



Histopathological diagnosis

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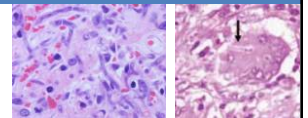


Need of histopathological diagnosis

- Fungi are ubiquitous & saprophytic
- Usual laboratory contaminant
- Infection versus colonization - a frequent problem
- Rapid & cost-effective means of providing a presumptive or definitive diagnosis of an invasive fungal infection
Help in knowing the load, tissue reaction, extent & invasion
- Difficulty – to get samples from deep tissue
- Advances in diagnostic radiology & patient support (platelet transfusions) have improved collection of tissue biopsy specimens

Learning histopathological diagnosis

- Learn tissue reaction to fungi
- Commonly performed H & E stain in histopathology will help you to observe tissue reaction
- Difficult to identify fungi on H & E (except *Histoplasma*, *Mucor* etc.)
- On H&E, all fungi show pink cytoplasm, blue nuclei & no colouration of the wall. You may see unstained area in the position of fungi
- Go ahead performing PAS, GMS
- Other specific stains – Alcian blue, Mucicarmine, Fontana Masson etc.
- Need training....



Other challenges

- Morphological characteristics of fungi are specific in few occasions
- Histopathology report - description fungus & the presence or absence of tissue invasion & the host reaction to the infection
- Comment - most frequent fungi associated with the morphology, other possible fungi considered in the differential diagnosis
- Alternate techniques - immunohistochemistry, in situ hybridization, & PCR
- Laser micro-dissection - detect dual fungal infections & the local environment in which this phenomenon occurs

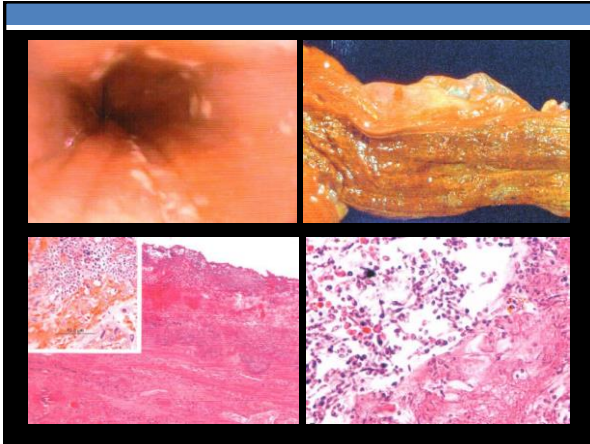
Tissue reaction depends on

- Host immunity
- Class of fungal pathogen

Superficial infections

Superficial *Candida* infection

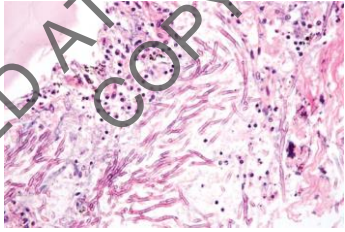
- Low level tissue destruction & inflammation compared to dermatophytes
- Pathogenic (vs. commensal) correlates with pro-inflammatory response & depends on fungal burden
- Steps – colonization, adhesion, invasion, damage
- Cell wall (mannan, glucan, chitin, protein) triggers host immune response (cytokines, antimicrobial molecule & attraction of immune effector cells)
- But it is not best interest of commensal *Candida*, as host response would cause elimination



Chronic mucocutaneous candidiasis

- Disease occurs in autoimmune polyendocrinopathy candidiasis ectodermal dystrophy syndrome (APECED), hypoparathyroidism, Addison disease or Hyper IgE syndrome
- CMC can occur in defective pathogen recognition pathway
- **Low level of inflammation**

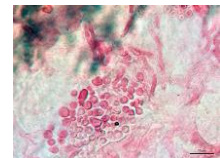
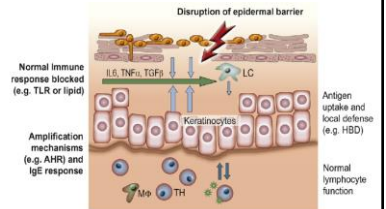
Dermatophyte infection



- Though dermatophytes alone have minimal capacity to damage host, consistently high level of host tissue destruction observed in dermatophytosis
- However, for long-term survival - ↓ tissue reaction required (tinea unguium – localized in nail & avoid host immune cells)

Malassezia infection

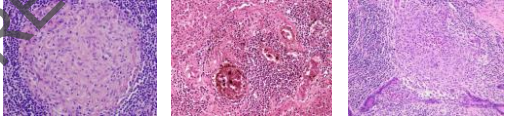
- Host secretion of β -endorphins increase the production of *Malassezia* phospholipases → disrupt epithelial barrier & provoke inflammation



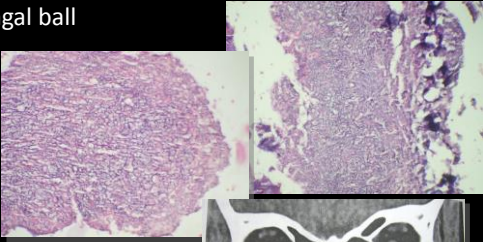
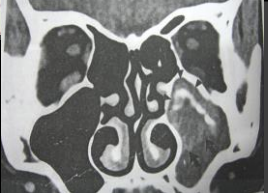
Hube et al. J Mycol Med 2015; 25: e44

Tissue reactions	Fungi can be suspected
Acute pyogenic or suppurative	<i>Candida, Aspergillus</i>
Suppurative with angio-invasion	<i>Aspergillus, Mucorales</i>
Mixed suppurative inflammation	<i>Blastomyces, Coccidioides</i>
Mixed suppurative & granulomatous	<i>Blastomyces, Coccidioides, Talaromyces, Paracoccidioides, Sporothrix, Phaeohiphomyces</i>
Predominantly granulomatous	<i>Cryptococcus, Histoplasma, Coccidioides</i>
Granulomatous with various degree of fibrosis	<i>Cryptococcus, Rhinosporidium, Chronic or sub-acute aspergillosis</i>
Nodules having vascular necrosis, lymphohistiocytic vasculitis, rare granuloma	<i>Histoplasma</i>
Granuloma with necrosis & calcification	<i>Histoplasma, Coccidioides</i>
Predominant fibrosis with granuloma, mixed eosinophilic inflammation	<i>Entomophthorales</i>
Diffuse alveolar damage (ARDS)	<i>Blastomyces, Histoplasma, Aspergillus</i>

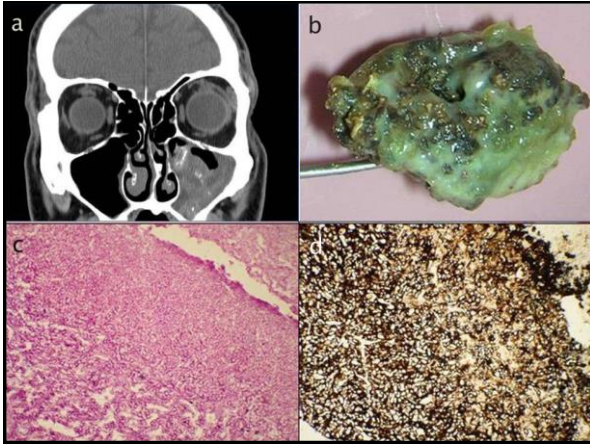
- ### Tissue reaction
- **Non-invasive colonization of pre-existing cavity** – fungal ball (paranasal sinus & pulmonary cavities)
 - **Allergic, mucin-producing, non-invasive fungal disease** – ABPA, AFRS
 - **No reaction, gelatinous** (Cryptococcus)
 - **Predominantly neutrophilic inflammatory response**
 - Mild neutropenia – localized lesion (neutrophilic exudate)
 - Severe neutropenia – disseminated (coagulative necrosis)
 - **Granuloma vs. diffuse macrophage infiltration**
 - **Mixed granulomatous & purulent inflammation** (mixture of epithelioid macrophages & neutrophils)

