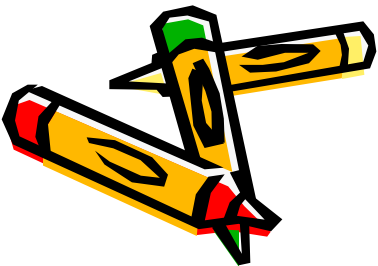


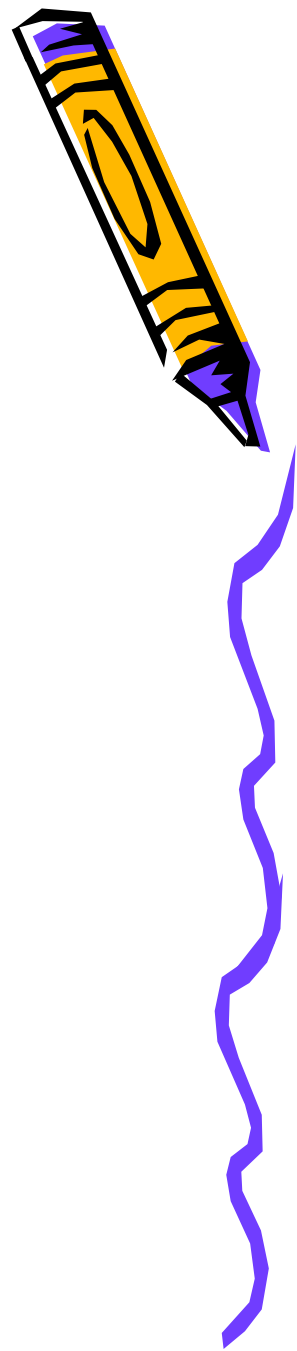
The Curse of the Pharaoh: Aspergillus

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Senior Consultant, Infectious Diseases,
Apollo Hospitals, Bangalore
Dec 7, 2013

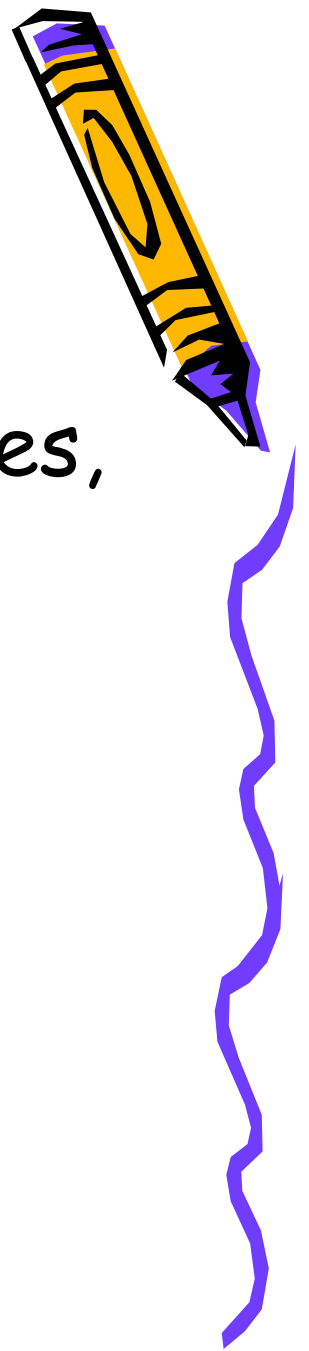


Discussion points

- Spectrum of disease
- Life threatening issues
- Treatment



Case



- 73 y o male, diabetic, h/o headaches, for the last few weeks. Went to different hospitals.
- Poorly controlled diabetes.
- Initial CT:

