MMTN
MEDICAL MYCOLOGY TRAINING NETWORK

Histopathological diagnosis

Professor Arunaloke Chakrabarti
Head, Department of Medical Microbiology
Postgraduate Institute of Medical Education and Research
Chandigarh, India
Co-chair, ISHAM Asia Fungal Working Group

ASIA FUNGAL WORKING GROUP
an ISHAM working group

ISHAM
INTERNATIONAL SOCIETY FOR HUMAN AND ANIMAL MYCOLOGY

Presented at MMTN Vietnam Conference
1–3 December 2017, Ho Chi Minh City, Vietnam

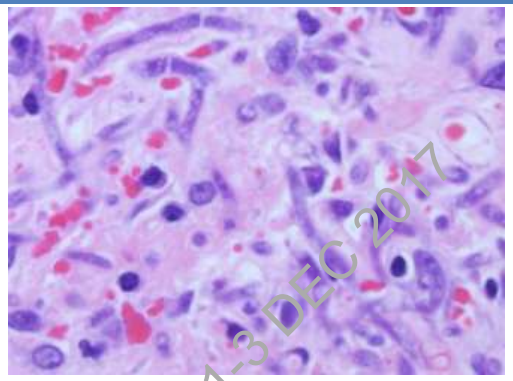
Histopathological diagnosis

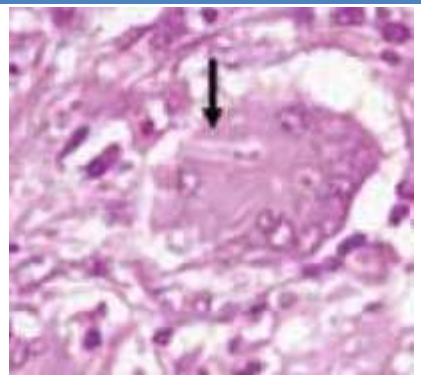
Arunaloke Chakrabarti
Professor & Head
Center for Advanced Research in Medical Mycology
& WHO Collaborating Center
Department of Medical Microbiology
Postgraduate Institute of Medical Education & Research
Chandigarh – 160012, India

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

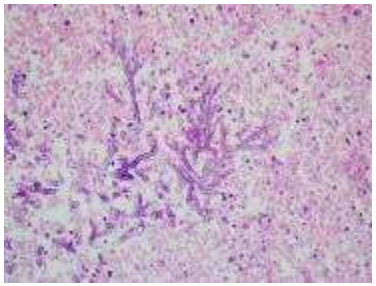




- Learn tissue reaction to fungi
- Commonly performed H & E stain in histopathology will help you to observe tissue reaction
- Difficult to identify fungi on H & E (except *Histoplasma, Mucor* etc.)
- On H&E, all fungi show pink cytoplasm, blue nuclei & no colouration of the wall. You may see unstained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

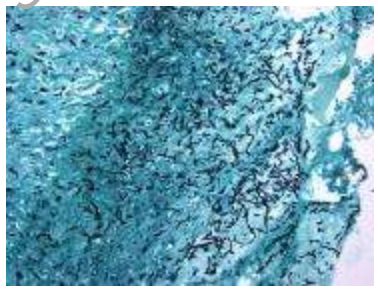
Other challenges

- Morphological characters of fungi are specific in few occasions
- Histopathology report - description fungus & the presence or absence of tissue invasion & the host reaction to the infection
- Other possible fungi with same morphology to be considered in the differential diagnosis

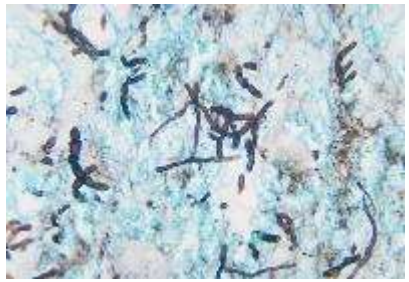


Aspergillosis

Fusariosis



Scedosporiosis



Phaeohyphomycosis

- Alternate techniques - immunohistochemistry, in situ hybridization, & PCR
- Laser micro-dissection - detect dual fungal infections & the local environment in which this phenomenon occurs

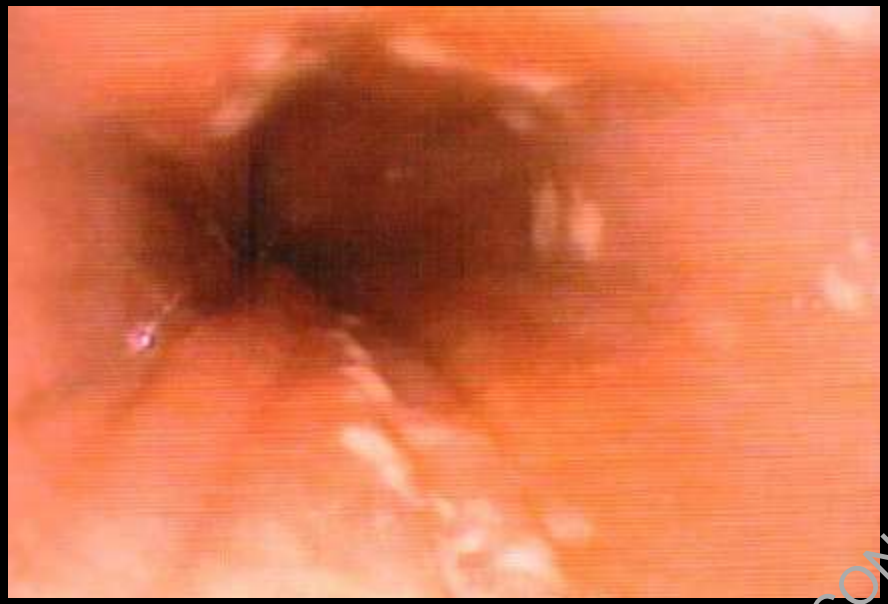
Tissue reaction depends on

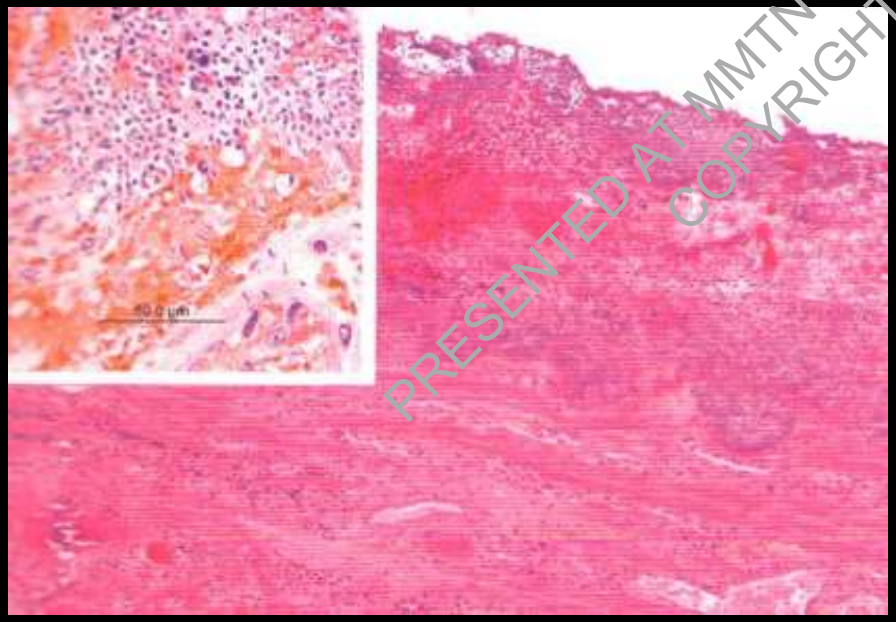
- Host immunity
- Class of fungal pathogen

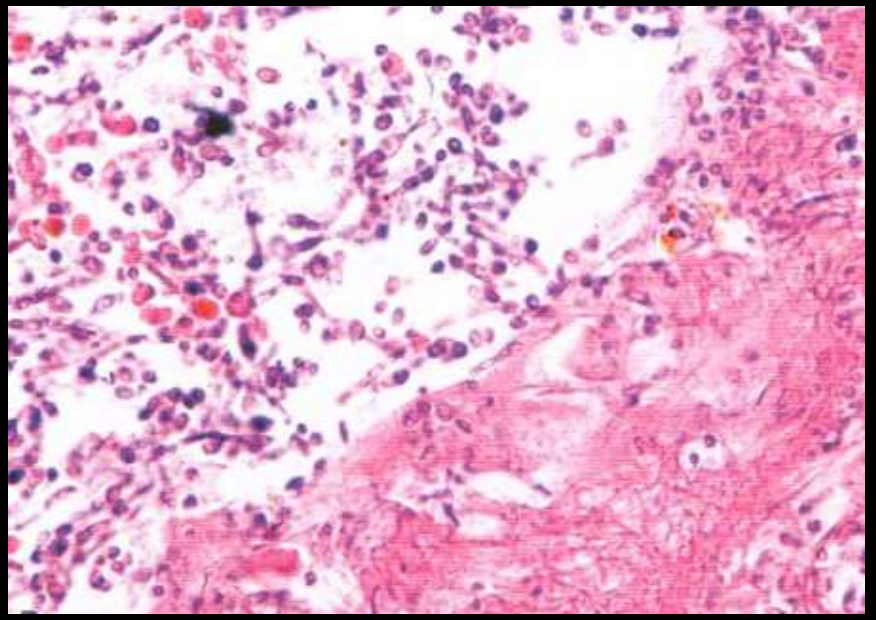
Superficial infections

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



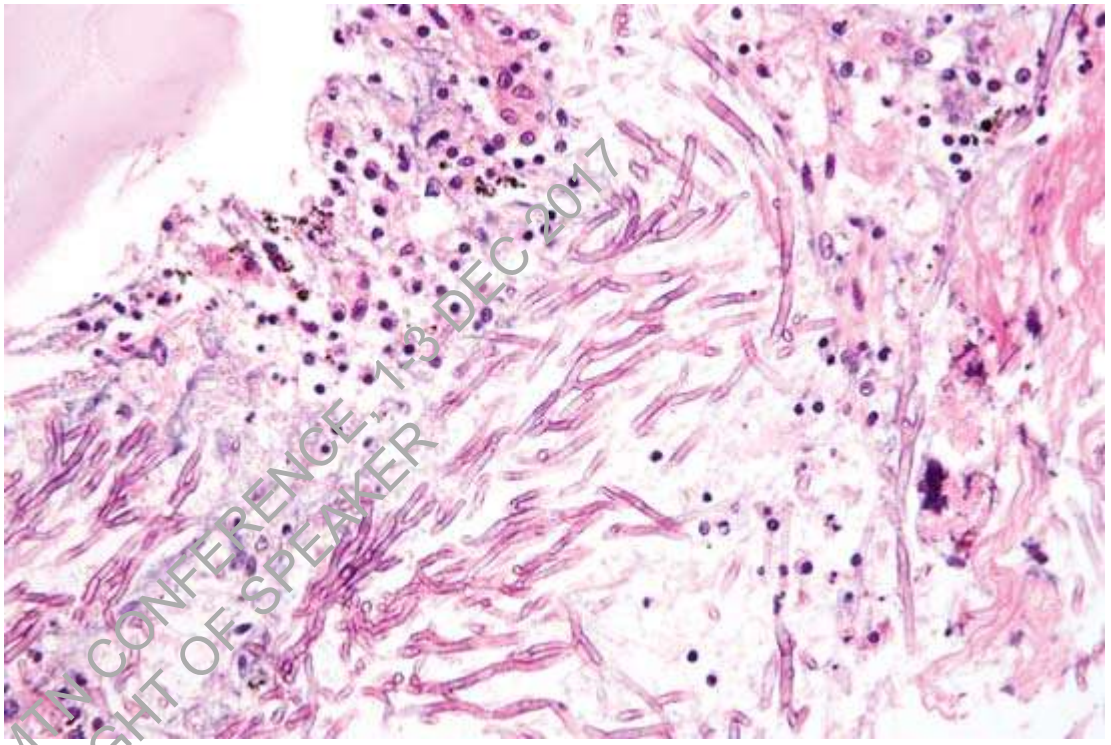




Chronic mucocutaneous candidiasis

- 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

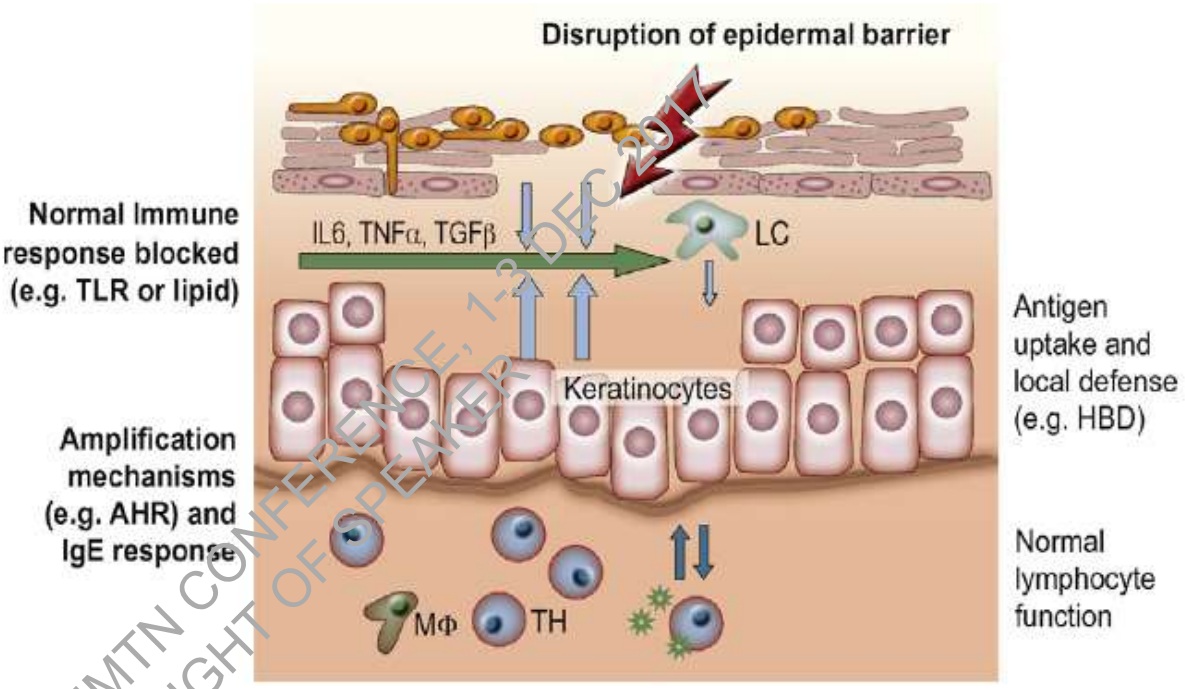


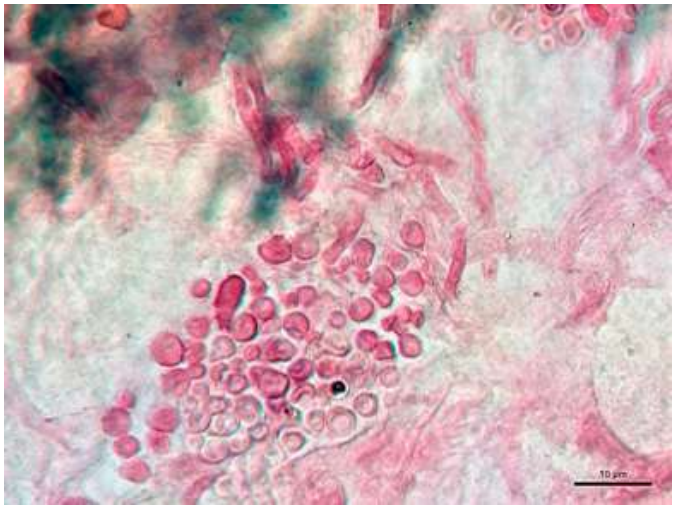
- Though dermatophytes alone have minimal capacity to damage host, consistently high level of host tissue destruction observed in dermatophytosis
- However, for long-term survival - ↓ tissue reaction required (tinea unguium – localized in nail & avoid host immune cells)

Malassezia infection

- Host secretion of β-endorphins increase the production of *Malssezia*

  phospholipases → disrupt epithelial barrier & provoke inflammation





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

Tissue reaction in subcutaneous & systemic fungal infections

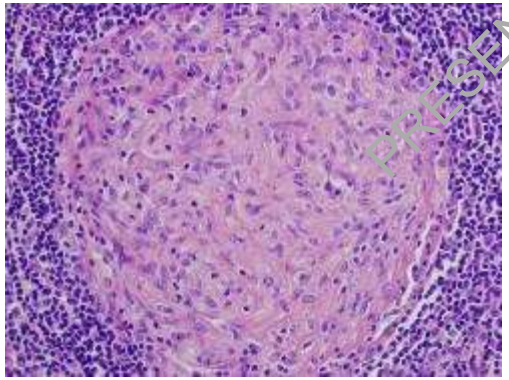
Tissue reactions	Fungi can be suspected
Acute pyogenic or suppurative	*Candida, Aspergillus*
Suppurative with angio-invasion	*Aspergillus, Mucorales*
Mixed suppurative inflammation	*Blastomyces, Coccidioides*
Mixed suppurative & granulomatous	*Blastomyces, Coccidioides, Talaromyces, Paracoccidioides,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

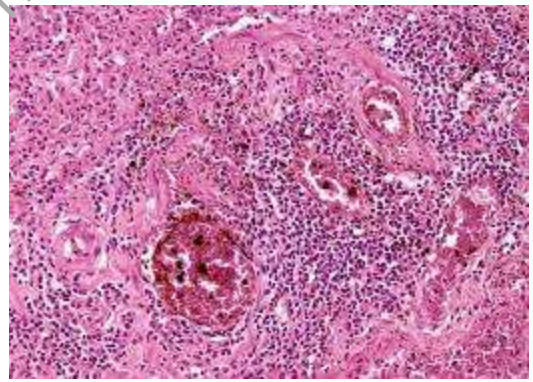
Tissue reaction

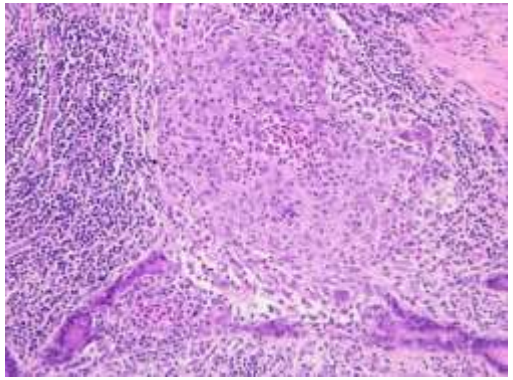
- Non-invasive colonization of pre-existing cavity – fungal ball (paranasal sinus & pulmonary cavities)
- Allergic, mucin-producing, non-invasive fungal disease –ABPA, AFRS
- No reaction, gelatinous (Cryptococcus)
- Predominantly neutrophilic inflammatory response
  - Mild neutropenia – localized lesion (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

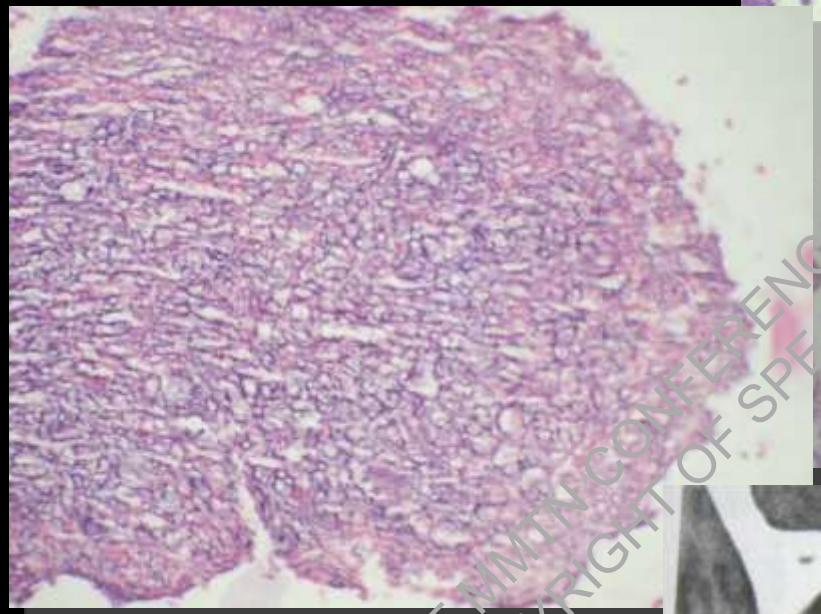
- Localized controlled infection – granuloma predominates, organism scanty (chronic granulomatous FRS)
- Fulminant infection – predominance of neutrophils, organism readily seen (dimorphic infection in AIDS)
- Mixed purulent & granulomatous inflammation (sporotrichosis, chromoblastomycosis)

