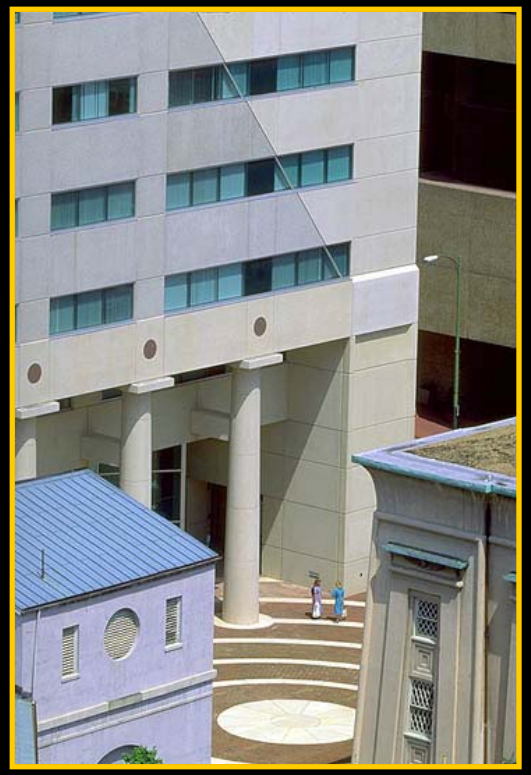
# Opportunistic and Transplant Related Infections

*For VCU Internal Medicine Residents*

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8.5.2008

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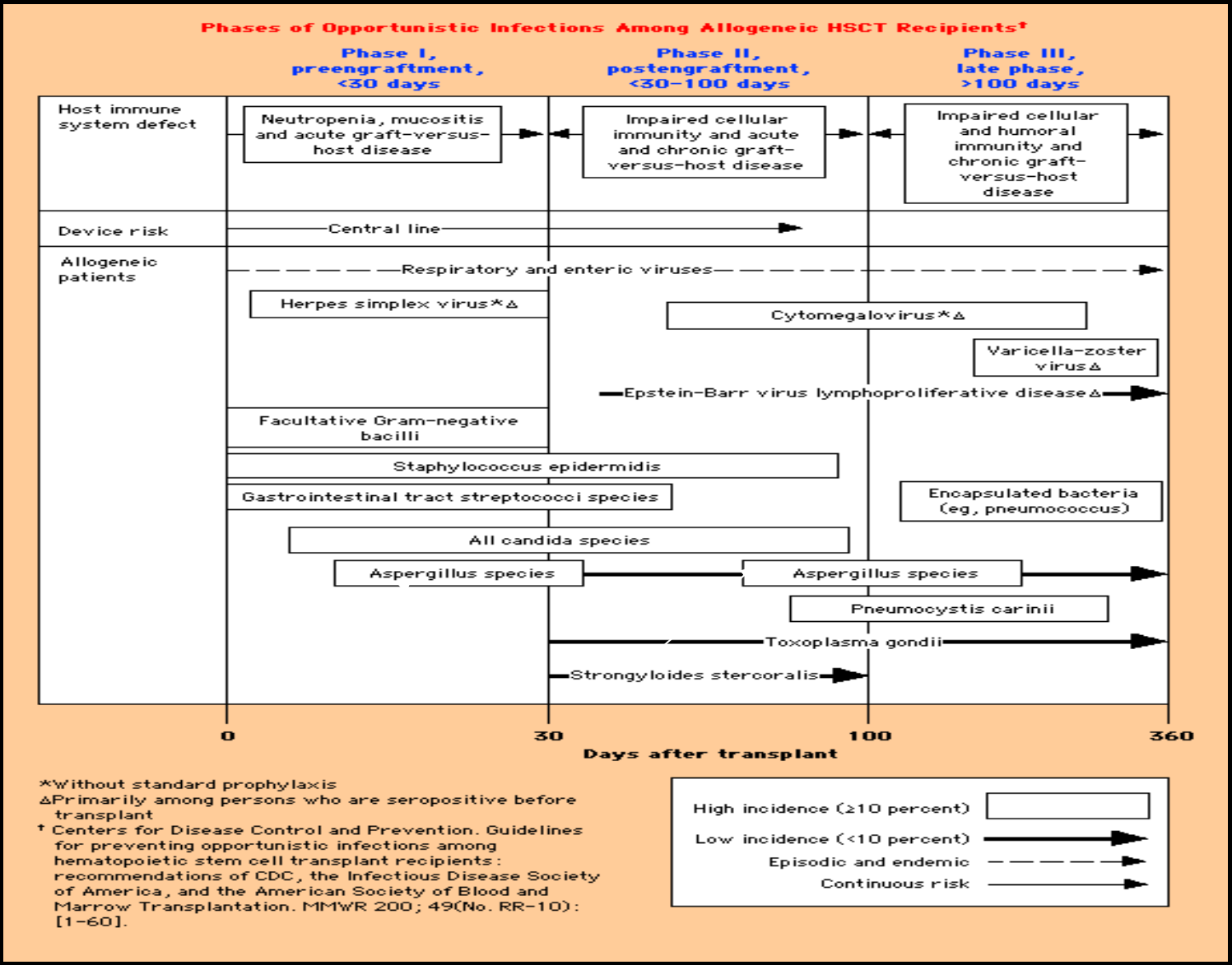
# Disclaimer

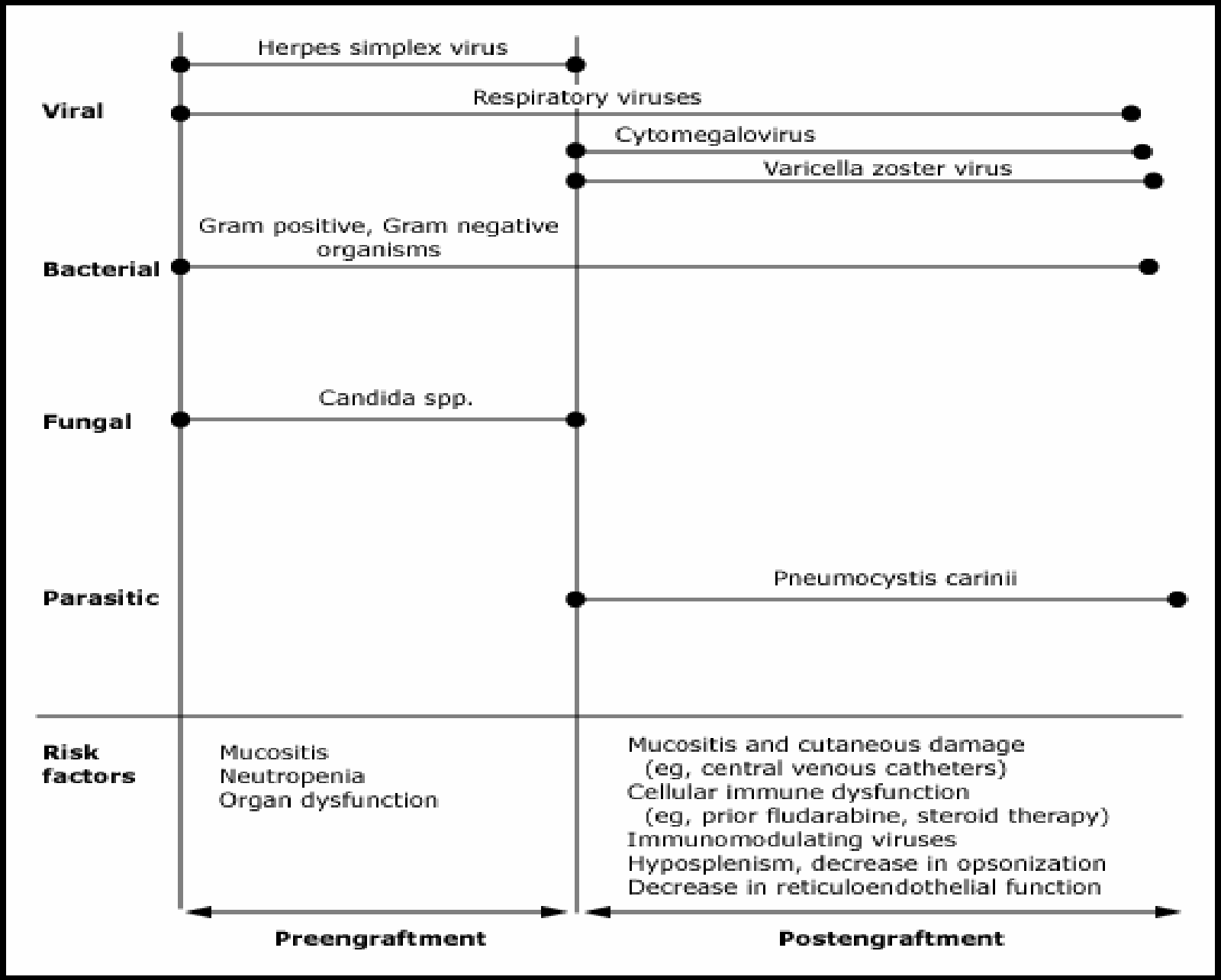
***Many physician/researchers dedicate entire careers to the study and treatment of opportunistic infections. One cannot possibly cover all 'opportunistic' infections in a 60 minute lecture. As such, the purpose of this lecture is to cover material deemed appropriate for an Internal Medicine Board Examination review.***

# Opportunistic Infection Defined

***An infection by a microorganism that normally does not cause disease but pathogenic when the body's immune system is impaired and unable to fight off infection, as in AIDS, neutropenia, and congenital or iatrogenic host defense defects.***

# OI Following BMT





# Preengraftment

- Preengraftment — less than three weeks
  - The major risk factors for infection during the preengraftment period in the first three weeks after HCT are mucositis and cutaneous damage, and neutropenia with resulting loss of phagocytic abilities

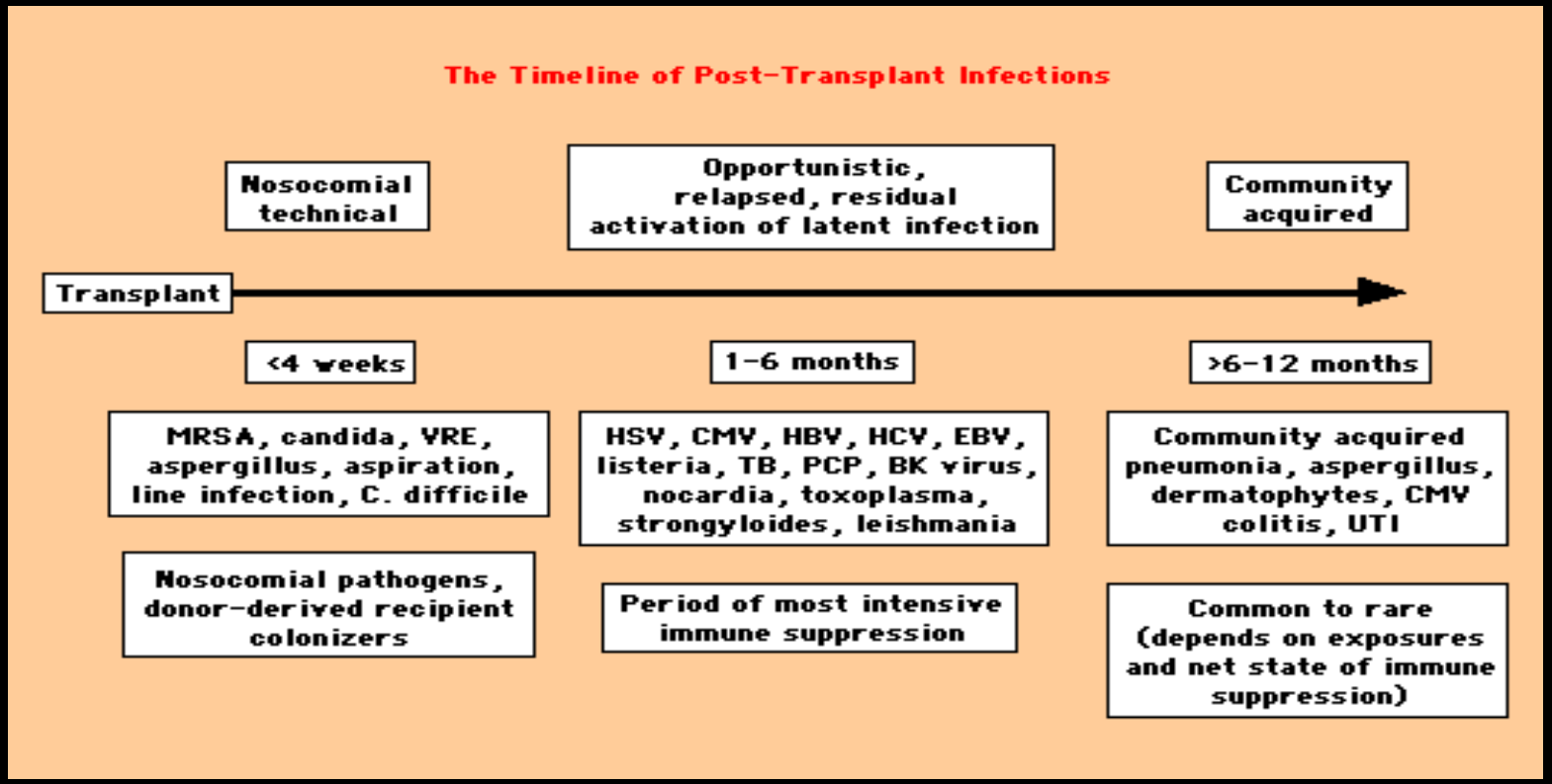
# Early Postengraftment

- Immediate postengraftment: three weeks to three months
  - Risk factors for infection during the immediate postengraftment period three weeks to three months after HCT are mucositis and cutaneous damage along with but also cellular immune dysfunction, decrease in opsonization, and diminished reticuloendothelial function.