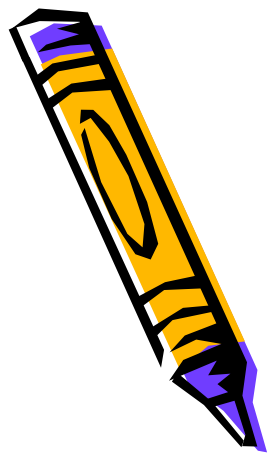


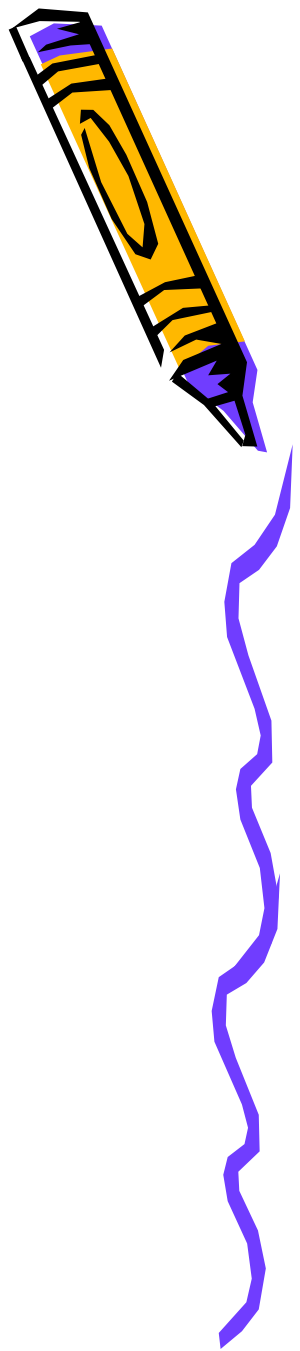
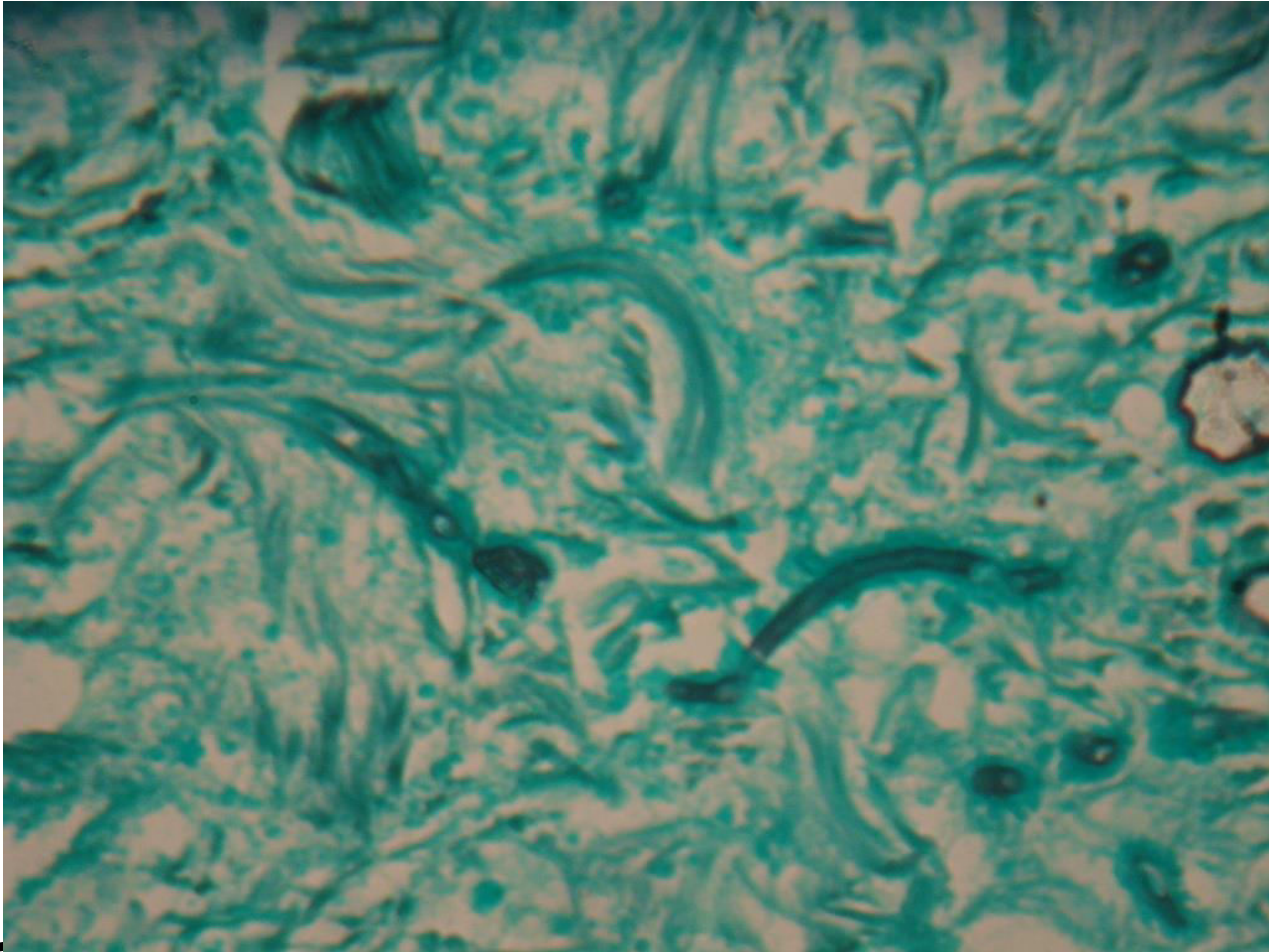
History continued...



- Sent to see Infectious Diseases after recurrence of headache, proptosis
- Repeat imaging of the orbit showed:







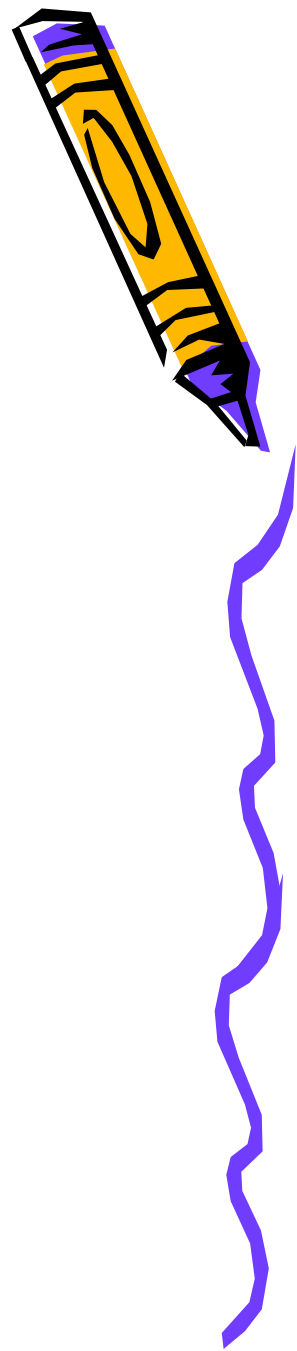
Risk Factors

- Neutropenia: severe and prolonged:
 - Chemotherapy for hematologic malignancies, MDS, aplastic anemia etc
 - Allogeneic HSCT: cumulative incidence at 12 months: 2.3% to 3.9%. 0.5% in autologous
- Immunosuppression: GVHD- depends on severity and amount of immunosuppressants
- Solid organ transplant: Lung, heart-lung, liver
 - Colonisation
 - Late onset (> 3 months)- immunosuppression to treat graft rejection



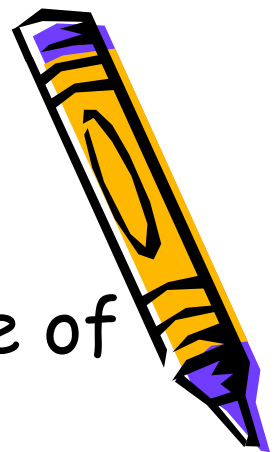
The Others...

