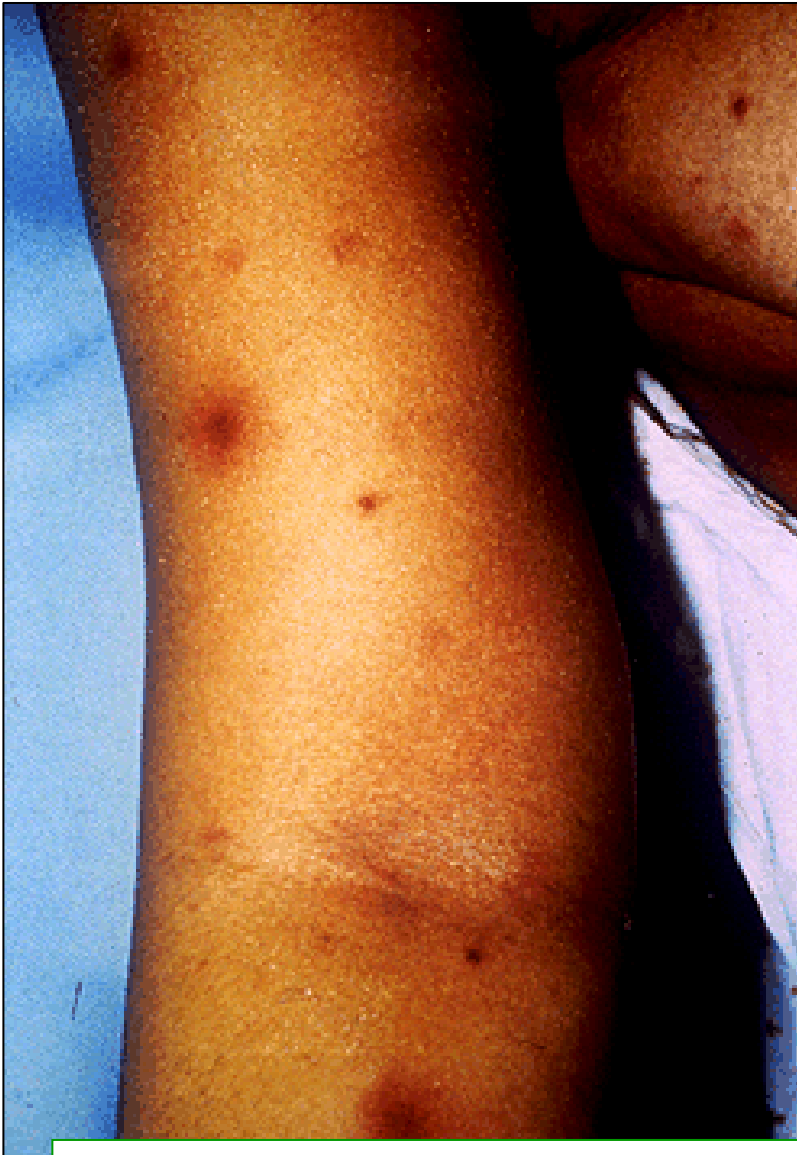


- Blurred vision and hemodynamic deterioration

: candida sepsis with disseminated candidiasis

Candida sepsis with disseminated candidiasis

- Presentation: minimal fever → full-blown sepsis
- Hematogenic spread → visceral involvement (eye, brain, kidney, heart)= disseminated candidiasis
- Skin lesions = clue to disseminated disease:
painless pustules on erythematous base
↔ nodular lesions with central necrosis
- Diagnosis: blood cultures, skin biopsy
- High mortality, especially when treatment is delayed (up to 45 %)



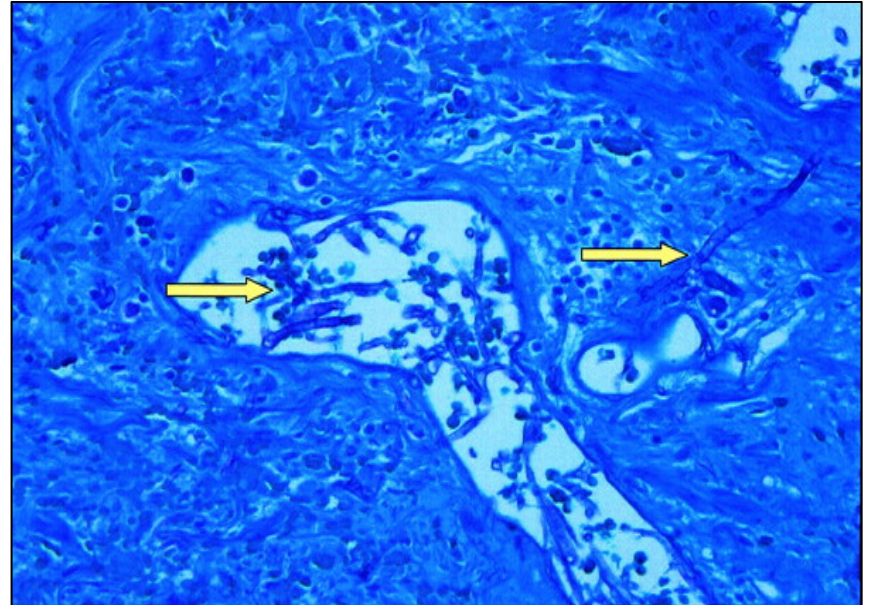
Nodular lesions in neutropenic patient



Disseminated lesions, later stage

Ptn: 53 years; AML, DMII

- New episod of fever at the end of chemotherapy
- Tender lesion on cheek, turning black over night



: Ecthyma gangrenosum (*Zygomycosis*)

Clin Infect Dis, 2006, 42:296-297

3. Cell-mediated immune dysfunction

- Increased risk of infection with intracellular bacteria, viruses, fungi and parasites
- Increased risk of extracellular pathogens such as *Pneumocystis carinii*, *strongyloides*, *candida*