# Late Postengraftment

- Late infectious complications are typically only seen among allogeneic recipients. The major risk factor for infection during this period is chronic GVHD and its immunosuppresive therapy
- This results in
  - Cellular and humoral immune dysfunction, hyposplenism, decrease in opsonization, and diminished reticuloendothelial function
  - Mucocutaneous damage

# OI following Solid Organ Transplantation



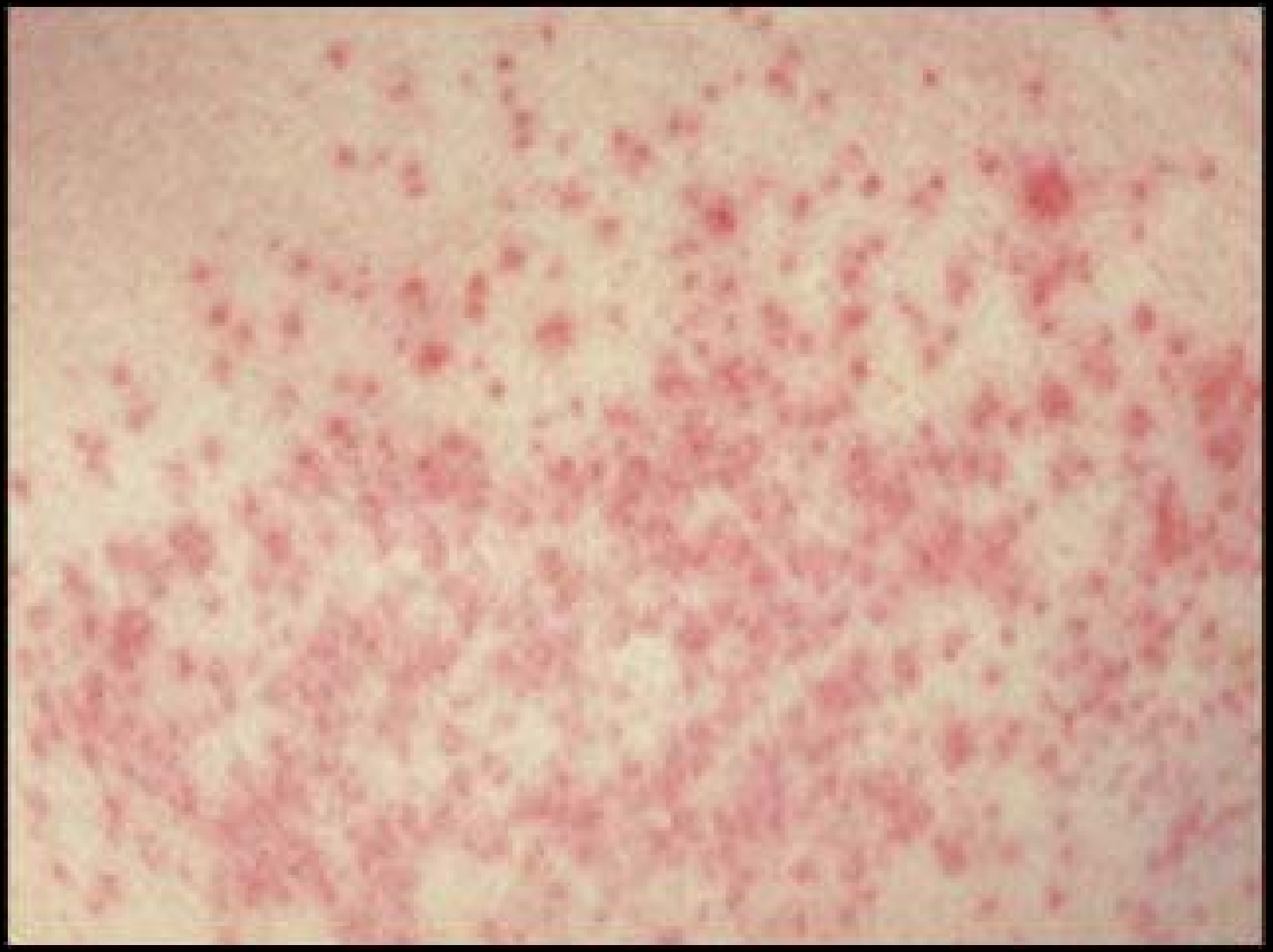
# Case 1

- 70 year old man with history of AML, S/P bone marrow tyransplant, hospitalized for 16 days with febrile neutropenia
- Despite 9 days of aggressive antibiotic therapy with vancomycin, piperacillin/tazobactam and ciprofloxacin
  - He is febrile and is complaining of rigors and blurred vision in the left eye.

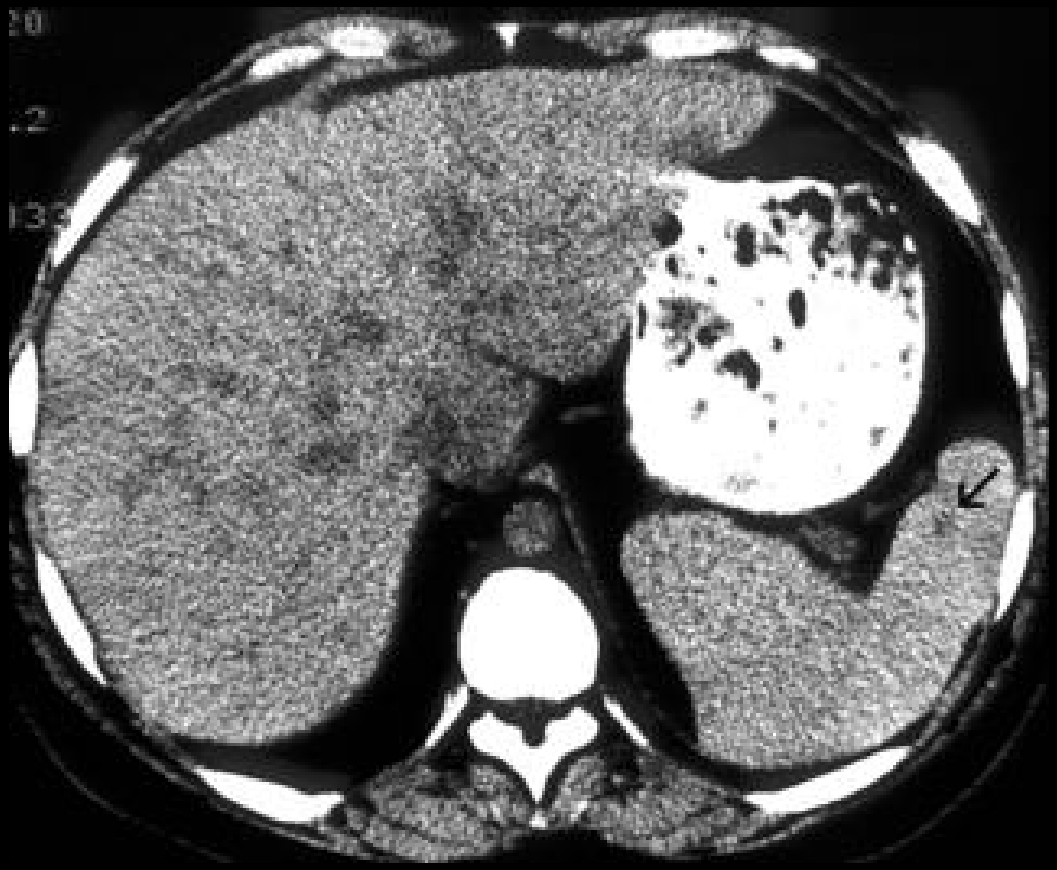
# Case 1

- T-39.7, P-120,RR-16, BP 130/75
- Ill appearing
- PERRLA; Mouth no lesions
- Chest:clear
- Cardiac- tachycardic, no mumurs or gallops
- Abd soft; mild tenderness RUQ, no hepatomegaly
- Mediport site: clean, no erythema, discharge or tenderness

# Case 1



# Case 1



WBC- 3.5

Hgb 12.1

AST 65

ALT-55

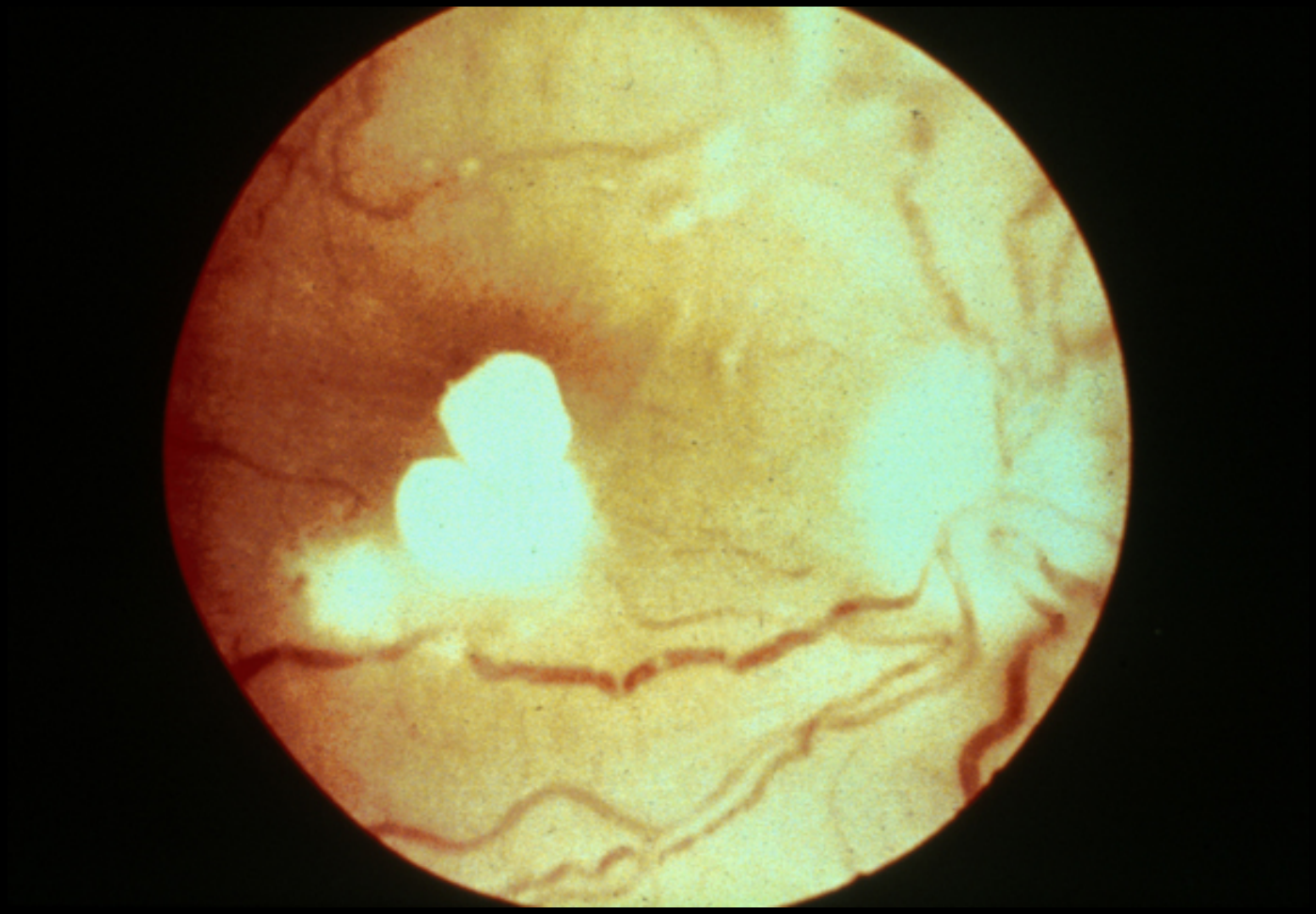
T.bili 0.9

ALP 185

Electrolytes, BUN/creatinine WNL

Blood cultures- negative

# Case 1



# *Candida*

- *Candida* species are ubiquitous fungi found throughout the world as normal body flora.
- Candidiasis can range from superficial disorders such as diaper rash to invasive, rapidly fatal infections in immunocompromised hosts.
- *Candida albicans* is commonly responsible for candidiasis.
  - *Candida tropicalis, Candida parapsilosis, Candida guilliermondi,* and *Torulopsis glabrata* are also causative organisms

# *Candida: laboratory diagnosis*

- Systemic candidiasis (eg, CNS, joint, blood)
- Cultures of cerebrospinal fluid (CSF), joint fluid, urine, or surgical specimens may be obtained to identify candidal infections.
- Blood culture is useful for diagnosing endocarditis and catheter-induced sepsis.
- Urinalysis (UA) positive for *Candida* species may predict 38-80% of systemic candidiasis.