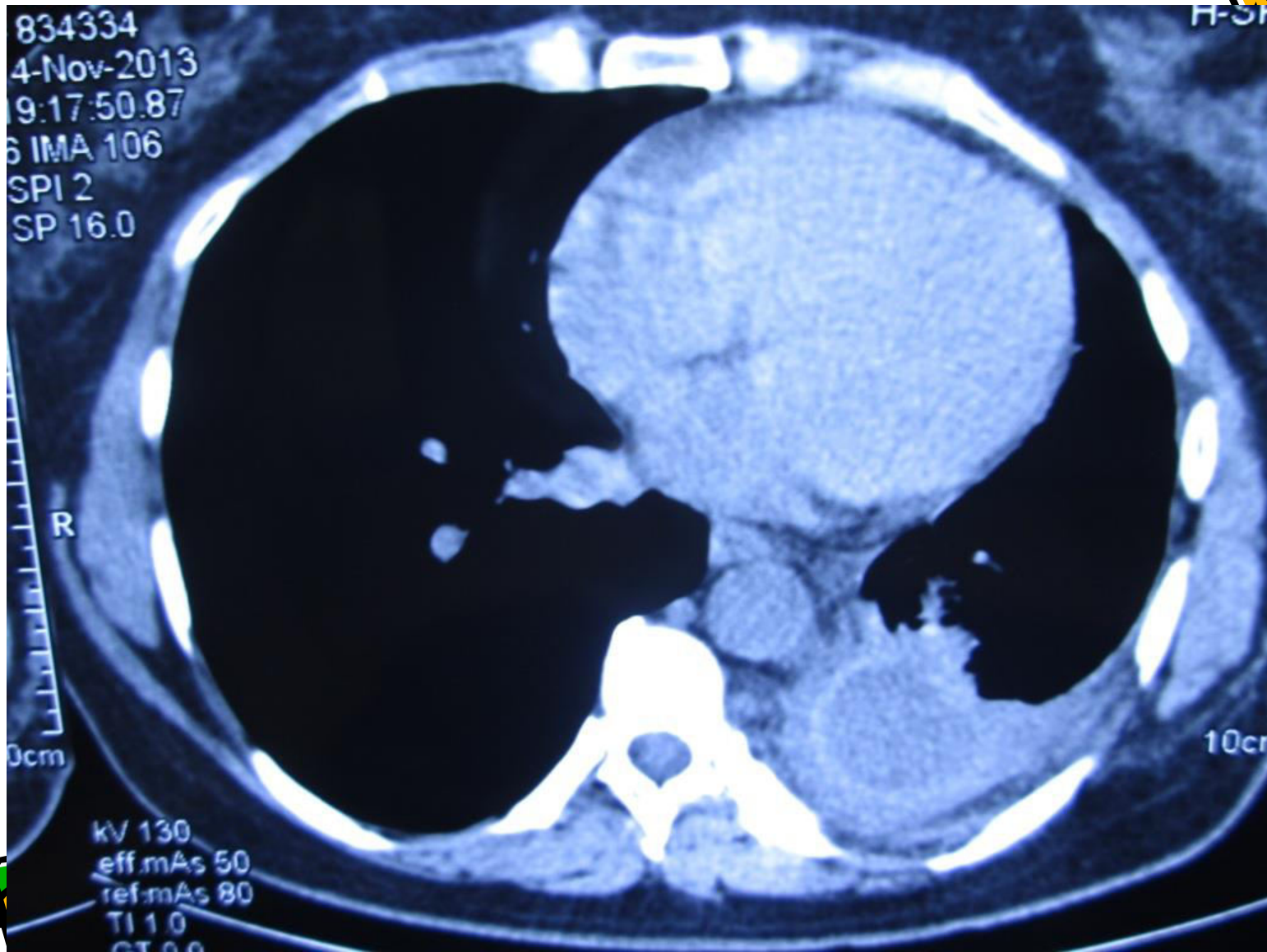
- High dose Steroid therapy:
- Defective NADH oxidase: CGD
- Mannose-binding lectin deficiency
- Preexisting lung disease- cavity
- Diabetes mellitus
- Advanced HIV
- ICU
- Drug abusers- inhaling marijuana contaminated with spores, 'shooting up'

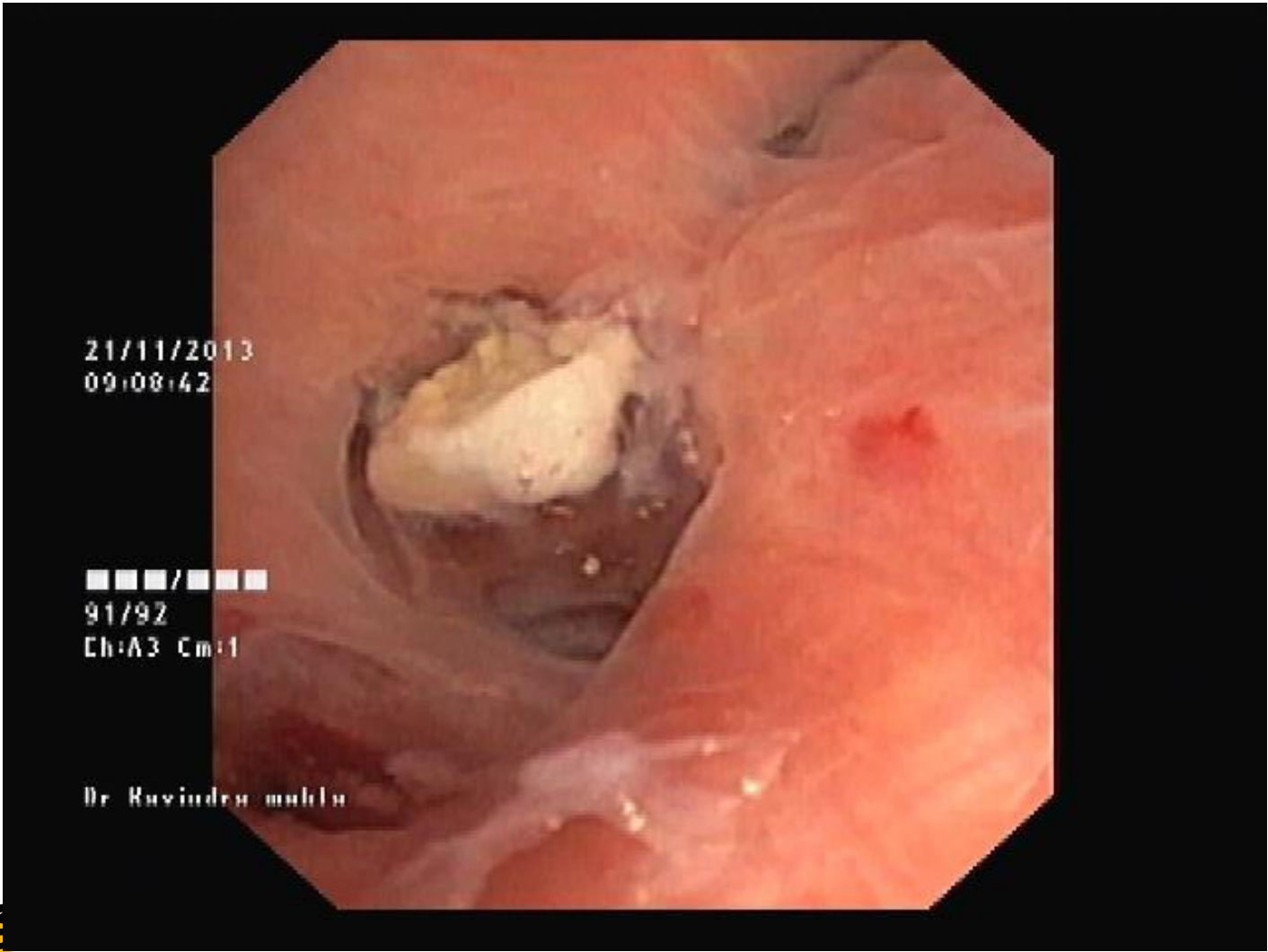


Spectrum of disease

- Depends on the degree, duration and type of immunosuppression
- Usually, inhalation route (Sinopulmonary). Less commonly, GIT/skin
- Invasive Aspergillosis: Sinuses, Lungs.
- Extra Pulmonary: any organ
- Chronic necrotising and chronic cavitary pulmonary aspergillosis (semi invasive)
- ABPA: Allergic Bronchopulmonary aspergillosis