- BACTERIAL INFECTIONS
 - *Nocardia*
 - *Tuberculosis*
 - Non-tuberculous mycobacteria
- VIRAL INFECTIONS
 - HSV
 - VZV
- FUNGAL INFECTIONS
 - *Cryptococcus neoformans*
 - Endemic fungi (*Histoplasma*, *Blastomyces*, *Coccidioides*)
 - *Pseudoallescheria boydii*



Cutaneous MAC



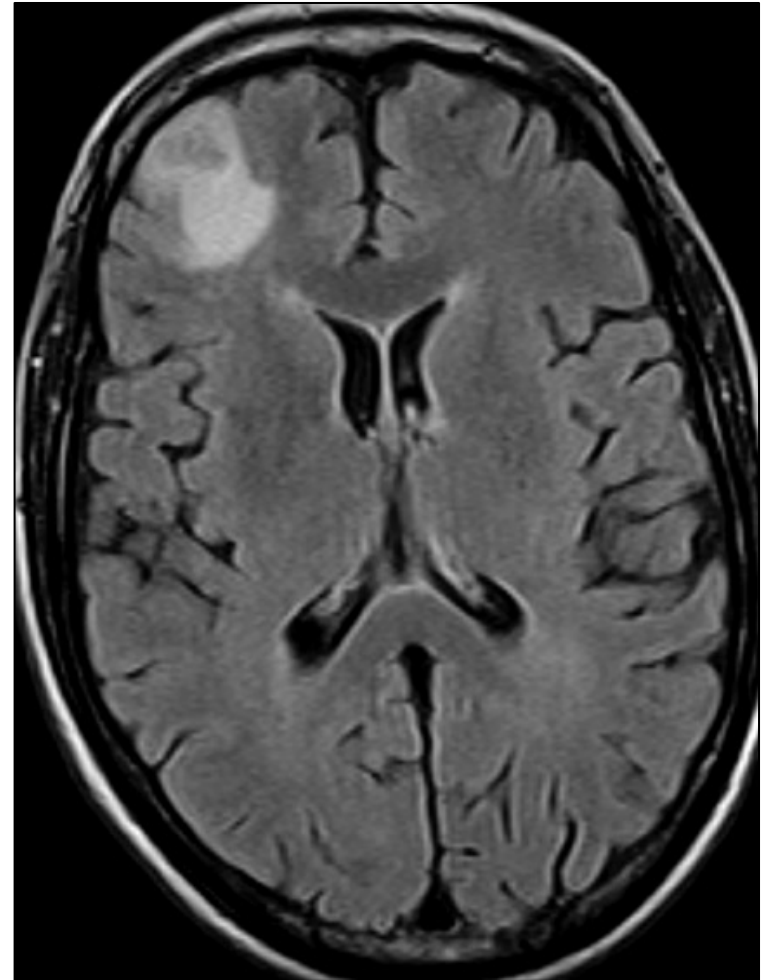
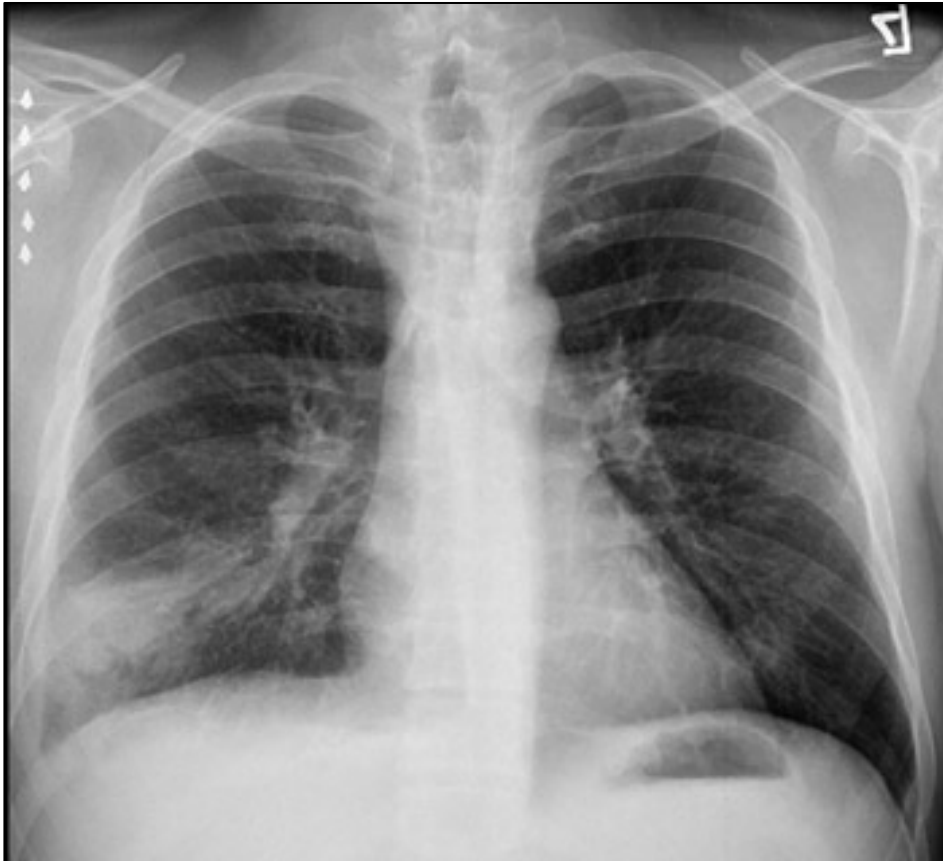
Herpes zoster