# Candida: Antifungal Susceptibility

**TYPICAL SUSCEPTIBILITY PATTERNS FOR MOST FREQUENT *CANDIDA* ISOLATES**

| Species | Typical Isolate Frequency | Interpretation, based on usual MIC | | | |
|---|---|---|---|---|---|
| | | Fluconazole | Itraconazole | Amphotericin B | Flucytosine |
| *C. albicans* | ≥50% | S | S | S | S |
| *C. parapsilosis* | 10-20% | S | S | S | S |
| *C. tropicalis* | 10-20% | S | S | S | S |
| *C. glabrata* | 10-30% | S-DD | S-DD | I | S |
| *C. krusei* | ≤1% | R | S-DD | S | I-R |
| *C. lusitaniae* | ≤1% | S | S-DD | R | R |

Based on data from many sources, typical isolate frequencies and MIC distributions have been used to produce an interpreted summary of typical susceptibility patterns. For fluconazole, itraconazole, and flucytosine, the table is based on MICs determined and interpreted using modifications of M27 that have shown to enhance detection of amphotericin B-resistant isolates.

Table 4

http://www.nfid.org/publications/clinicalupdates/fungal/candida.html

# *Candida* Treatment Guidelines *CID* 2004

| Category | Definition |
|---|---|
| A | Both strong evidence for efficacy and substantial clinical benefit support recommendation for use. **Should always be offered.** |
| B | Moderate evidence for efficacy – or strong evidence for efficacy but only limited clinical benefit – support recommendation for use. **Should generally be offered.** |
| C | Evidence for efficacy is insufficient to support a recommendation for or against use. Or evidence for efficacy might not outweigh adverse consequences (e.g. drug toxicity, drug interactions) or cost of the treatment under consideration. **Optional.** |
| D | Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use. **Should generally not be offered.** |
| E | Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use. **Should never be offered.** |
| **Quality of evidence supporting the recommendation** | |
| I | Evidence from at least one properly designed randomized, controlled trial. |
| II | Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), or from multiple time-series studies. Or dramatic results from uncontrolled experiments. |
| III | Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees. |

| Disseminated *Candidiasis* Treatment Intervention: | Category |
|---|---|
| Remove all existing CVC | BII |
| ***Candidemia (non-neutropenic patient)***<br>Amphotericin B 0.7-1.0 mg/kg/d or LFAmpB 3.0-6.0 mg/kg/day or Fluconazole 6mg/kg/d, or Caspofungin | AI |
| ***Candidemia (neutropenic patient)***<br>Amphotericin B 0.7-1.0 mg/kg/d or LFAmpB 3.0-6.0 mg/kg/day or Caspofungin | AI |
| ***Candida Endophthalmitis***<br>Amphotericin B 0.7-1.0 mg/kg/d or Fluconazole 6mg/kg/day<br>Vitrectomy is usually performed | BIII |
| ***Hepatosplenic Candidiasis***<br>Fluconazole 6mg/kg/day for stable patient<br>Amphotericin B 0.7-1.0 mg/kg/d or LFAmpB 3.0-6.0 mg/kg/day for critically ill | BIII |

| Echinocandins for Candidemia in adults without neutropenia | |
|---|---|
| Caspofungin | •**Choice of an echinocandin vs. an azole for candidemia in a non-neutropenic patient is not well established**<br>•**Echinocandins may be preferred preferred when *C. glabrata* or *C. krusei* is identified or suspected**<br>•**Fluconazole interacts with cytochrome P450 resulting in many drug-drug interactions.**<br>–**This may dictate a preference for treatment with an echinocandin** |
| Micafungin | |
| Anidulafungin | |

# Case II

- 31 year old Caucasian woman with a history of multiple ‘sinus’ infections over the last 8-9 years. Over the last 3 years she has had an episode of ‘bronchitis’ and 2 bouts of pneumonia.
- She presents to the ambulatory care clinic with a 4 days history of fever, right maxillary tenderness, and purulent nasal discharge
- She does not smoke and has no history of either seasonal or perennial allergies.
- Family history of ‘sinus’ problems and pneumonias in older sister

# Case II

T- 101.7, p-65, RR-16, 125/75

No apparent distress

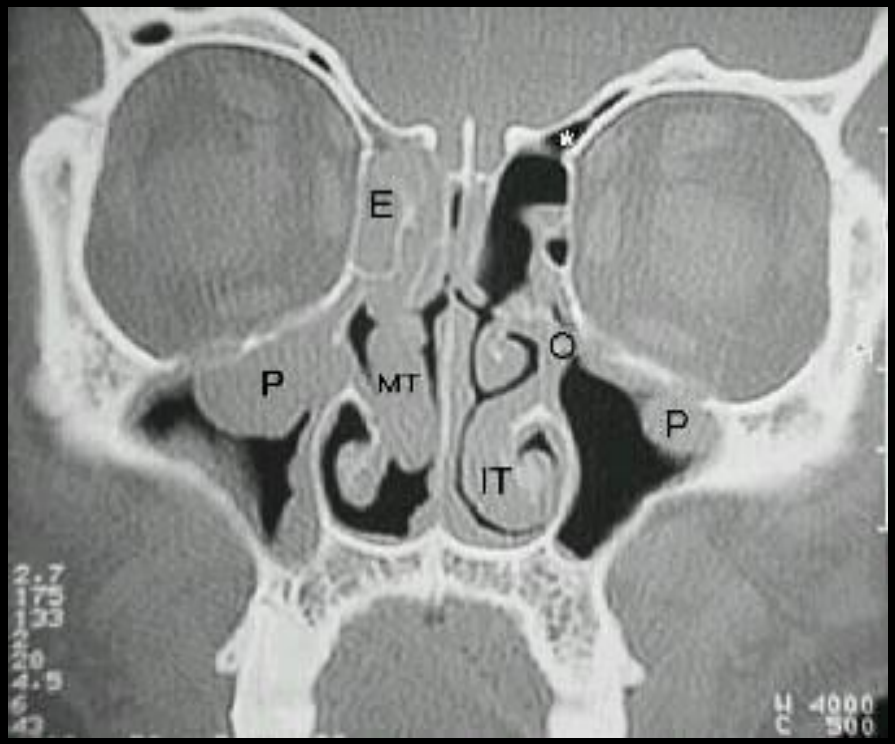
Tenderness over right maxillary sinus

Purulent nasal discharge from right nares

Pharynx mildly inflamed, no exudate on tonsils

Mild anterior cervical LAN

Remainder of exam Unremarkable




***Why should a young, healthy woman have so many sinopulmonary infections?***

# Common Variable Immunodeficiency

- Common variable immunodeficiency (CVID) involves the following:
  - (1) low levels of most or all of the immunoglobulin (Ig) classes
  - (2) Qualitative defect in B lymphocytes or plasma cells – defective *Antibody* production
  - (3) frequent bacterial infections.
  - (4) Association with autoimmune disorders

# Common Variable Immunodeficiency

| More Common | Infection | Autoimmune Diseases | Other |
|---|---|---|---|
| ↑ | Sinusitis, otitis media, pneumonia (encapsulated organisms) | Hemolytic Anemia | Lymphadenopathy<br>Splenomegaly |
| | Infectious diarrhea (*Giardia, Salmonella, campylobacter species*) | Autoimmune thyroid disease | Bronchiectasis |
| | Septic arthritis (*S.aureus, mycoplasma*) | Rheumatoid Arthritis<br>JRA | |
| Less Common | Meningitis (encapsulated organisms) | SLE<br>Sjogren's<br>UC/Crohn's | Malignancy (gastric CA) |

# Immunodeficiencies and Chronic or Recurrent Infections

| Organism | Immune Defect |
|---|---|
| **Encapsulated organisms:**<br>***S.pneumoniae, H. influenza*** | **Hypogammaglobulinemia**<br>**Abnormal neutrophil content**<br>**Complement deficiency**<br>**T-cell deficiency** |
| **Fungal infections**<br>**HSV**<br>***Pneumocystis* pneumonia**<br>**Mycobacterial infections** | **T-cell deficiency** |
| ***Neisseria* infections** | **Complement deficiencies (C5,C6,C7,C8,C9)** |

# Select Immunodeficiencies

| Immune Deficiency | Diagnostic Test |
|---|---|
| **Selective IgA (most common)** | **Measure IgA antibody level** |
| **IgG subclass deficiency** | **IgG2 most common**<br>**Obtain IgG subclass measurements**<br>**Measure response pre/post vaccination with polysaccharide and protein antigens** |
| **Complement deficiency** | **Measure CH 50- functional measurement of complement in serum** |
| **Functional neutrophil defect (oxidative burst/phagocytic activity)** | **Neutrophil Oxidative Burst Assay** |
| **Common Variable Immunodeficiency (develops during adulthood)** | **IgM,IgA,IgG and IgG Subclasses**<br>**Measure response pre/post vaccination with polysaccharide and protein antigens** |

# Case III

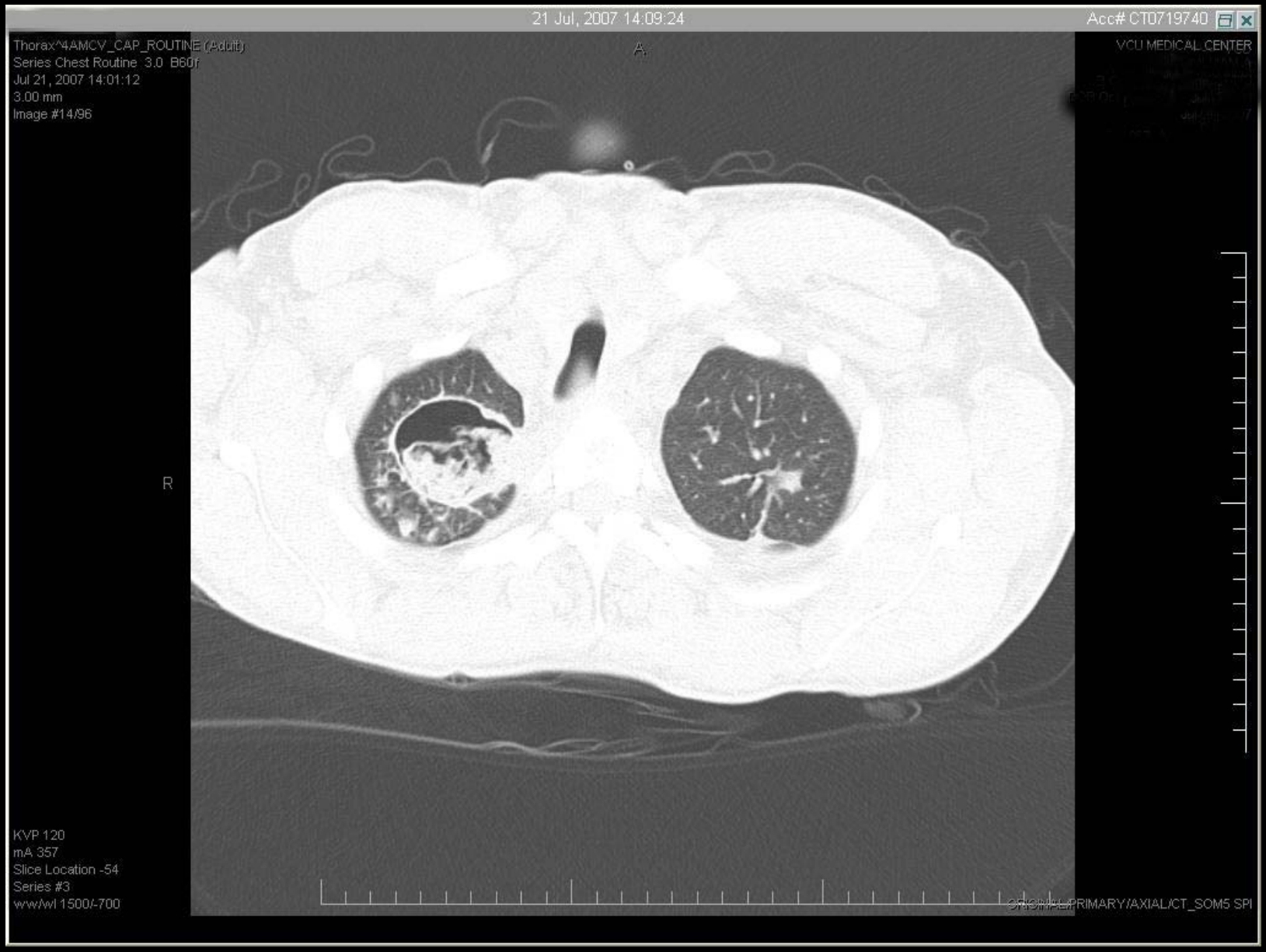
- 21-year old woman with AML is hospitalized for a febrile neutropenic episode
- She is S/P chemotherapy and had been placed on broad-spectrum antibiotic coverage that resulted in rapid defervescence and clinical improvement
- A few days later, she develops fever to 39.6C, accompanied by fever and pleuritic chest pain.