- ### Mixed granulomatous & purulent inflammation
- **Localized controlled infection** – granuloma predominates, organism scanty (chronic granulomatous PRS)
 - **Fulminant infection** – predominance of neutrophils, organism readily seen (dimorphic infection in AIDS)
 - **Mixed purulent & granulomatous inflammation** (sporotrichosis, chromoblastomycosis)
- 

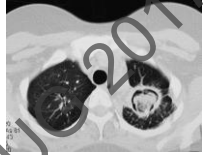
Fungal ball

- Usually unilateral
- Involves the maxillary sinus
- Well defined, high attenuation mass
- Occasional flocculent Ca
- Reactive sclerosis of sinus wall
- No invasion



Aspergilloma

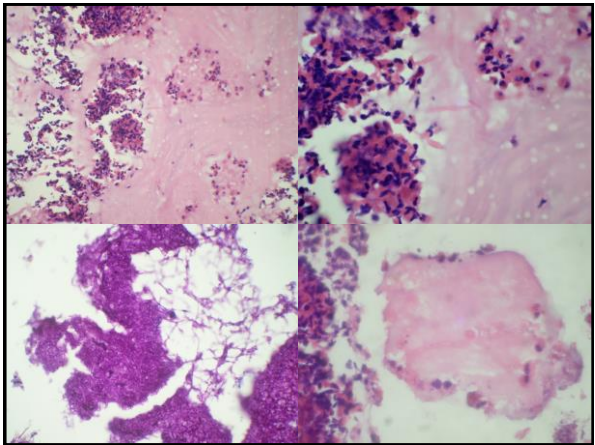


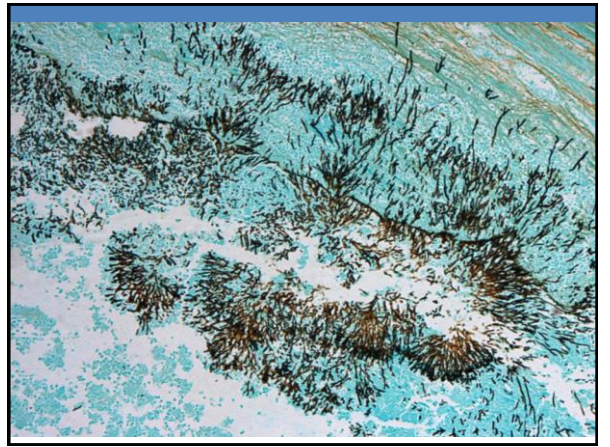
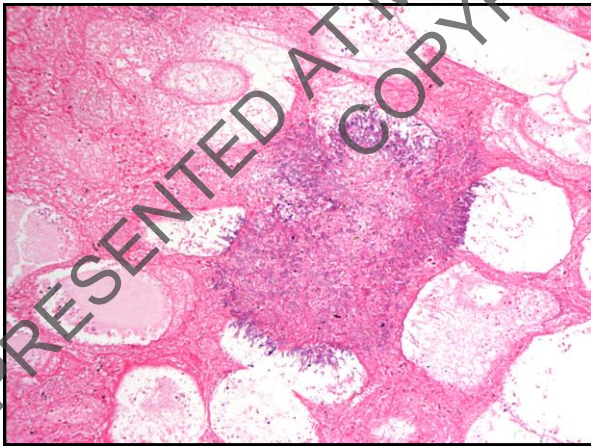
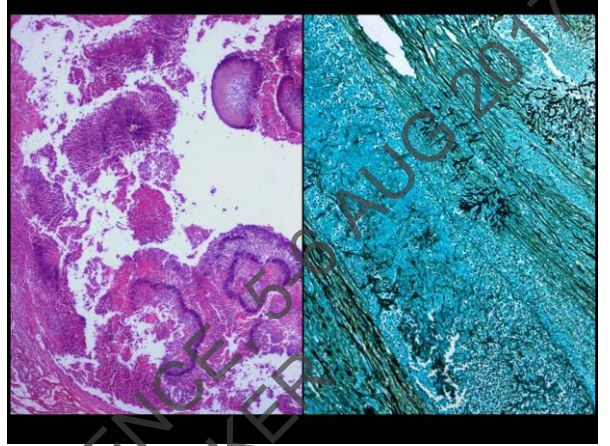
- Fungus ball composed of *Aspergillus* hyphae & cellular debris within a pulmonary cavity
- Preexisting pulmonary cavities that have become colonized with *Aspergillus* spp.
- Fungal ball is single cavity stable over months
- Patient has few symptoms (mild cough only) and little evidence of systemic inflammation

Allergic fungal rhinosinusitis

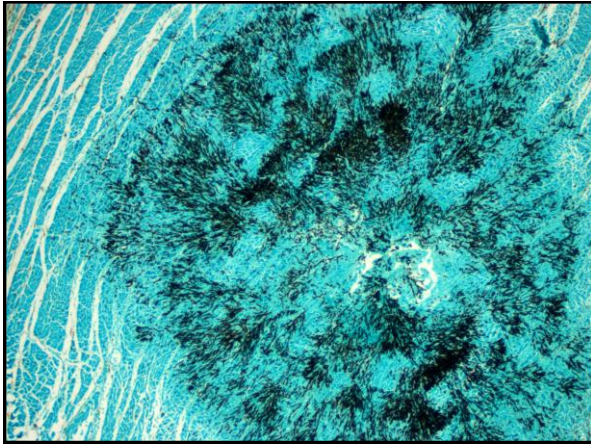
- Type I hypersensitivity
- Nasal polyposis
- Characteristic CT findings
- Allergic mucin without mucosal invasion
- Positive fungal culture of sinus content

Bent & Kuhn, Otolaryngol Head Neck Surg, 1994; 111: 580-8

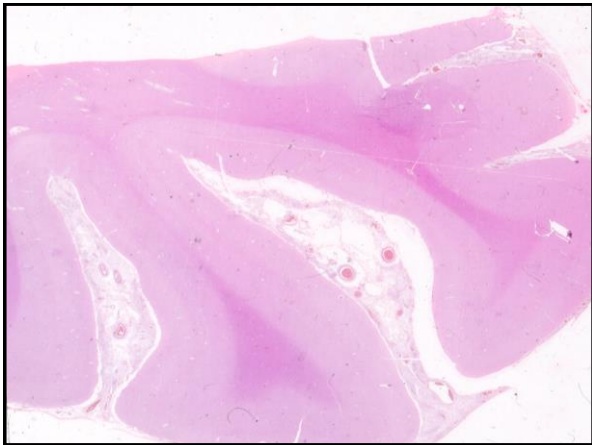
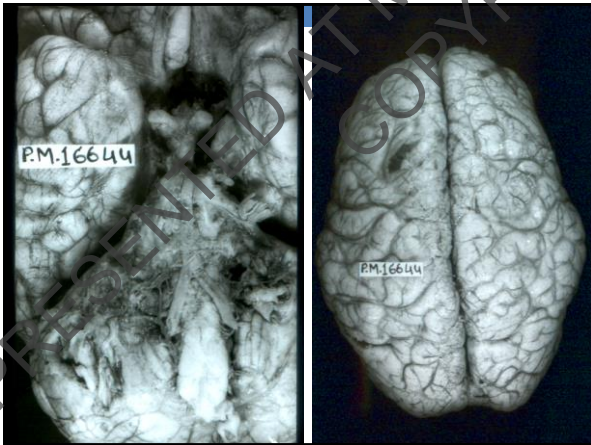