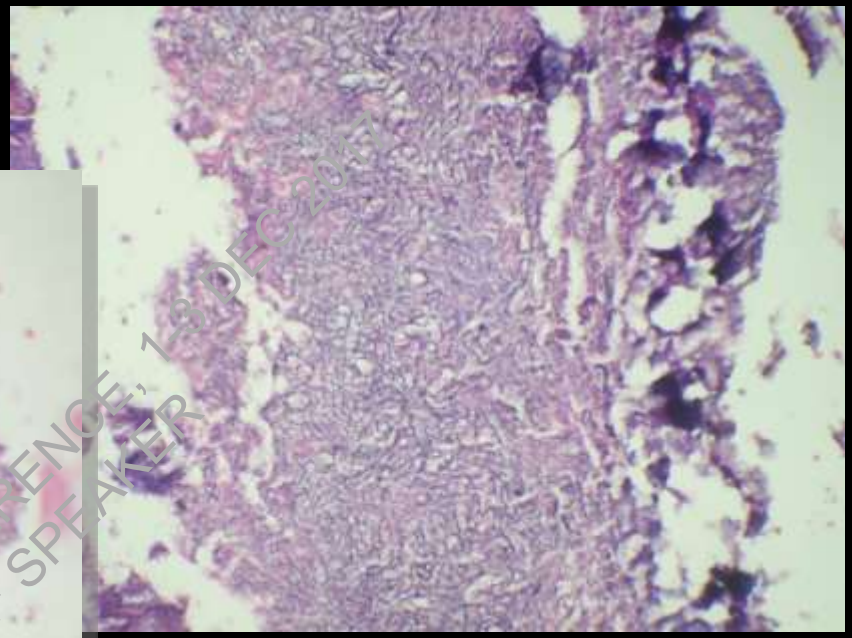




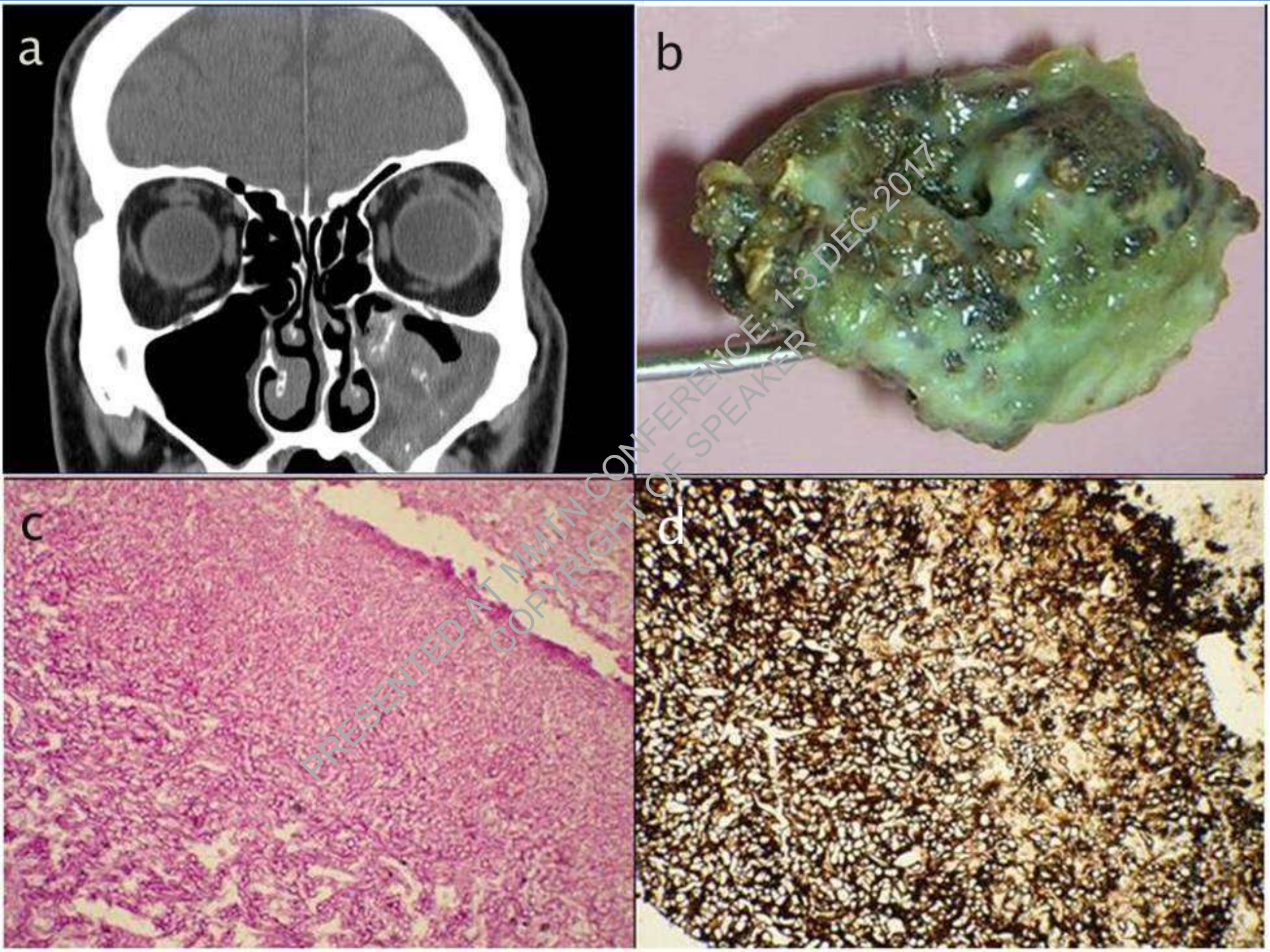


Fungal ball





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



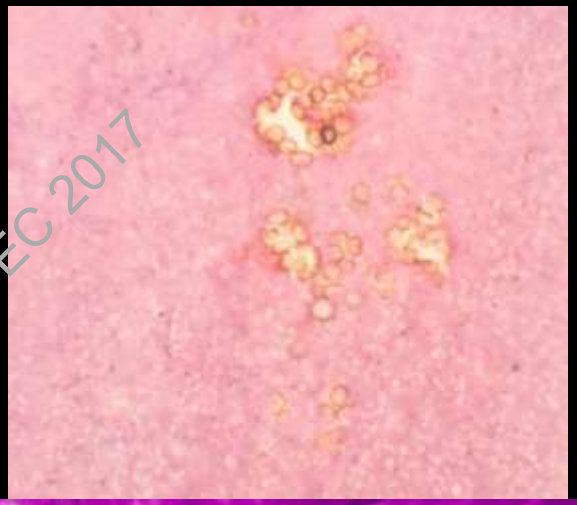
Aspergilloma

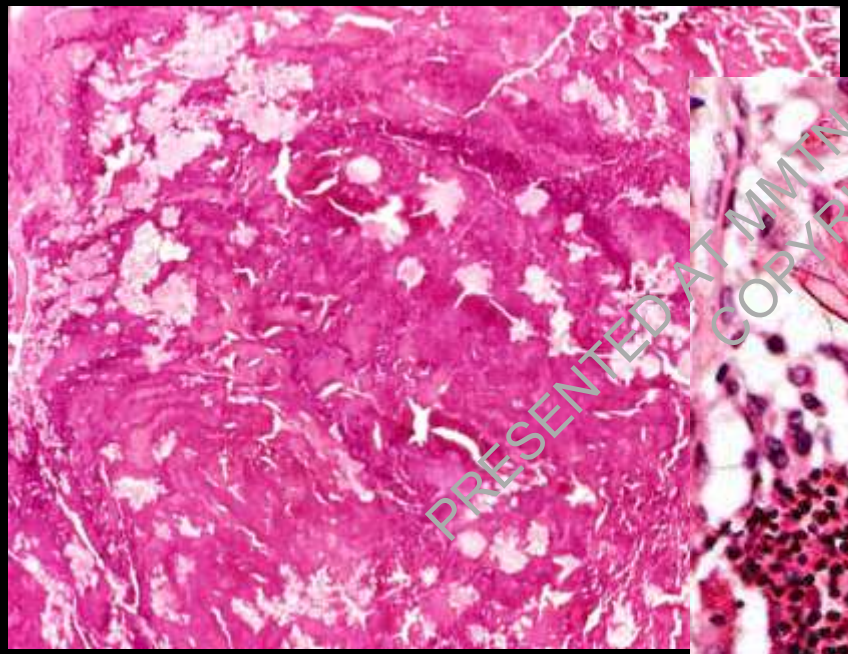
- Fungus ball composed of *Aspergillus* hyphae & cellular debris within a pulmonary cavity
- Preexisting pulmonary cavities that have become colonized with *Aspergillus* spp.
- Fungal ball is single, cavity stable over months
- Patient has few symptoms (mild cough only) and little evidence of systemic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

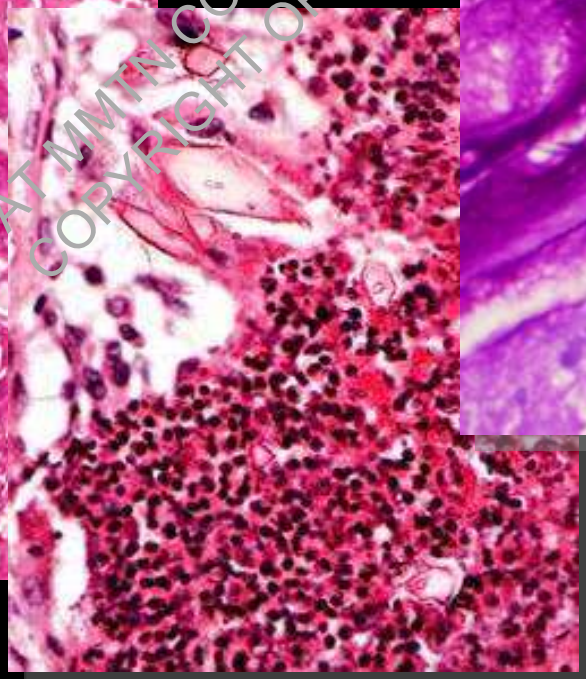
Allergic fungal rhinosinusitis

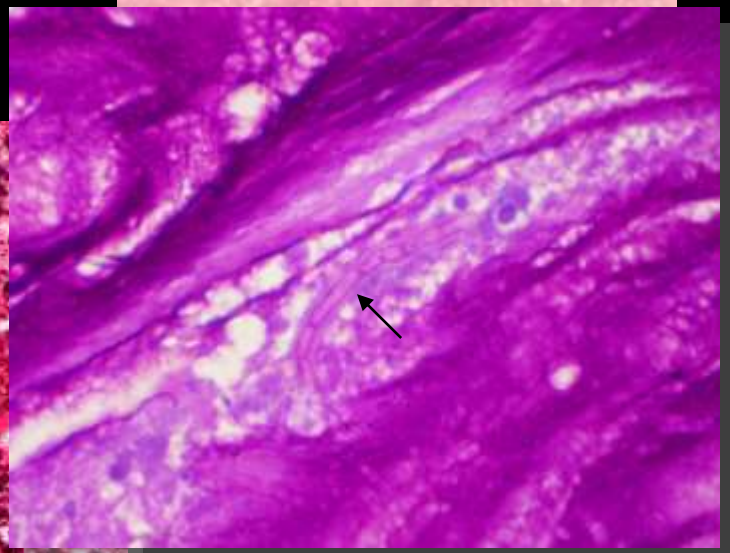
- Type I hypersensitivity
- Nasal polyposis
- Characteristic CT findings
- Allergic mucin without mucosal invasion
- Positive fungal culture of sinus content

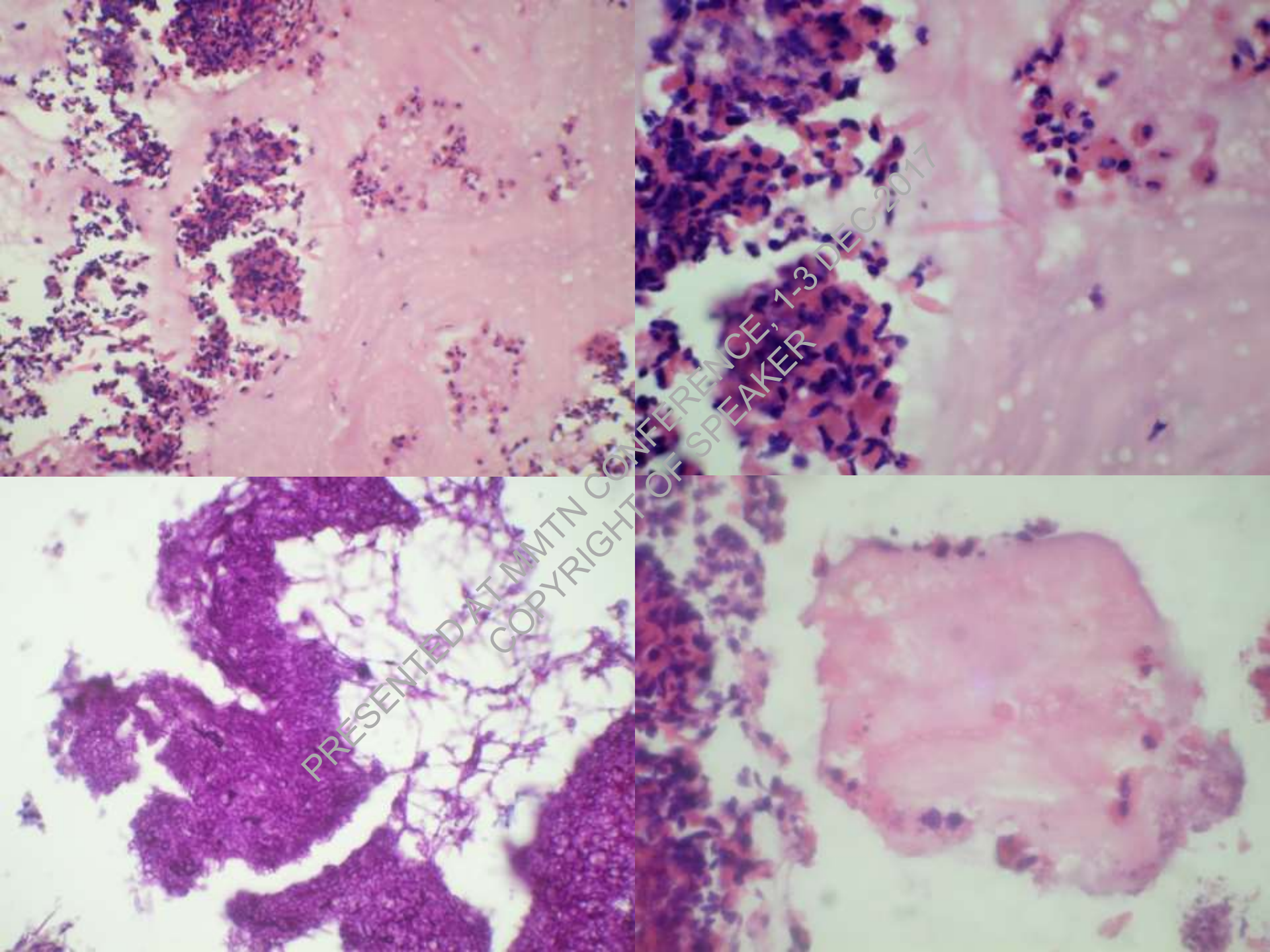
Bent & Kuhn, Otolaryngol Head Neck Surg, 1994; 111: 580-8