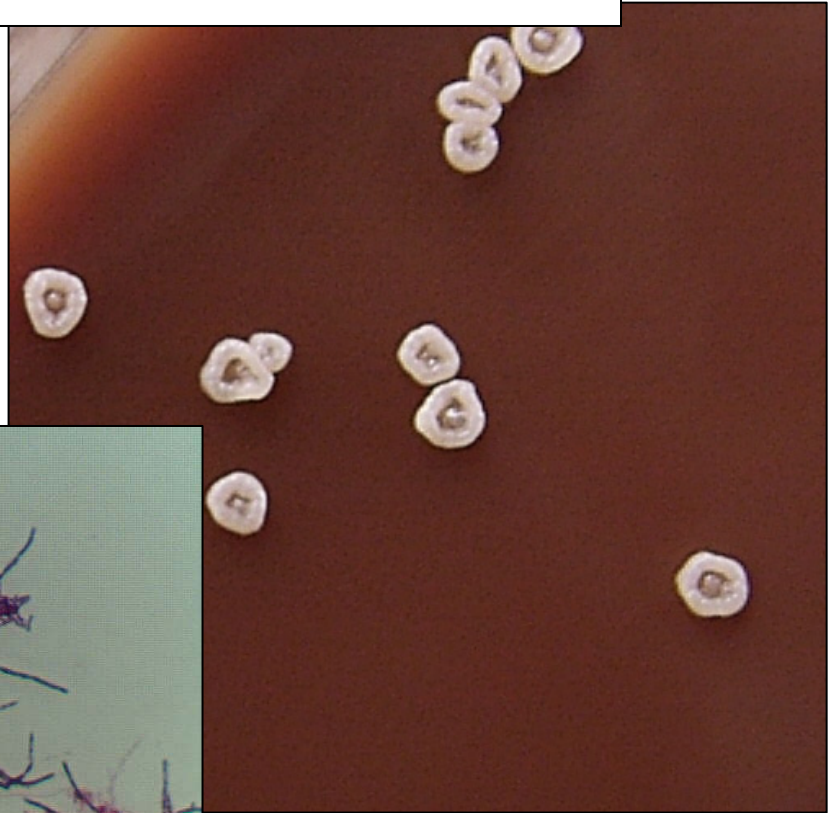
Histoplasmosis

Ptn: 45 y old recipient of kidney/pancreatic transplant since 6 months

- Persistent cough since weeks and new onset hallucinations



Associated skin lesion



: disseminated nocardia infection

Nocardia infections

- Immune deficiency is major risk factor; associated with disseminated/more severe infection
- gram-positive, partially acid-fast, soil-born aerobic actinomycete – prolonged incubation !!
- Actinomycetomata: progressive local destructive infection
- Pathology: suppurative granulomata, progressive fibrosis and necrosis, sinus formation with destruction of adjacent structures, and macroscopically visible infective granules
- Disseminated infection mainly affecting lung, CNS, kidney

Ptn: Kidney transplantation 25 years ago

- Chronic, small, intermittent draining lesions on the left index finger
- Slowly deformative arthritis of all fingers of the same hand



**: *Mycobacterium chelonae* infection +
tuberculous pseudo-rheuma**

Non-tuberculous mycobacterial infections

- Skin/soft tissue + disseminated infections in compromised hosts
- MAC, *M. kansasii*, Rapidly growing mycobacteria (*M. fortuitum*, *M. chelonae*, and *M. abscessus*), *M. marinum*
- Painless nodules; abscesses; cellulitis; intermittent draining (watery) lesions; ...
- Notify laboratory: prolonged incubation, optimal temperature
- R/ clarithromycin + rifampin/ethambutol + ...:
prolonged therapy

4. HIV infected hosts

- Progressive and ultimately severe defect in cellular immunity (T4-lymphocytes)
- Cutaneous reactions are extremely common in HIV infected ptns (79 % of ptns over 3 y)
- Drug reactions are the leading cause of skin problems
- Patients with AIDS used to be/are much more likely to have skin problems than HIV positives

NEJM, 1993, 328:1670-1674

Arch Intern Med, 1991, 1295-1303

- BACTERIAL INFECTIONS

- *Staphylococcus aureus*
- Bacillary angiomatosis
- *Neisseria gonorrhoea*
- Syphilis
 - Primary syphilis
 - Secondary syphilis
 - Tertiary syphilis
- *Pneumococcus*
- *Helicobacter cinadei*

- MYCOBACTERIAL INFECTIONS

- VIRAL INFECTIONS

- Acute HIV infection
- Genital herpes virus
- Varicella zoster virus
- Parvovirus
- Hepatitis B
- *Molluscum contagiosum*
- Human papillomavirus



- PARASITIC INFECTIONS
 - Scabies
 - Leishmaniasis
- KAPOSII'S SARCOMA
- DRUG REACTIONS
- FUNGAL INFECTIONS
 - Cutaneous and/or systemic
 - *Cryptococcus*
 - *Histoplasmosis*
 - *Blastomycosis*
 - *Coccidioidomycosis*
 - *Sporotrichosis*
 - *Penicillium marneffeii*
 - *Pneumocystis*
 - Candidiasis
 - *Pityriasis versicolor*
 - *Pityrosporon folliculitis*
 - Proximal subungual onychomycosis