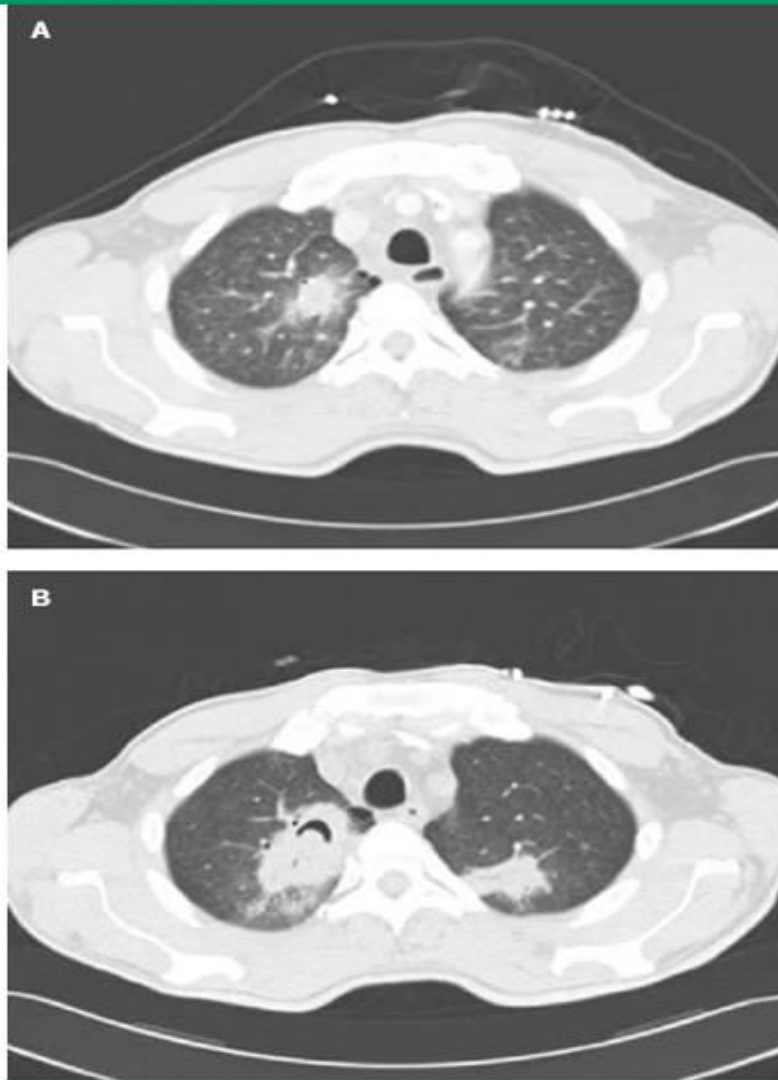
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Dr. Ravindra maha

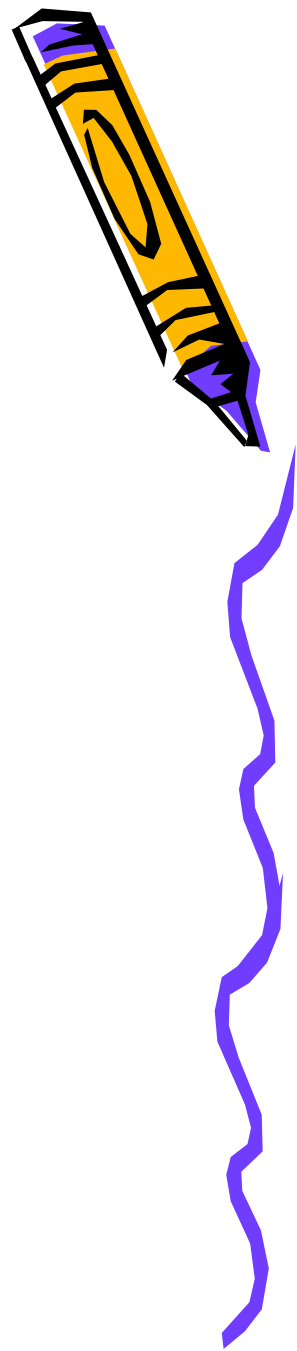


CT pulmonary aspergillosis

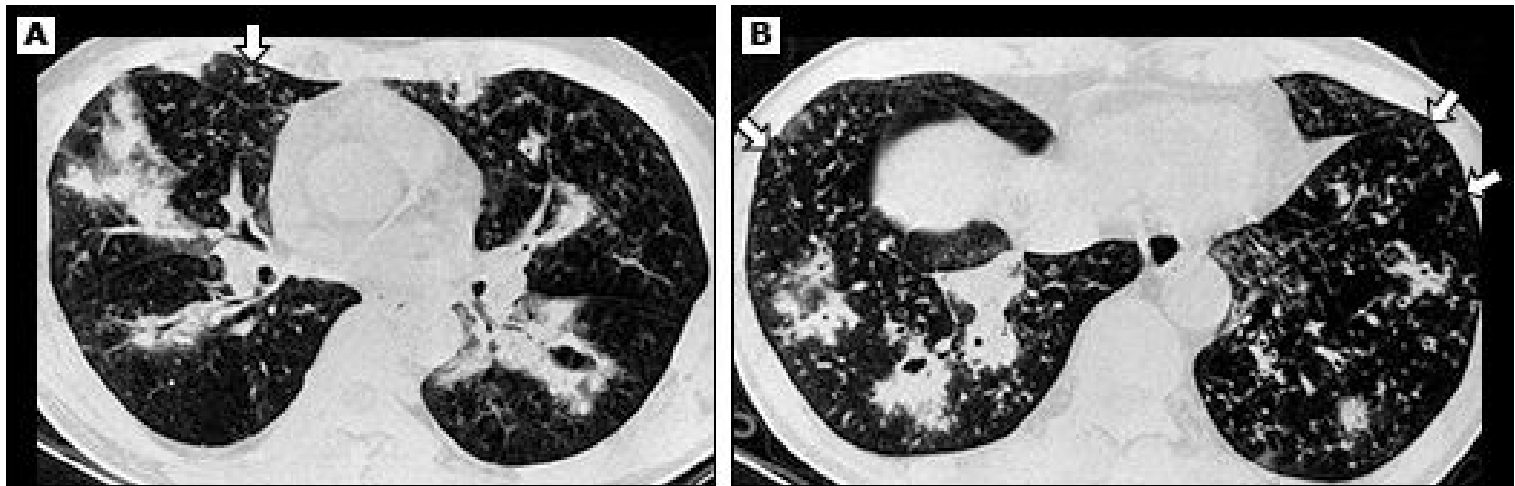


Halo sign (A) converting to an air-crescent sign (B) after neutrophil recovery.