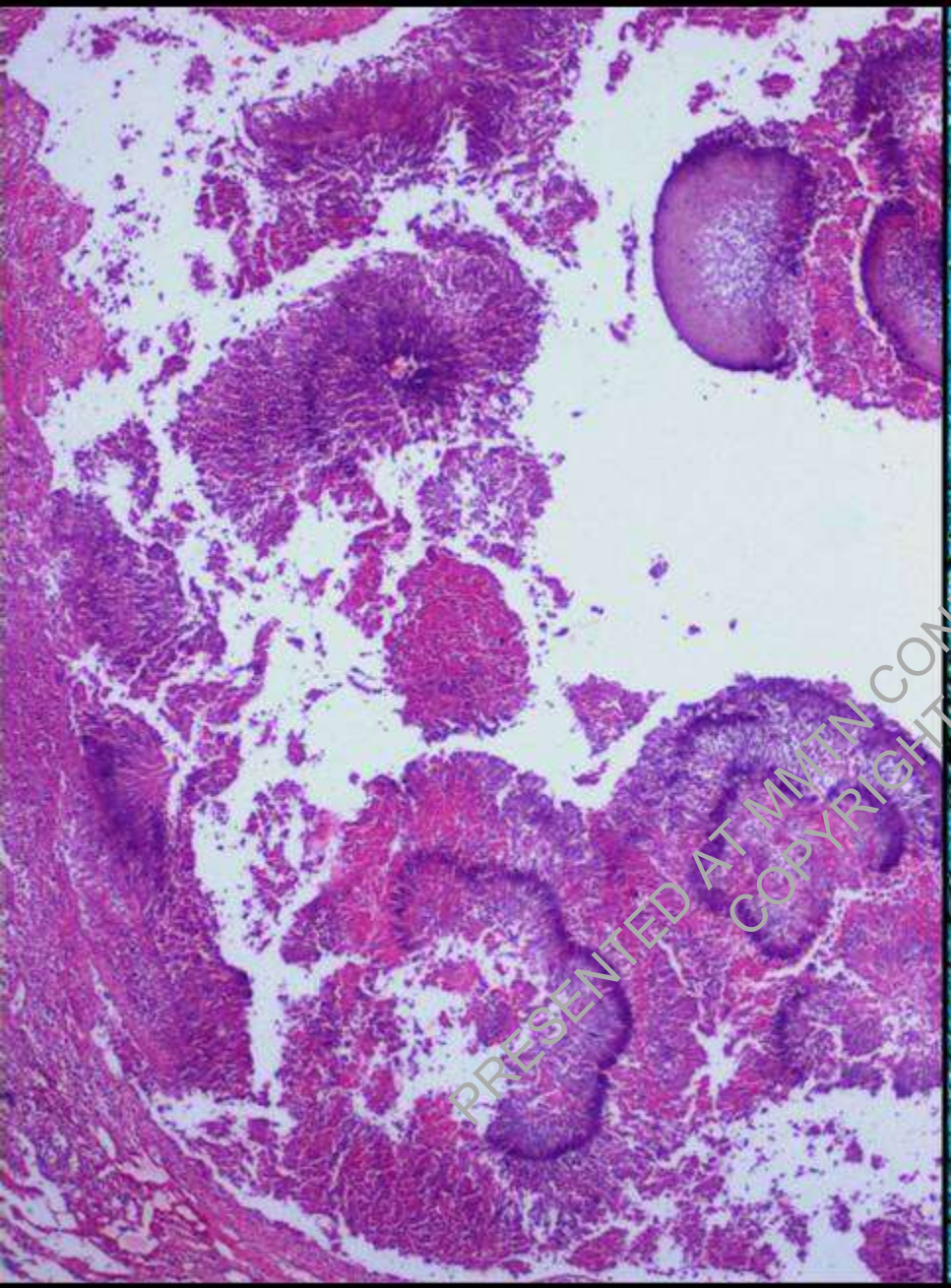


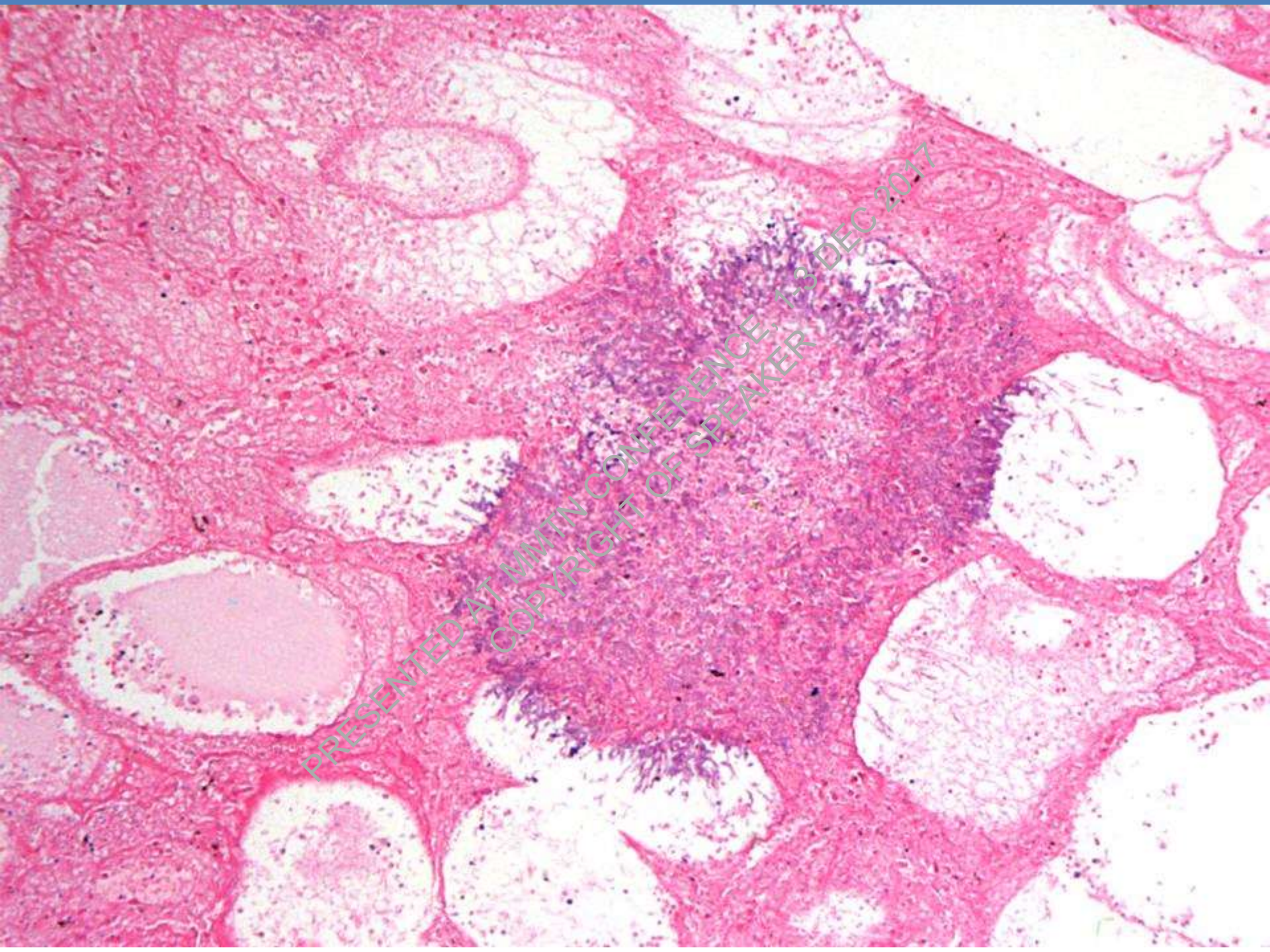


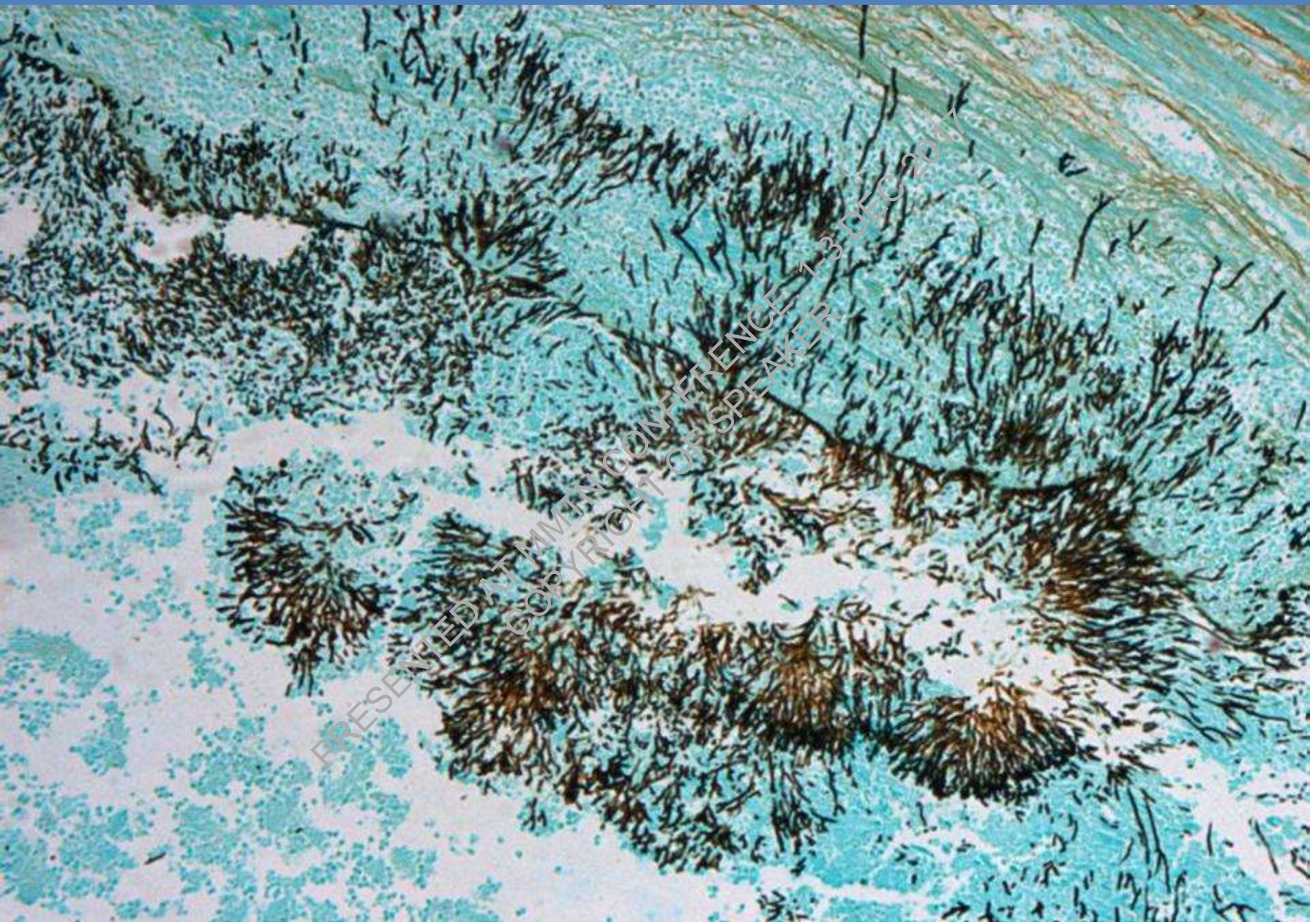


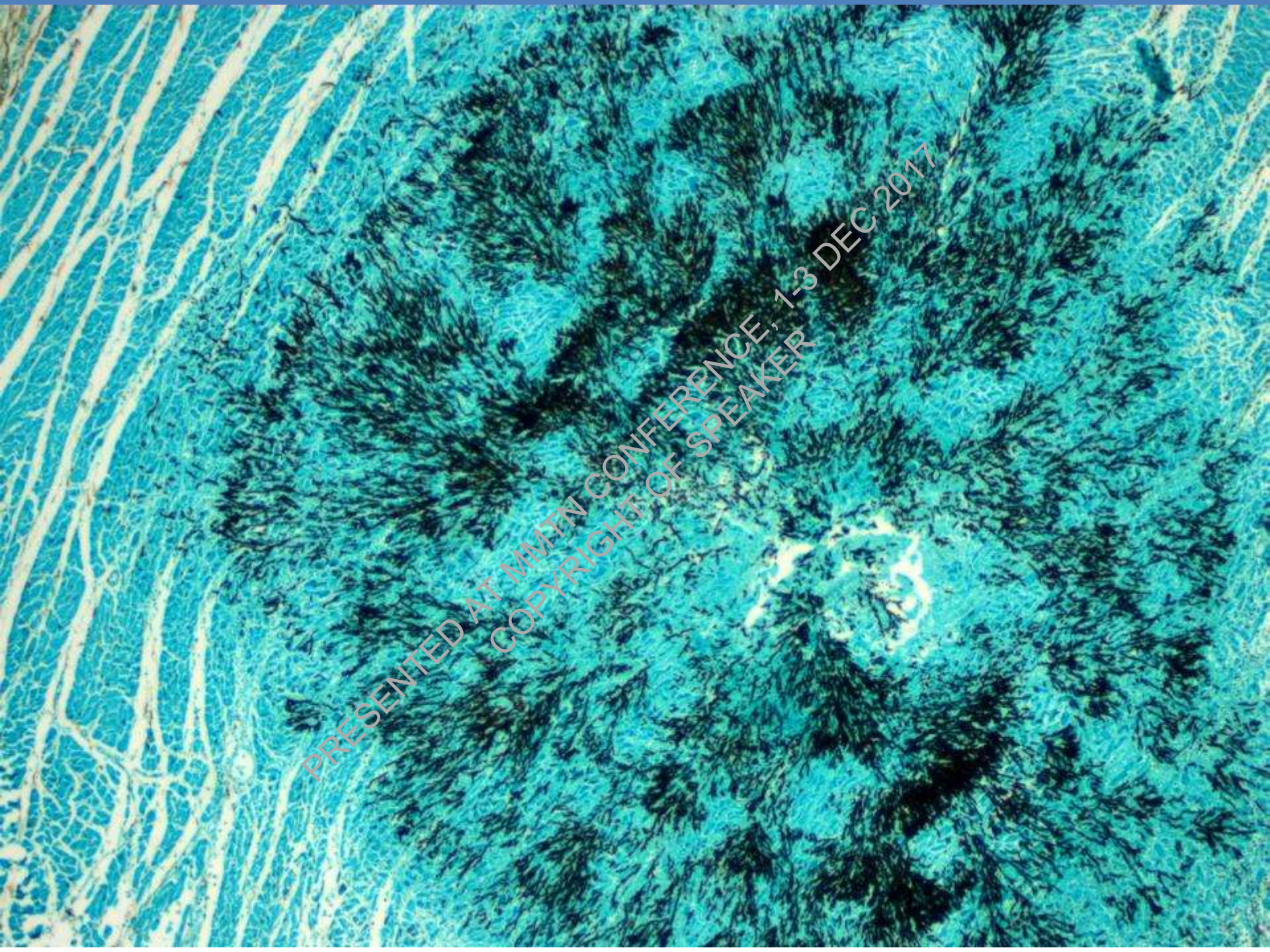




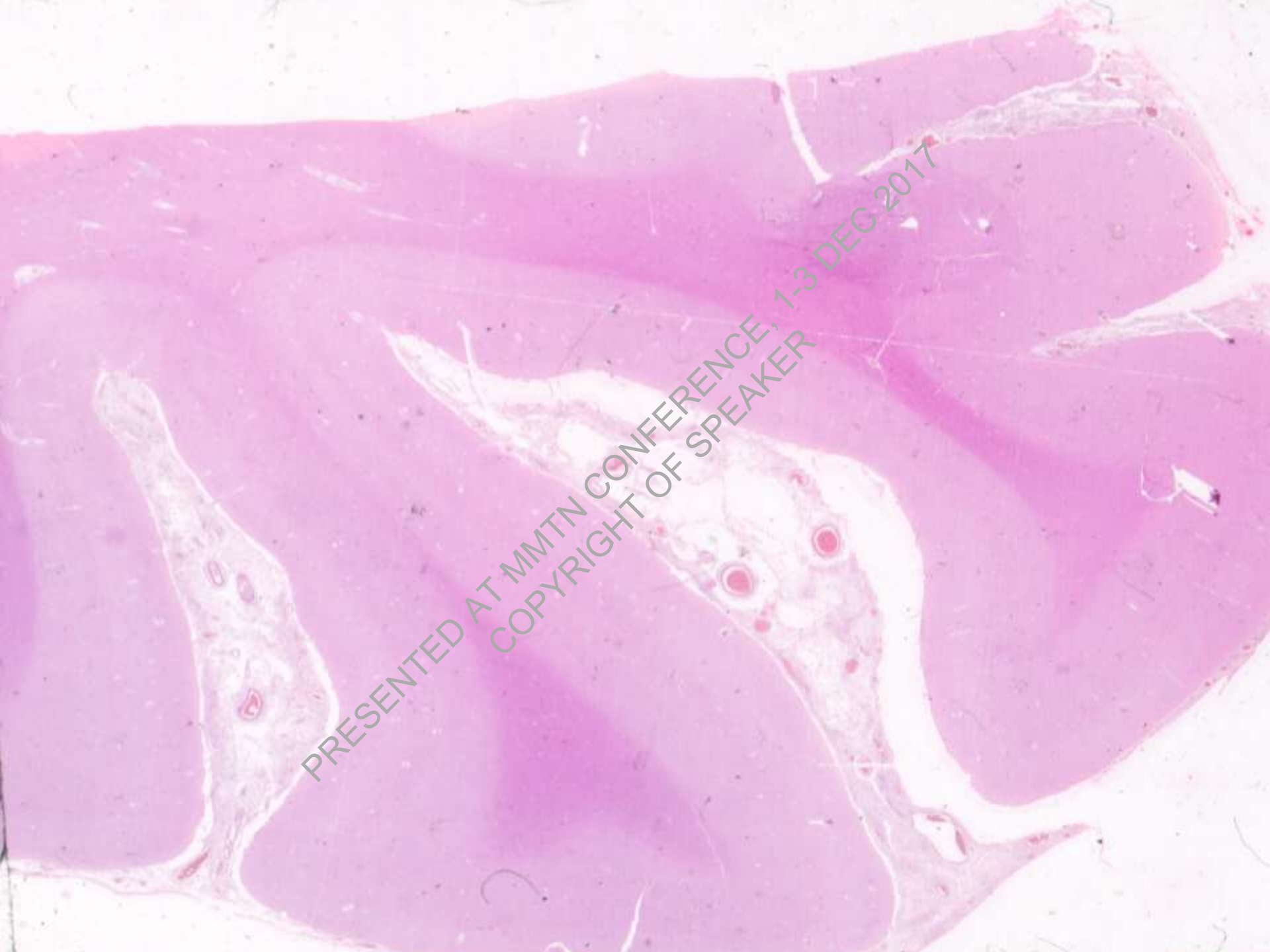


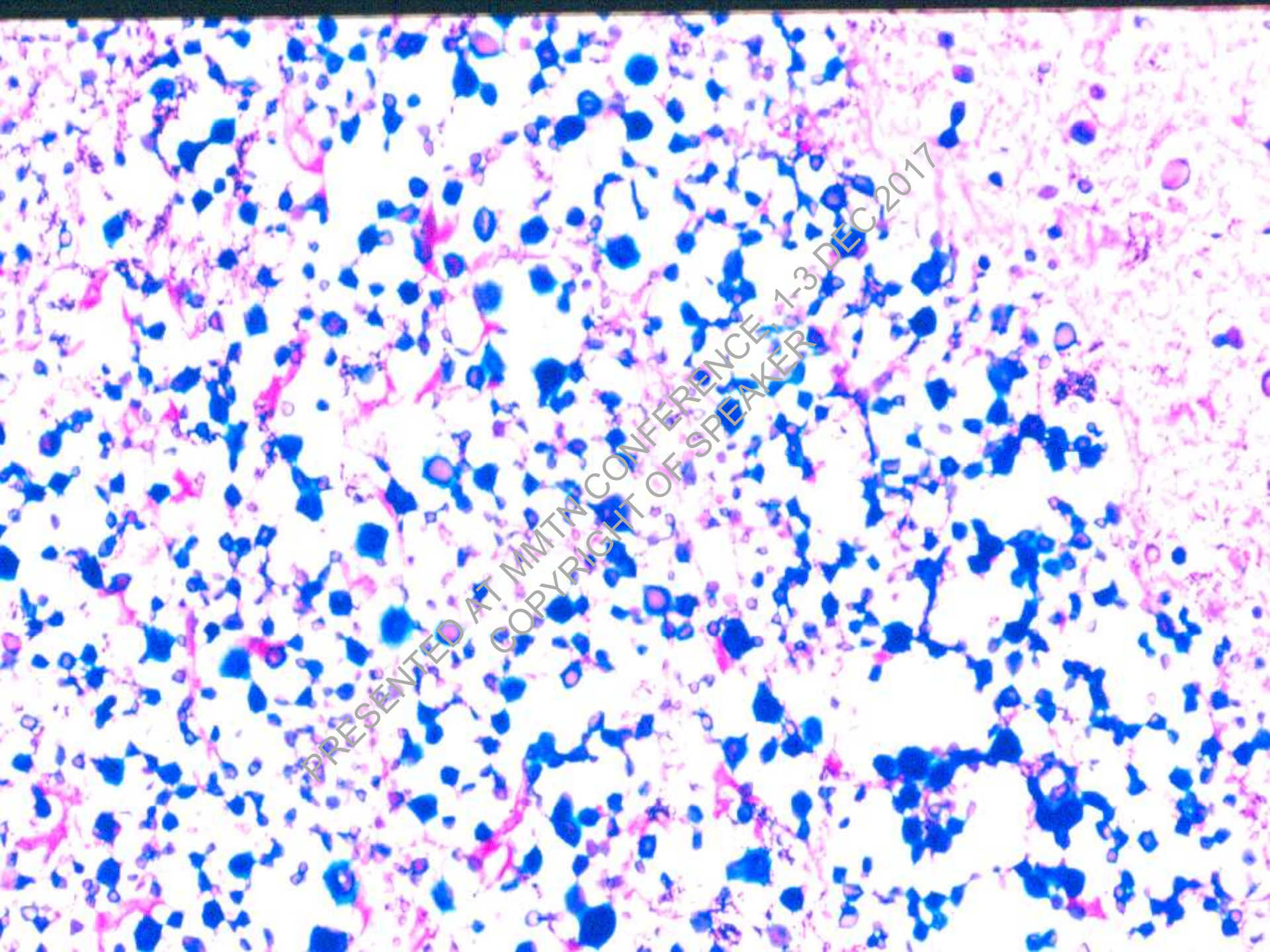


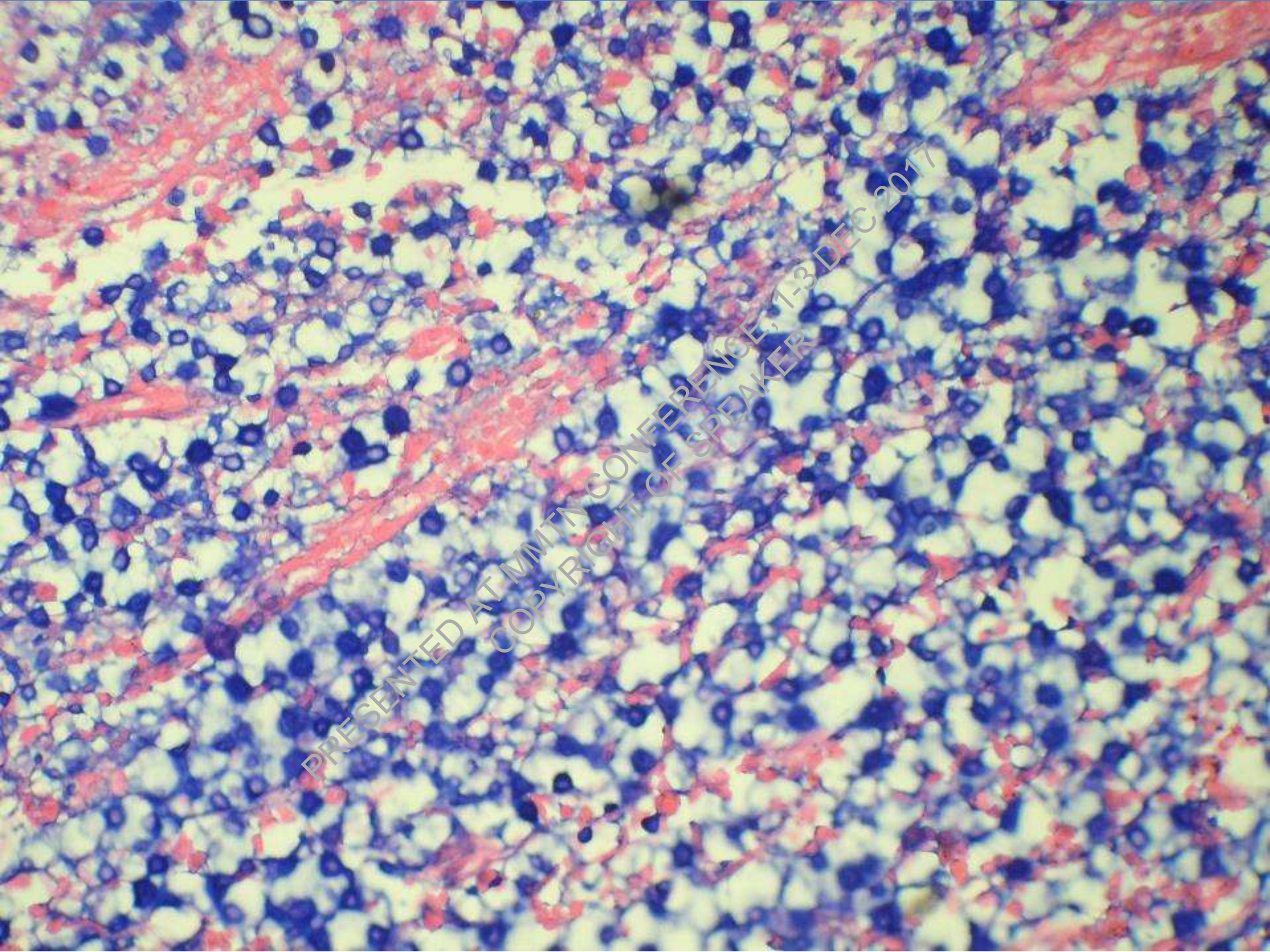




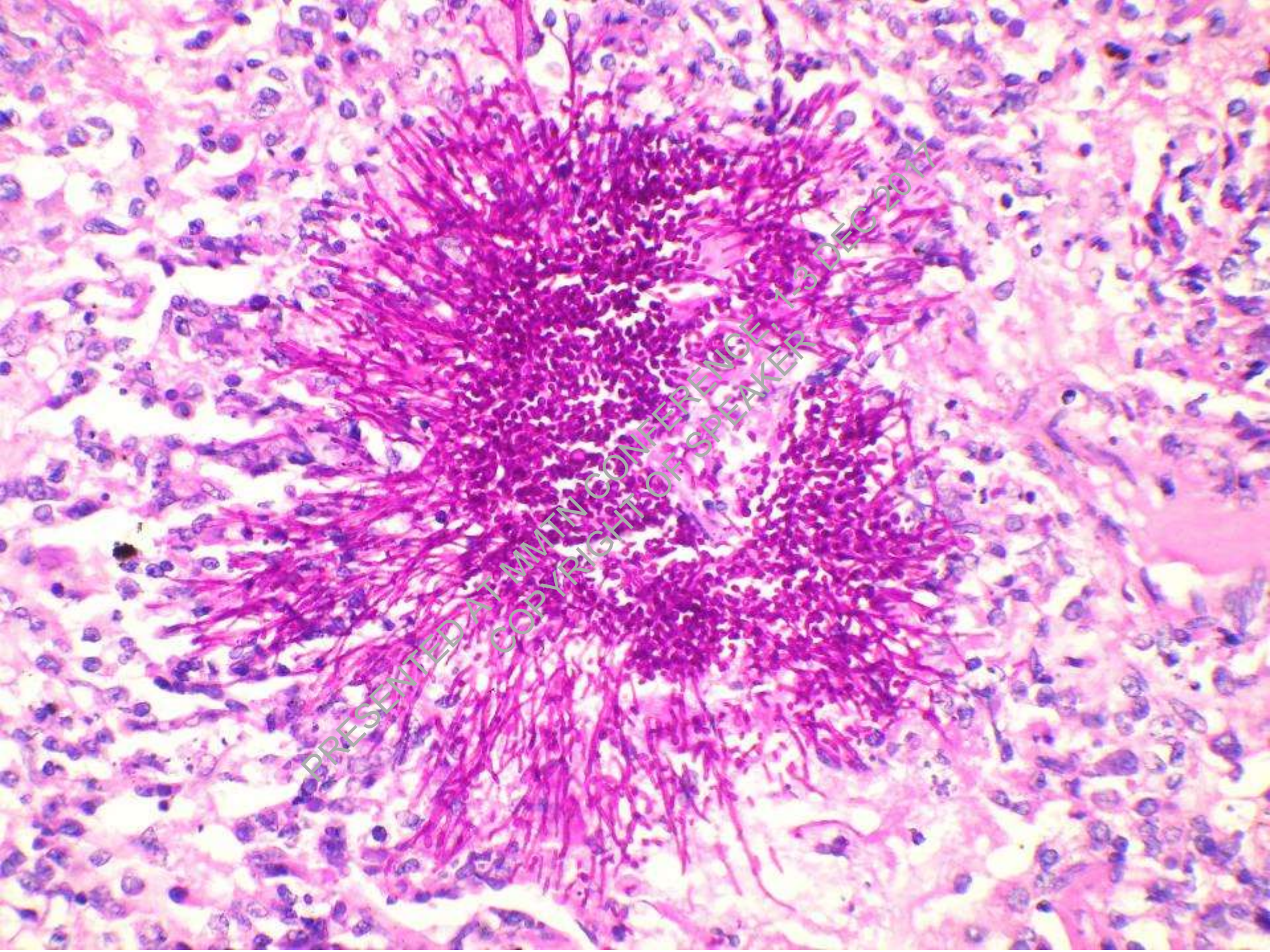
Gelatinous inflammation