Cunha, B. ***Infectious Diseases Pearls***. 1999

# Case III

- T 39.6, pulse 130, RR 22, BP 90/58
- Ill appearing
- HEENT: no abnormalities
- Chest: bibasilar crackles
- Cardiac: S1, S2 with II/VI SM
- Abd:WNL
- Ext: trace pedal edema
- Skin- no rashes or dermatitis

Cunha, B. ***Infectious Diseases Pearls***. 1999


21 Jul, 2007 14:09:24
Acc# CT0719740
Thorax^4AMCV_CAP_ROUTINE (Adult)
Series Chest Routine 3.0 B60f
Jul 21, 2007 14:01:12
3.00 mm
Image #14/96
A
R
VCU MEDICAL CENTER
KVP 120
mA 357
Slice Location -54
Series #3
ww/wl 1500/-700
ORIGINAL/PRIMARY/AXIAL/CT_SOM5 SPI

Aspergillus can be seen with conventional stains but GMS is recommended. The fungus exhibits long uniform and septate hyphae. The hyphae have parallel contours and branch at 45 degrees

www.cytology-asc.com/cec/respiratory/resp83.html

# Clinical Presentations

- Invasive Aspergillosis-
  - Pulmonary Aspergillosis (most common)

    - CNS aspergillosis
    - Sinonasal aspergillosis
    - Osteomyelitis
    - Endophthalmitis
    - Endocarditis
    - Renal abscesses
    - Cutaneous

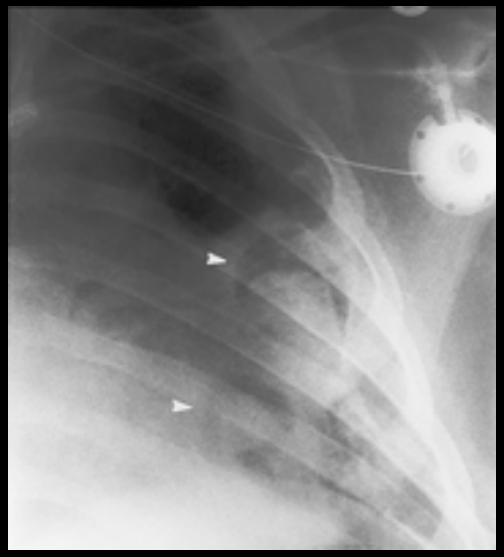
# Diagnosis

- Definitive diagnosis
  - Requires the demonstration of tissue invasion seen on biopsy specimen.
  - Positive culture obtained from tissue obtained by invasive procedure.
  - ***These patients are typically very sick/debilitated thereby precluding them form invasive diagnostic procedures.***

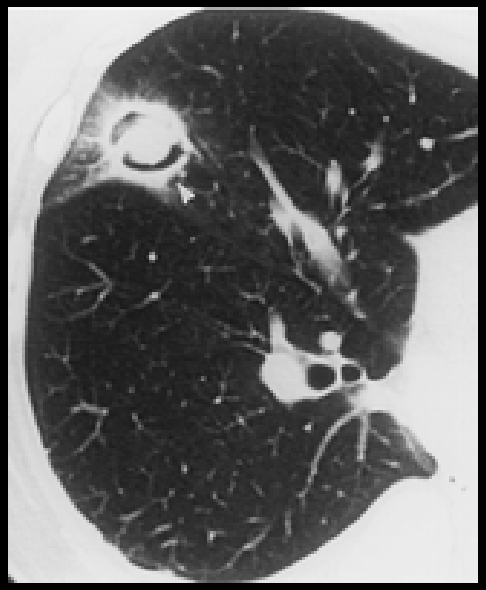
# Diagnosis

- Less or non-invasive tests in the setting of the appropriate clinical setting may ***suggest*** the diagnosis.
  - Blood cultures are typically negative.
  - In high risk patient, isolation of isolation of ***Aspergillus*** from sputum or BAL is strongly suggestive of IA.
  - Serologic ***Aspergillus*** precipitin assays are rarely elevated in IA and thus are of little clinical value

# Radiographic Presentations

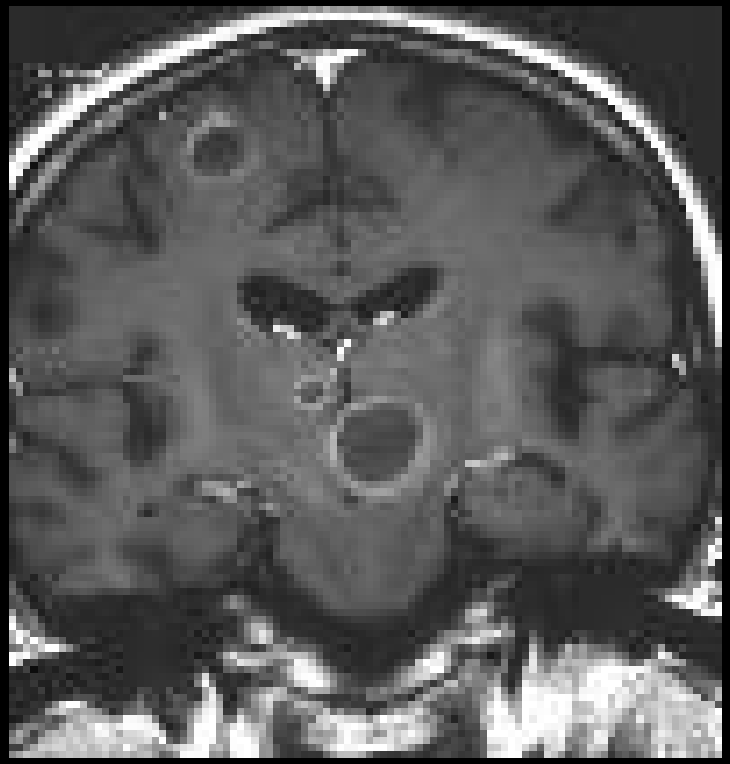


Invasive aspergillosis in a 6-year-old girl with neutropenia and acute lymphocytic leukemia.



Invasive aspergillosis in a 58-year-old woman with acute myelocytic leukemia. Transverse CT image depicts the CT halo sign

# Radiographic Presentations



Multiple aspergillomas in the brain of an HIV positive patient with AIDS

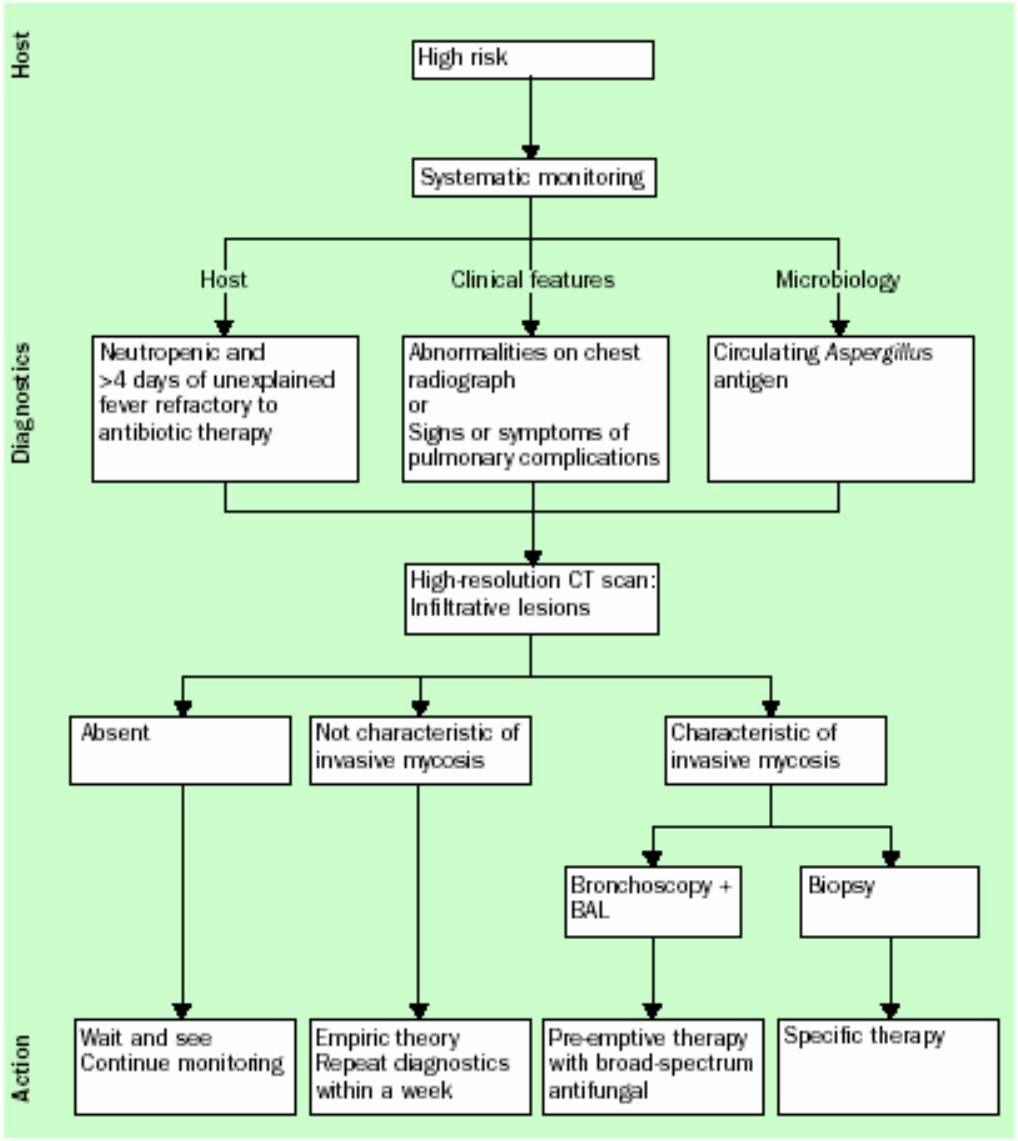
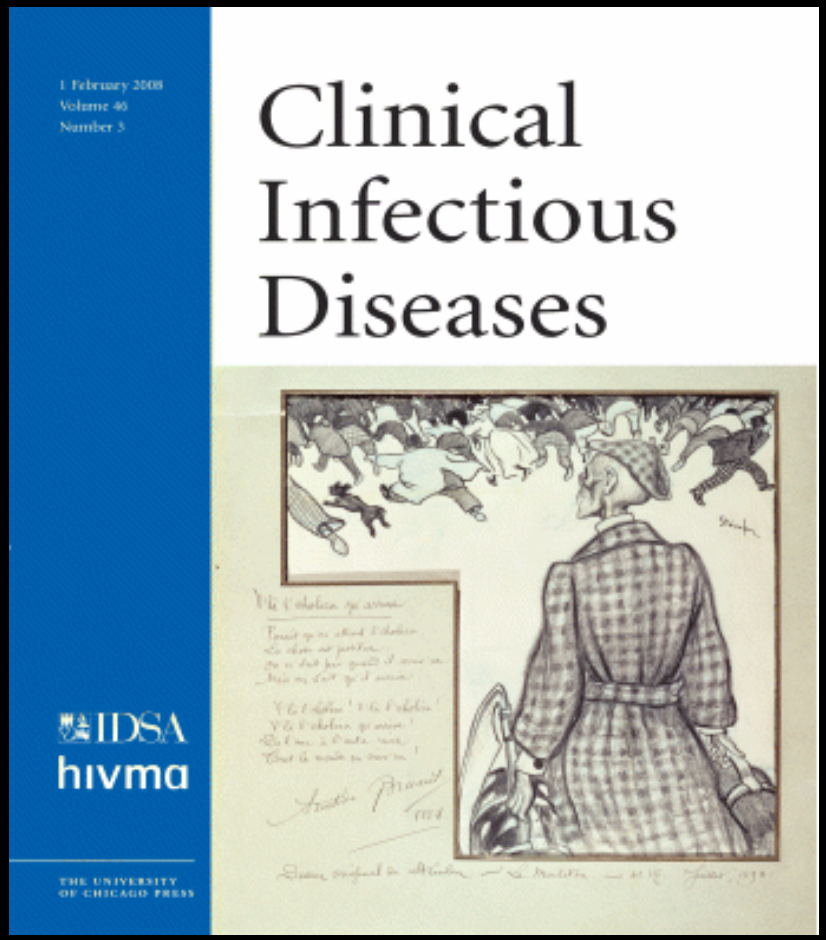



*Figure 8. A strategy for managing patients at high risk of developing invasive pulmonary aspergillosis.*

**Twice weekly monitoring for patients at high risk**

*The Lancet* Infectious Diseases Vol 4 June 2004. 349-357




# Treatment of Aspergillosis: Clinical Practice Guidelines of the Infectious Diseases Society of America

*Clinical Infectious Diseases* 2008;46:327–360

# Treatment of Aspergillosis: Clinical Practice Guidelines of the Infectious Diseases Society of America

**Table 2. Summary of recommendations for the treatment of aspergillosis.**

| Condition | Therapy[a] | | Comments |
|---|---|---|---|
| | Primary | Alternative[b] | |
| Invasive pulmonary aspergillosis | Voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h; oral dosage is 200 mg every 12 h) | L-AMB (3–5 mg/kg/day IV), ABLC (5 mg/kg/day IV), caspofungin (70 mg day 1 IV and 50 mg/day IV thereafter), micafungin (IV 100–150 mg/day; dose not established[c]), posaconazole (200 mg QID initially, then 400 mg BID PO after stabilization of disease[d]), itraconazole (dosage depends upon formulation)[e] | Primary combination therapy is not routinely recommended based on lack of clinical data; addition of another agent or switch to another drug class for salvage therapy may be considered in individual patients; dosage in pediatric patients for voriconazole is 5–7 mg/kg IV every 12 h and for caspofungin is 50 mg/$m^2$/day; limited clinical experience is reported with anidulafungin; dosage of posaconazole in pediatric patients has not been defined; indications for surgical intervention are outlined in table 3 |

*Clinical Infectious Diseases* 2008;46:327–360

# Empirical Antifungal Therapy of Neutropenic Patients with Prolonged Fever Despite Antibacterial Therapy

- Empirical antifungal therapy with AMB, an LFAB, itraconazole, voriconazole, or caspofungin is recommended for high-risk patients with prolonged neutropenia who remain persistently febrile despite broad-spectrum antibiotic therapy (A-I).
- Empirical antifungal therapy is not recommended for patients who are anticipated to have short durations of neutropenia (duration of neutropenia, <10 days), unless other findings indicate the presence of an invasive fungal infection (B-III).