Reproduced with permission from: Maertens J, Meersseman W, Van Bleyenbergh P. New therapies for fungal pneumonia. Curr Opin Infect Dis 2009; 22:183. Copyright © 2009 Lippincott Williams & Wilkins.



Aspergillus bronchiolitis and bronchopneumonia



High-resolution computed tomography images (1.0-mm collimation) at the level of the right middle lobe bronchus (A) and liver dome (B) show patchy peribronchial consolidation, centrilobular nodules, and branching linear structures (arrows). Cavity formation is seen in both lower lobes.

Reproduced with permission from: Müller NL, Fraser RS, Lee KS, Johkoh T. Pulmonary infections. In: Diseases of the Lung, Lippincott Williams & Wilkins, Philadelphia 2002.

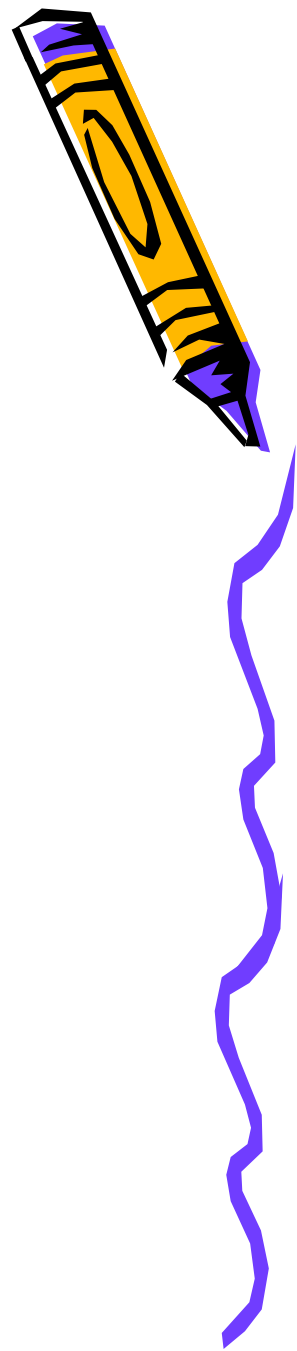
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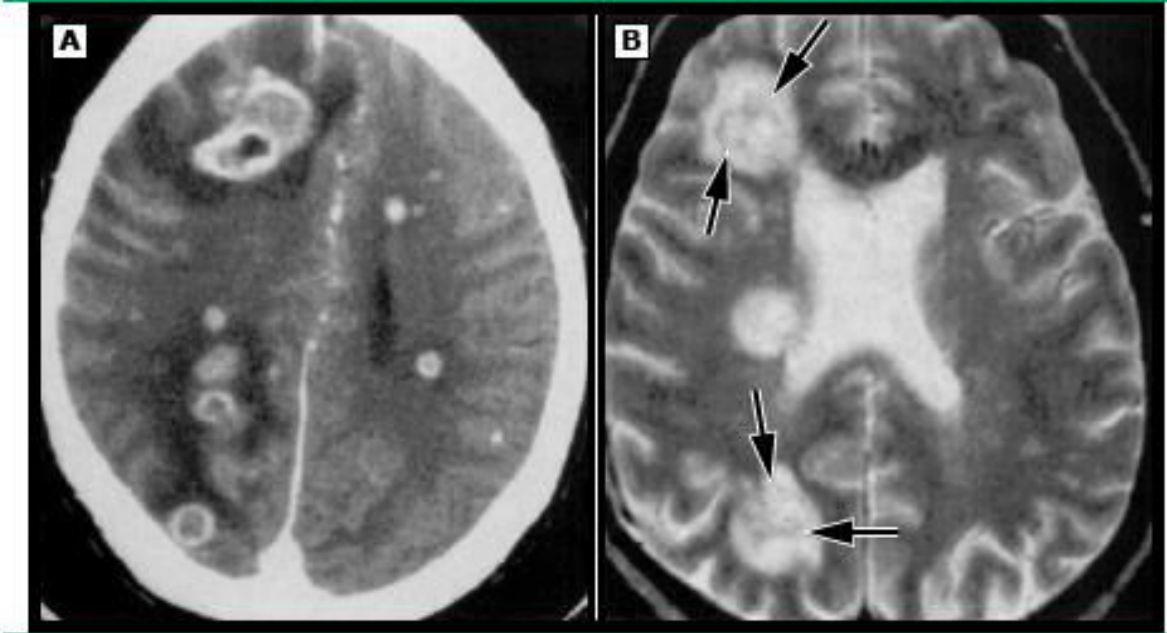


Life threatening issues

- Does not respect tissue planes
- Angio-invasive
- Dissemination



Aspergillus brain abscesses



44-year-old man with hairy-cell leukemia and biopsy-proved cerebral aspergillosis.

(A) CT scan obtained after injection of contrast material shows multiple ring-enhancing lesions with surrounding edema and mass effect.

(B) T2-weighted MR image (at slightly lower level than A) shows multiple hypointense rings (arrows) with surrounding edema in right cerebral hemisphere. Rings are irregular and relatively poorly formed.

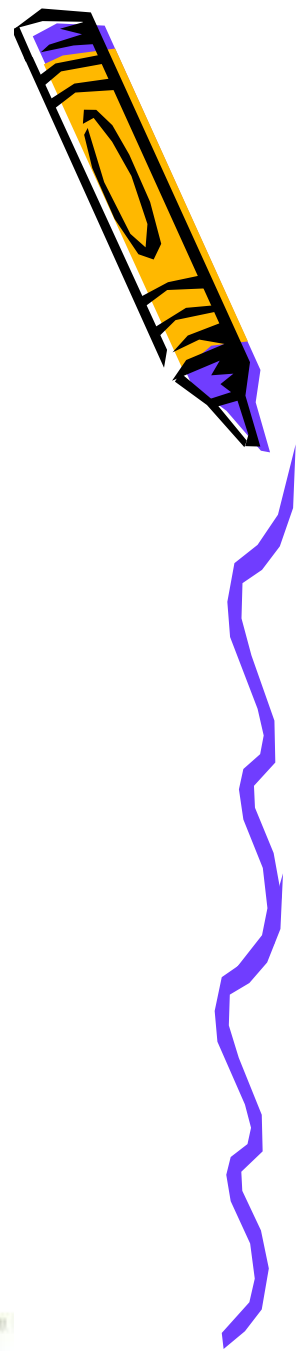
From: Ashdown BC, Tien RD, Felsberg GJ. Aspergillosis of the brain and paranasal sinuses in immunocompromised patients: CT and MR imaging findings. AJR Am J Roentgenol 1994; 162:155. Reprinted with permission from: the American Journal of Roentgenology.