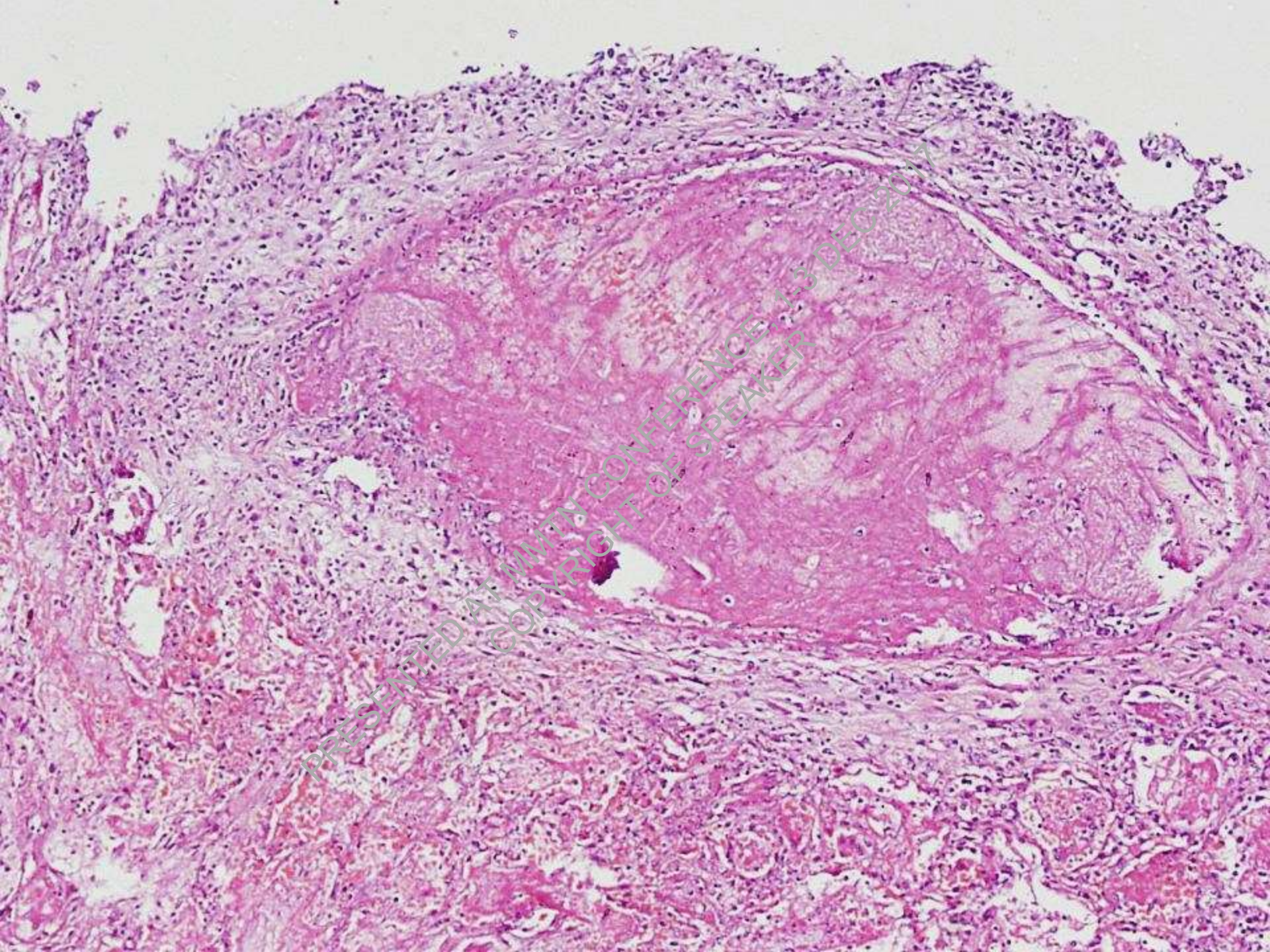


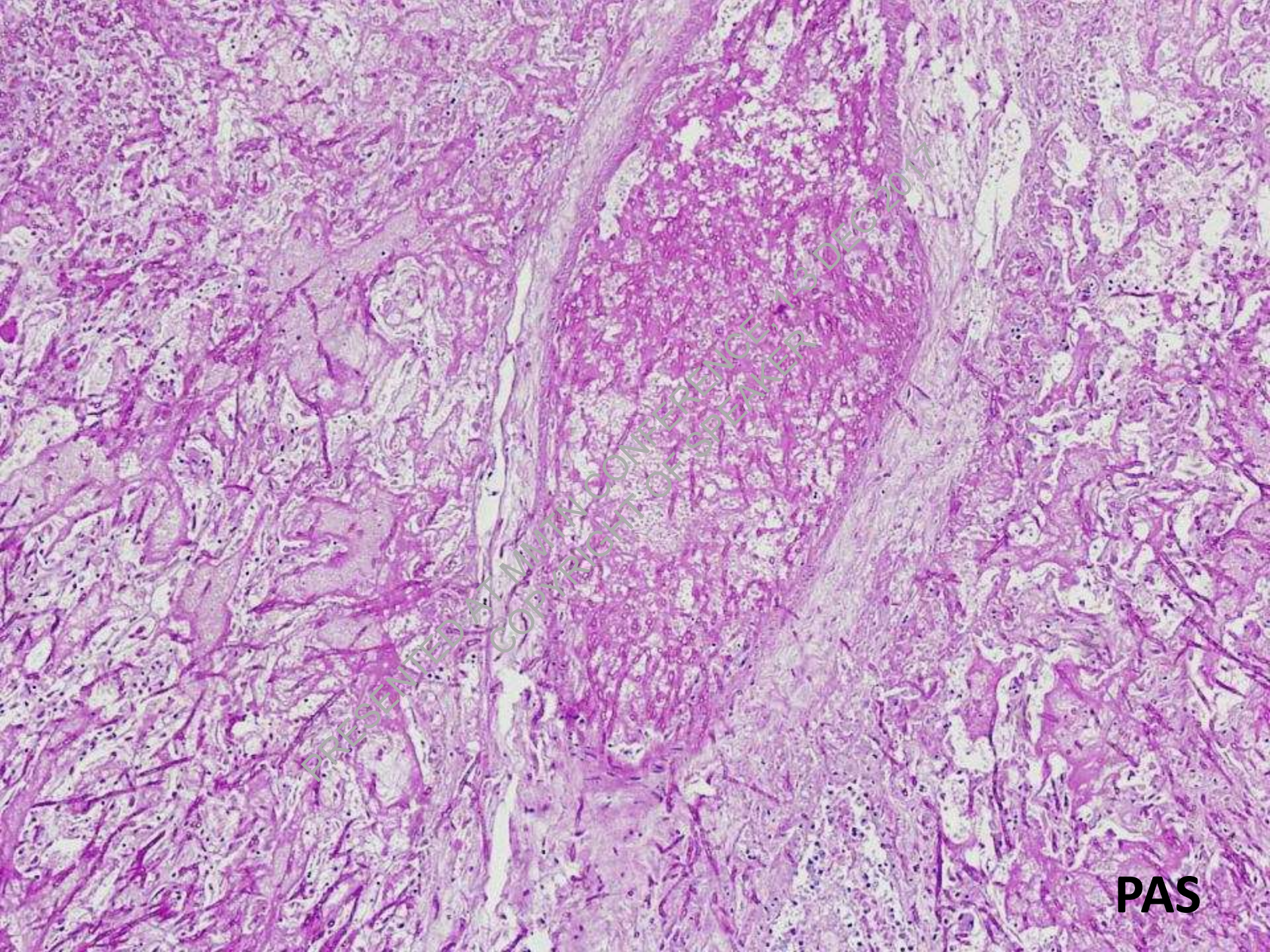


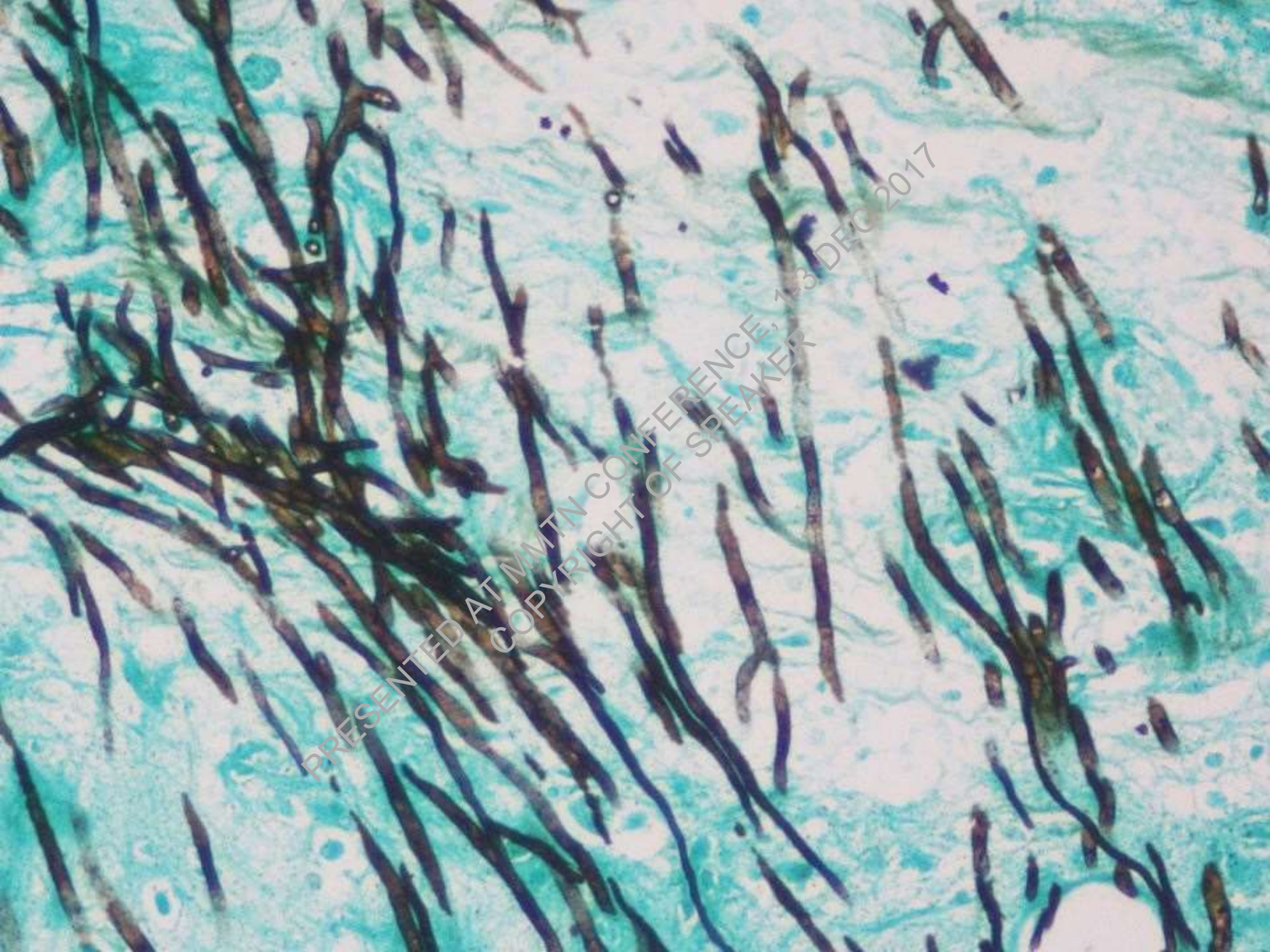


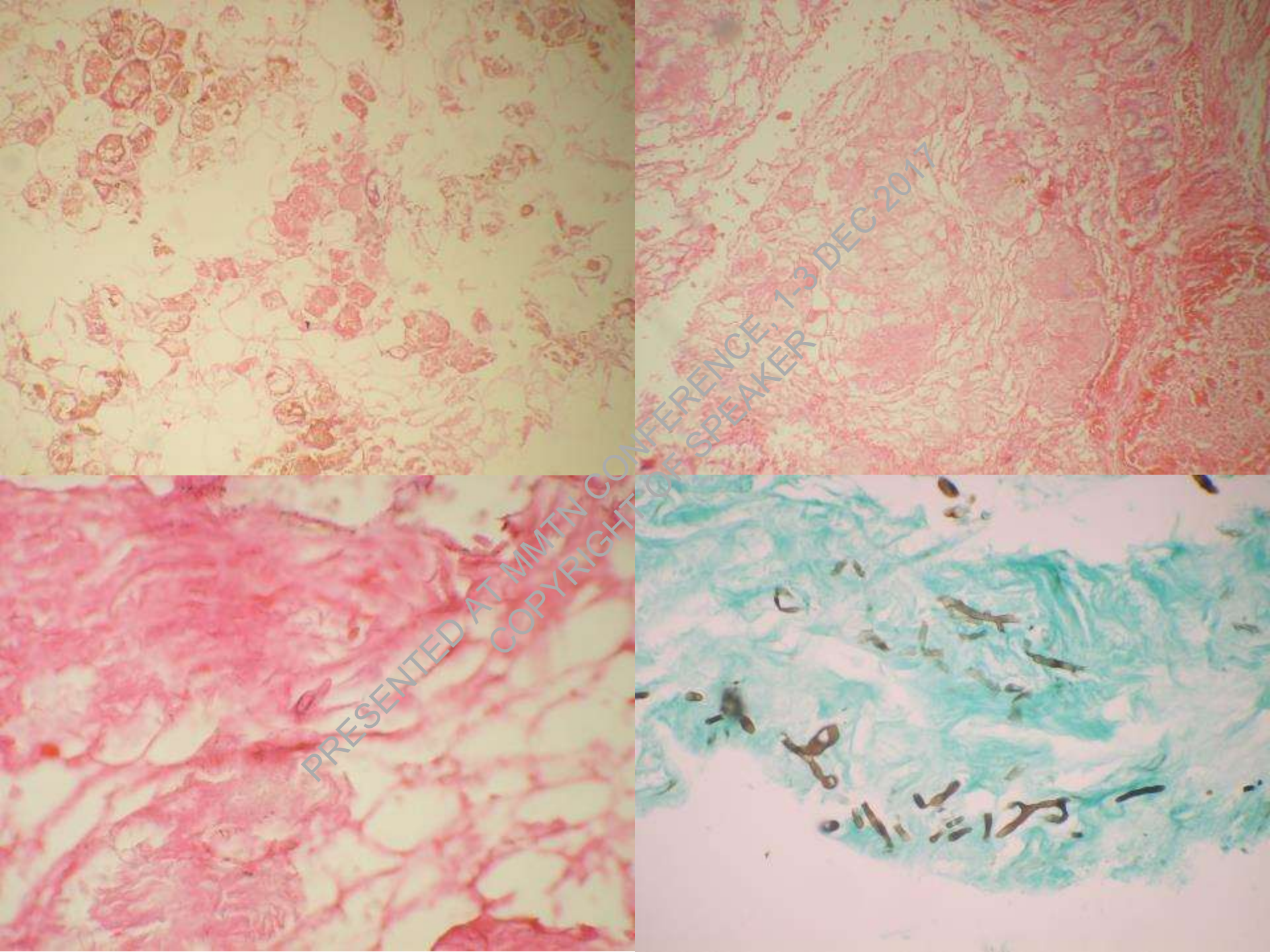
Acute pyogenic

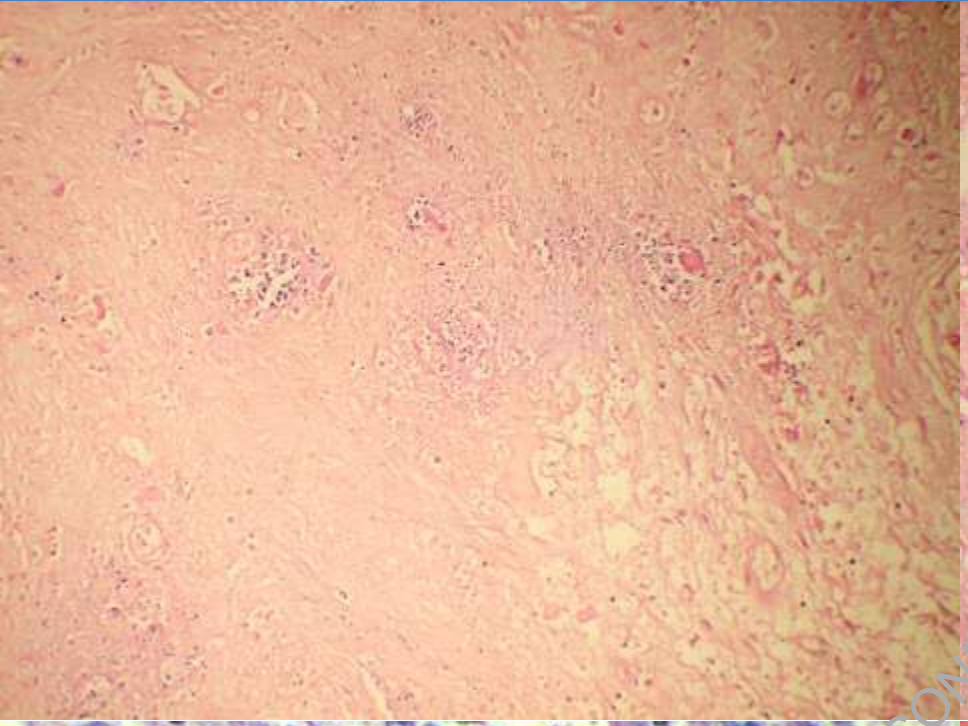
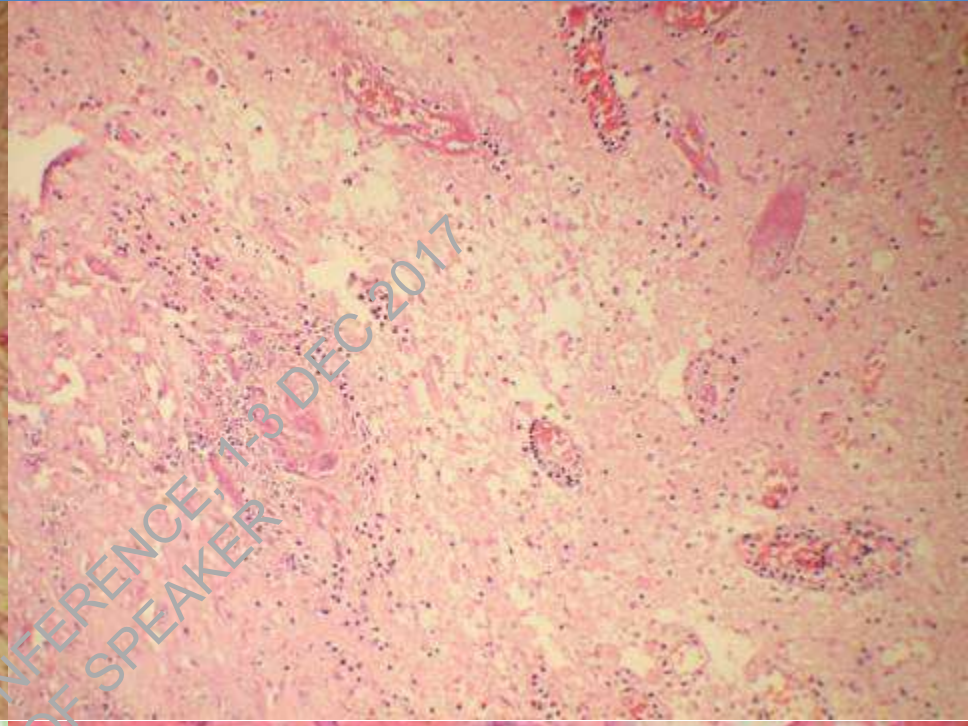
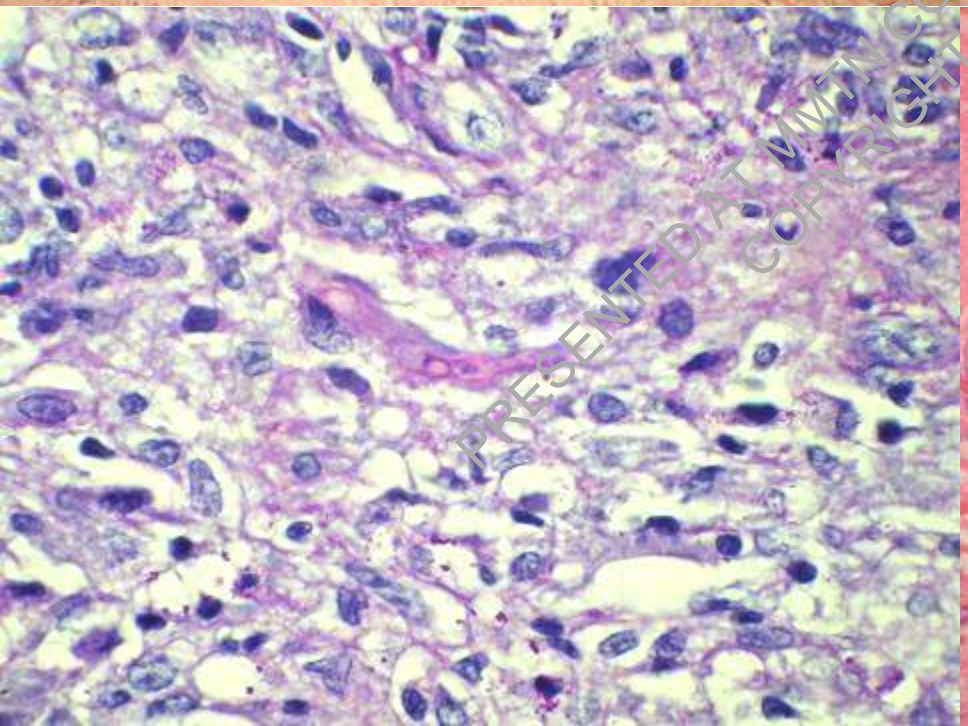
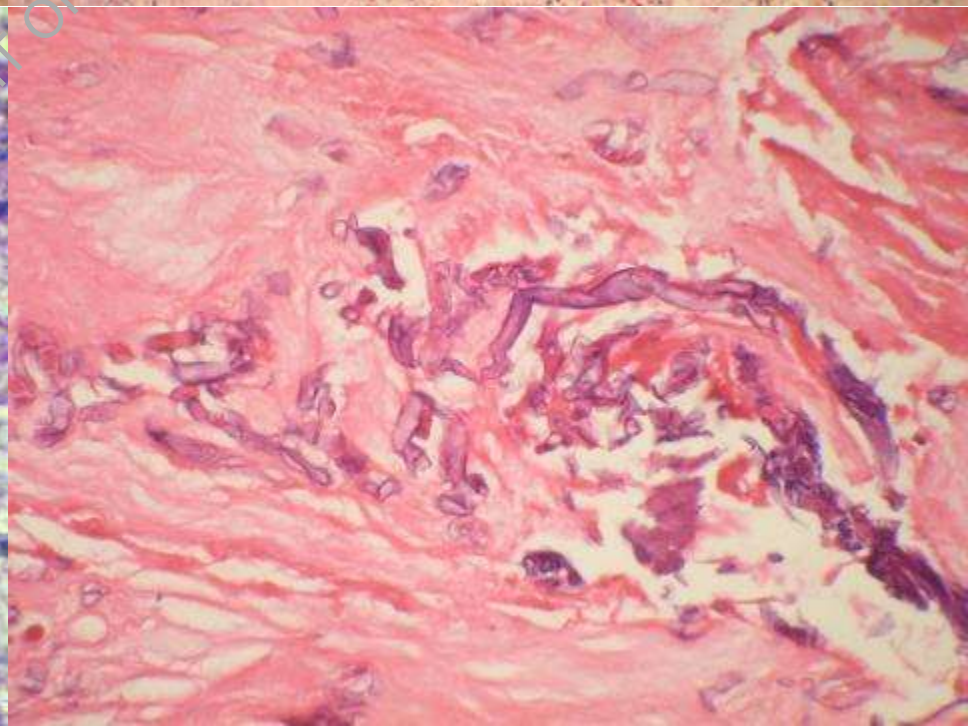