Scabies



Disseminated Cryptococcosis



Fixed drug eruption
HIV + cotrimoxazole

| DIAGNOSIS | TOTAL PATIENTS | HIV STATUS AT 1ST VISIT FOR SKIN CONDITION† | | | | | |
|------------------------------------|-------------------|---|------------------|---------------------|------------------|------------------|------------------|
| | | BEFORE HIV DOCUMENTATION | | HIV WITHOUT AIDS | | AIDS | |
| | | <i>rate/1000</i> | | <i>rate/1000</i> | | <i>rate/1000</i> | |
| | | <i>no.</i> | <i>person-yr</i> | <i>no.</i> | <i>person-yr</i> | <i>no.</i> | <i>person-yr</i> |
| Dermatitis | | | | | | | |
| Seborrheic | 92 | 18 | 42 | 48 | 64 | 26 | 87 |
| Contact | 34 | 9 | 21 | 18 | 23 | 7 | 21 |
| Nummular | 16 | 2 | 5 | 6 | 8 | 8 | 24 |
| Other or unspecified‡ | 183 | 43 | 104 | 86 | 113 | 54 | 207 |
| Viral infections | | | | | | | |
| Herpes simplex | 133 | 30 | 70 | 61 | 86 | 42 | 156 |
| Herpes zoster | 67 | 15 | 34 | 32 | 42 | 20 | 63 |
| Verruca vulgaris | 83 | 24 | 56 | 43 | 59 | 16 | 52 |
| Condyloma | 45 | 9 | 21 | 27 | 36 | 9 | 28 |
| Molluscum | 55 | 7 | 16 | 19 | 24 | 29 | 96 |
| Oral hairy leukoplakia | 29 | 1 | 2 | 17 | 22 | 11 | 32 |
| Infections, often bacterial | | | | | | | |
| Folliculitis | 75 | 18 | 42 | 37 | 49 | 20 | 64 |
| Cellulitis | 70 | 18 | 42 | 17 | 22 | 35 | 113 |
| Skin abscess | 57 | 9 | 21 | 18 | 23 | 30 | 94 |
| Impetigo | 26 | 6 | 14 | 10 | 13 | 10 | 30 |
| Furunculosis | 25 | 9 | 21 | 8 | 10 | 8 | 24 |
| Paronychia | 22 | 2 | 5 | 12 | 15 | 8 | 24 |

4.1. Lesions indicative for HIV infection

Ptn: male, 34 y, fever, headache, sore throat and anorexia 3 weeks after a great trip to Thailand



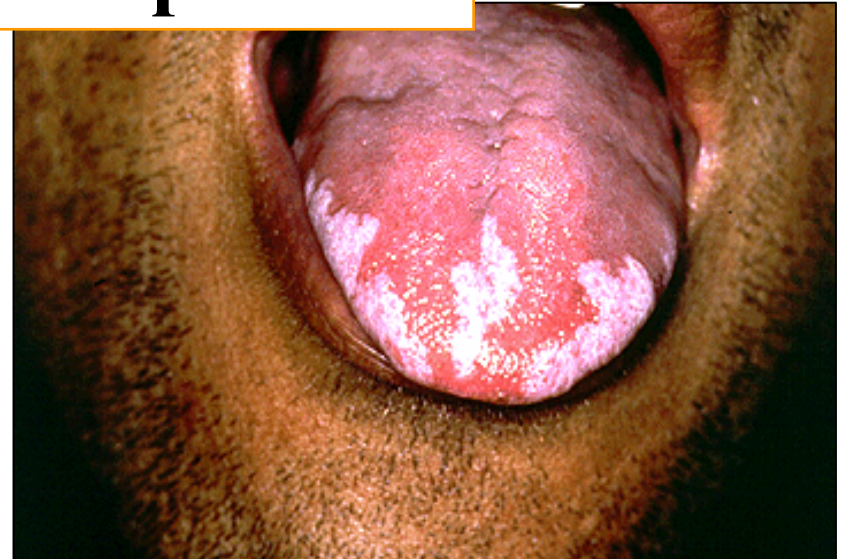
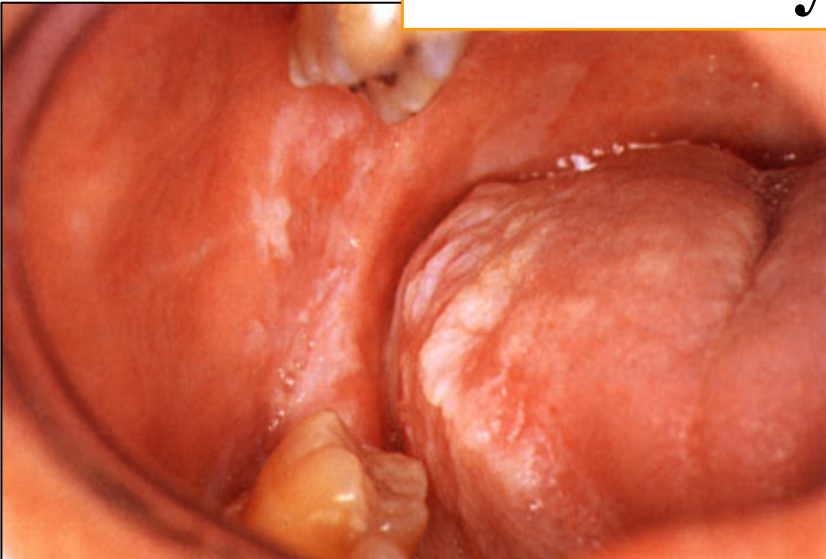
• Enlarged lymph nodes, moderately ill patient

: primary HIV infection

Ptn: male, 34 y, fatigue and moderate weight loss



: oral hairy leukoplakia



Hairy leukoplakia

- Most frequently, but not exclusively associated with HIV
- Indicates bad HIV prognosis (without cART)
- Florid EBV replication *in vivo*
- **Table 1.** Clinical features of oral hairy leukoplakia.