*Clinical Infectious Diseases* 2008;46:327–360

# An opportunistic infection from paradise?

# Case IV

- A 51-year-old Korean woman was brought to the hospital after a close friend found her semiconscious and obtunded.
- The previous day, the woman was seen at church where she appeared healthy.On admission, she began to experience episodic chills lasting 30 to 40 minutes.
- That evening she was extremely lethargic.
- The patient had a medical history of chronic active hepatitis B virus (HBV) infection.

Resident & Staff Physician
A Peer-Reviewed Medical Education Journal

**http://www.residentandstaff.com/article.cfm?ID=281**

# Case IV

- The patient presented to the ED where she was lethargic and diaphoretic.
- She was tachypneic (25-32 breaths/min) and mildly tachycardic (95-105 beats/min) with a temperature of 103°F and systolic blood pressure between 90 and 100 mm Hg.
- Physical examination revealed that she was obtunded and lethargic. Her sclera was icteric, and her skin was jaundiced with mild generalized edema.
- No cardiac murmurs or a rub were heard on auscultation. An audible wheeze was heard bilaterally on expiration.
- Auscultation of her abdomen revealed decreased bowel sounds.
- Palpation of the abdomen revealed diffuse tenderness, and a liver edge was noted 2 to 3 cm below the costodiaphragmatic angle.

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# Case IV

- Edema of the legs was noted, with the right being more swollen than the left.
- Two prominent blisters, approximately 4 and 6 cm in diameter, soft and compressible and filled with serous fluid

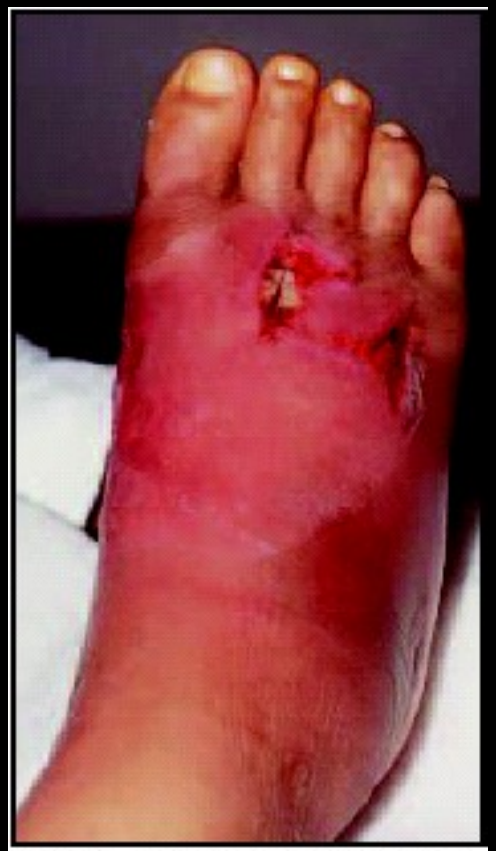

Figure 2—Dorsum of patient's right foot.

http://www.residentandstaff.com/article.cfm?ID=281

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# Case IV

- The surgical specimen taken from the right ankle grew a bacillus species later identified as *Vibrio vulnificus.*
- *It was discovered that she had purchased a can of oysters but could not recall if she consumed it.*

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**http://www.residentandstaff.com/article.cfm?ID=281**

# *Vibrio vulnificus*

<>

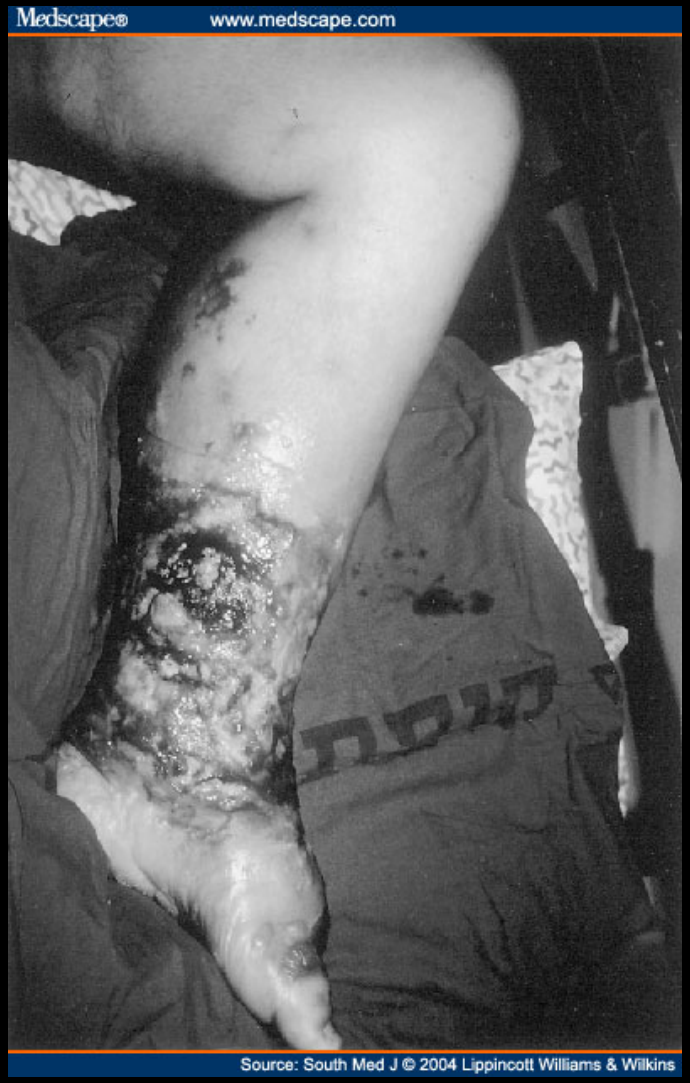
June 04, 1993 / 42(21);405-407

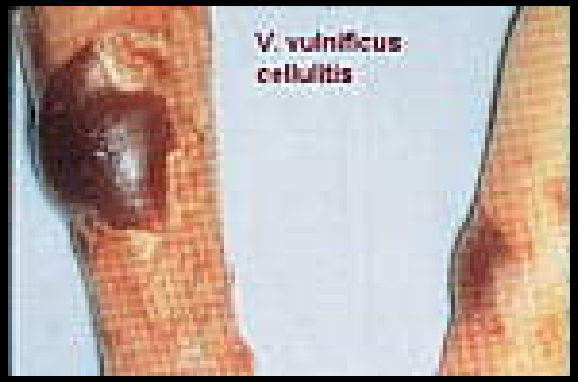
**Vibrio vulnificus Infections Associated with Raw Oyster Consumption -- Florida, 1981-1992**

July 26, 1996 / 45(29);621-624

**Vibrio vulnificus Infections Associated with Eating Raw Oysters -- Los Angeles, 1996**

# *Vibrio vulnificus*

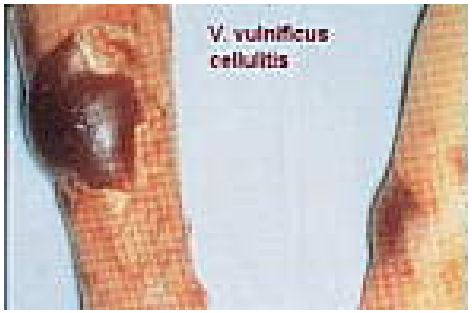



***Vibrio vulnificus*** **causes wound infections, gastroenteritis or a serious syndrome known as "primary septicema."**

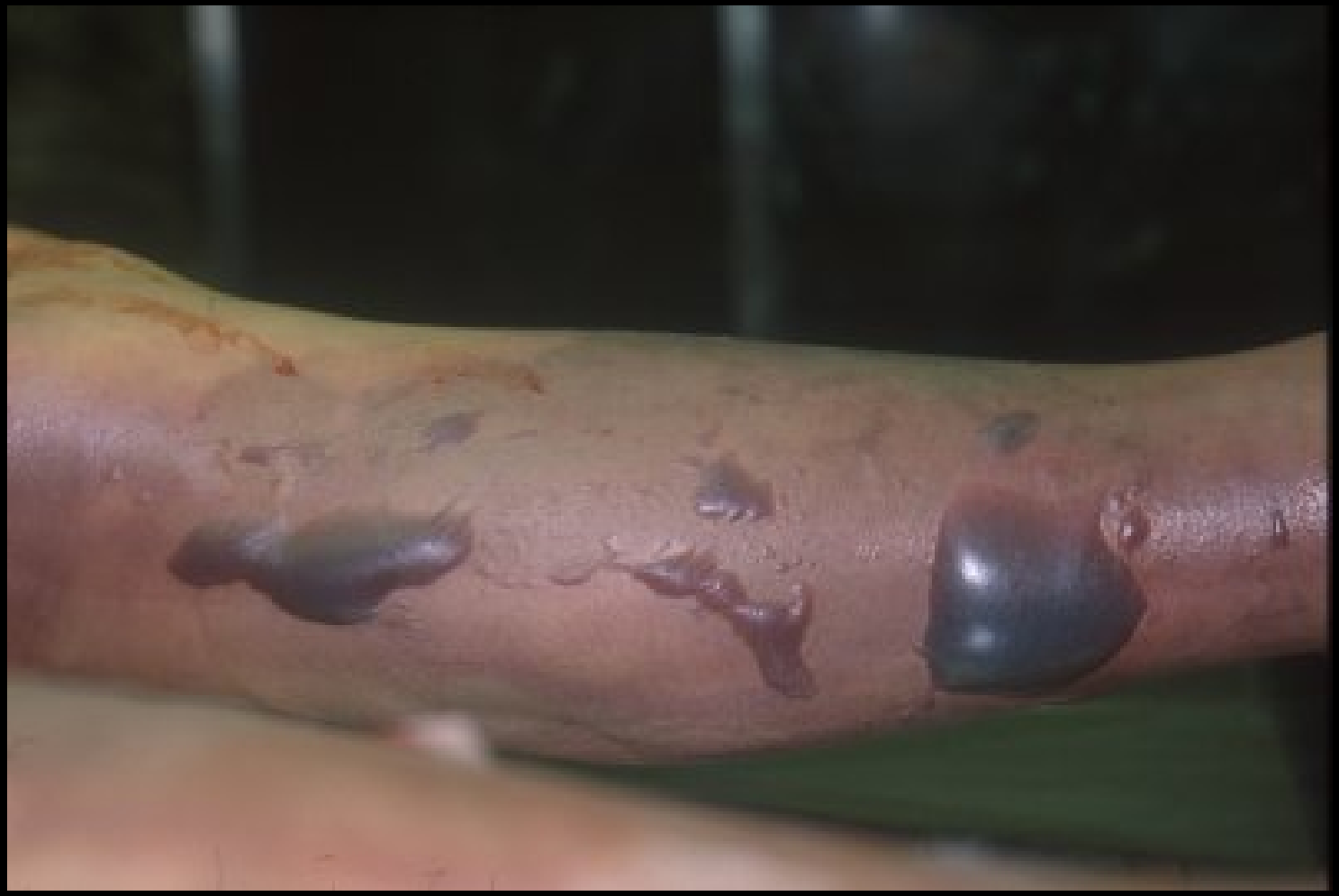
www.medscape.com

# *Vibrio vulnificus*

| Mode of Transmission | Clinical Manifestations | Dermatologic Manifestations |
|---|---|---|
| Transmitted to humans through open wounds in <u>contact</u> with seawater <u>or</u> through <u>consumption</u> of certain improperly cooked or raw shellfish.<br>**AVOID RAW CLAMS and OYSTERS!** | -Gastroenteritis: usually develops within 16 hours of eating the contaminated food<br>-Sepsis: 60% case fatality<br>Over 70 percent of infected individuals have distinctive bullous skin lesions. | From hematogenous spread or from direct innoculation<br>Bullous skin lesions<br>  |

www.dermnet.com

# *Vibrio vulnificus*



www.dermnet.com

# *Vibrio vulnificus*

- **High Risk Conditions Predisposing to *Vibrio vulnificus* infection:**
  - **Liver disease:**
    - **alcohol intake, viral hepatitis or other causes**
  - **Hemochromatosis**
  - **Diabetes**
  - **GI disorders:gastric surgery and achlorhydia**
  - **Malignancies**
  - **Immune disorders, including HIV infection**
  - **Long-term steroid use (as for asthma and arthritis).**

# *Vibrio vulnificus*

| Diagnostic Pearls | Culture |
| --- | --- |
| -Consumption of shellfish, clams<br><br>-Exposure to seawater (bathing/swimming)<br>-Violaceous, large bullous lesions<br>-Sepsis<br>***-A physician should suspect V. vulnificus if a patient has watery diarrhea and has eaten raw or undercooked oysters or when a wound infection occurs after exposure to seawater*** | Vibrio organisms can be isolated from cultures of stool, wound, or blood.<br>*V. vulnificus* infection is diagnosed by routine stool, wound, or blood cultures;<br><br>Notify the lab since a special growth medium can be used to increase the diagnostic yield |
| | **RX:**<br>Doxycycline or a third-generation cephalosporin (e.g., ceftazidime) |

# Case V

- 65 year old caucasian man with a history of RPGN is S/P cadaveric renal transplant 180 days ago.
- Over the last several days he has felt fatigued, with a low grade fever. His appetite has been poor.
- He is currently on prednisone and Imuran for chronic immunosuppression.