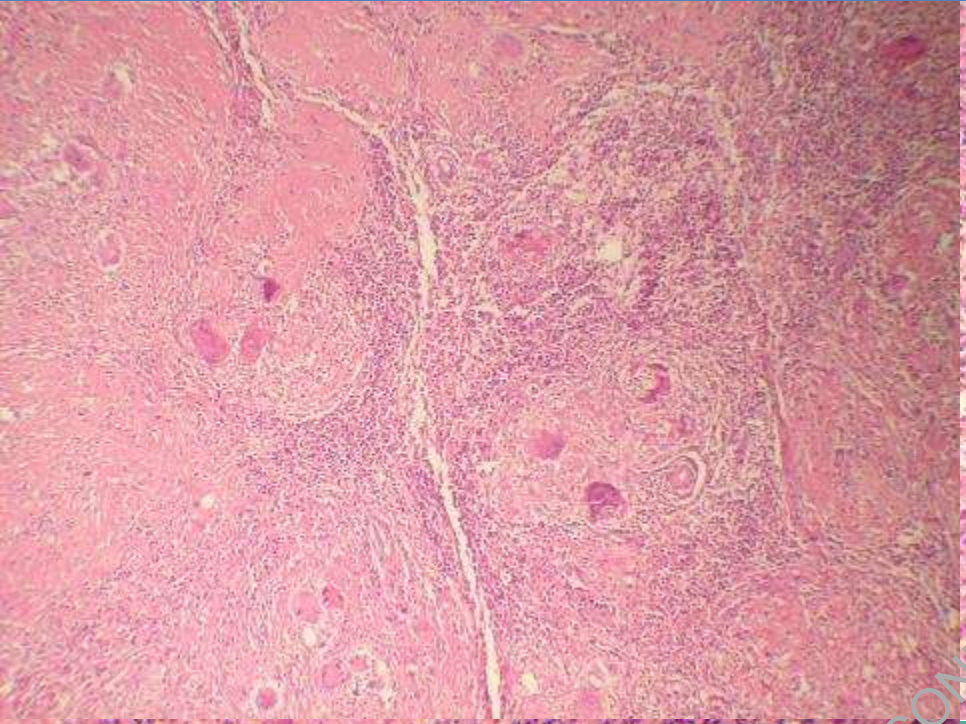
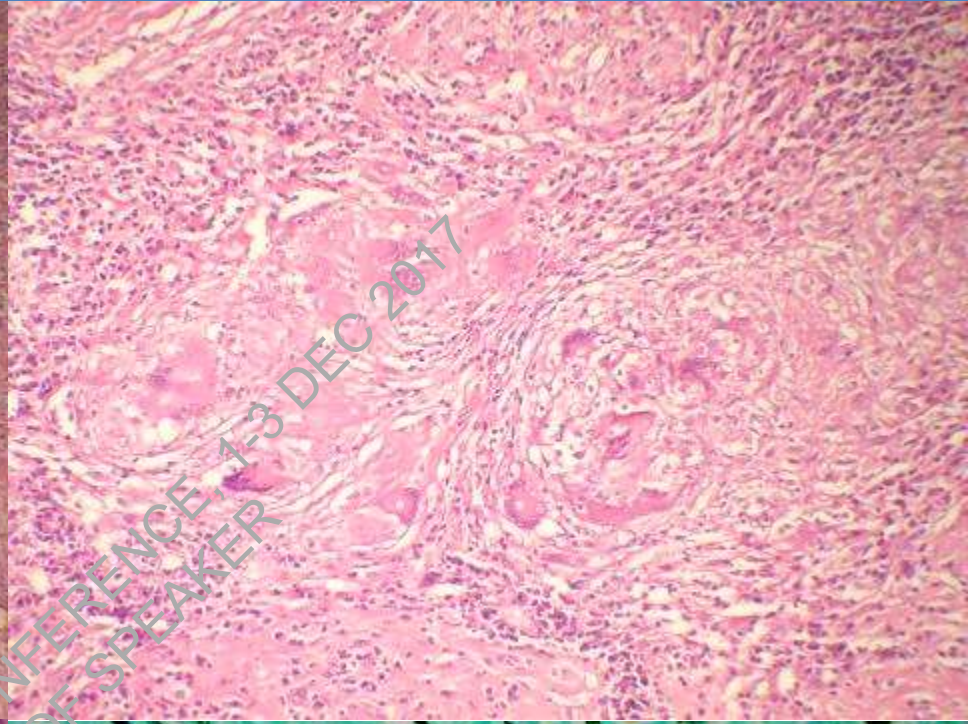
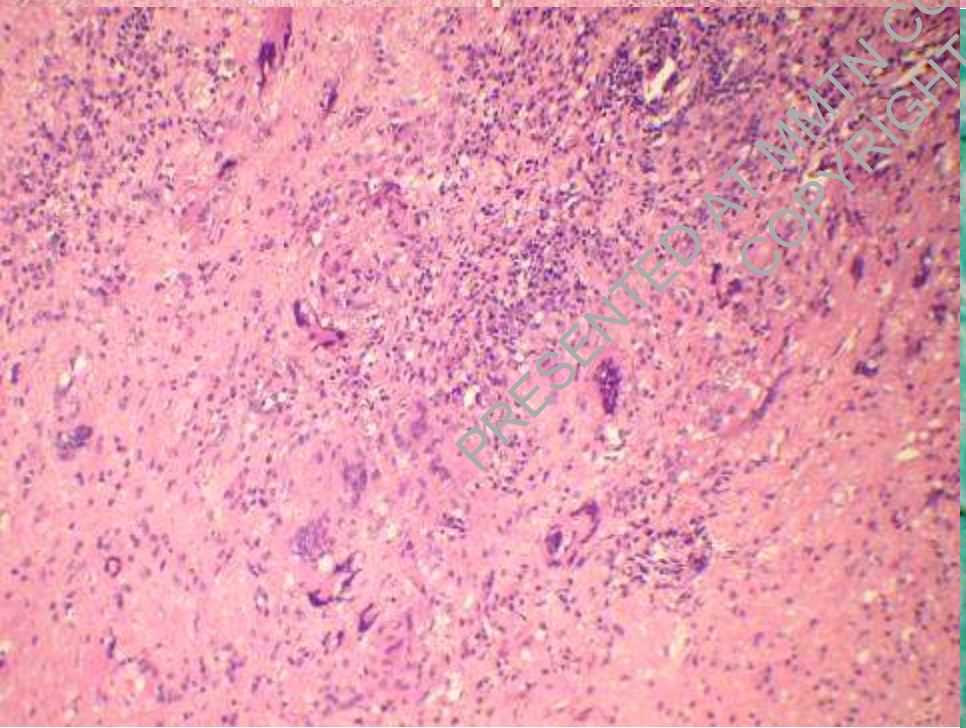
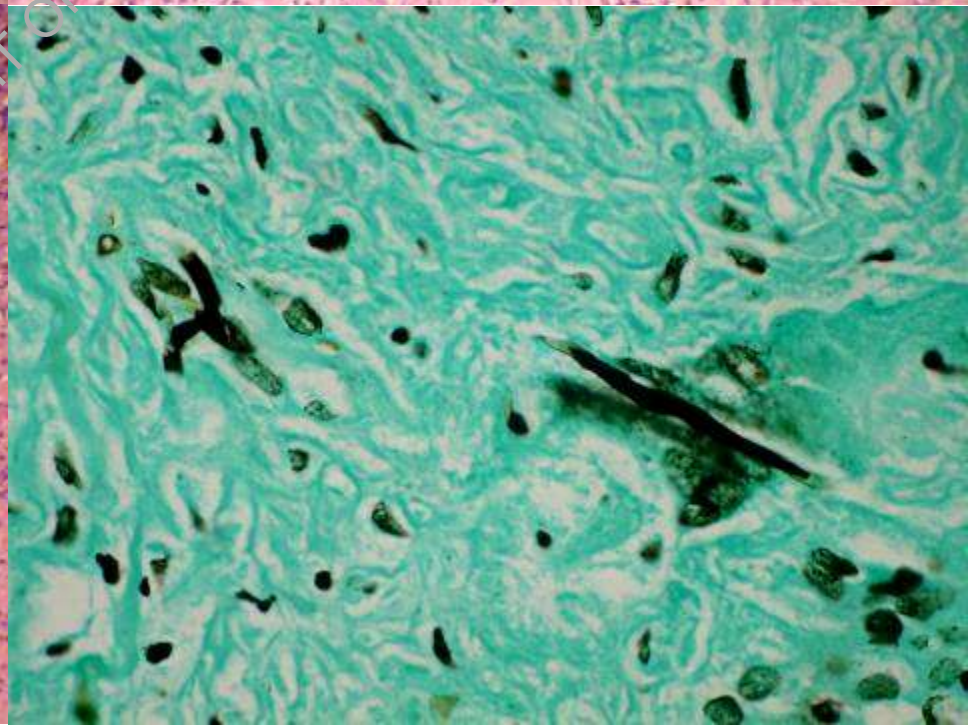