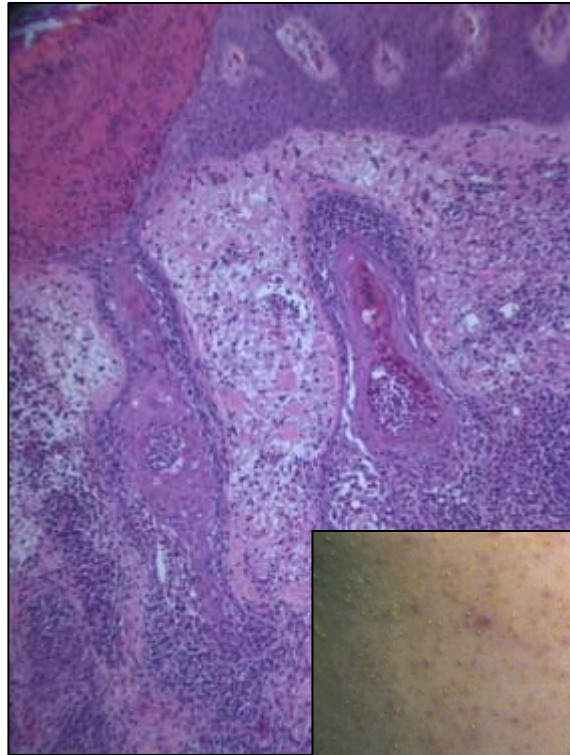
Typically unilateral or bilateral, adherent, slightly elevated whitish or gray patches

Principally located mainly on lateral margins, dorsum, or ventrum of the tongue

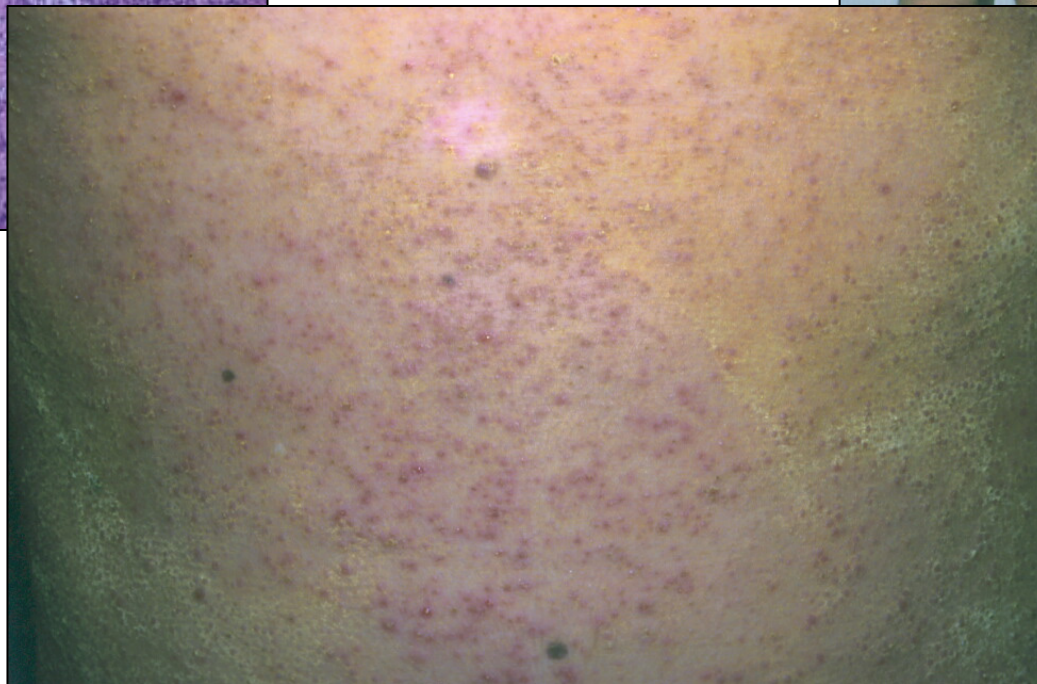
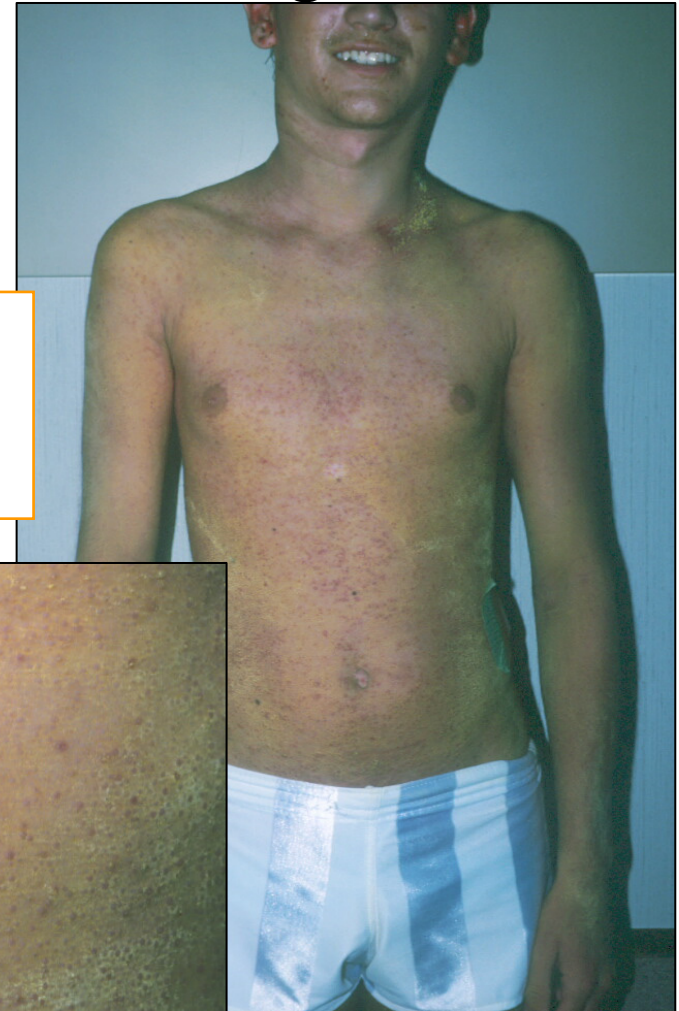
Occasionally observed over the floor of the mouth, palate, or oropharynx