T=101.5, p-97, RR 18, 125/78

No apparent distress

No oral lesions

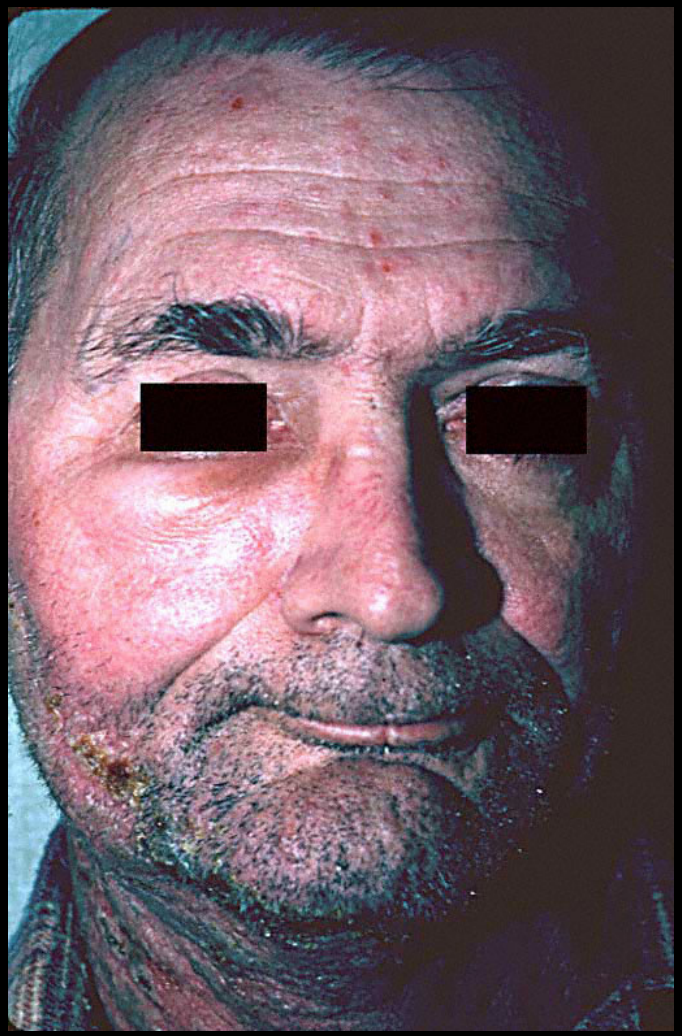
Mild anterior cervical lymphadenopathy

No murmurs or gallops

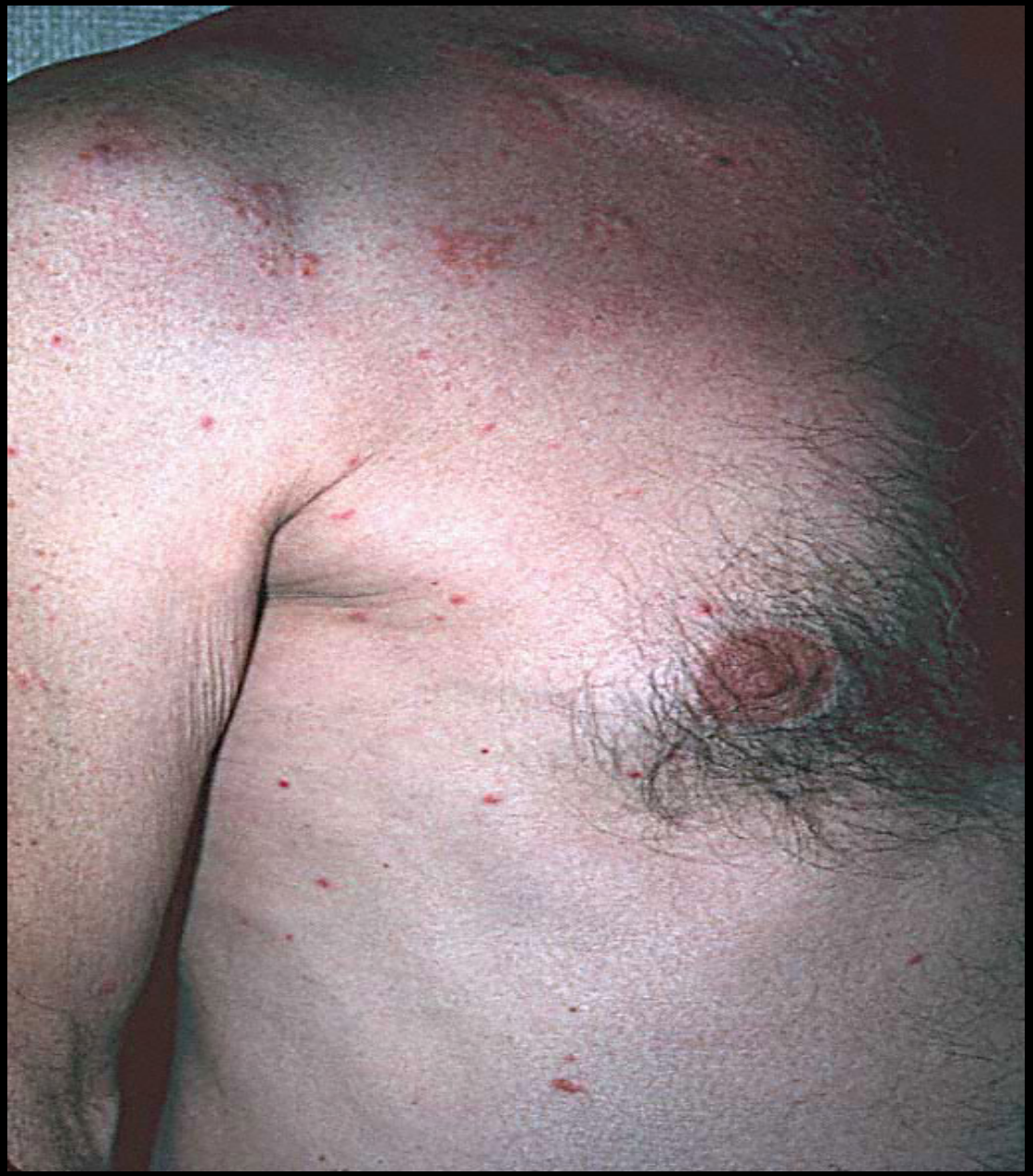
Abdomen soft with normal bowel sounds and no masses

No clubbing, cyanosis, or edema

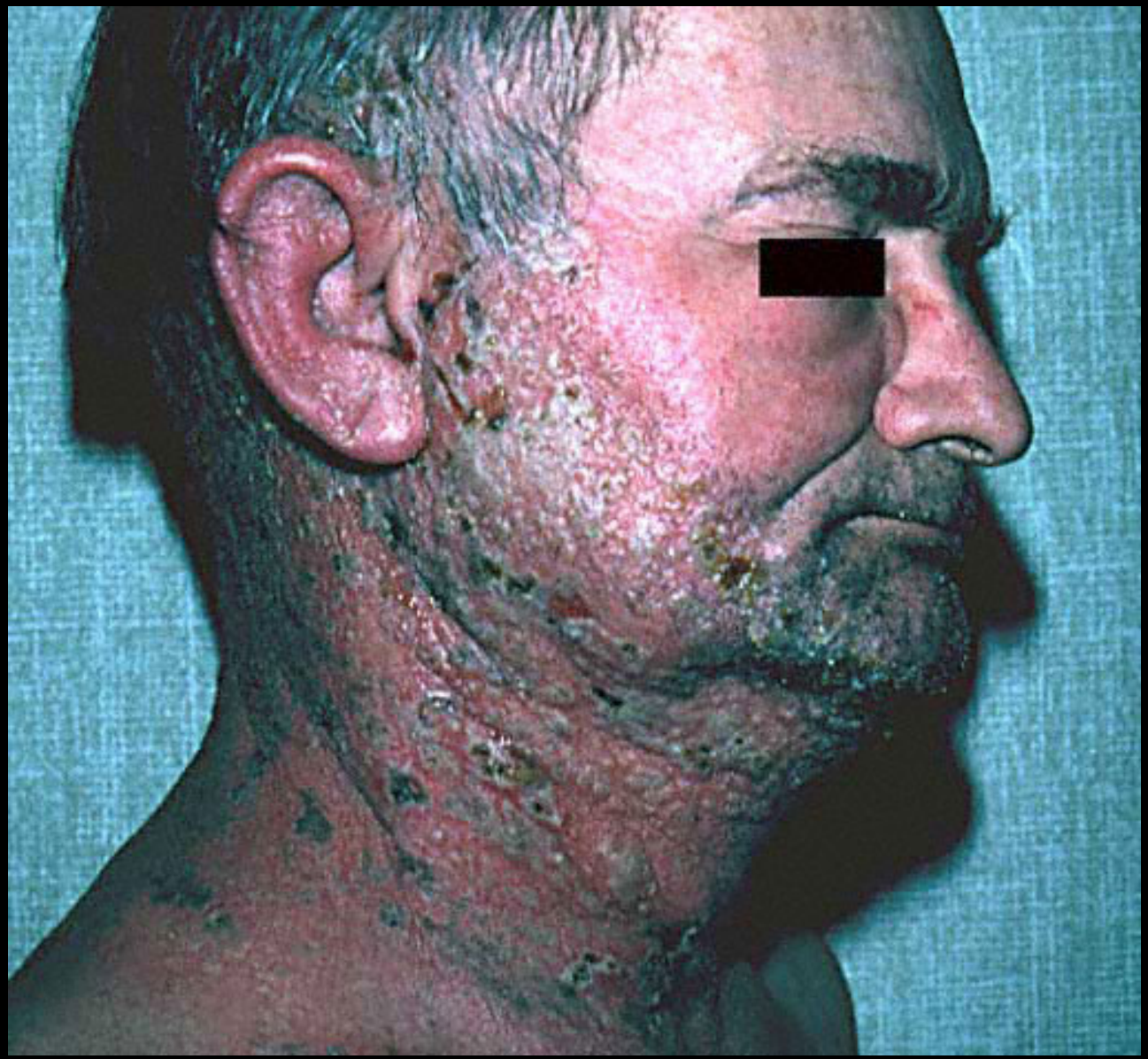
Cutaneous exam:



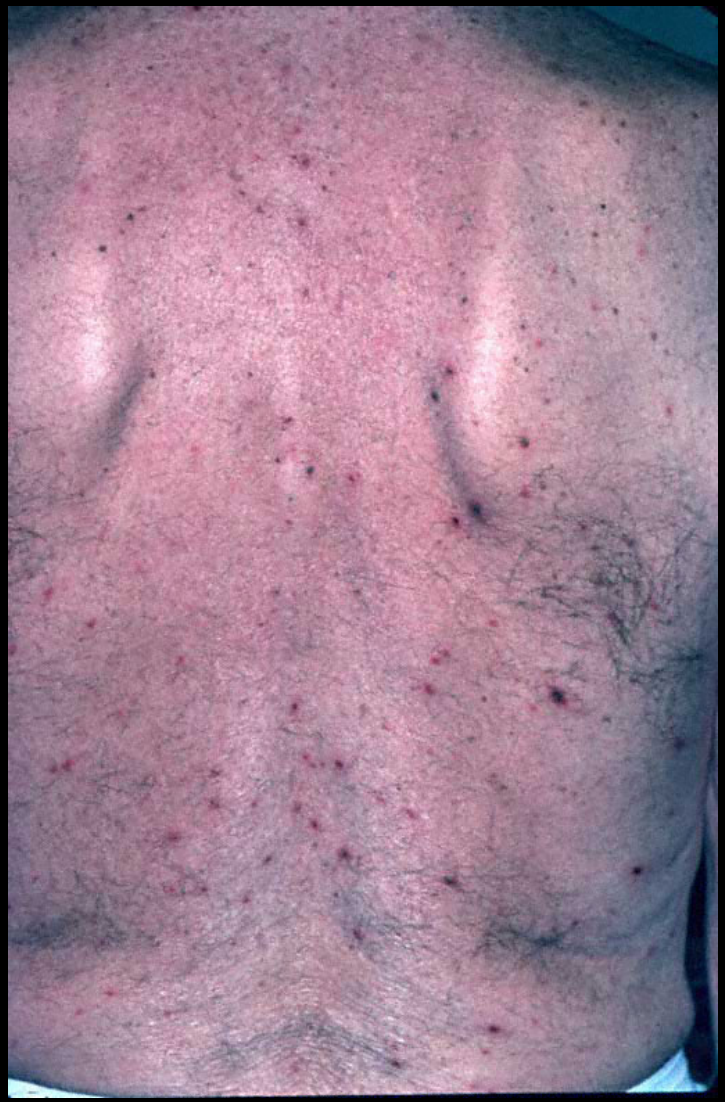
www.dermnet.com



www.dermnet.com



www.dermnet.com



www.dermnet.com


http://tray.dermatology.uiowa.edu

# Varicella Zoster Virus

- About 95% of adults in the United States have antibodies to the varicella-zoster virus.
  - Herpes zoster occurs annually in 300,000-500,000 individuals
  - Incidence of herpes zoster increases with age.
    - 80% of cases occur in persons> 20 years of age
  - A minority of the cases are non-dermatomal or disseminated

# Disseminated Zoster

- Disseminated zoster seen in immunocompromised patients.
  - hematogenous spread:
    - results in the involvement of multiple dermatomes.
    - Visceral involvement.
      - can lead to death due to encephalitis, hepatitis, or pneumonitis.