Aspergillus sinusitis

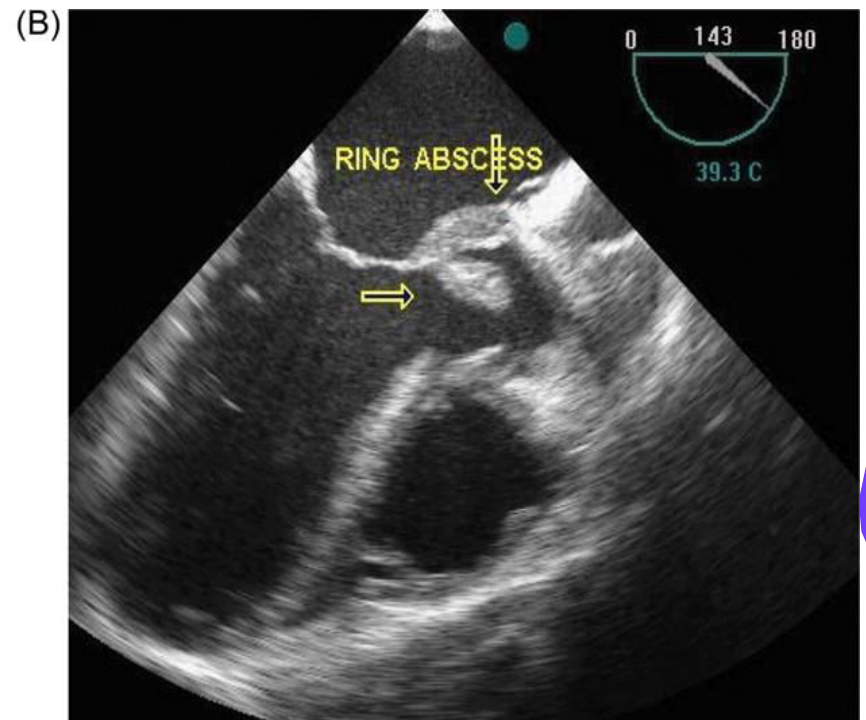


87-year-old man with diabetes mellitus and biopsy-proved aspergillosis of paranasal sinuses. Coronal T1-weighted MR image obtained after injection of contrast material shows abnormal soft tissue filling ethmoidal air cell complex, nasal cavity, and maxillary sinus. Note subfrontal intracranial extension with dural thickening and abnormal enhancement (arrows).

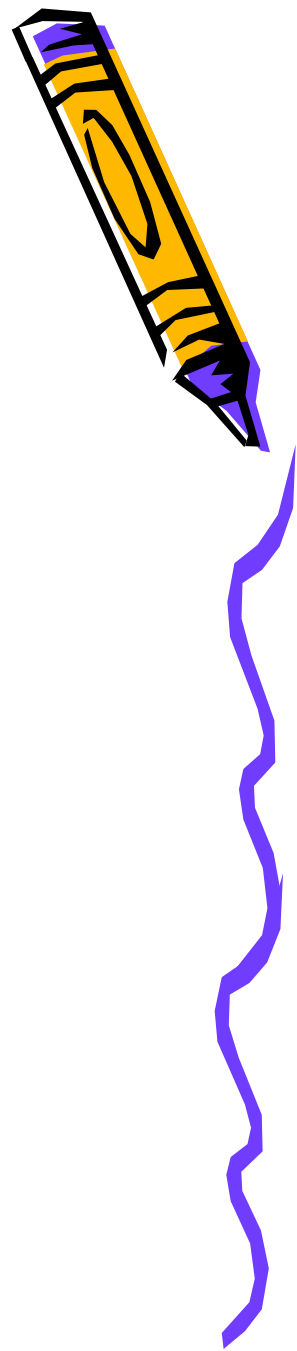
From: Ashdown BC, Tien RD, Felsberg GJ. Aspergillosis of the brain and paranasal sinuses in immunocompromised patients: CT and MR imaging findings. AJR Am J Roentgenol 1994; 162:155. Reprinted with permission from the American Journal of Roentgenology.