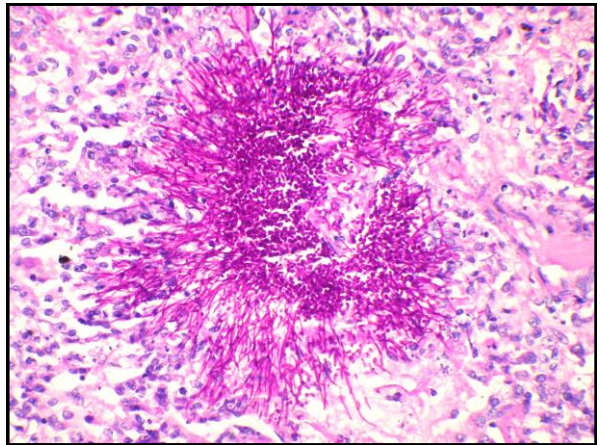
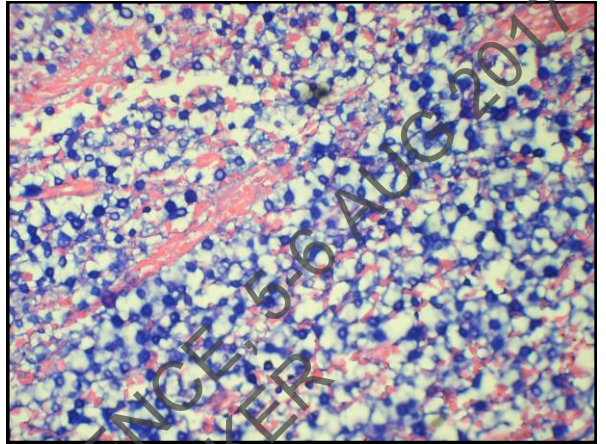
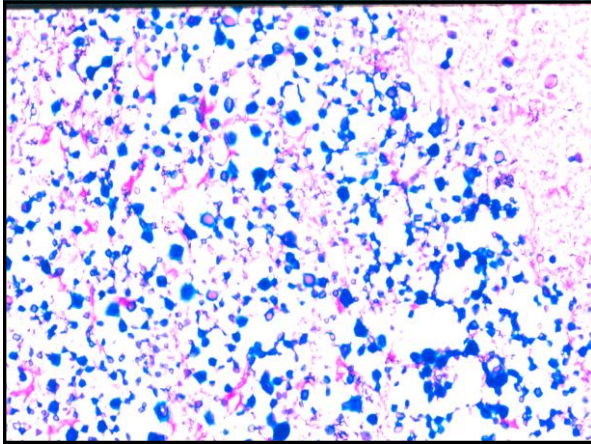
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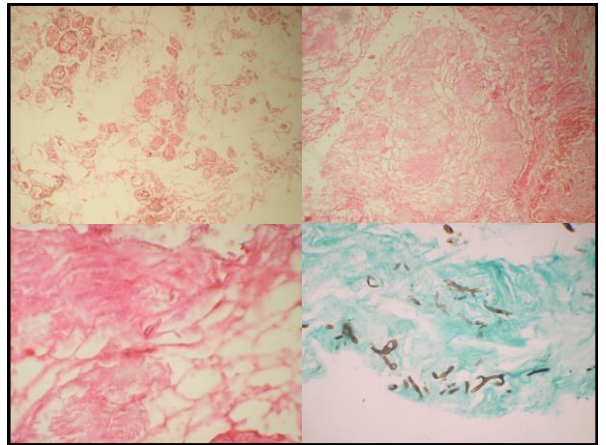
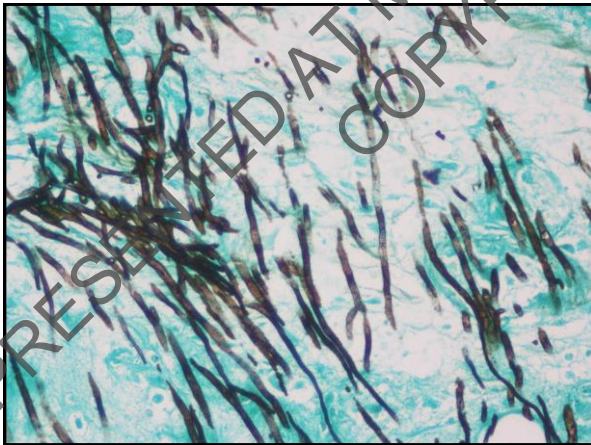
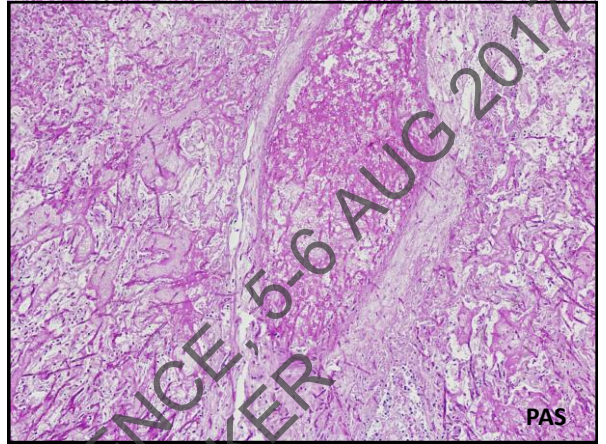
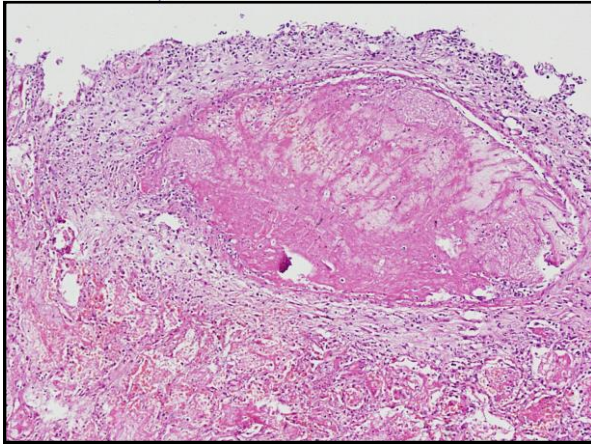
Gelatinous inflammation