# Disseminated Zoster

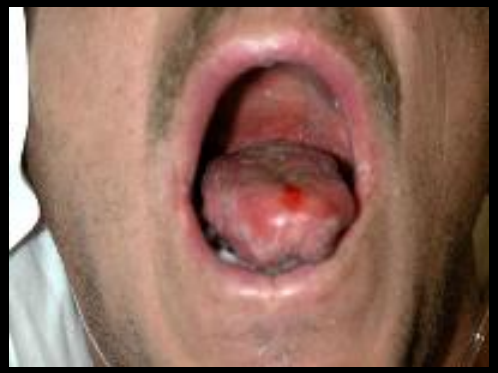
| Diagnosis | Treatment |
| --- | --- |
| •Herpes zoster is based primarily on clinical findings<br>•Varicella-zoster virus culture<br>•Tzanck smear (vesicular lesions)<br>•Biopsy for direct immunofluorescence | Acyclovir:<br>Immunocompromised adults:<br>800 mg PO q4h (5 times/d) for 7-10 d; or 10 mg/kg/dose or 500 mg/$m^2$/dose IV q8h |

# Case VI

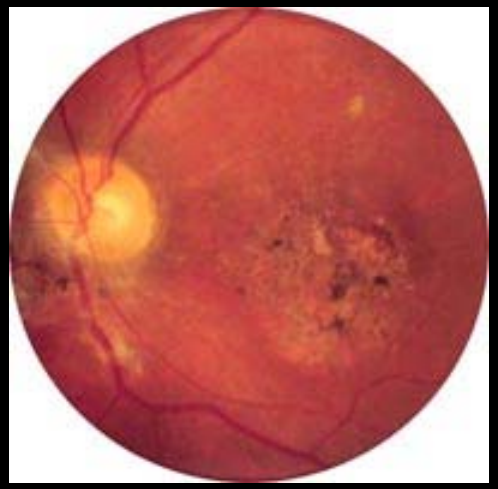
- 34 year old caucasian male,  HIV positive since 1993.
- Past history significant for PCP and thrush.
- Was on antiretrovirals on and off for years but had problems with medication adherence .
- Had been lost to follow up but presents to clinic with a history of progressive weight loss, anorexia, malaise, odynophagia and subjective fever.
- Additionally, he has complained of ‘floaters’ in the right eye, but no pain or change in visual acuity

# Case VI

- Physical examination
- T 101.8F otherwise WNL
- Height 6’1’, 140 lbs
- No murmurs or gallops
- Lungs clear
- Abdomen; soft, liver edge 2cm below costal margin
- Skin warm, dry, no significant lesions



http://www.emedicine.com/



http://www.eyemdlink.com

# Case VI

- Laboratory
  - Chemistry panel WNL
  - LFT:
    - AST 65
    - ALT 55
    - T.bili 0.9
  - WBC 3.0; Hgb 9.7; Plt 170,000

# CMV

- CMV:
  - CMV is a member of the herpesvirus group
  - Found universally throughout all geographic locations and socioeconomic groups
  - Infects between 50% and 85% of adults in the United States by 40 years of age
  - Typically remains dormant within the body

# CMV

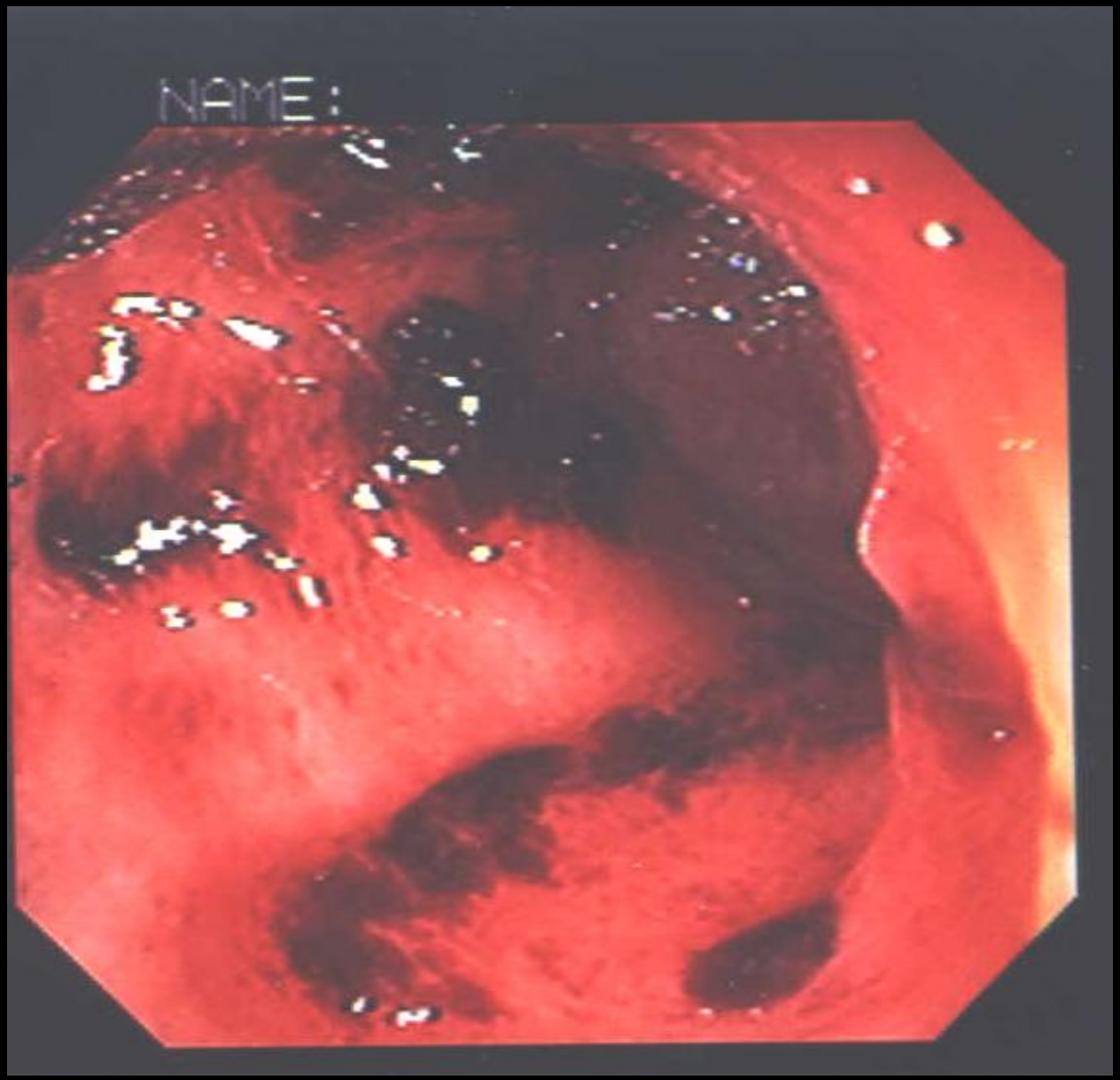
- Transmission:
  - Transmission occurs from person to person.
  - Infection requires close, intimate contact with a person excreting the virus:
    - saliva, urine, breast milk, transplanted organs, and rarely from blood transfusions and other body fluids
    - Sexual transmission has been documented
  - In most adults, ***reactivation***, is the cause of symptomatic disease

# CMV

| Host | Presentation |
| --- | --- |
| **Immunocompetent** | **Heterophile negative mononucleosis syndrome** |
| **Immunocompromised** | **Retinitis**<br>**Hepatitis**<br>**Pneumonitis**<br>**Gastritis**<br>**Esophagitis**<br>**Polyradiculopathy**<br>**Myelitis** |

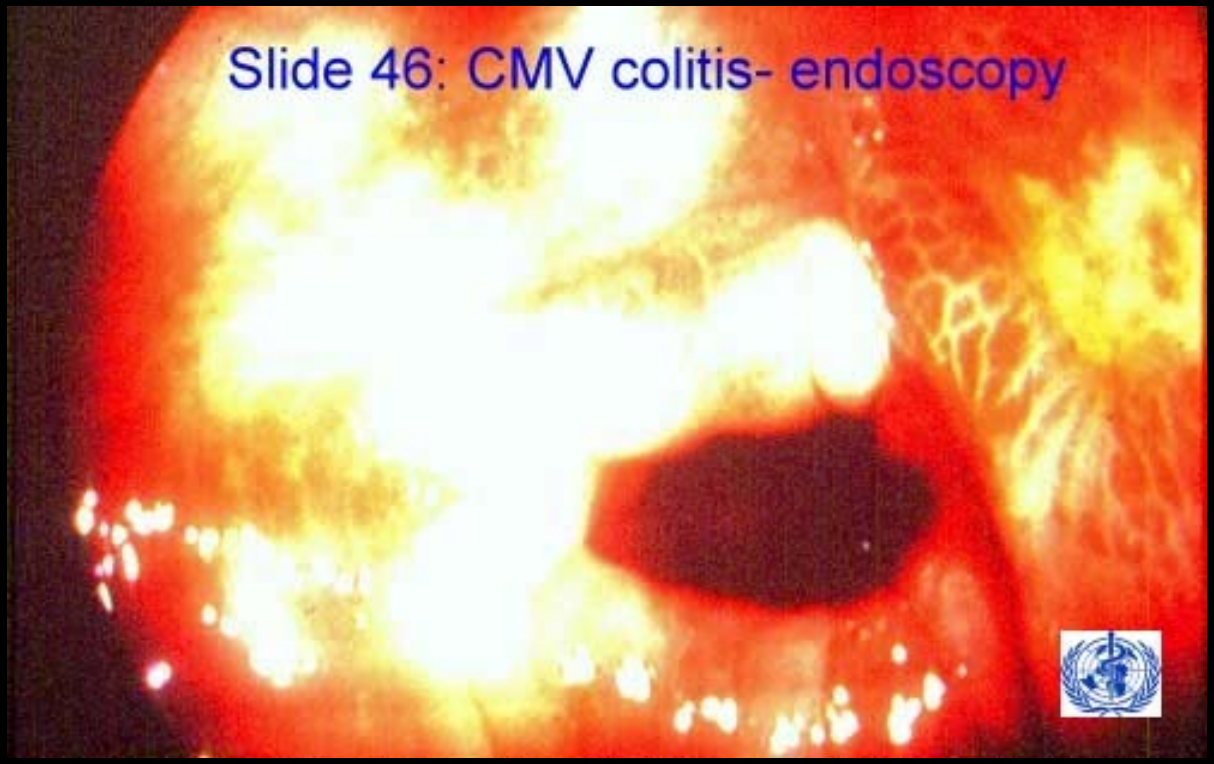
# CMV: HIV/AIDS Population

| Clinical Manifestation | Comment |
|---|---|
| CMV Retinitis | •Most commonly in patients whose CD4 count is less than 50 cells/μL<br>•Retinitis begins as a unilateral disease<br>• It may progresses to bilateral involvement.<br>•Retinitis may be accompanied by CMV systemic disease. |
| CMV Esophagitis/Colitis | •Upper GI tract: CMV has been isolated from esophageal ulcers, gastric ulcers, and duodenal ulcers.<br>•Lower GI tract: CMV may present with colitis<br>–These patients usually present with diarhea |
| CMV Pneumonia | •CMV pneumonia in HIV Positive Patients is very rare<br>•CMV pneumonia without a co-infecting pathogen is uncommon |