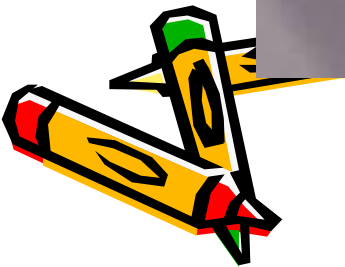


Aspergillus endocarditis after CABG

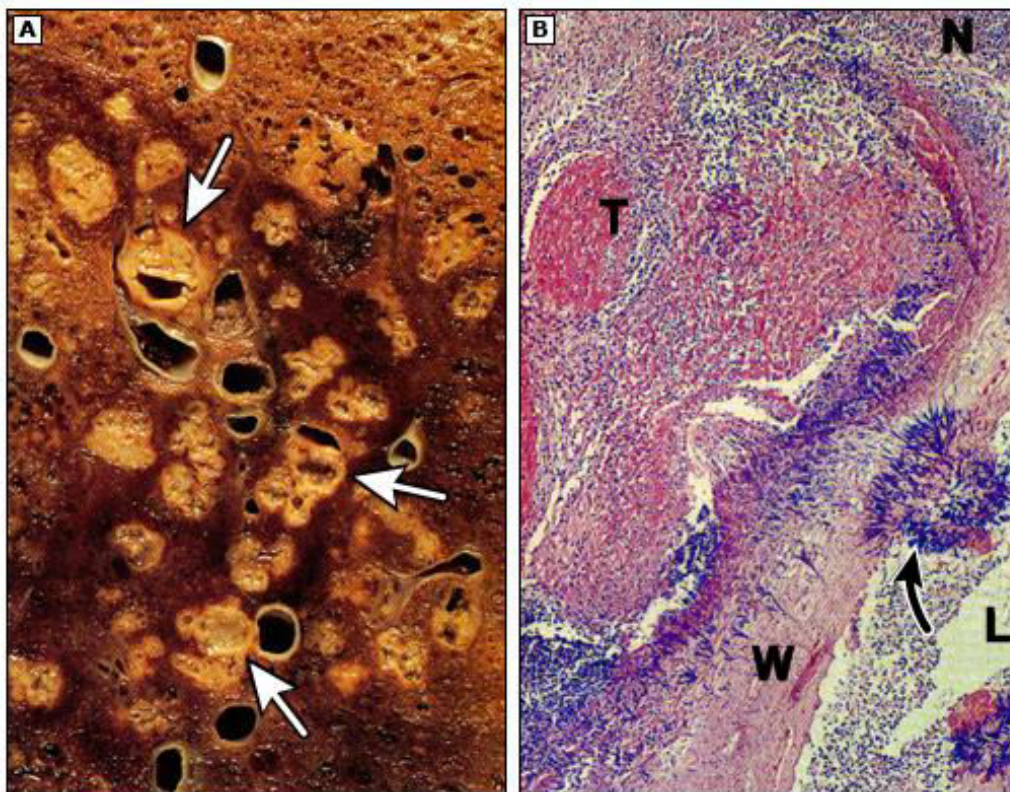


Aspergillus vertebral osteomyelitis





Aspergillus bronchopneumonia histopathology



(Panel A) Magnified view of a slice of lower lobe shows multiple foci of necrosis, some clearly centered on airways (arrows) as indicated by their intimate association with pulmonary arteries. The lung parenchyma adjacent to the necrotic regions is hemorrhagic.

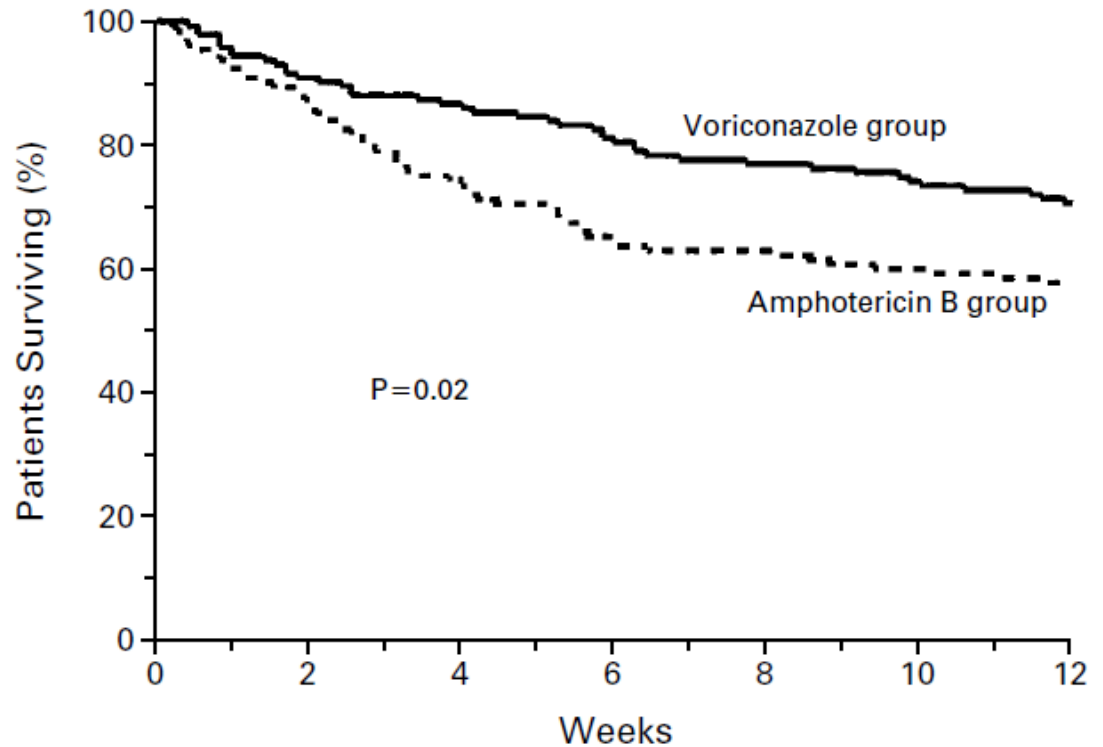
(Panel B) Photomicrograph shows small colonies of Aspergillus (arrow) within a bronchial lumen (L) and wall (W). Extension of fungus can also be seen into the adjacent pulmonary artery, which is partly occluded by thrombus (T). An infiltrate of neutrophils (N) is evident in the adjacent lung.

Reproduced with permission from: Müller NL, Fraser RS, Lee KS, Johkoh T. Pulmonary infections. In: *Diseases of the Lung*, Lippincott Williams & Wilkins, Philadelphia 2002. Copyright © 2002 Lippincott Williams & Wilkins. <http://www.lww.com>

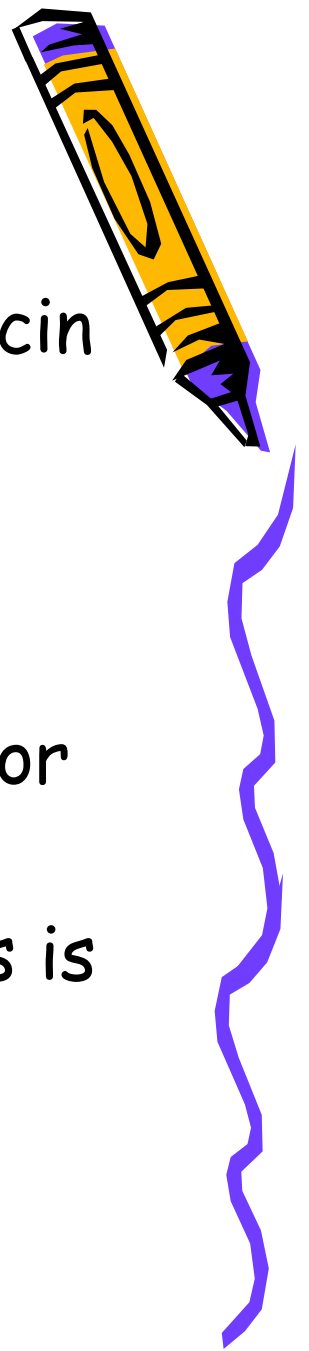
VORICONAZOLE VERSUS AMPHOTERICIN B FOR PRIMARY THERAPY OF INVASIVE ASPERGILLOSIS

N Engl J Med, Vol. 347, No. 6 · August 8, 2002 ·

- 95 centers, 19 countries
- Randomised, unblinded
- Vori=144, ampho=133
- At week 12- survival rate:
 - vori= 70.8
 - ampho B= 57.9



Therapeutic strategies



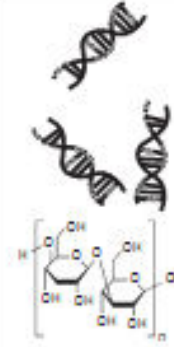
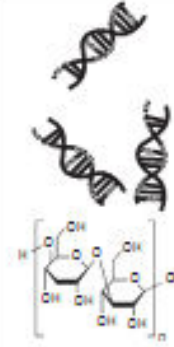