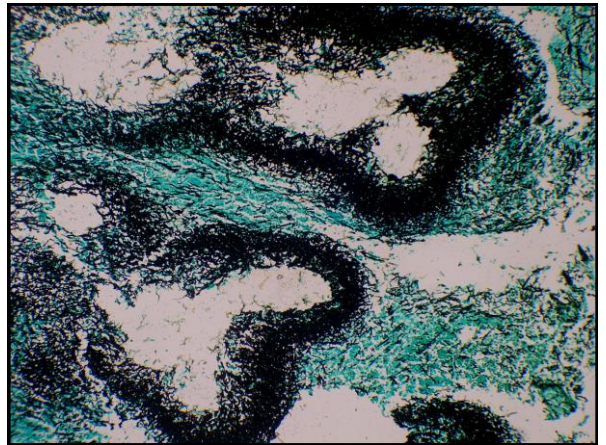
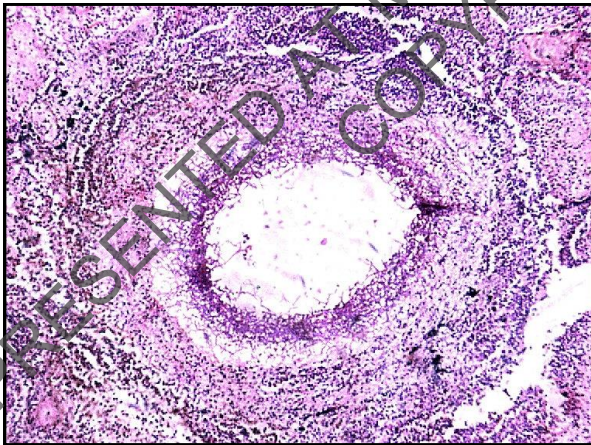
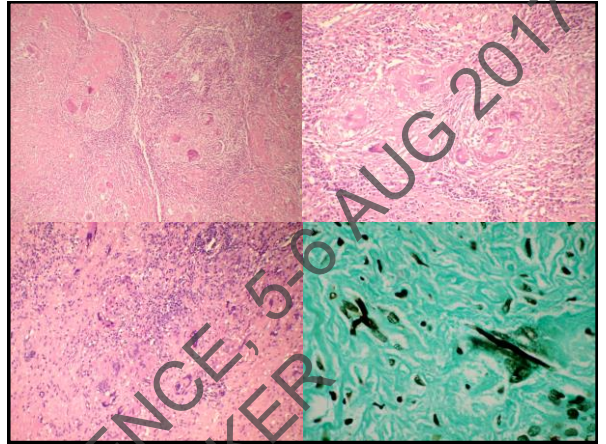
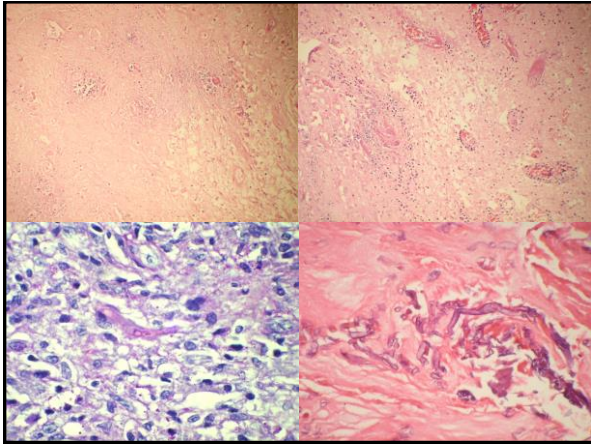
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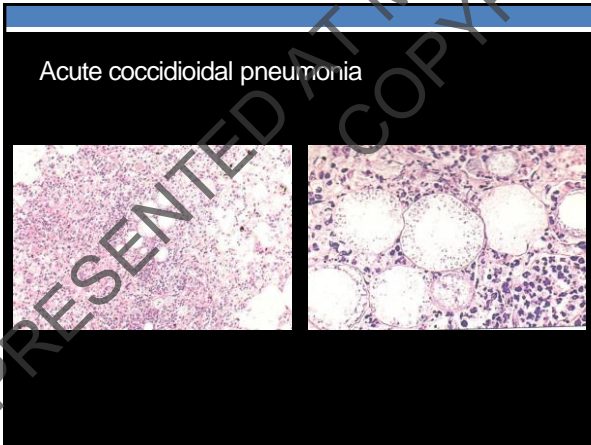
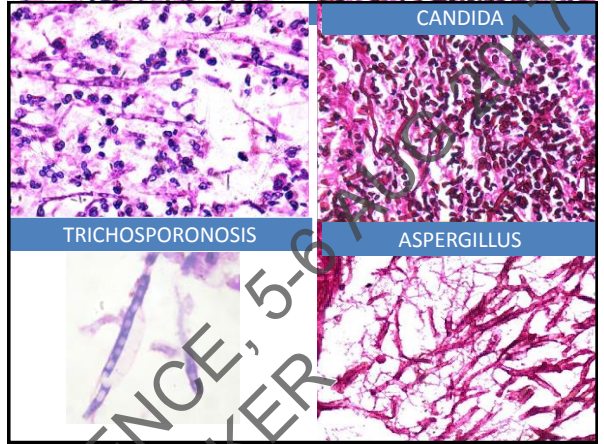
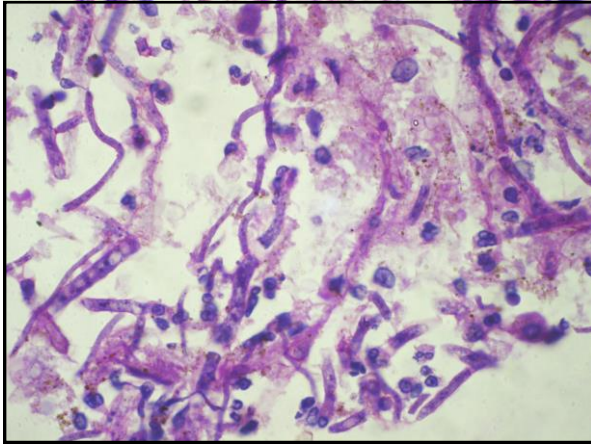
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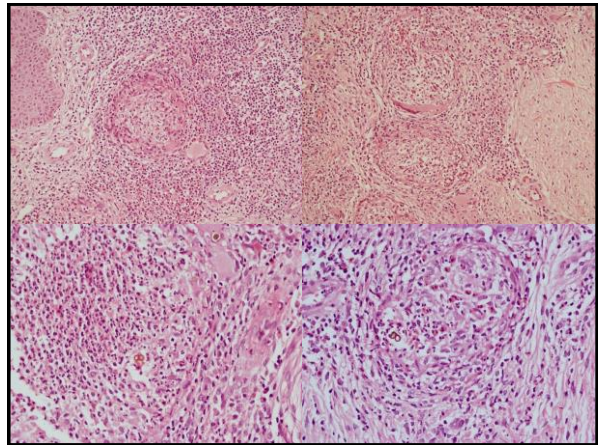
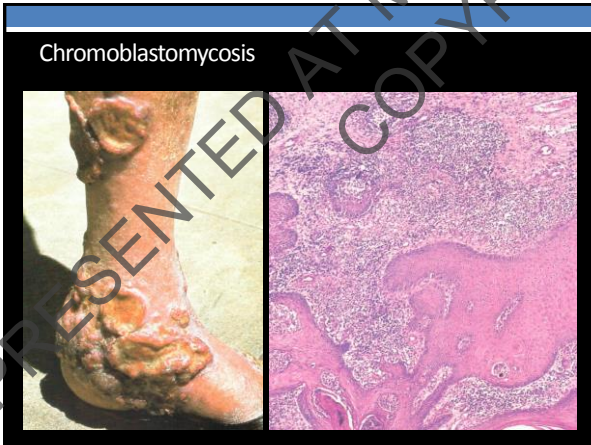
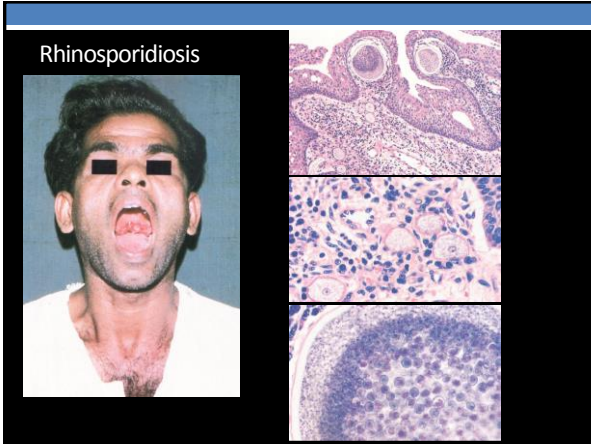
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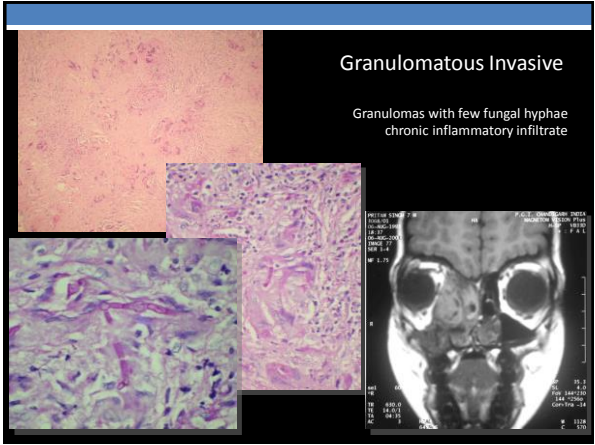
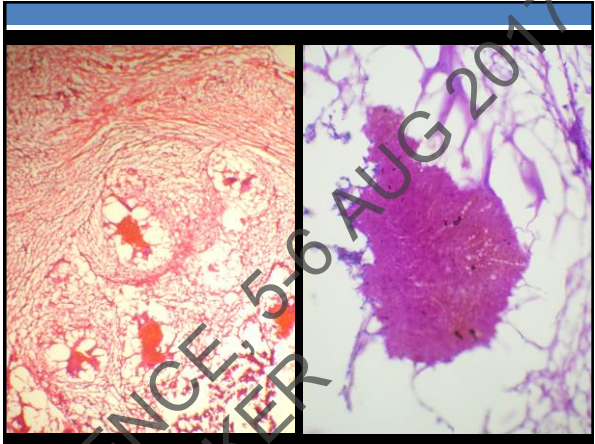