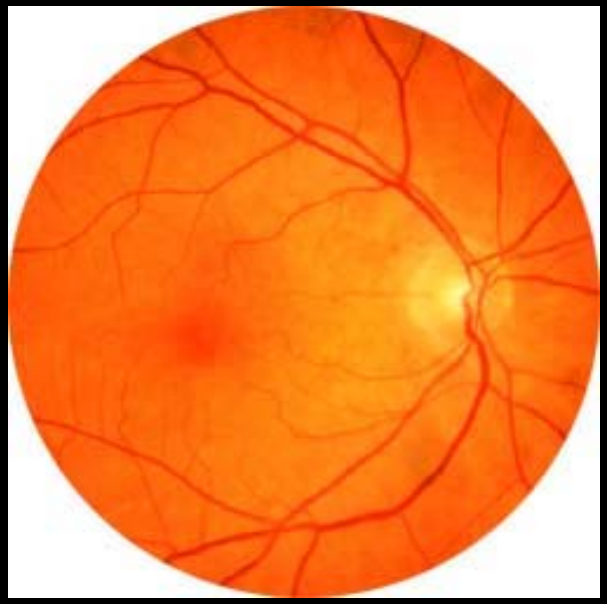


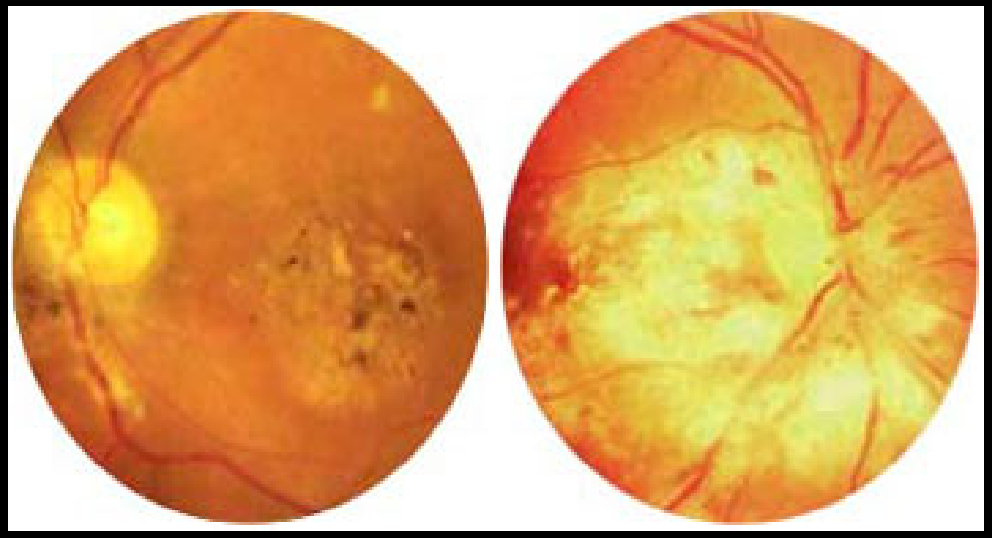

CMV Esophagitis

http://www.giatlas.com



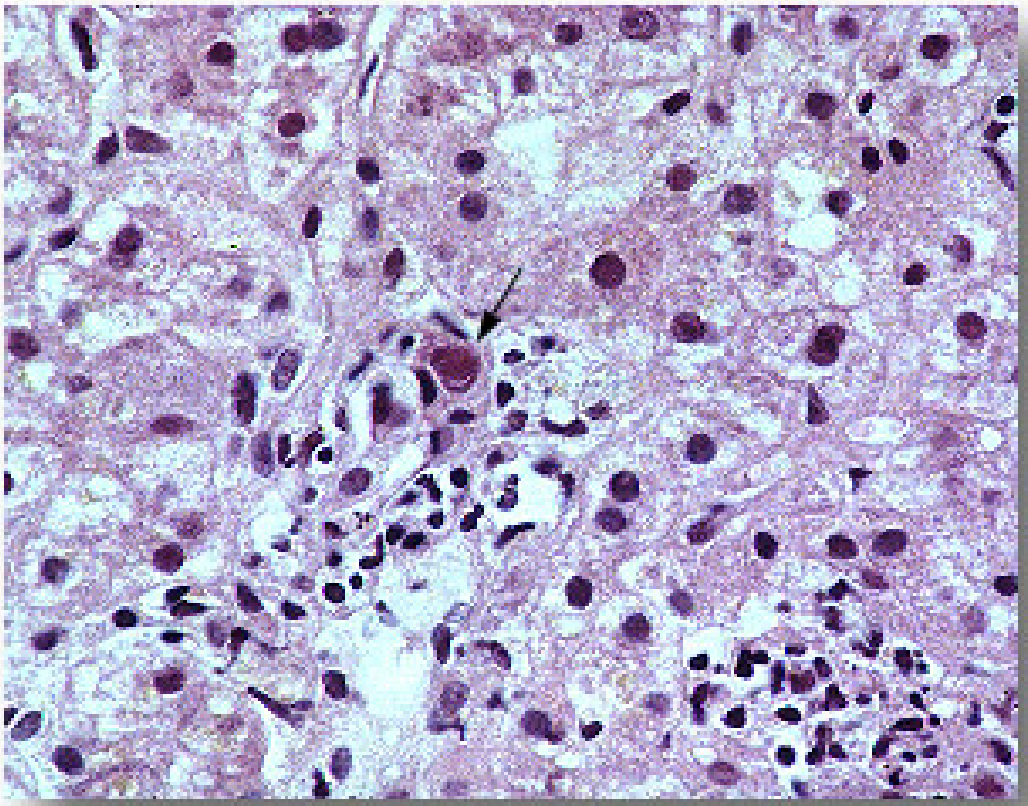

http://www.who.or.id





**Retinal hemmorrhages and inflamation can lead to permanent loss of vision, retinal detachment and blindness**

http://www.stlukeseye.com



•Diagnosis of CMV gastrointestinal disease by biopsy specimen demonstrating the CMV intranuclear inclusions

http://www.ulb.ac.be/erasme/edu/gastrocd/Case35/C35c03.htm

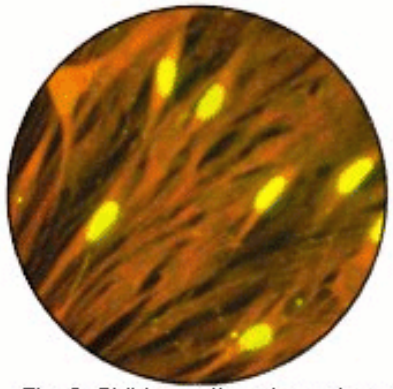
# CMV- Organ transplantation

| Clinical Manifestation | Comment |
| --- | --- |
| CMV pneumonia | •Incidence varies depending on the transplant population<br>–Higher incidence and high mortality (86%) in allogeneic bone marrow transplant recipients<br>–Less common and lower mortality in solid organ transplant recipients.<br>–Major risk factor is a CMV seronegative transplant recipient receiving a CMV positive organ |

# CMV- Laboratory Confirmation

| Test | Comment |
|---|---|
| **CMV-specific IgG**<br>**CMV-specific IgM** | **•Paired serum samples ( 2 weeks apart) show a fourfold rise in IgG antibody and a significant level of IgM antibody, meaning equal to at least 30% of the IgG value**<br>**•A positive IgG result does not automatically mean that active CMV infection is present** |
| **CMV Antigenemia** | **•Antigenemia can predict CMV pneumonia in transplant recipients**<br>**•A positive antigenemia test can trigger the use ganciclovir as preventive therapy of CMV disease in transplant patients**<br>**–Viremia is associated with CMV pneumonia in allogeneic BM transplant recipients** |

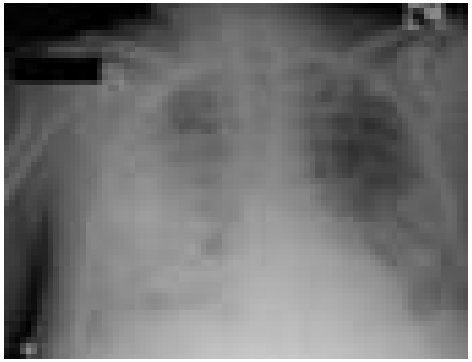
# CMV- Laboratory Confirmation

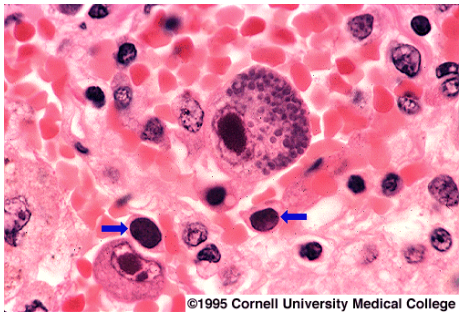
| Test | Comment |
| --- | --- |
| **CMV Shell Vial Cell Culture Technique**  Fig. 2, CMV centrifugation culture fixed and stained 16 hrs after inoculation showing viral proteins in nuclei of infected human fibroblast cells | **•Clinical specimen is transferred to a vial containing a permissive cell line for CMV-shell vial**<br>**•The shell vials are centrifuged and placed in an incubator.**<br>**•After 24-48 hours, the tissue culture is removed and the cells are stained using a fluorescein-labeled anti-CMV antibody.**<br>**•The cells are read using a fluorescent microscope** |

**https://labs-sec.uhs-sa.com/clinical_ext/dols/CMVshell.gif**

# CMV- Laboratory Confirmation

## CMV Pneumonia





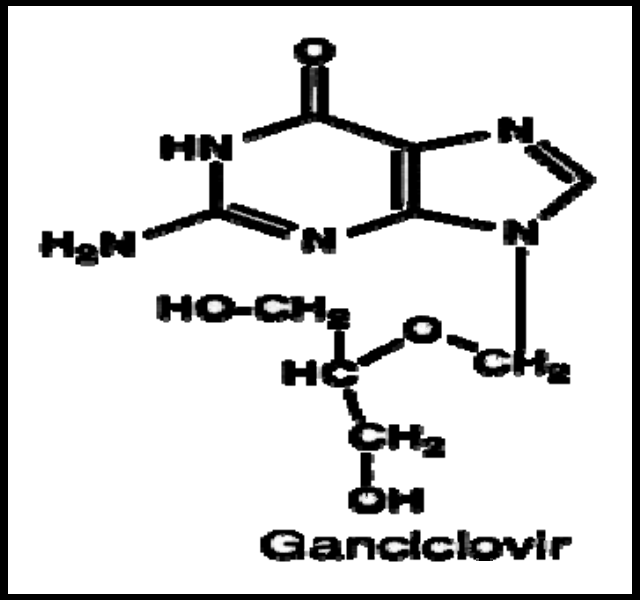

- **The diagnosis of CMV pneumonia:**
  - **–Appropriate clinical context**
  - **–Recovering CMV from patients with an infiltrate on chest radiograph and appropriate clinical signs.**
  - **–CMV may be isolated from the lung by bronchoalveolar lavage (BAL) or by open lung biopsy.**
  - **–CMV antigen or inclusions are found by histological examination.**

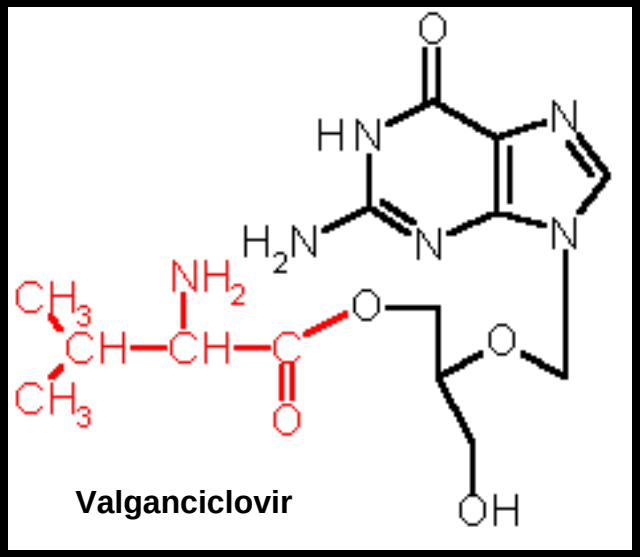
edcenter.med.cornell.edu

rad.usuhs.mil/medpix/ medpix.html

# CMV Treatment-Ganciclovir

- Nucleoside analogue that inhibits DNA synthesis
- Major adverse effects of are neutropenia and thrombocytopenia.
- Valganciclovir is the prodrug for ganciclovir
  - Absolute oral bioavailability is approximately 60%
  - FDA approved for Rx of CMV retinitis



# Management

| Clinical Manifestation | |
|---|---|
| CMV Retinitis | •Intraocular ganciclovir implant AND:<br>–Valganciclovir 900mg PO bid x 3 wks; then 900 mg po qd<br>–OR- Ganciclovir 5 mg/kg IV bid x 2 wks; then ganciclovir 5 mg/kp IV qd |
| CMV Esophagitis/Colitis | •Valganciclovir 900mg PO bid x 3 wks; then 900 mg po qd<br>•Ganciclovir 5 mg/kg IV bid x 2 wks; then valganciclovir 900 mg po qd<br>• Foscarnet 40-60mg/kg IV q 8h x 2wks, then 90 mg/kg/d |
| CMV Pneumonia | •Ganciclovir 5 mg/kg IV bid >21 days<br>•Foscarnet 60mg/kg IV q 8h x 2wks, then 90 mg/kg IV q 12 for >21 days<br>•Valganciclovir 900mg PO bid x 21 days |

# Conclusion

- Opportunistic Infection- an infection by a microorganism that normally does not cause disease but pathogenic when the body's immune system is impaired and unable to fight off infection
  - Prolonged Neutropenia- disseminated Candidiasis
  - Pre and post engraftment- invasive fungal infections
  - Common Variable Immunodeficiency- recurrent bacterial infections
  - Chronic liver disease- Vibrio infections
  - Advanced age, steroid use, laten post engraftment: VZV (disseminated)
  - HIV/AIDS, BM/Solid organ transplants: CMV

THE END