Usually asymptomatic

Ptn: 34 y, fatigue, weight loss and itching



**: eosinophilic
folliculitis**



HIV-associated eosinophilic folliculitis

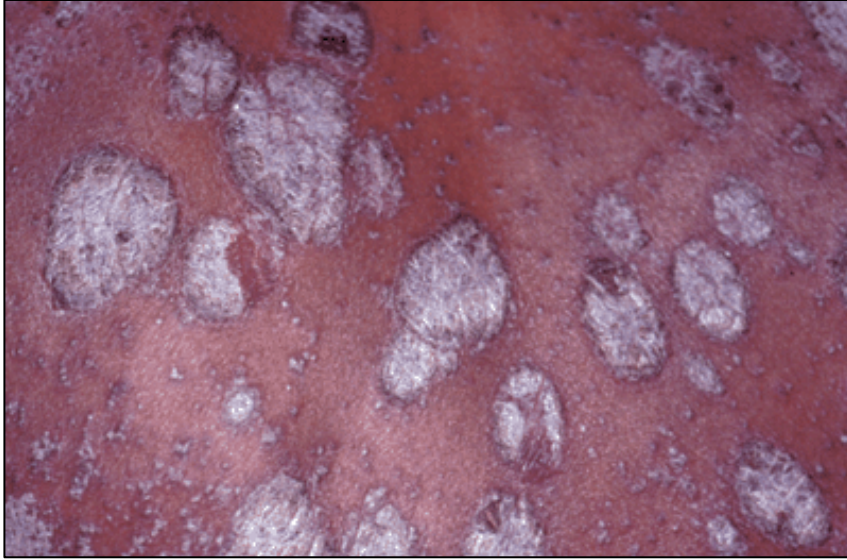
- chronic pruritic skin eruption of uncertain etiology, associated with low CD4 counts and later stage disease
- Diagnosis:
 - clinical suspicion with intensely pruritic follicular lesions (generally on the upper trunk, face, neck, or scalp)
 - histological confirmation
 - Eosinophilia, increased IgE
- Treatment: cART

Ptn: 54 y, long standing lesions on nails



: Proximal subungual onychomycosis, HIV related

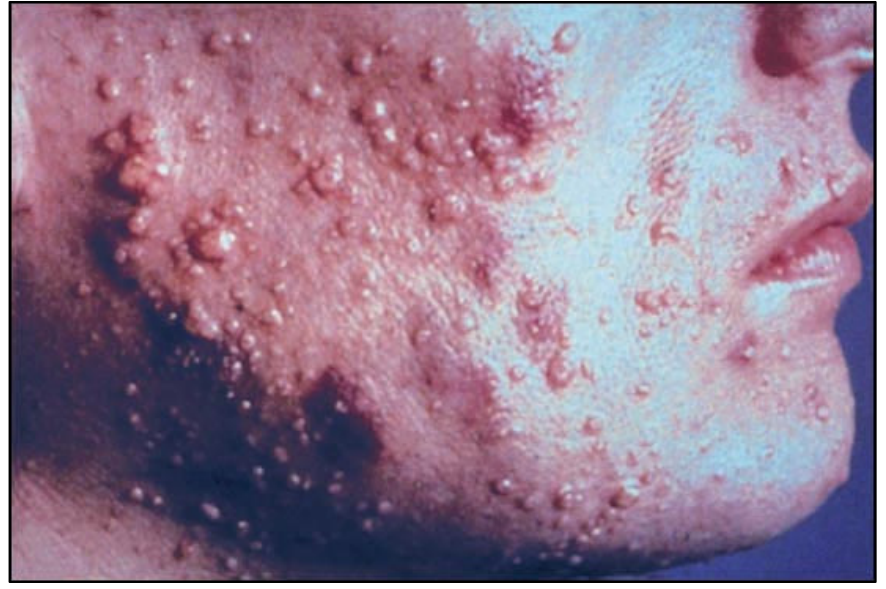
Ptn: 34 y, new onset generalized skin lesions since 3 months



: psoriasis, associated to HIV

- Incidence ~ general presentation, but generalisation and atypic presentation (erythrodermic, pustular, with arthropathy)

Ptn: 34 y, new onset generalized skin lesions since 3 months



: molluscum contagiosum, associated to HIV

- Incidence ~ 10-20 %
- More and bigger lesions in HIV
- Extensive molluscum → HIV ??

Ptn: 34 y, male, painful skin lesions peri-anal initially frequently recurrent, now persistent



**: Chronic HSV-2 ulcer,
HIV associated**

- HSV-2 → OR 3.1 HIV
- More asymptomatic and symptomatic episodes
- Very frequently recurrent/
persistent HSV-2 → HIV ?

J AIDS, 2004, 35:435-445,
Infect Dis Clin North Am, 1994, 583-606

genital ulcer disease (GUD)



HSV :
Usually multiple
Tender
Vesicles - ulcers



genital ulcer disease (GUD)