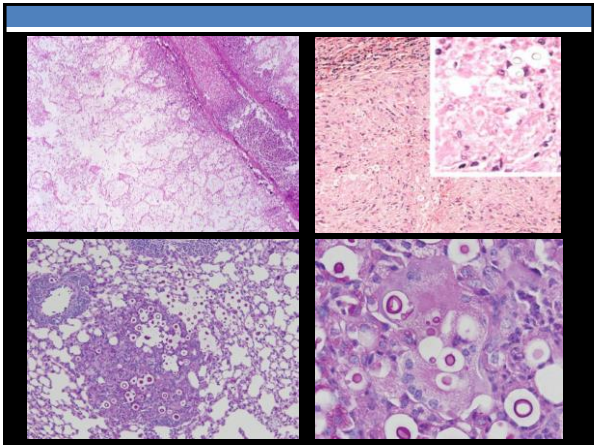
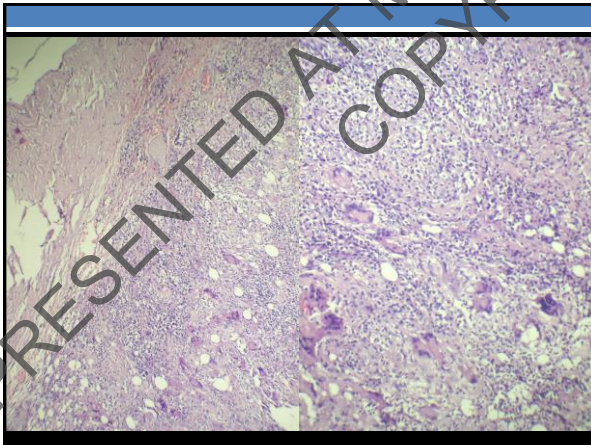
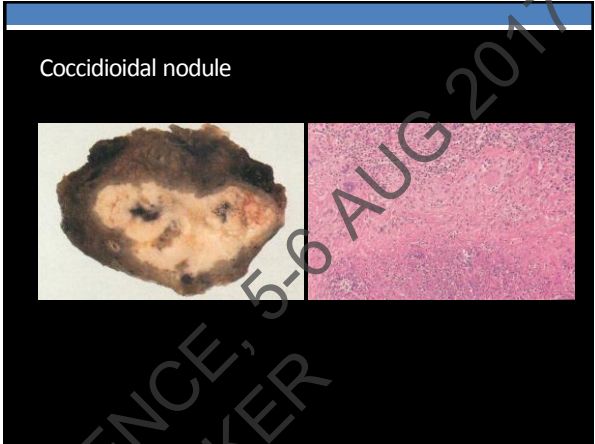
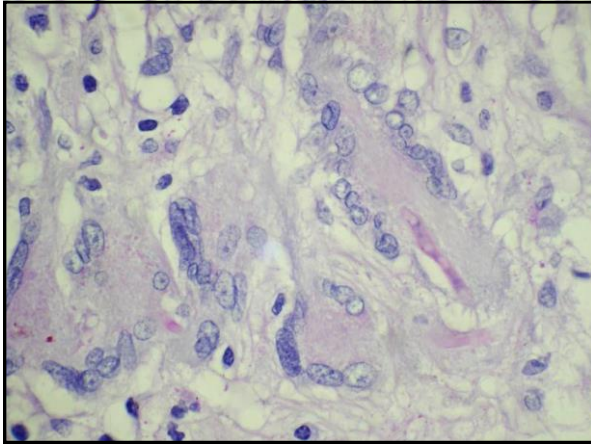
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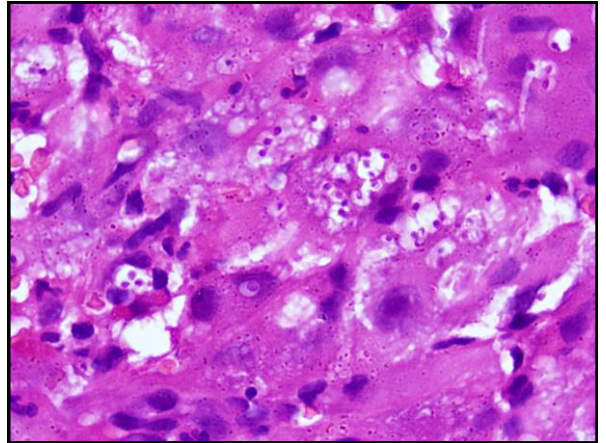
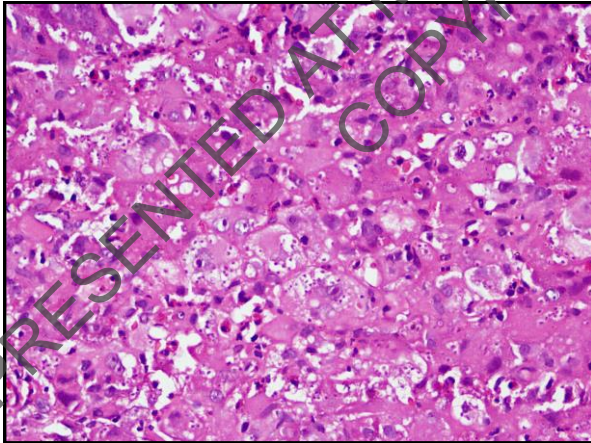
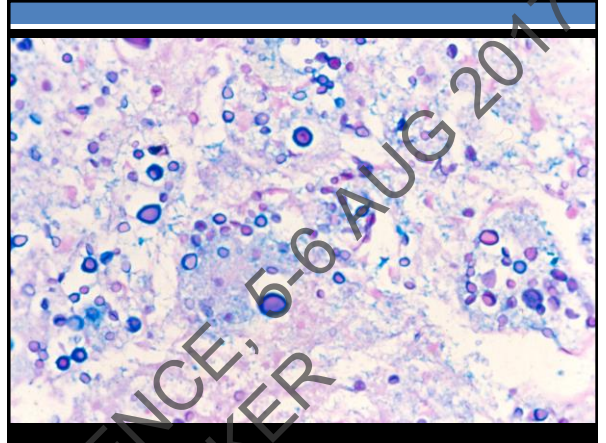
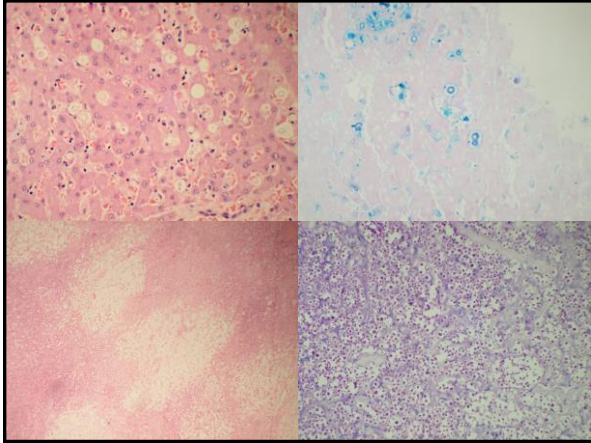
Mixed purulent & granulomatous