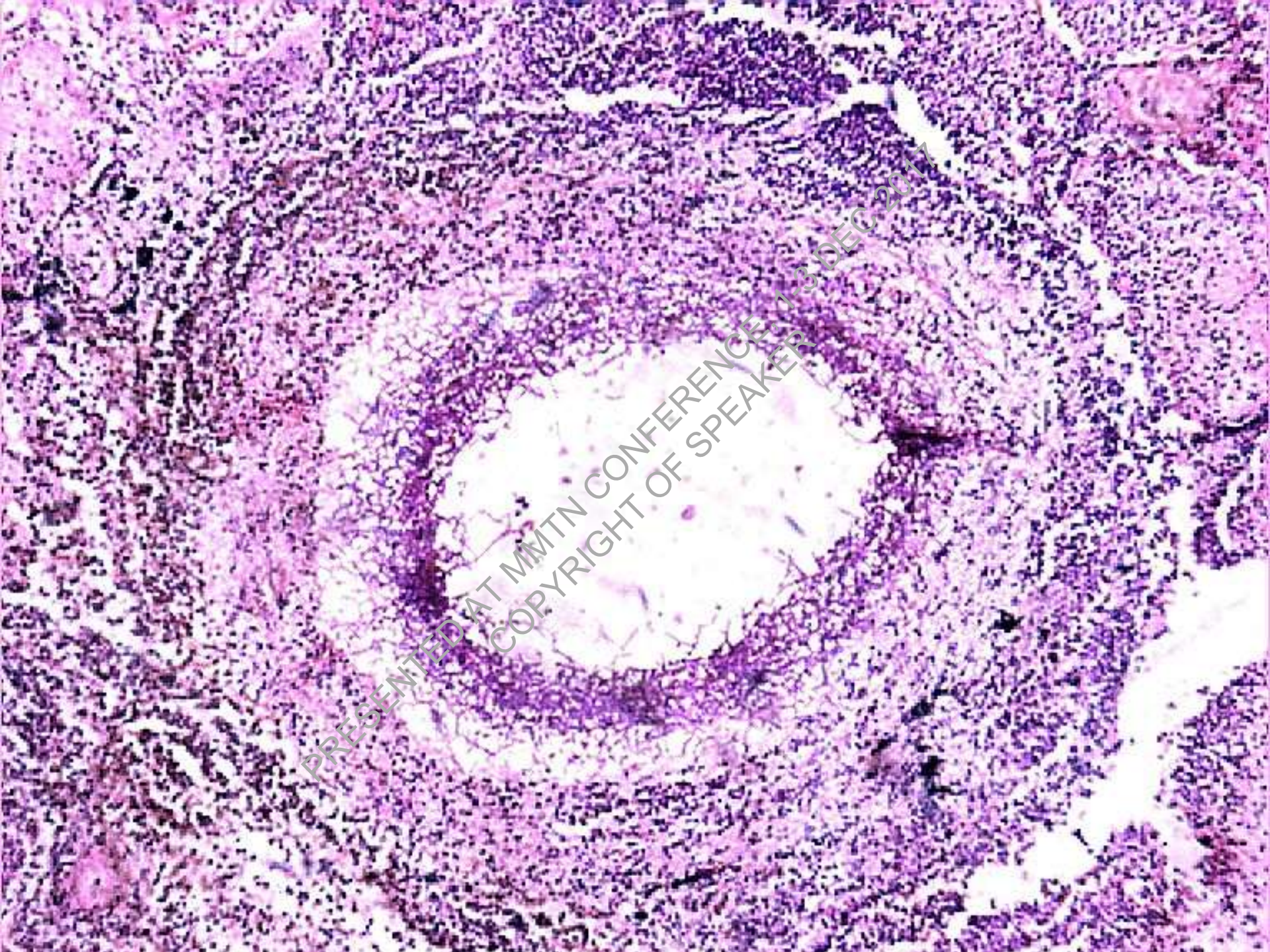




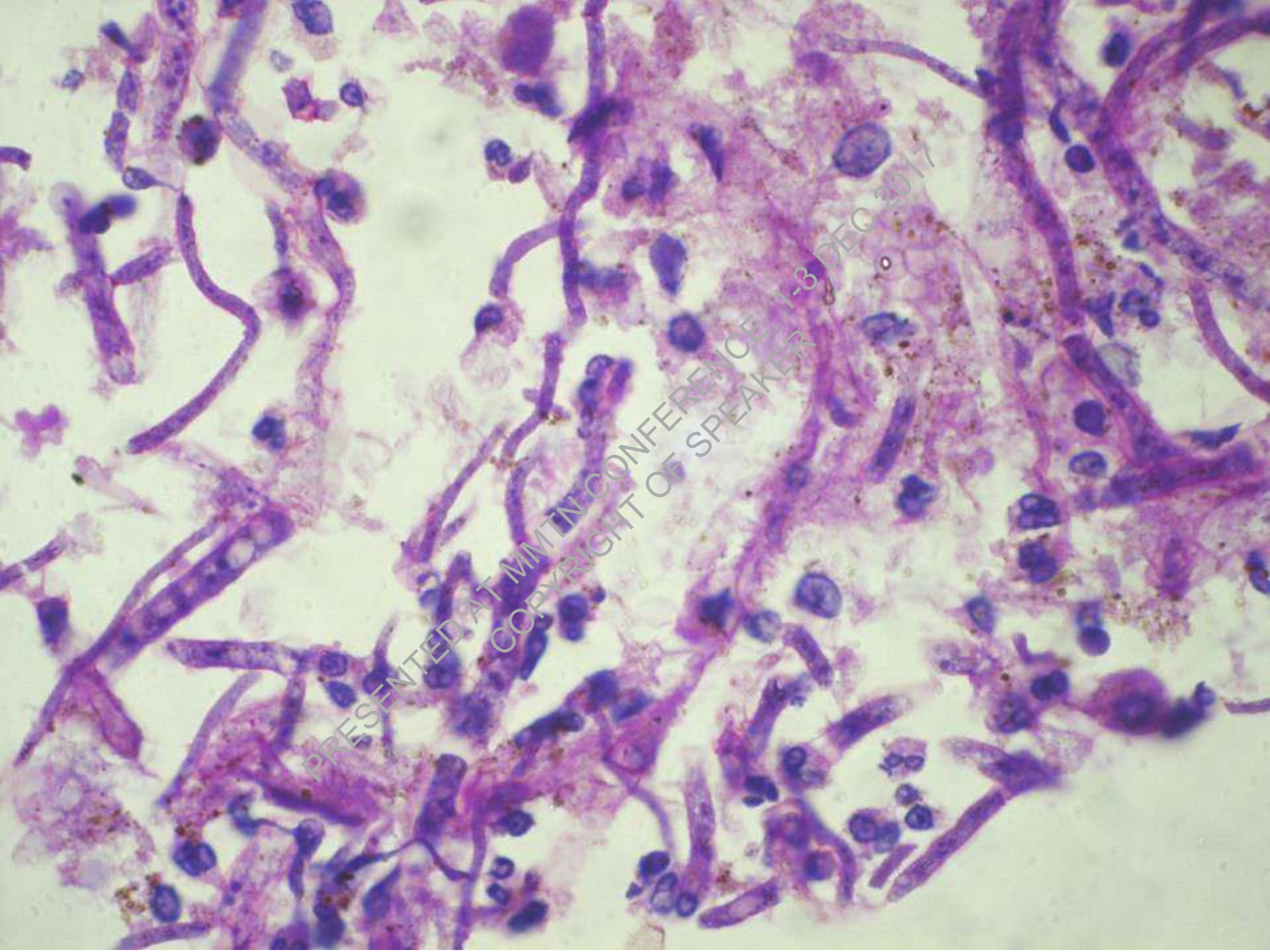


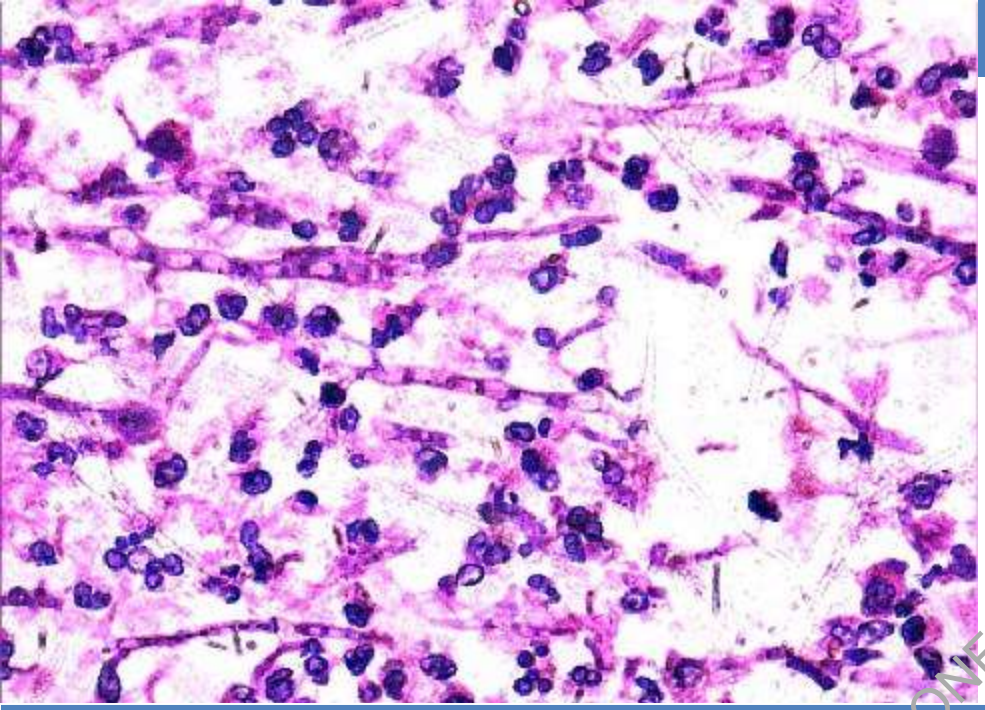





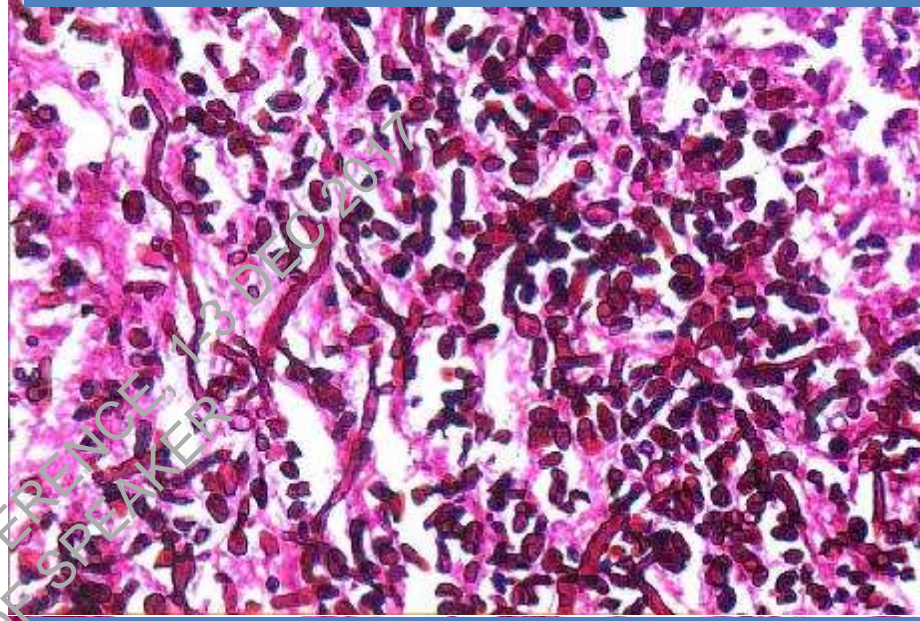


MMTN CONFERENCE
PRESENTER COPYRIGHT

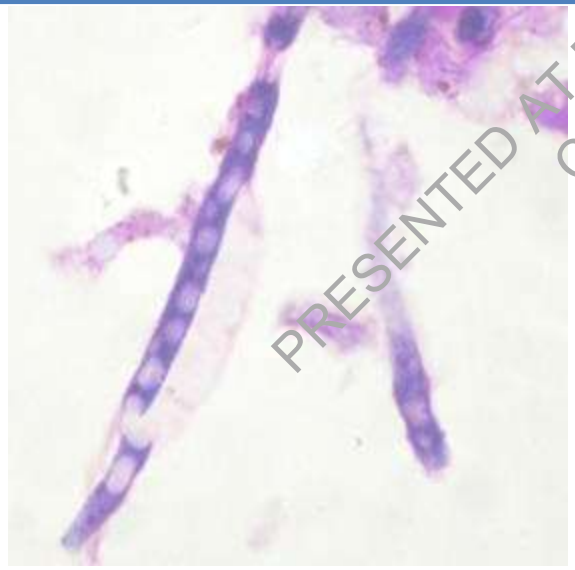




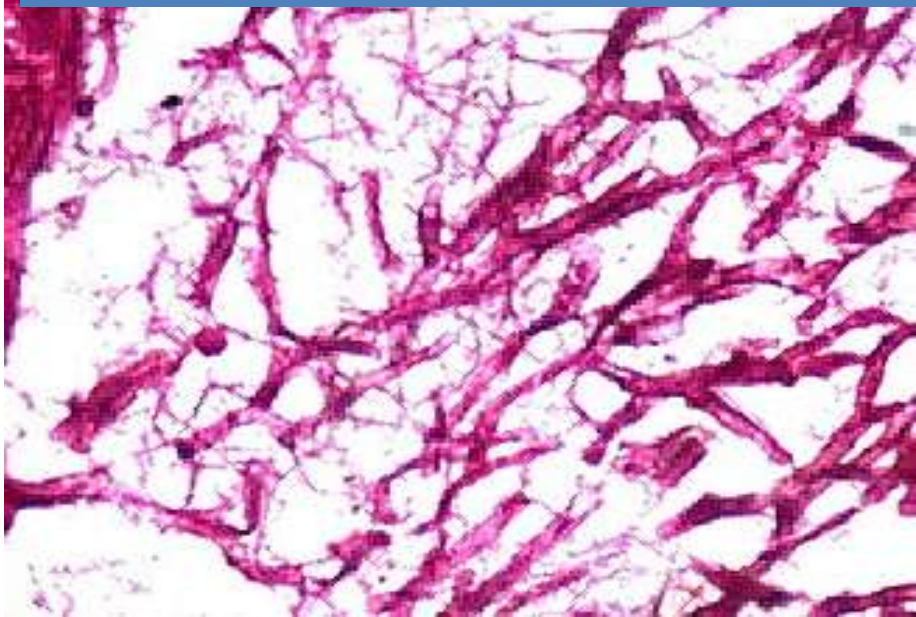
CANDIDA



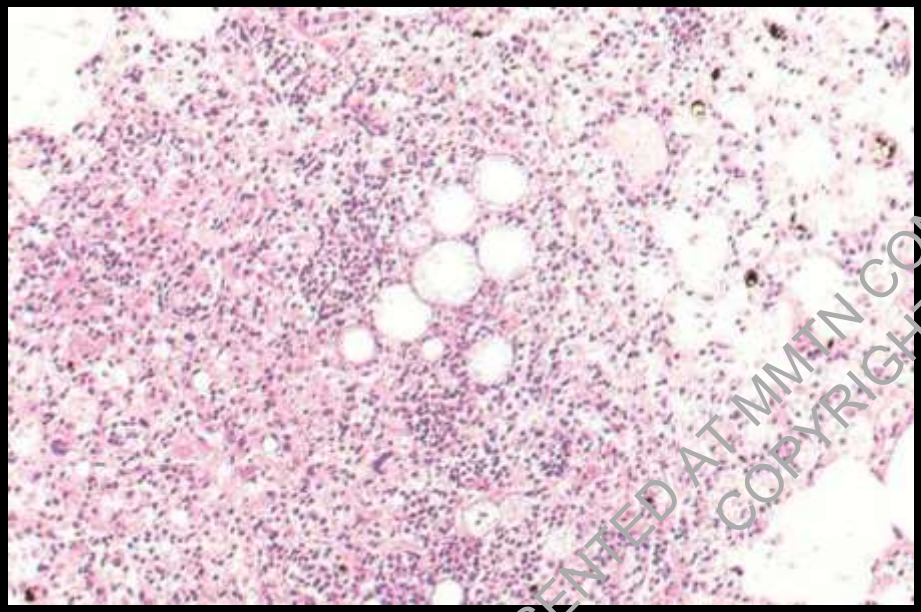
TRICHOSPORONOSIS

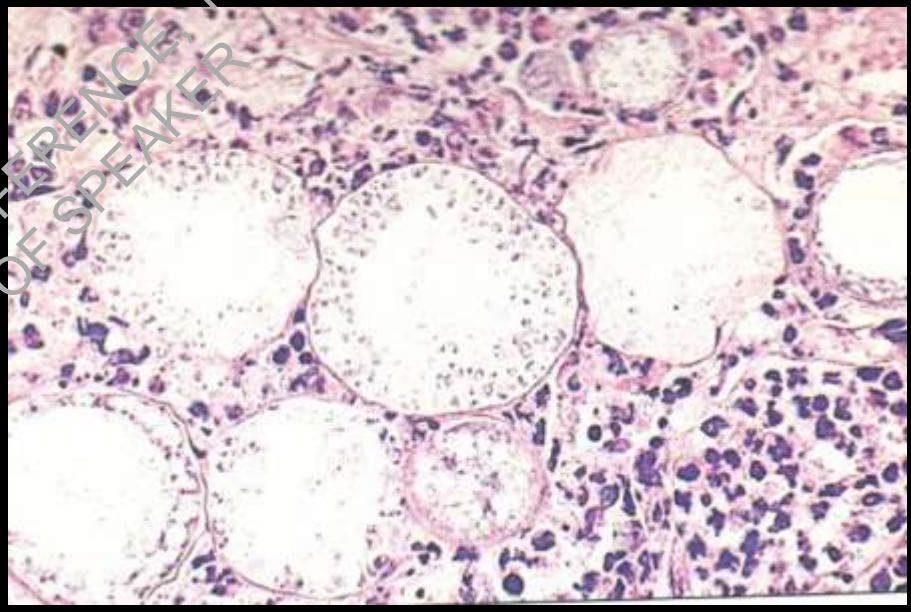


ASPERGILLUS



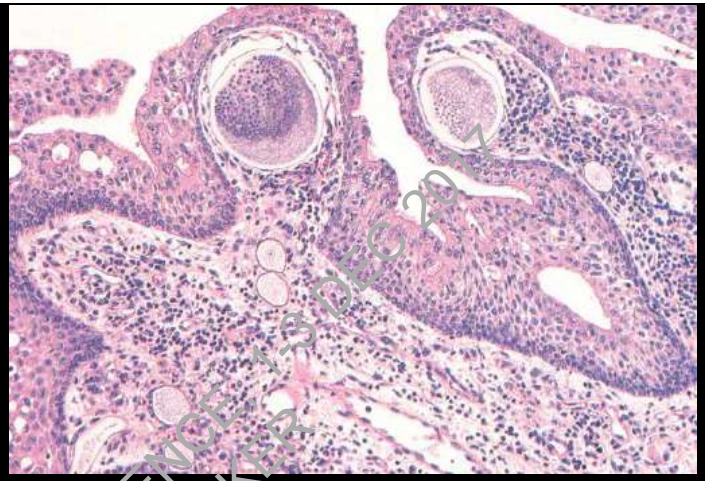
Acute coccidioidal pneumonia

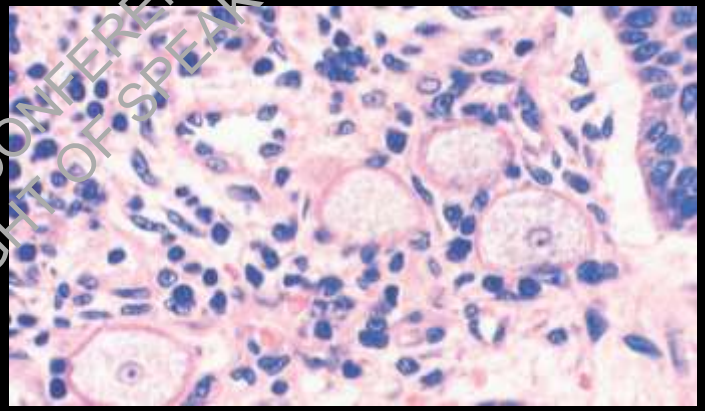


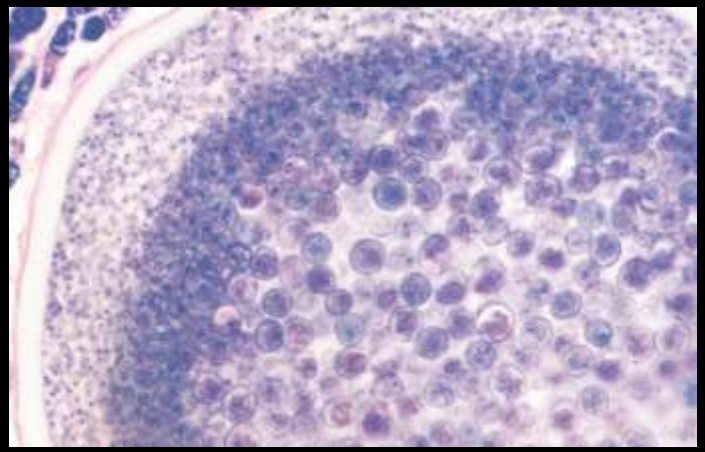


Mixed purulent & granulomatous

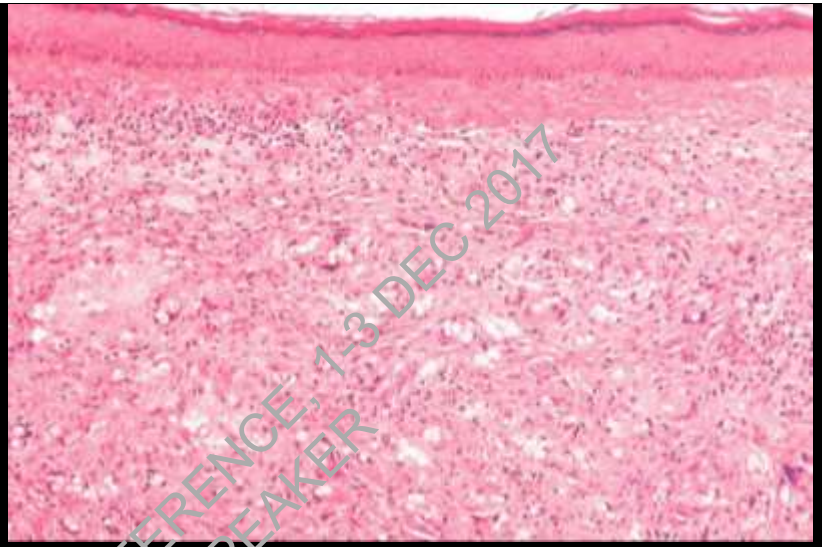
Rhinosporidiosis