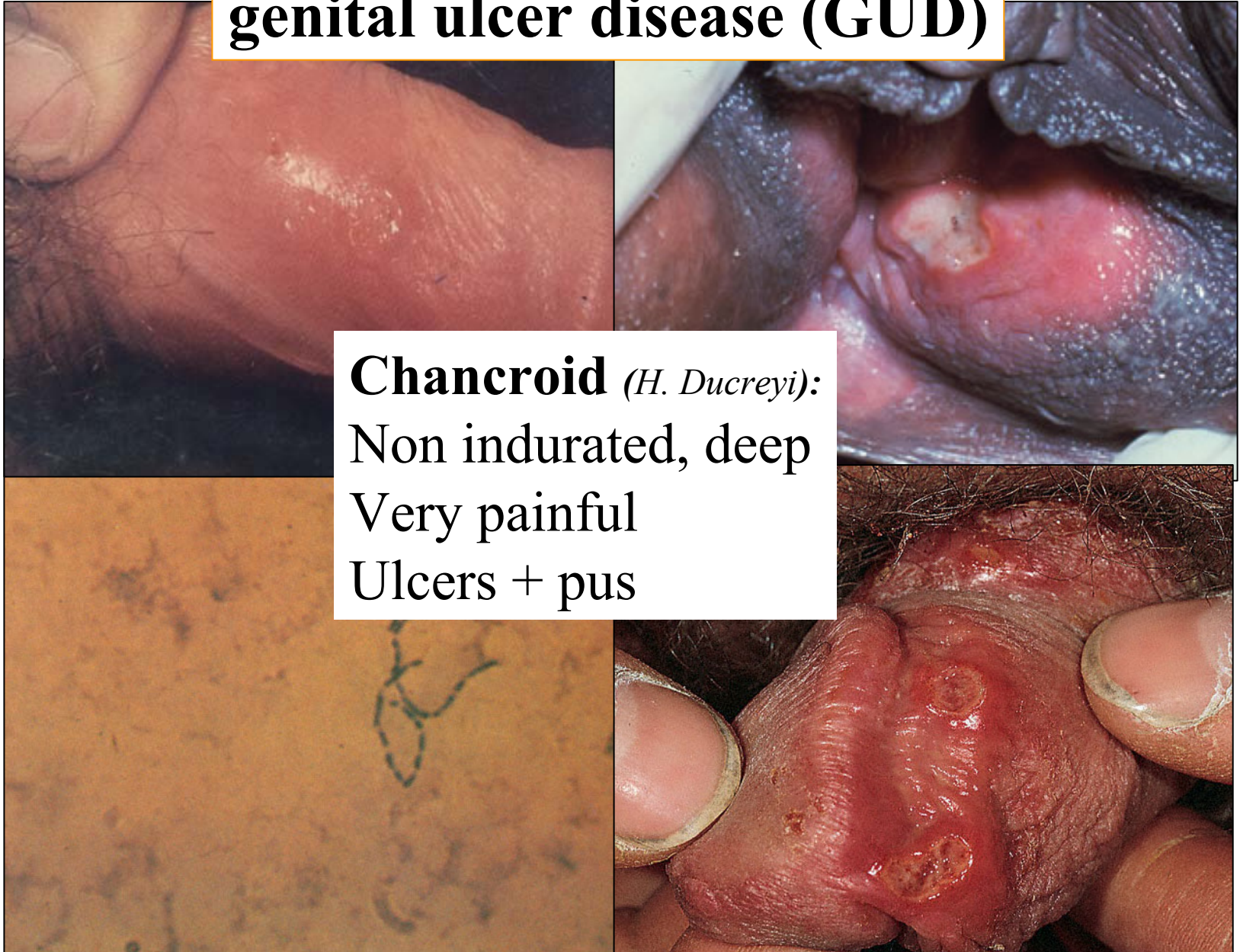
Lues chancre :

Indurated

Smooth firm borders

painless

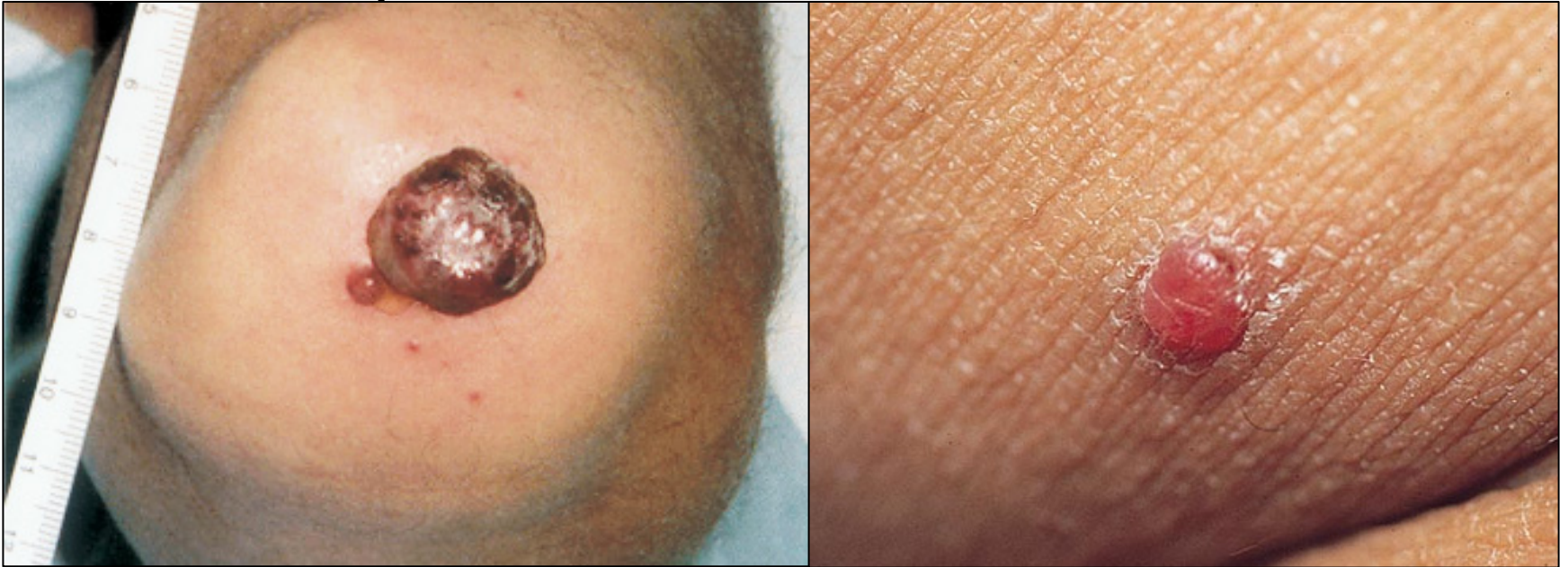
genital ulcer disease (GUD)



Chancroid (*H. Ducreyi*):
Non indurated, deep
Very painful
Ulcers + pus

4.2. Dermatological complications of AIDS

Ptn: 25 T4 cells; prolonged fever; weight loss; non-tender adenopathia



: bacillary angiomatosis

Bacillary angiomatosis

- *Bartonella quintana* > *B. henselae*
- Cutaneous lesions:
 - papular, nodular, pedunculated, verrucous
 - Purple papels ↔ friable lesions
- Subcutaneous nodules; mucosal lesions; osseous lesions
- D/ biopsy/culture/pathology/(serology)

Clin Infect Dis 1996 May;22(5):794-800.