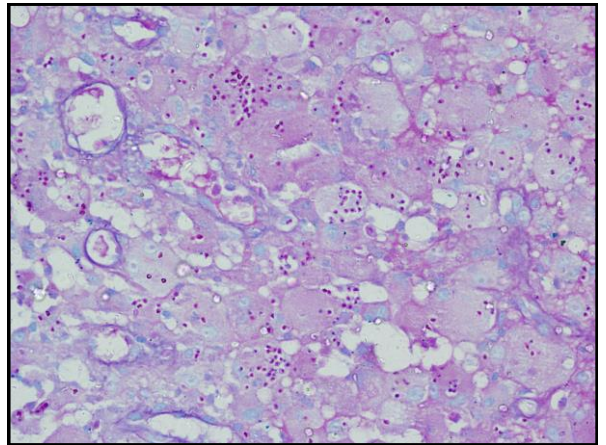
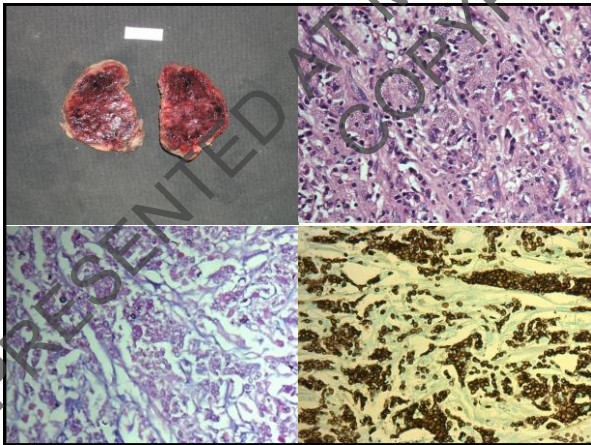
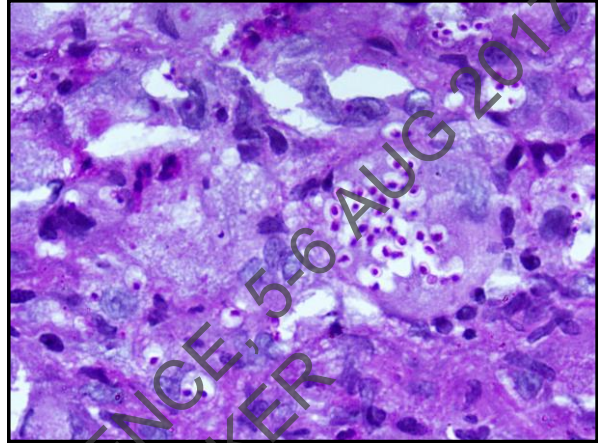
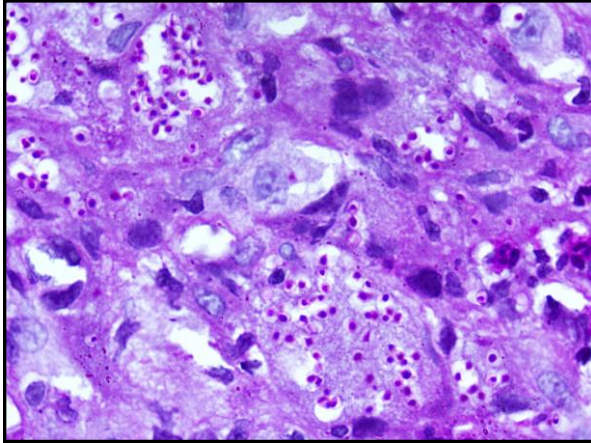




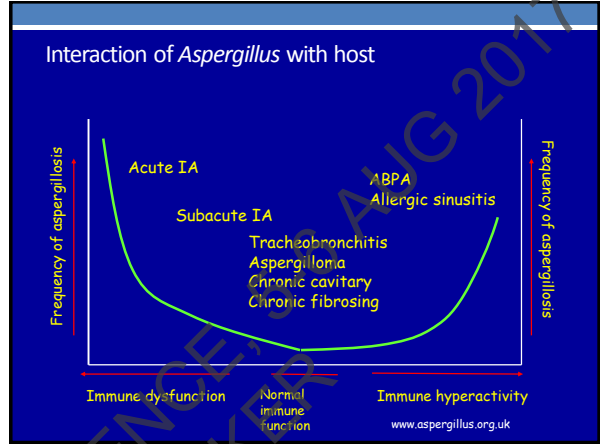
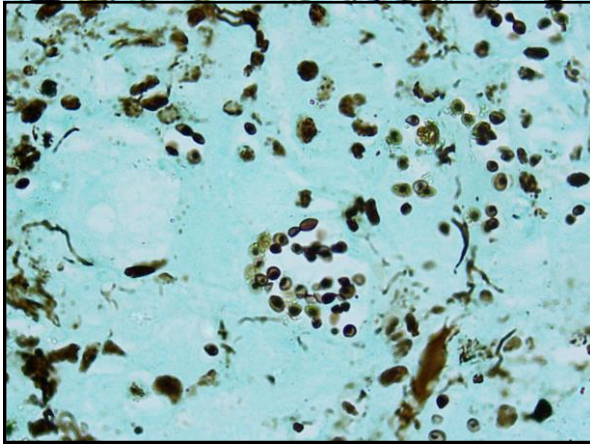
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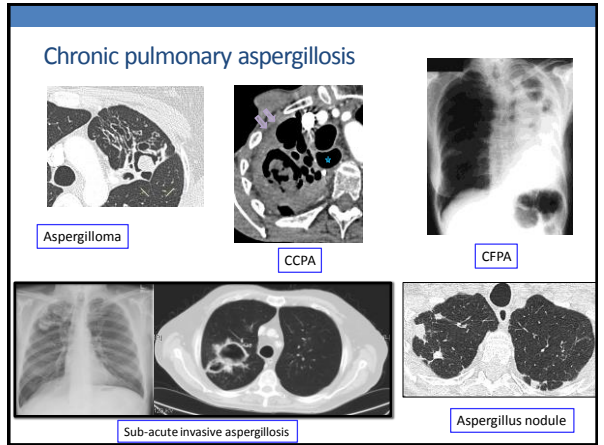
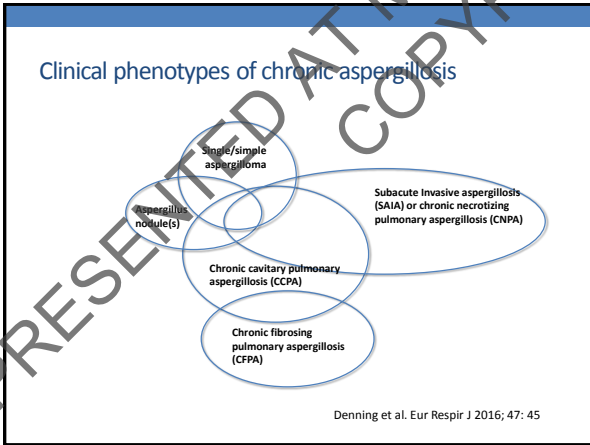
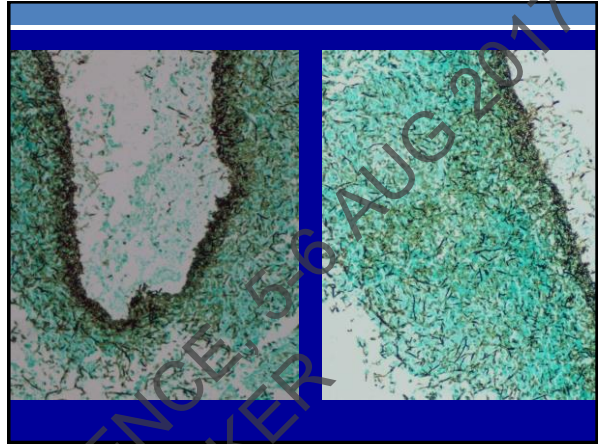
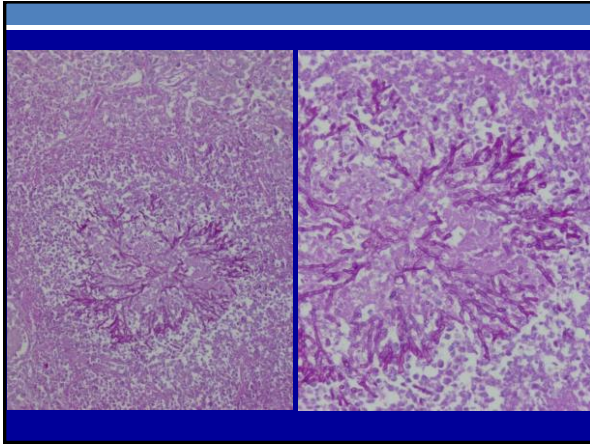
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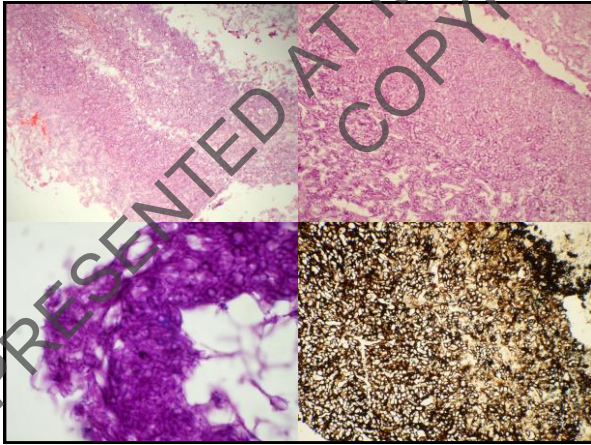
Acute invasive aspergillosis