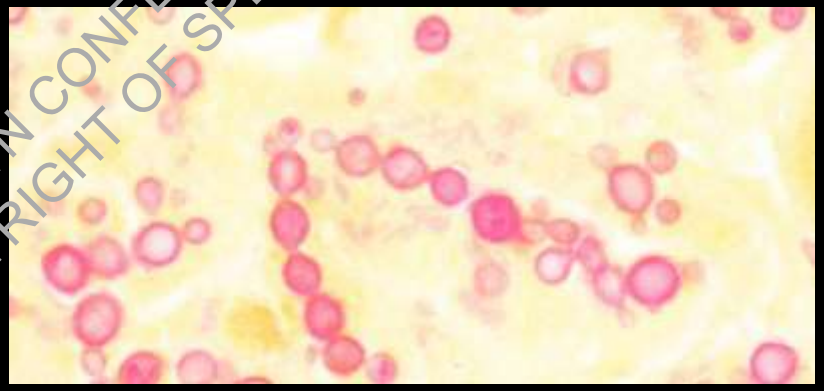


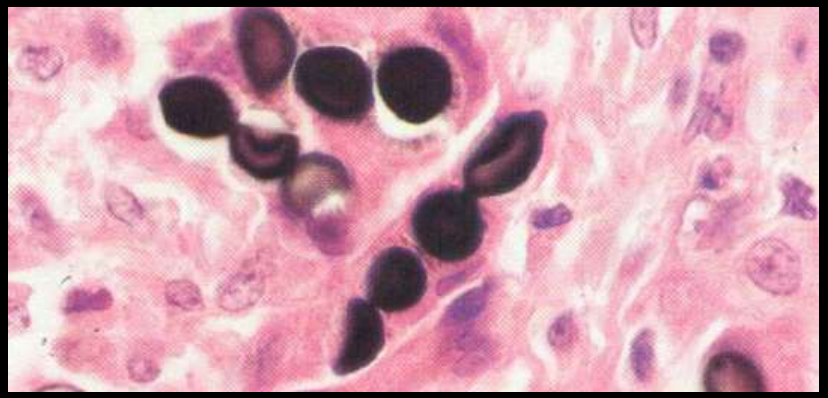




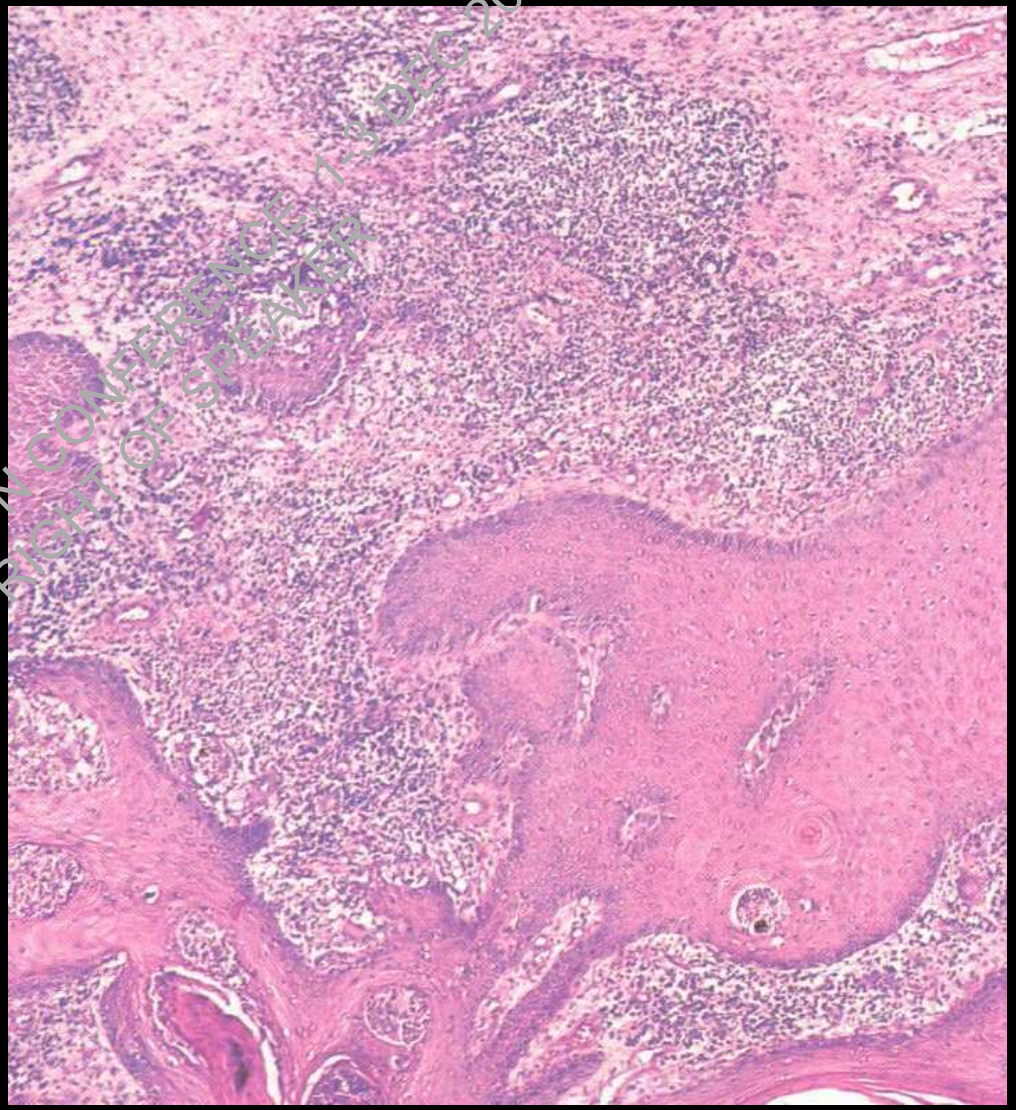
Lobomycosis

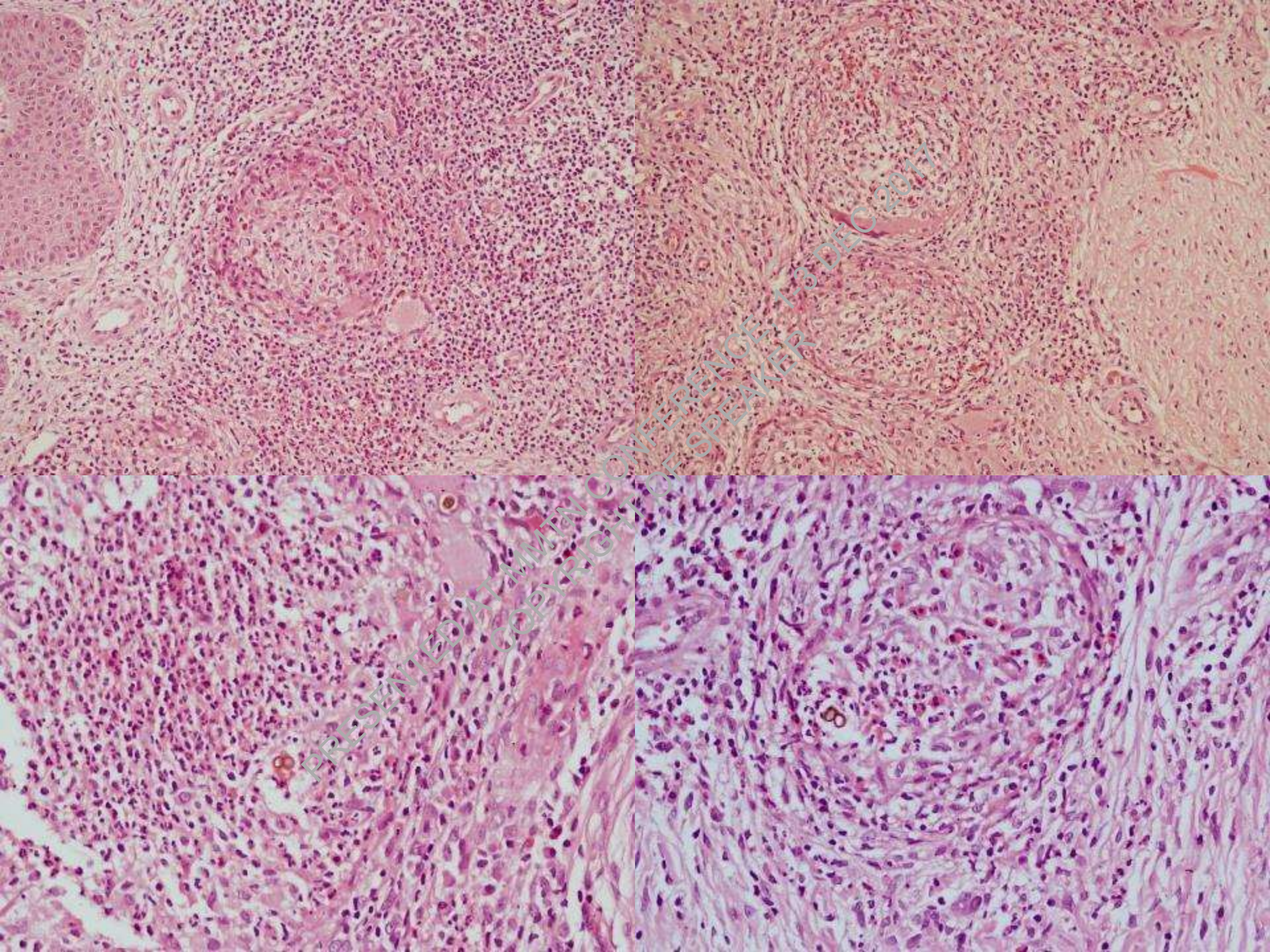




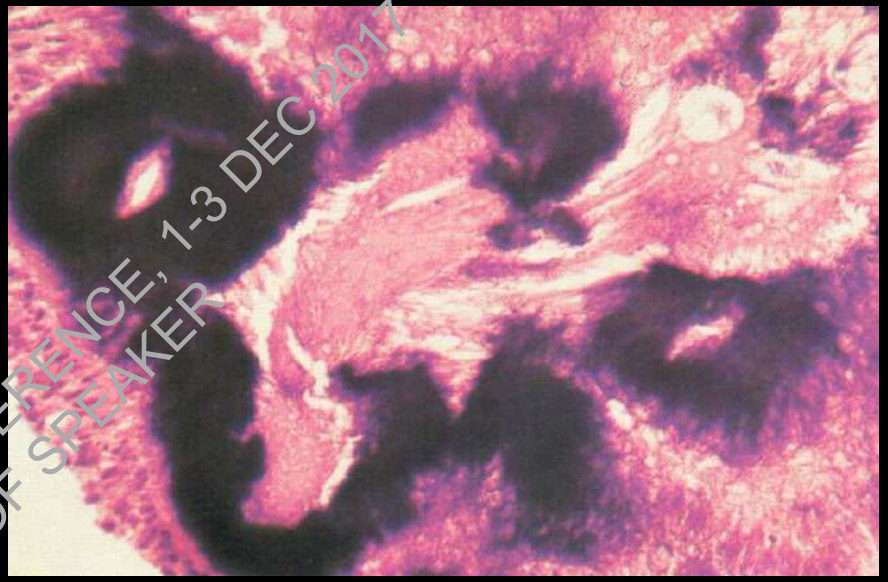


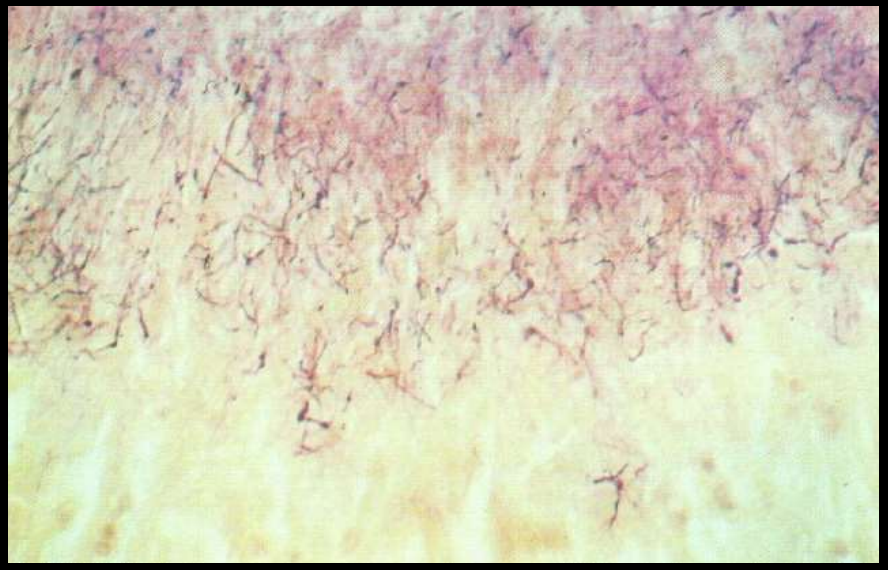
Chromoblastomycosis

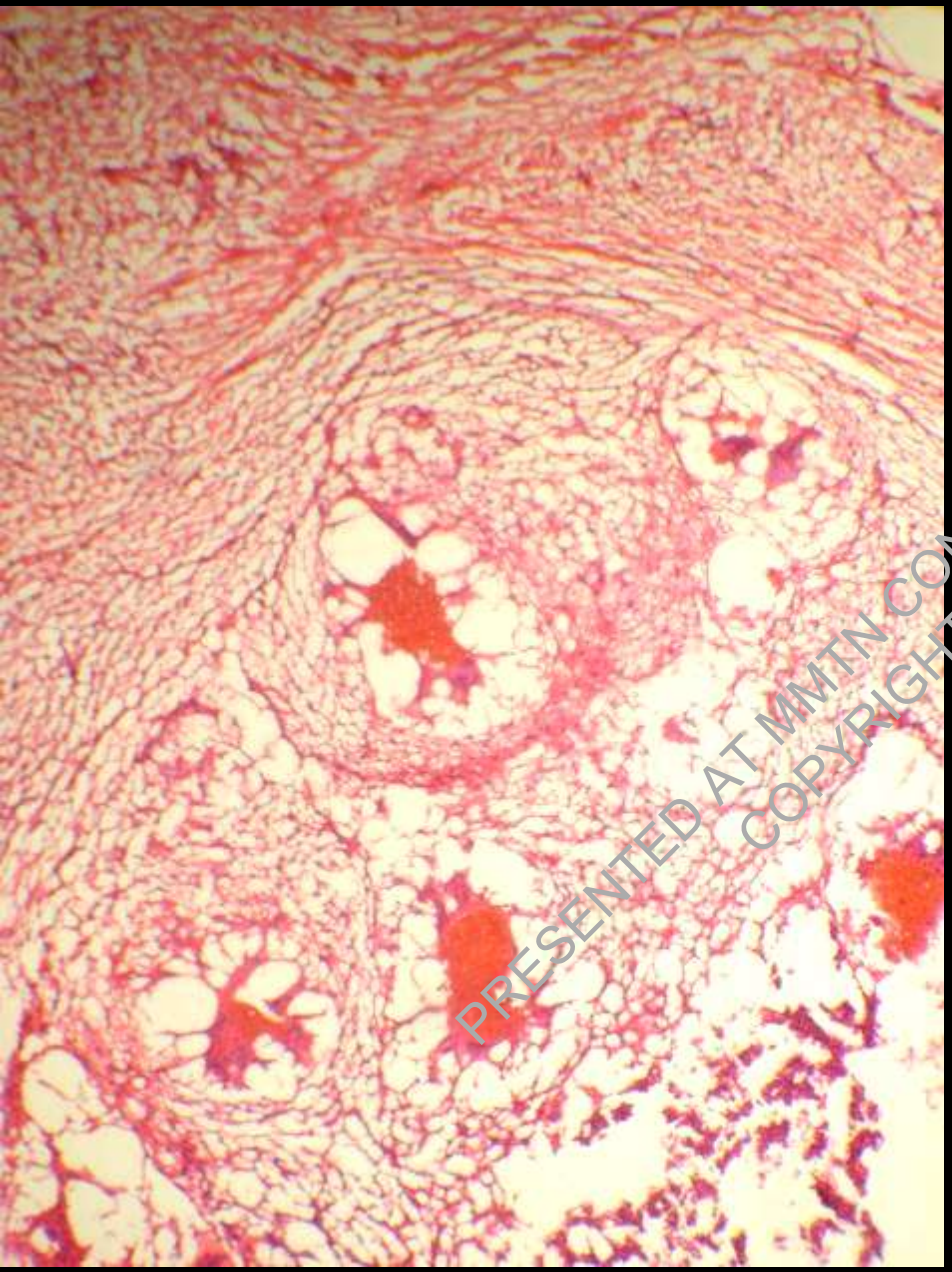




Mycetoma



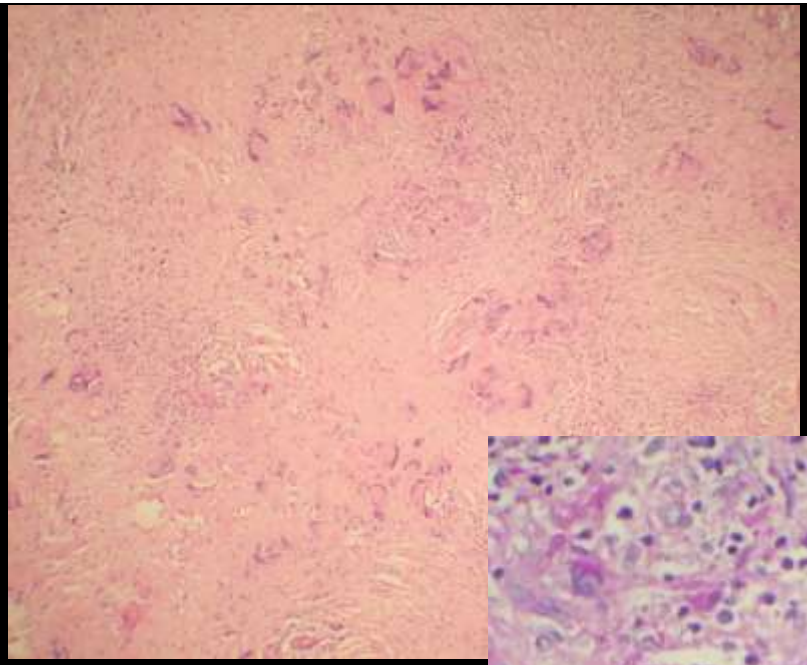


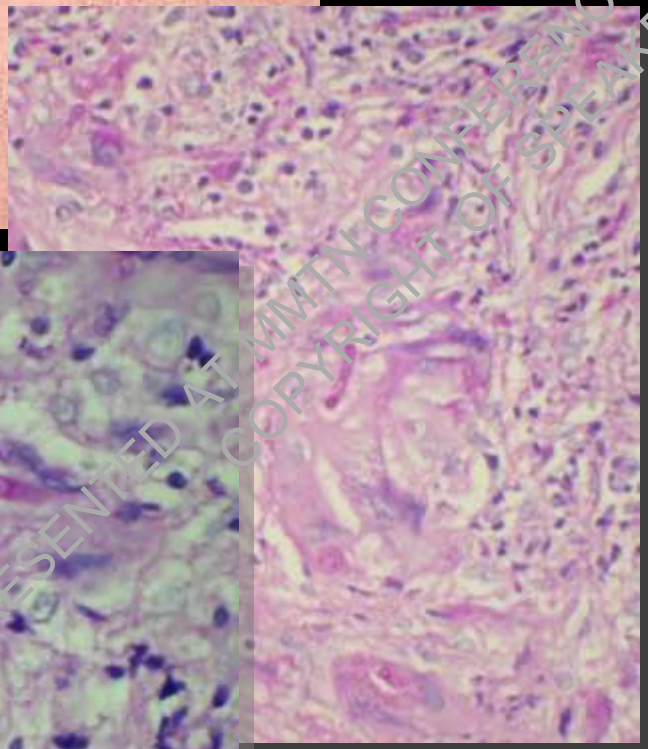


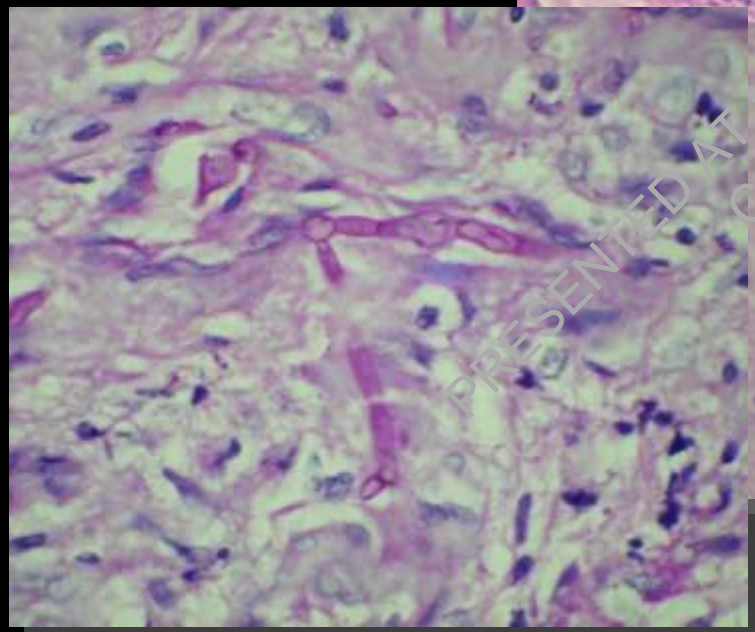
Granulomatous pathology

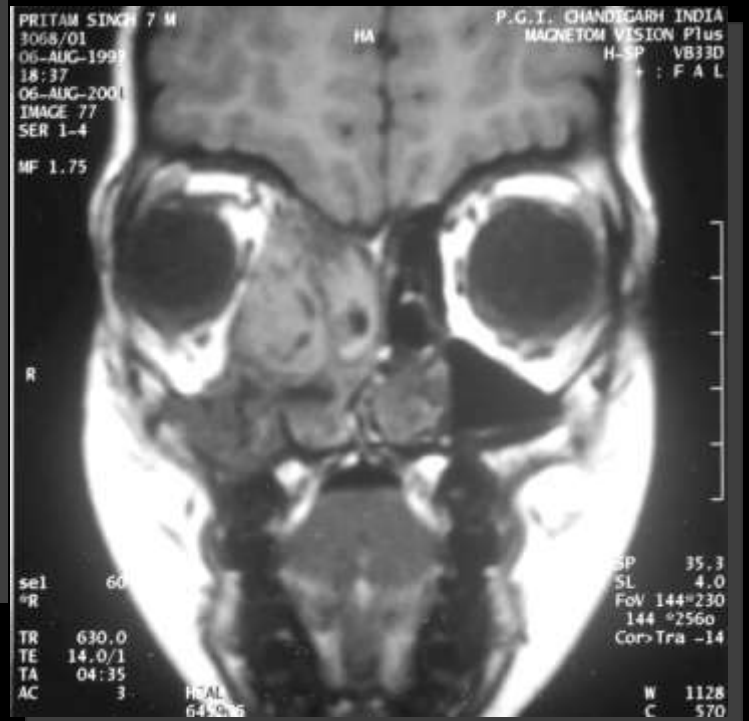
Granulomatous Invasive

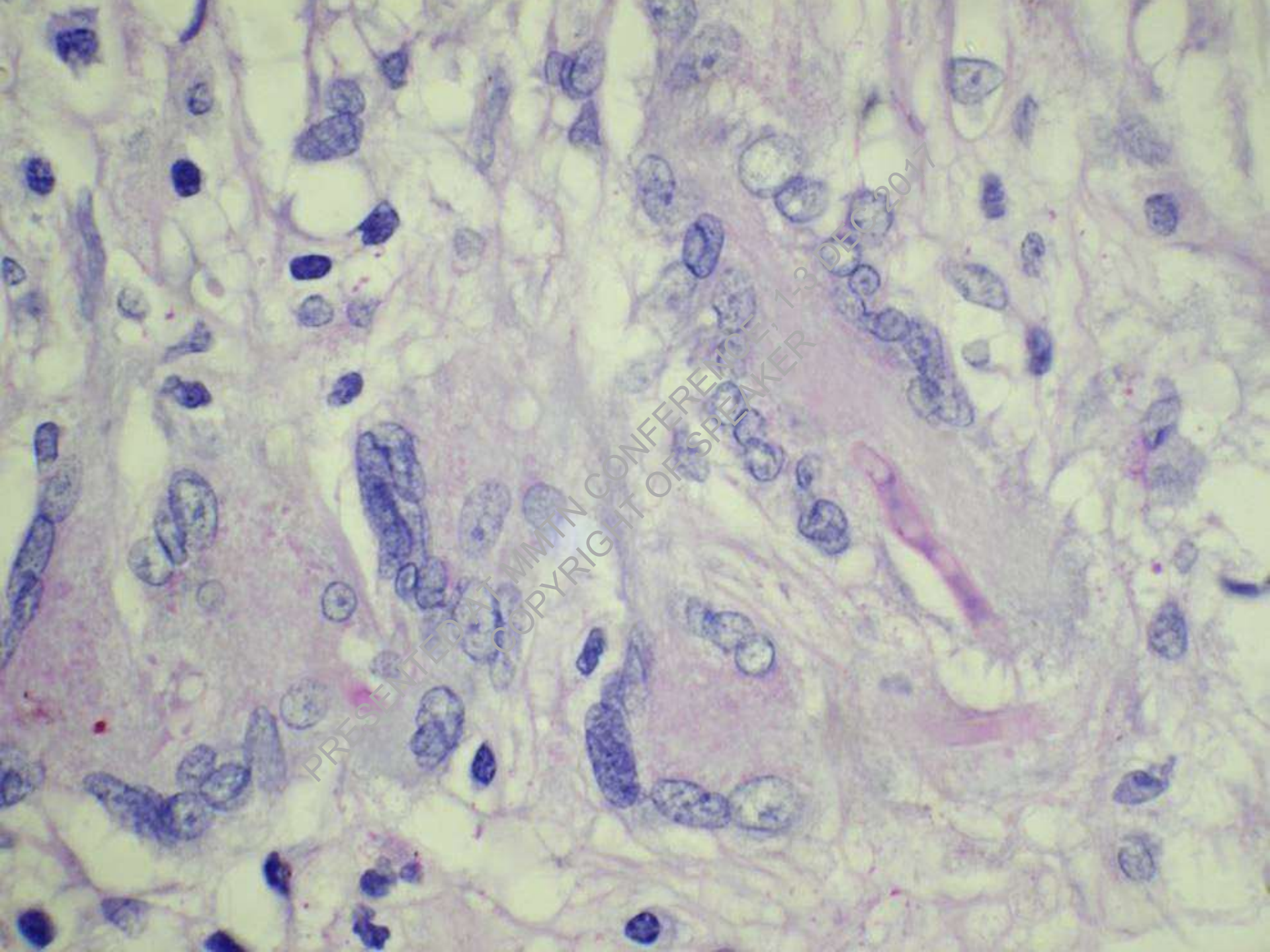
Granulomas with few fungal hyphae
chronic inflammatory infiltrate