Ptn: 25 T4 cells; pauci-symptomatic nodular skin lesions



• Presentation with gastro-intestinal bleeding

: AIDS Kaposi Sarcoma

Kaposi sarcoma

- HHV-8 associated vascular tumor
- Frequency in AIDS: 20.000× (population); 300× (other immunodeficiency)
- Skin: legs, face, mouth, genital
- Visceral involvement
- D/ biopsy/culture/pathology/(serology)

Clin Infect Dis 1996 May;22(5):794-800.



5. Diseases with immunodeficiency

- **Cirrhosis:**
 - phagocytosis, chemotaxis, complement levels
 - More bacterial infections
- **Diabetes mellitus:**
 - Neutrophilic and T-cell function
 - Skin and soft tissue infections (ulcers, abscesses, cellulitis, necrotizing infections)
 - Keto-acidosis: mucormycosis
- **SLE:**
 - Bacterial skin infections, HSV

Diabetes mellitus

- Affects +/- 5 % of population
- Diabetic foot infections = leading cause of amputation in western world
 - Superficial infections
 - Cellulitis
 - Osteomyelitis

Infect Dis Clin North Am, 1994, 523-32.
Clin Infect Dis 2004; 39:885-910



Diabetes mellitus:

- paronychia, skin and soft tissue infections
- Necrotizing soft tissue infections
- osteomyelitis
- Superficial yeast infections



III. Conclusions

- **Skin lesions may be:**
 - An early clue to underlying infectious disease
 - The hallmark of contagious diseases
 - The first signs of life-threatening infections



Secondary syphilis



Meningococcal meningitis

Epidemiologic clues:

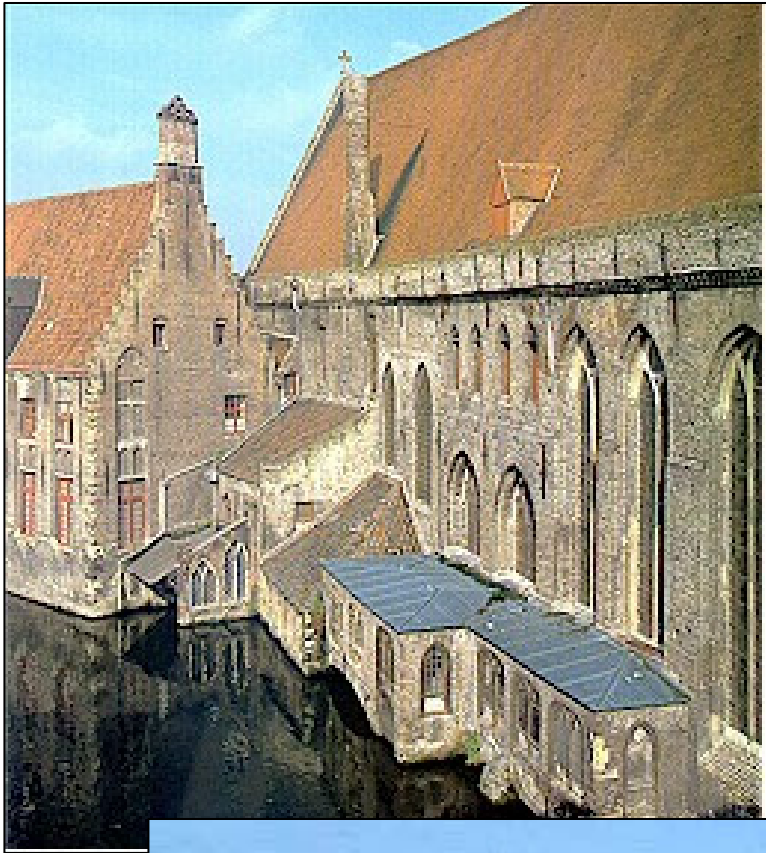
- Age of the patient, immunization and history of childhood illnesses: chickenpox, erythema infectiosum, exanthem subitum, ...
- Season of the year: non-polio enteroviruses (summer and fall), parvovirus (winter/early fall), tick-borne diseases (spring/summer), ...
- Geographic location and travel history: cutaneous leishmaniasis (old world/new world), dengue (caribbean, latin america, asia, ...), creeping eruption, onchocerciasis, ...
- Occupational history/exposure history: toxoplasma/cat scratch (kitten), cryptococcosis (pigeon), rat bite fever (rats), fish tank granuloma (mycobacterium marinum), sporothrix schenckii (florist, gardeners), ...
- Medication history (do not over-estimate relationship between rash and drug fever)
- Immune state of the host ...

NEJM, 1994, 331, 1272

Mandell, 2005, Ch 49, 729-746

Diagnostic approach:

- HISTORY
- CLINICAL ASPECT (macula, papule, nodule, plaque, vesicle, pustule, bulla, ulcer,)
- PHYSICAL EXAM (vital signs, general appearance, lymph nodes, mucous membranes, conjunctivae, genitalia, meningism, HSM, joints, ...)
- LAB (blood count, urinalysis, blood cultures, serology when appropriate)
- MICROBIOLOGY (fluid, viral culture, darkfield microscopy, ...)
- SKIN BIOPSY (for microbiology and pathology)



S.J. Vandecasteele, MD, PhD
Inwendige Ziekten - Nierziekten – Infectieziekten

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Dermatologie

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