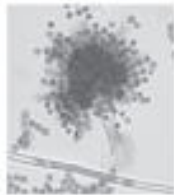


- Empirical therapy: Liposomal amphotericin
- Invasive Aspergillosis: Voriconazole
 - Watch for drug interactions
- Other azoles:
- Caspofungin (or other echinocandins): for salvage therapy
- Remember resistant species: *A. terreus* is resistant to ampho B

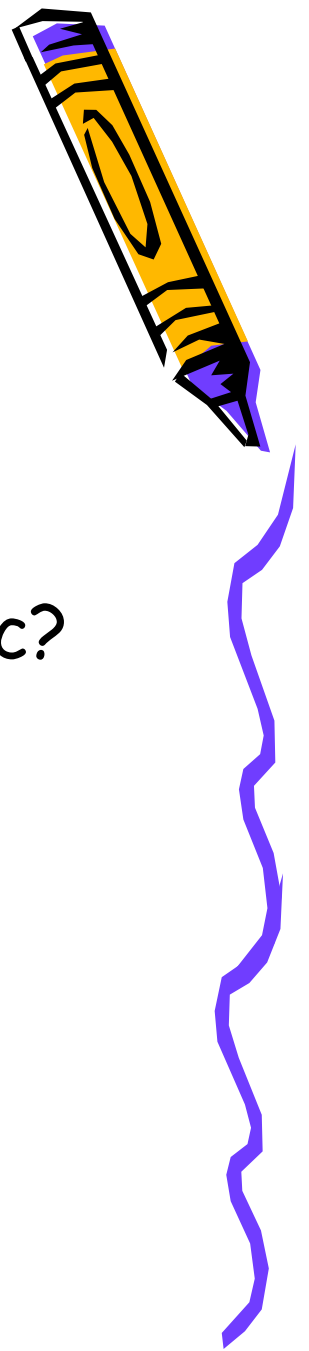


Directed therapy for fungal infections: focus on aspergillosis

Journal of Antimicrobial Therapy. July 9, 2013

No clinical signs of infection		Clinical signs of infection (fever, etc.)		Specific radiological evidence of disease (nodules±halo, cavitating lesions)		Microbiologically/histologically documented disease
						 
Biomarker negative	Biomarker positive	Biomarker negative	Biomarker positive	Biomarker negative	Biomarker positive	
EORTC/MSG criteria: no evidence of IFD				Possible IFD	Probable IFD	Proven IFD
Prophylaxis	Targeted prophylaxis	Empirical therapy	Pre-emptive therapy	Targeted therapy		Definitive therapy

Combination Therapy



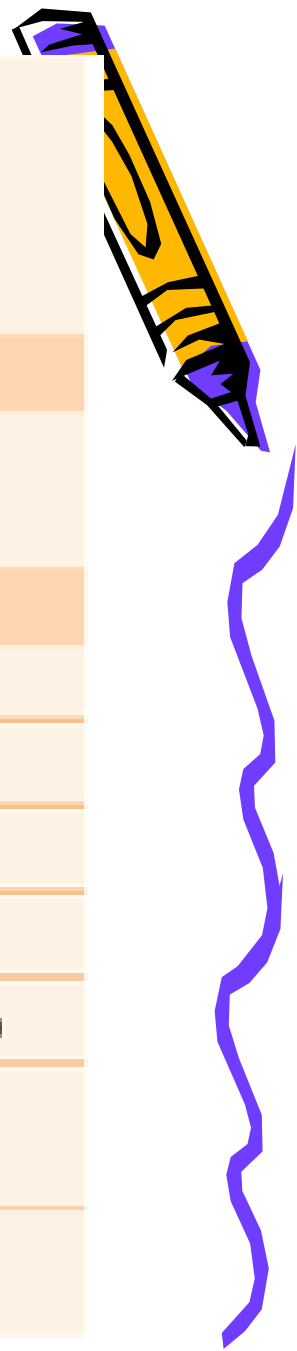
- Voriconazole with caspofungin (echinocandin)
- Ampho B with caspo
- Ampho B with voriconazole- antagonistic? Not recommended at present time.
- Immunomodulation
- Colony stimulating factors
- Surgery- source control



Table 2. Recommended Dosages for Invasive Aspergillosis Treatment

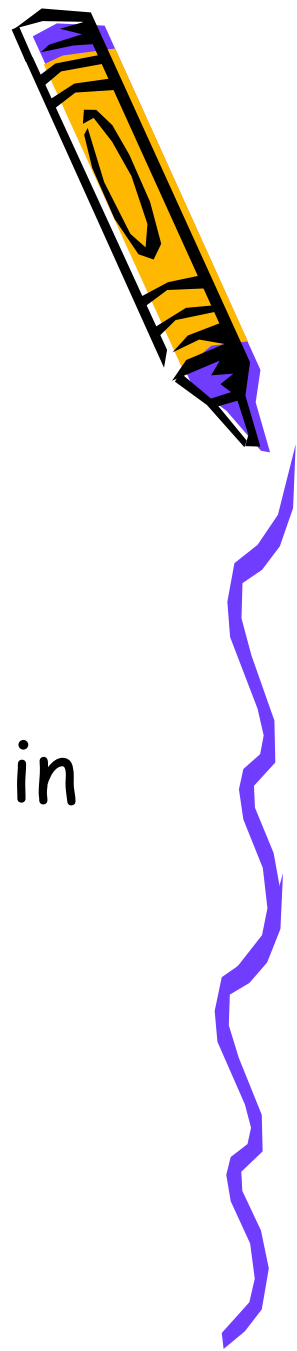
Agent	Dosage
<i>1st-Line Treatment</i>	
Voriconazole	IV: 6 mg/kg q12h on day 1, then 4 mg/kg q12h Oral form: 200 mg q12h
<i>Alternative Agents</i>	
L-AmB (primary option)	3-5 mg/kg/day IV
ABLc	5 mg/kg/day IV
Caspofungin	70 mg IV day 1, then 50 mg/day
Micafungin	100-150 mg/day IV
Posaconazole	200 mg 4 times/day po; after stabilization, 400 mg bid po
Itraconazole	IV: 200 mg q12h for 2 days, then 200 mg/day Oral form: 600 mg/day for 3 days, then 400 mg/day

*ABLc: amphotericin B lipid complex; L-AmB: liposomal amphotericin B.
Source: Reference 2.*



Prevention

- Prophylaxis with azoles (posaconazole)
- Infection Control: construction/renovation activities in the hospital, damp walls...



Questions?