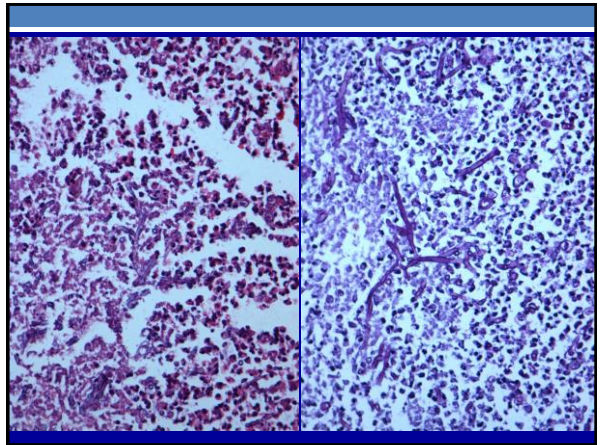
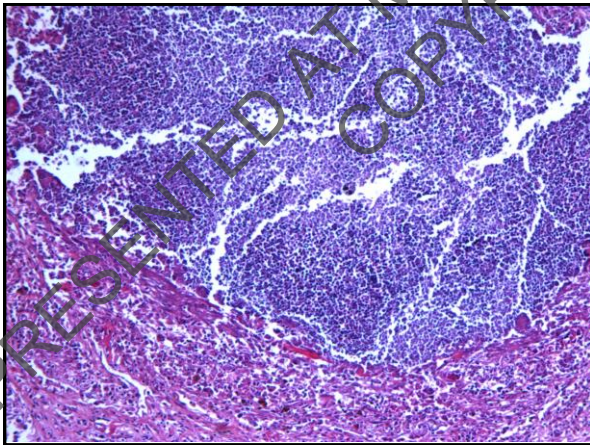
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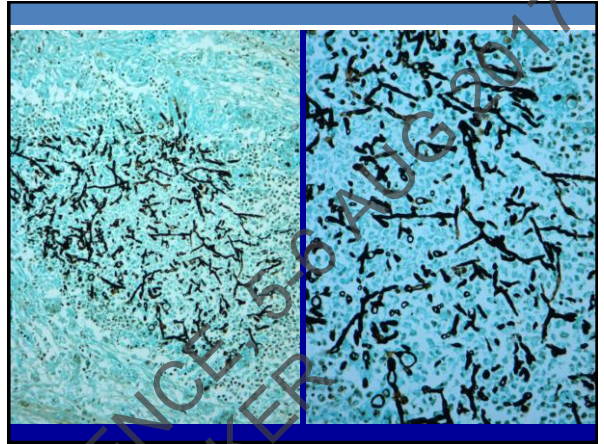
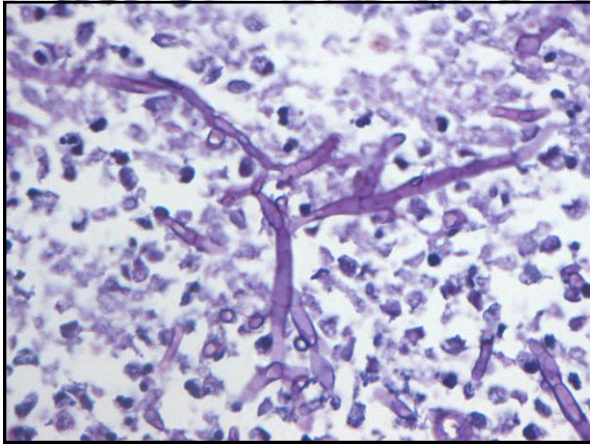


Aspergilloma



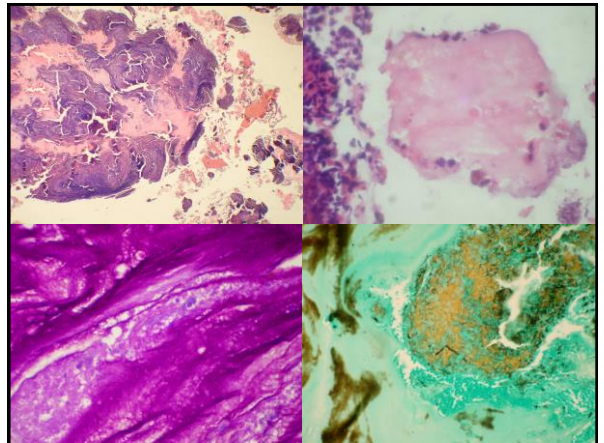
Chronic necrotizing pulmonary aspergillosis

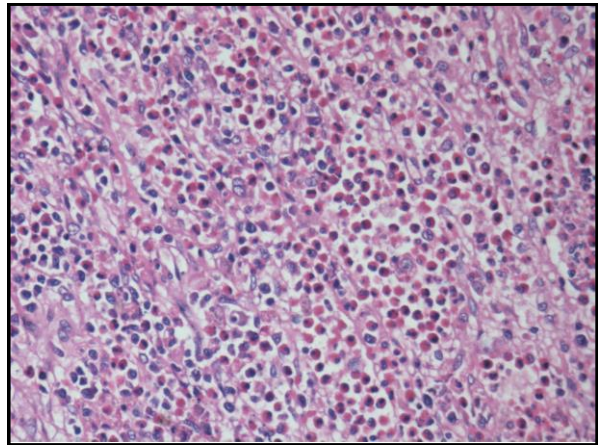
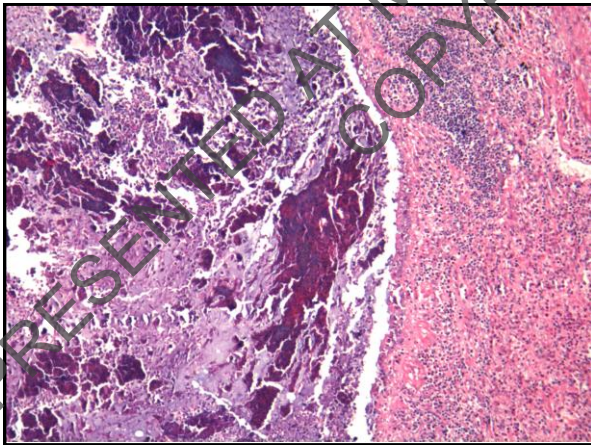




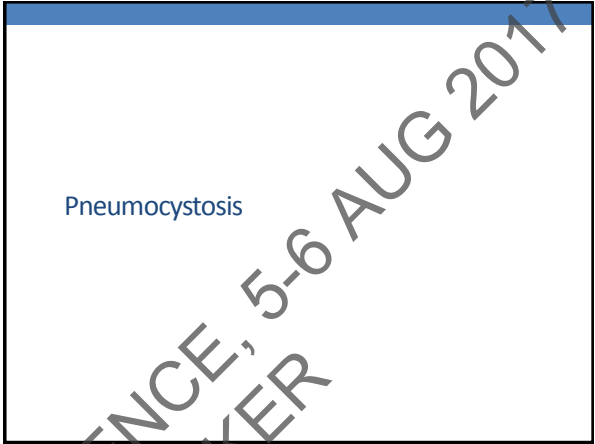
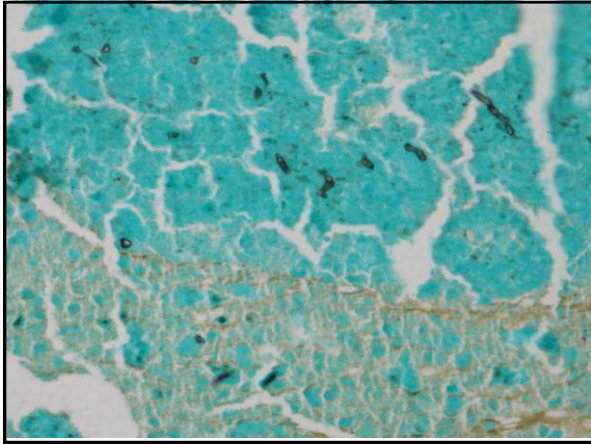
Allergic aspergillosis

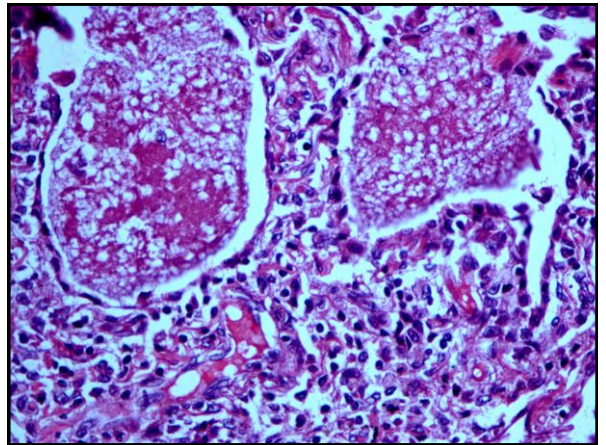
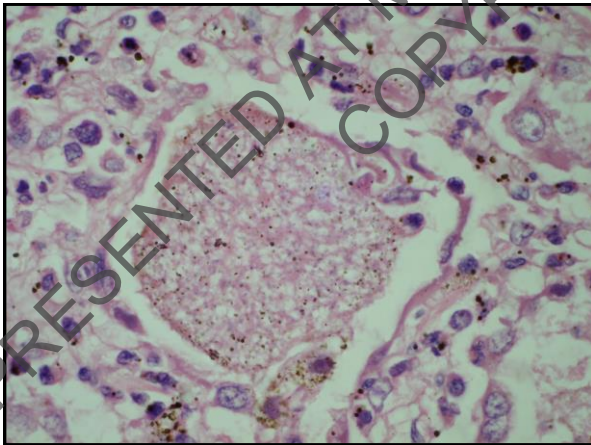
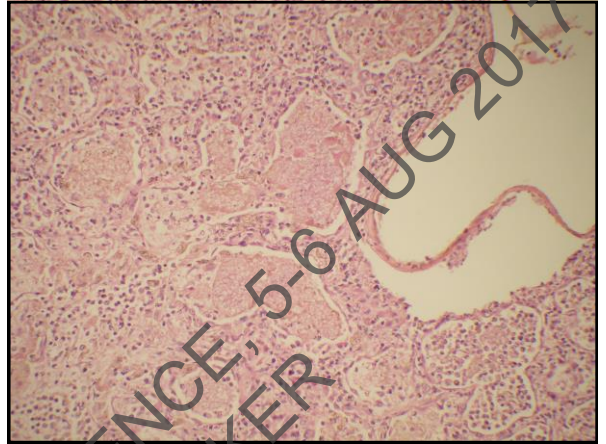
- allergic fungal rhinosinusitis
- allergic bronchopulmonary aspergillosis (ABPA)



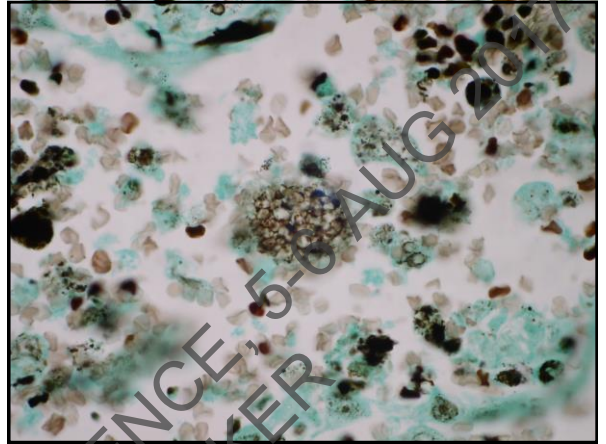
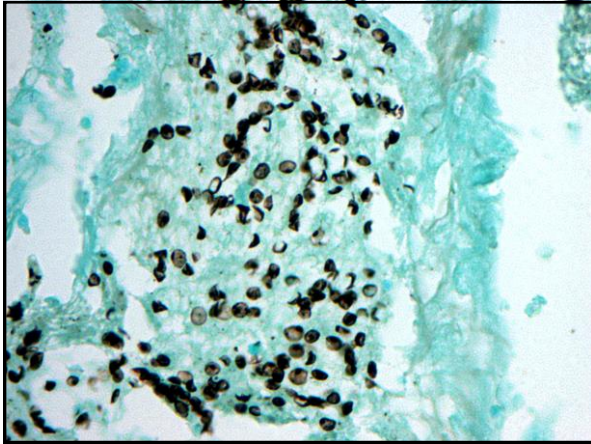


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