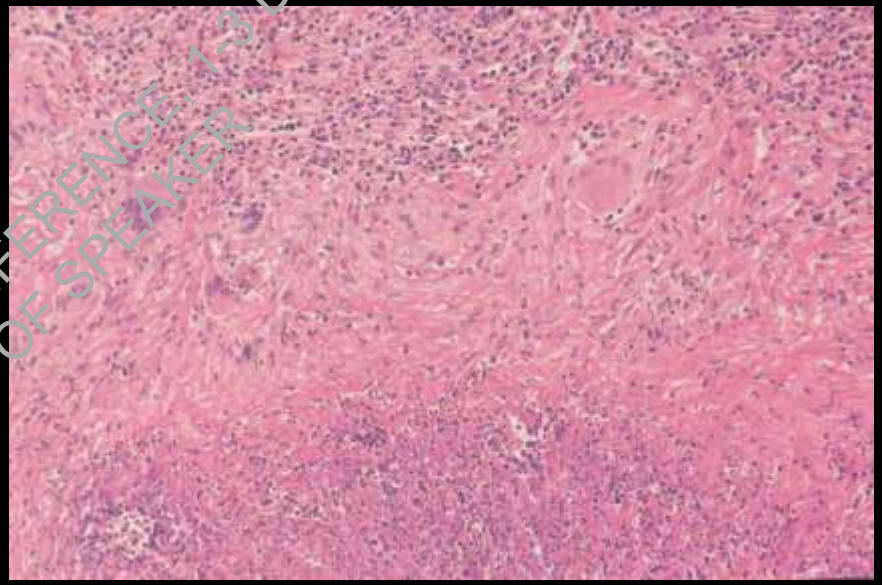


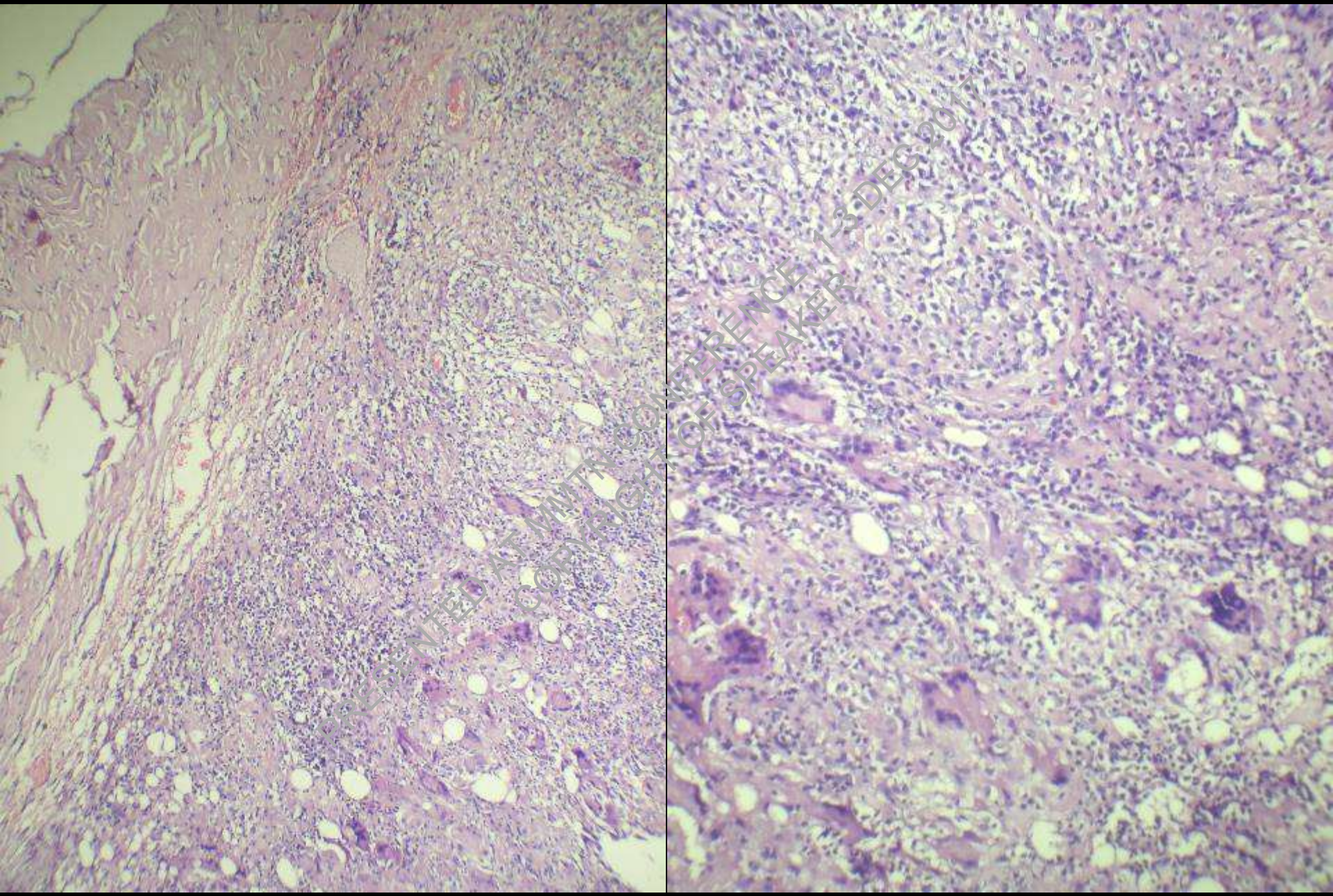


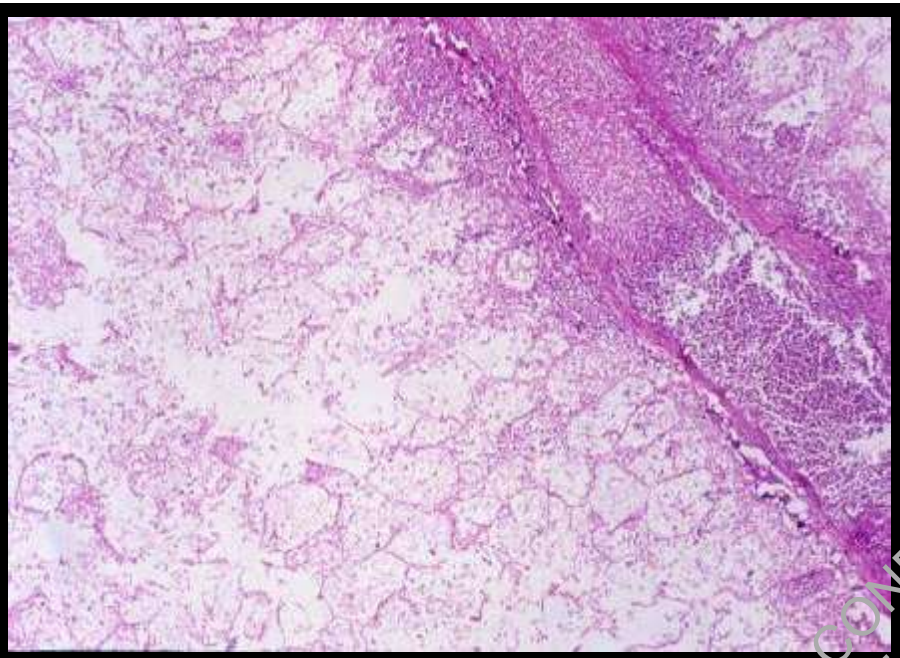


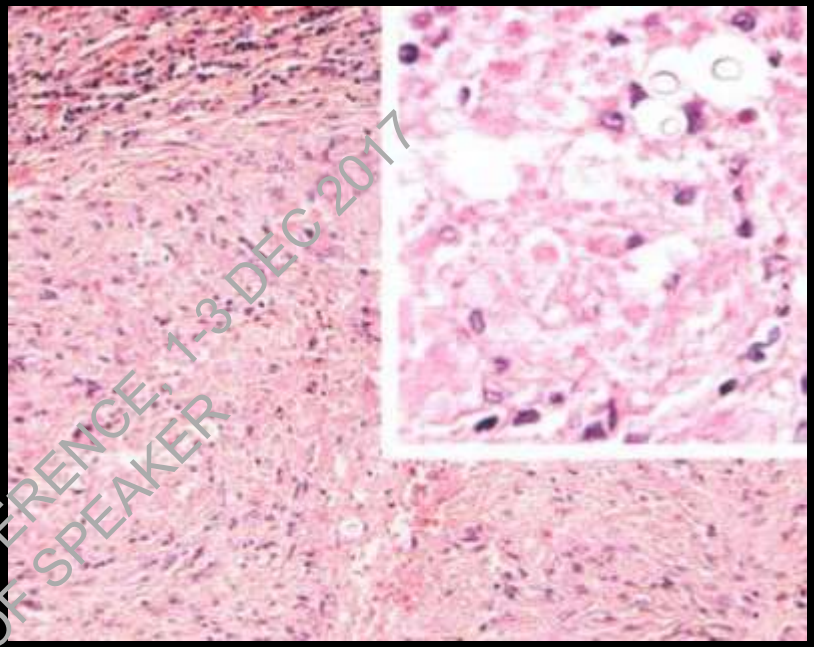


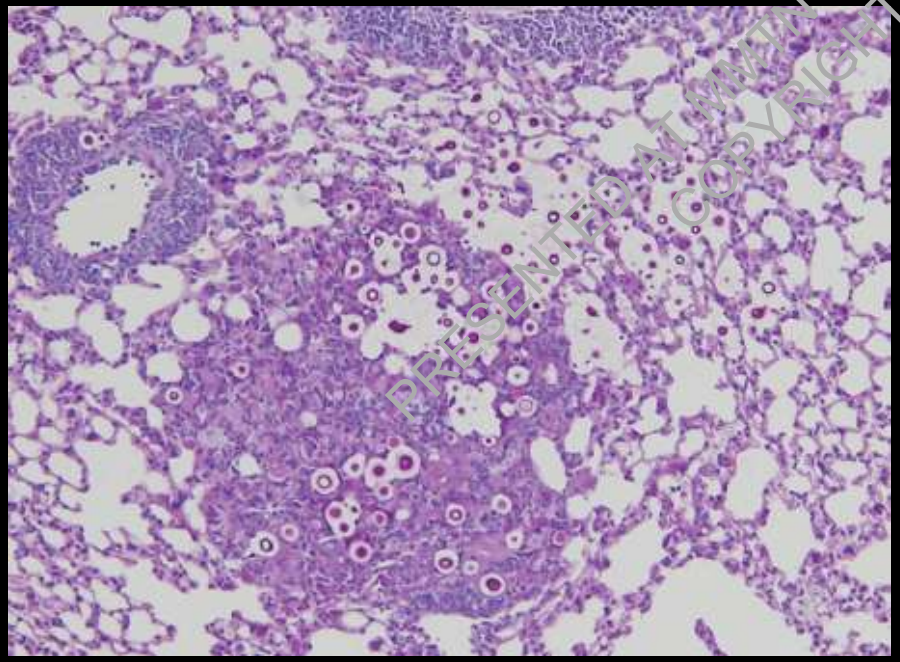
Coccidioidal nodule

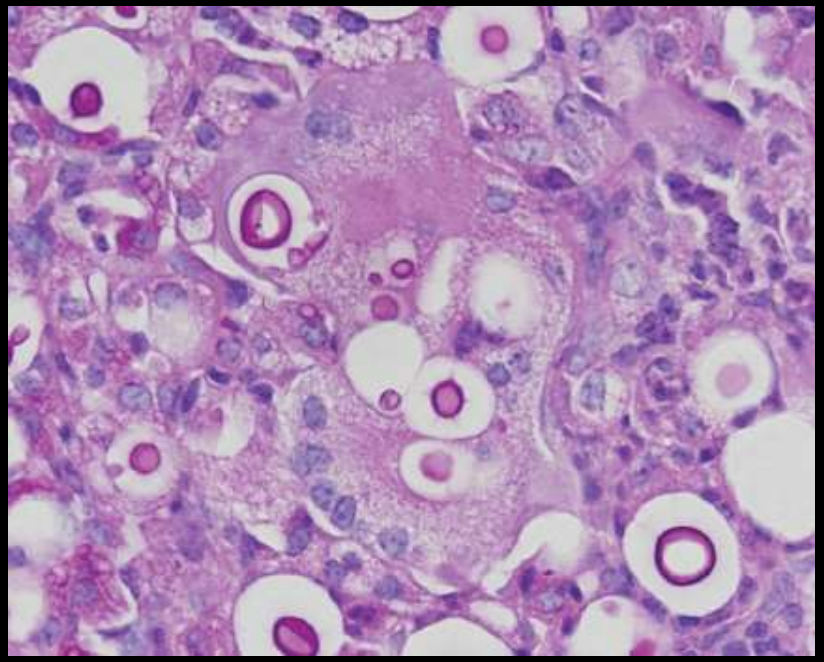


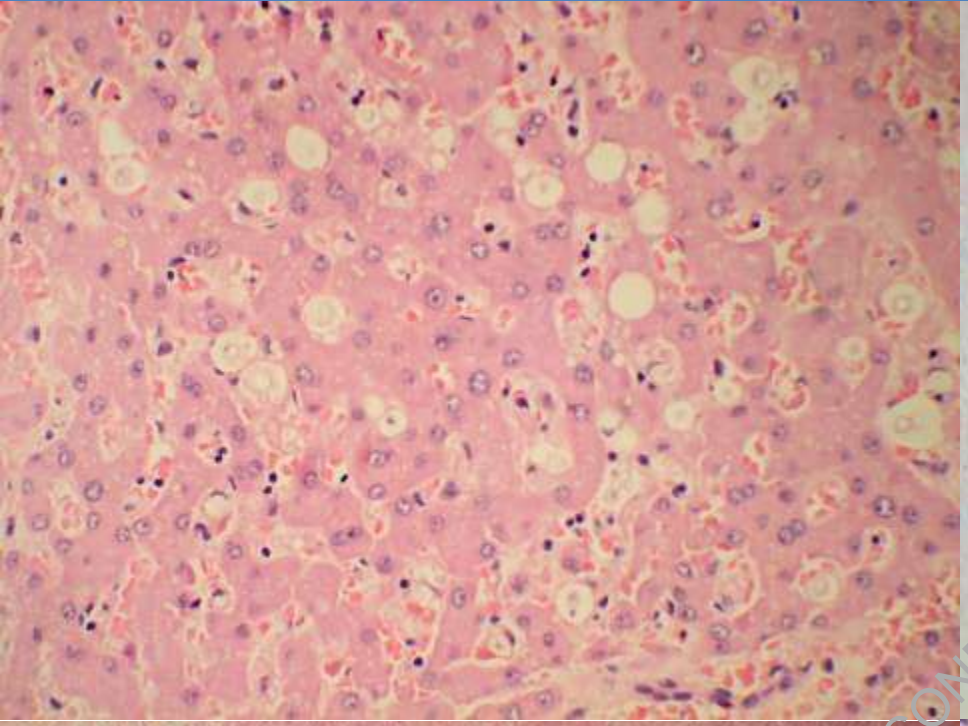


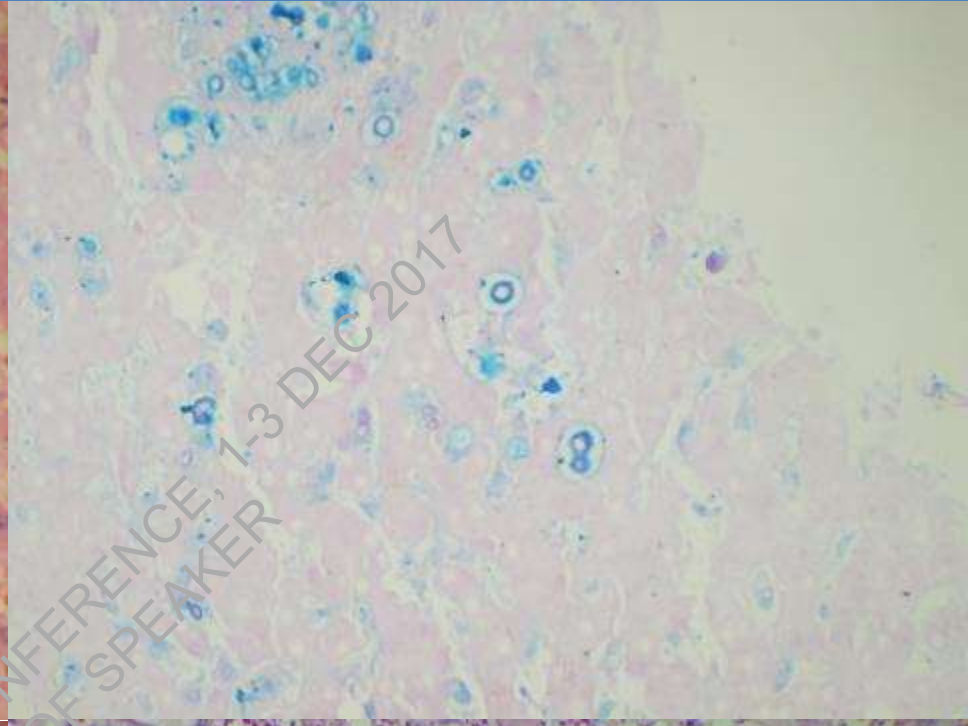


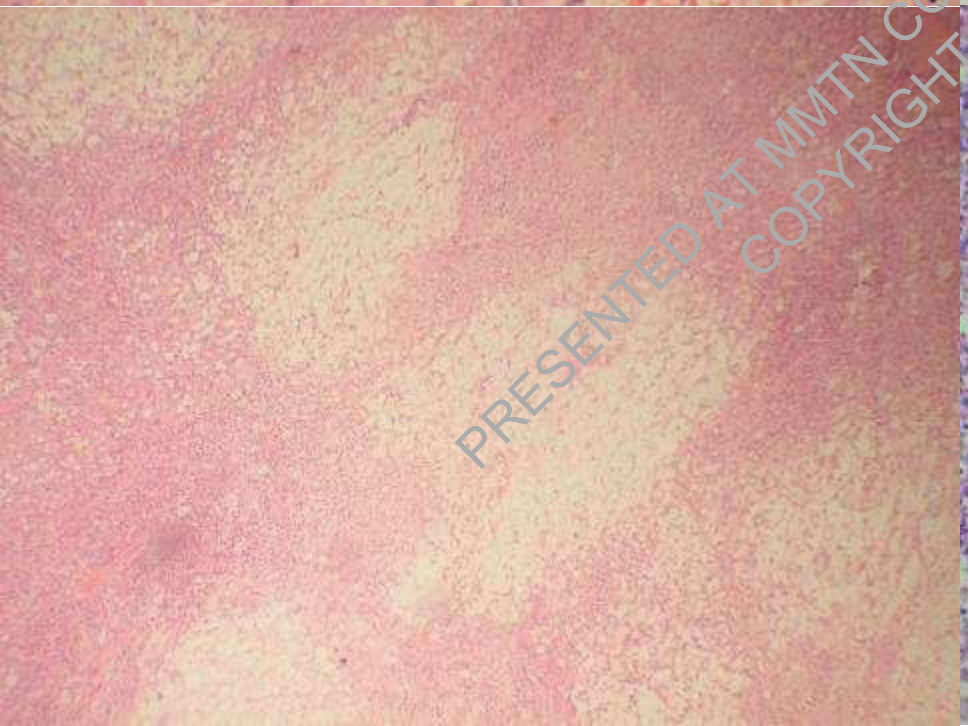


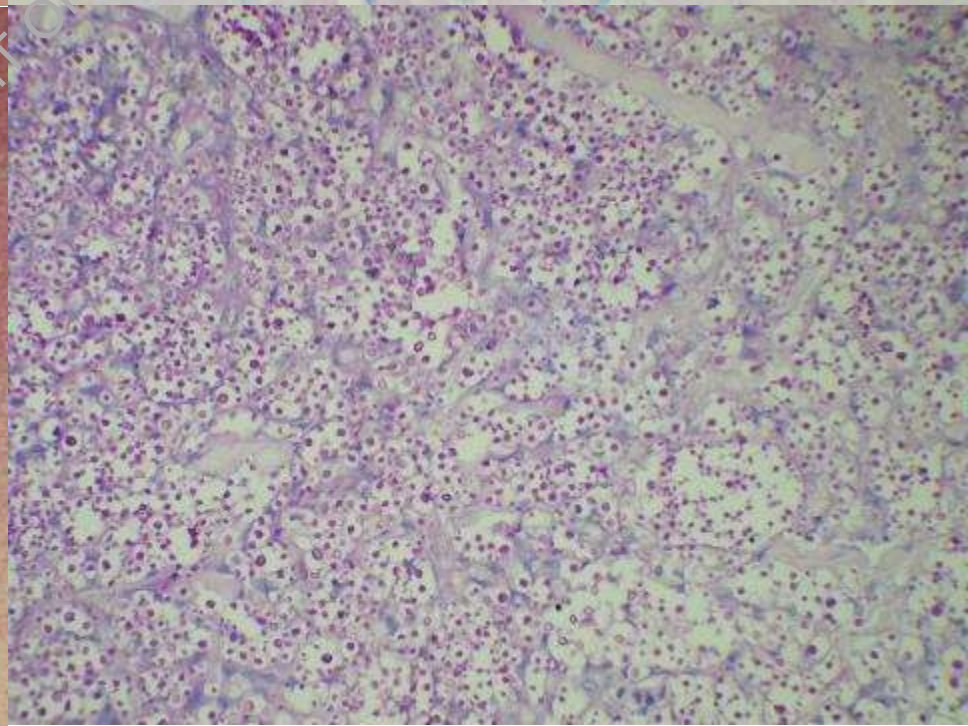


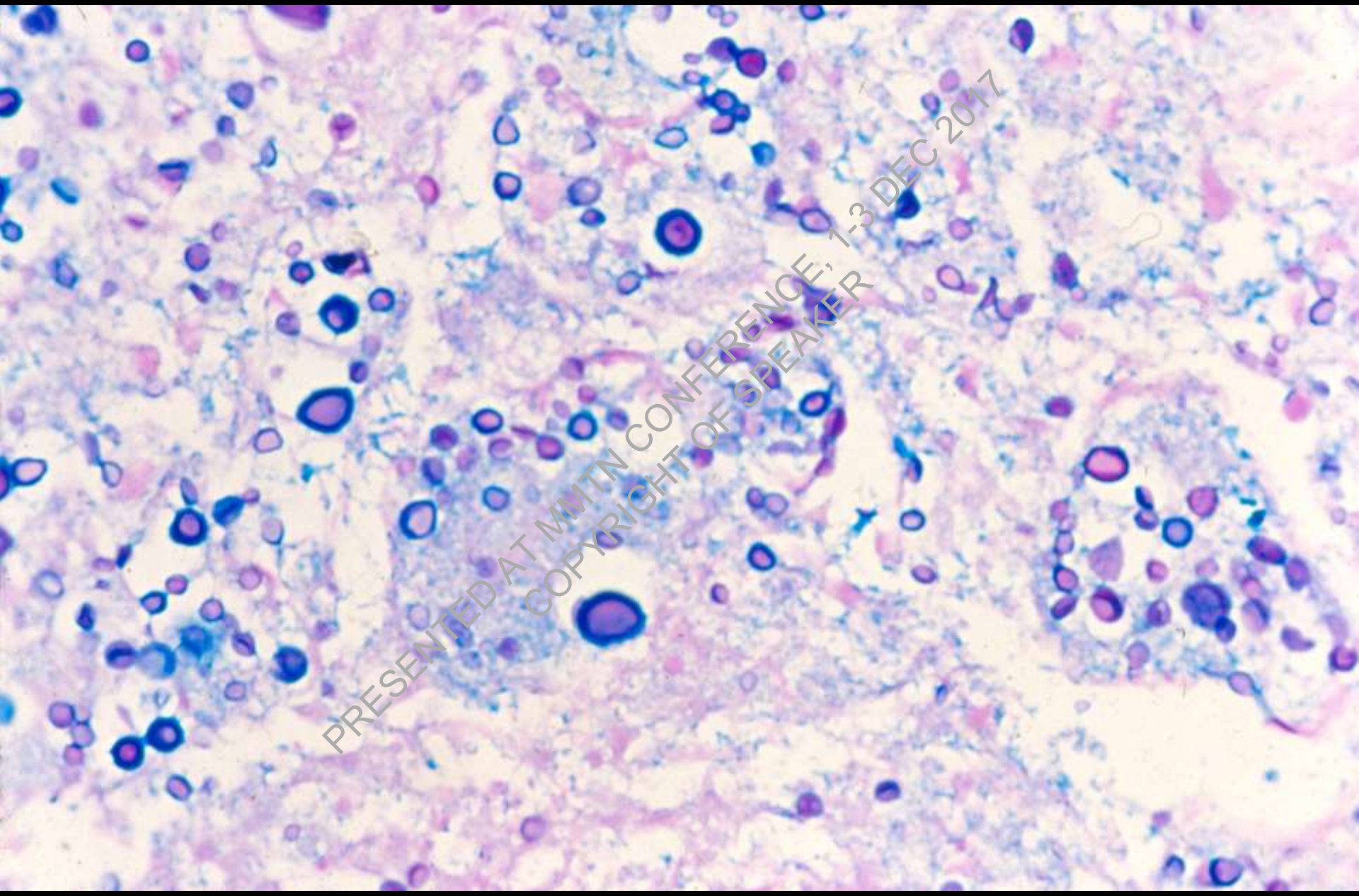


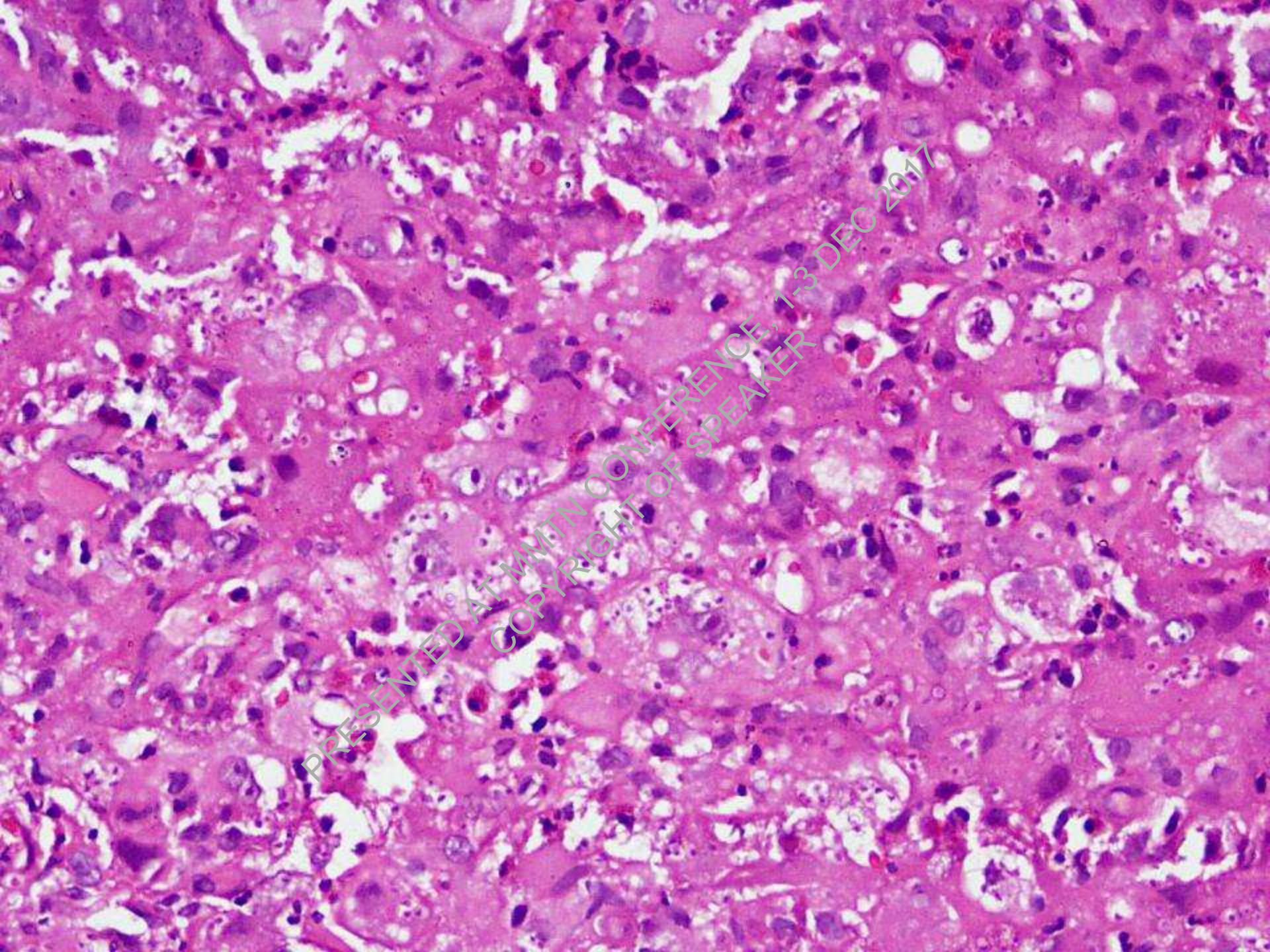


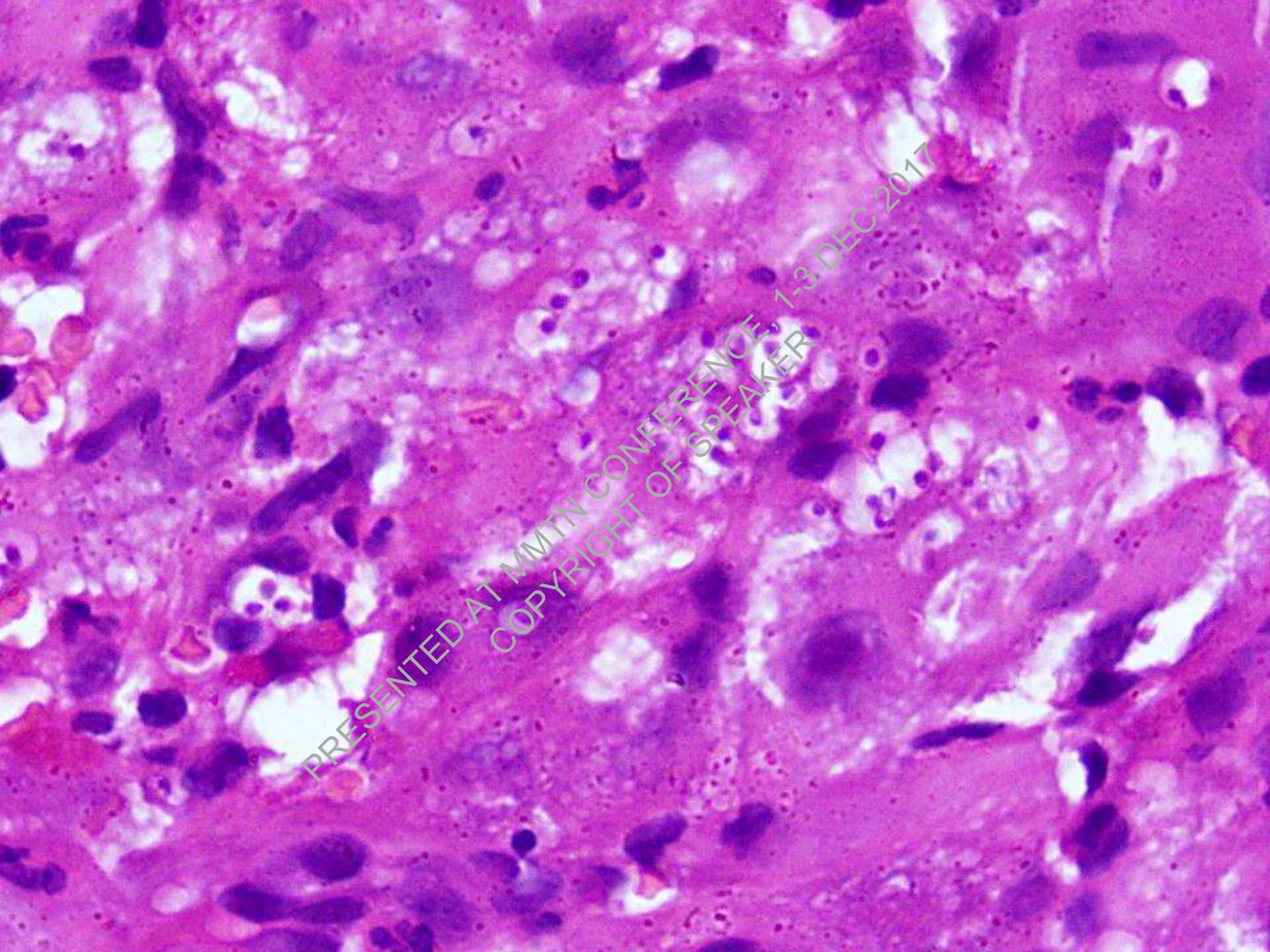


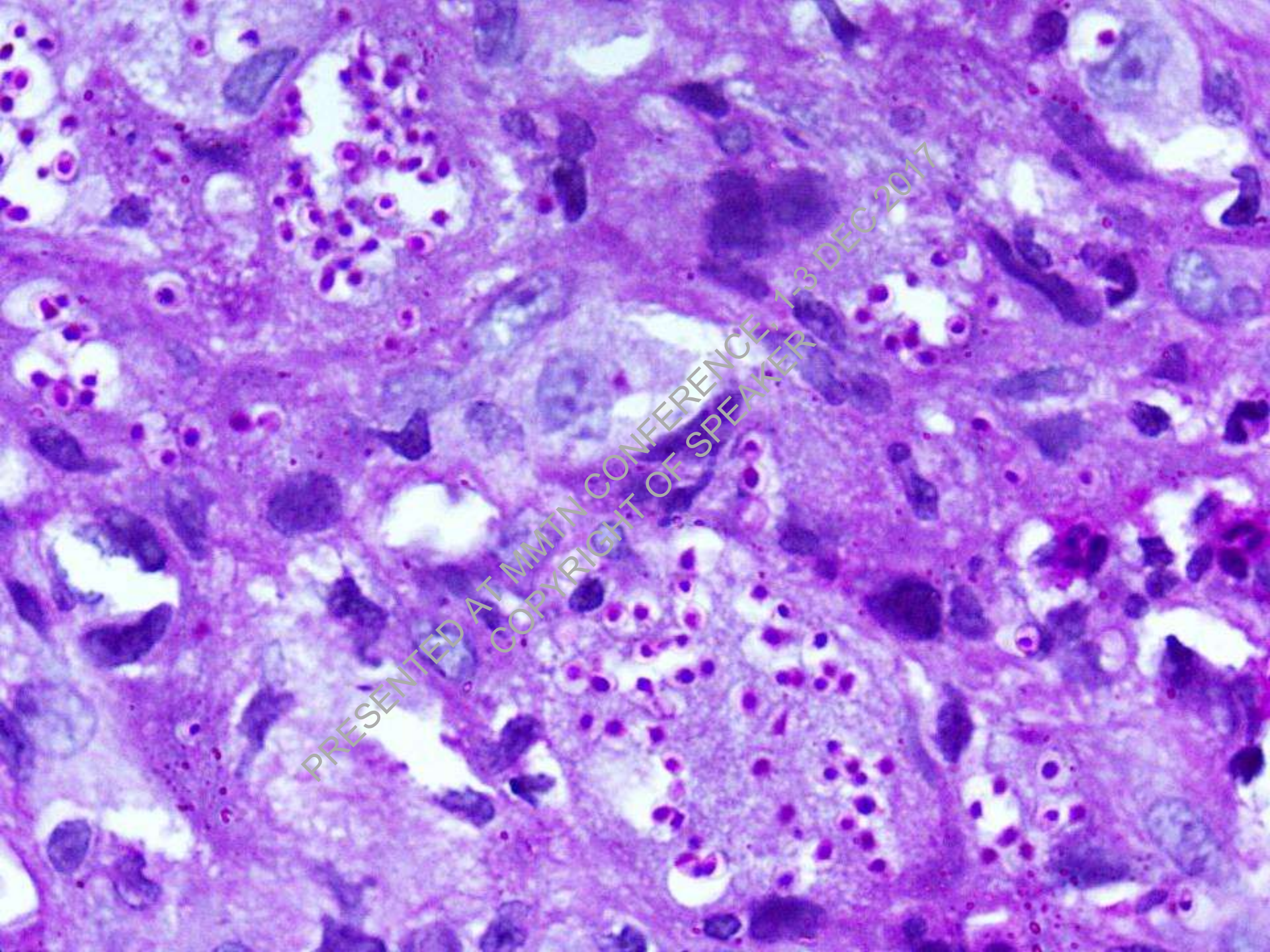


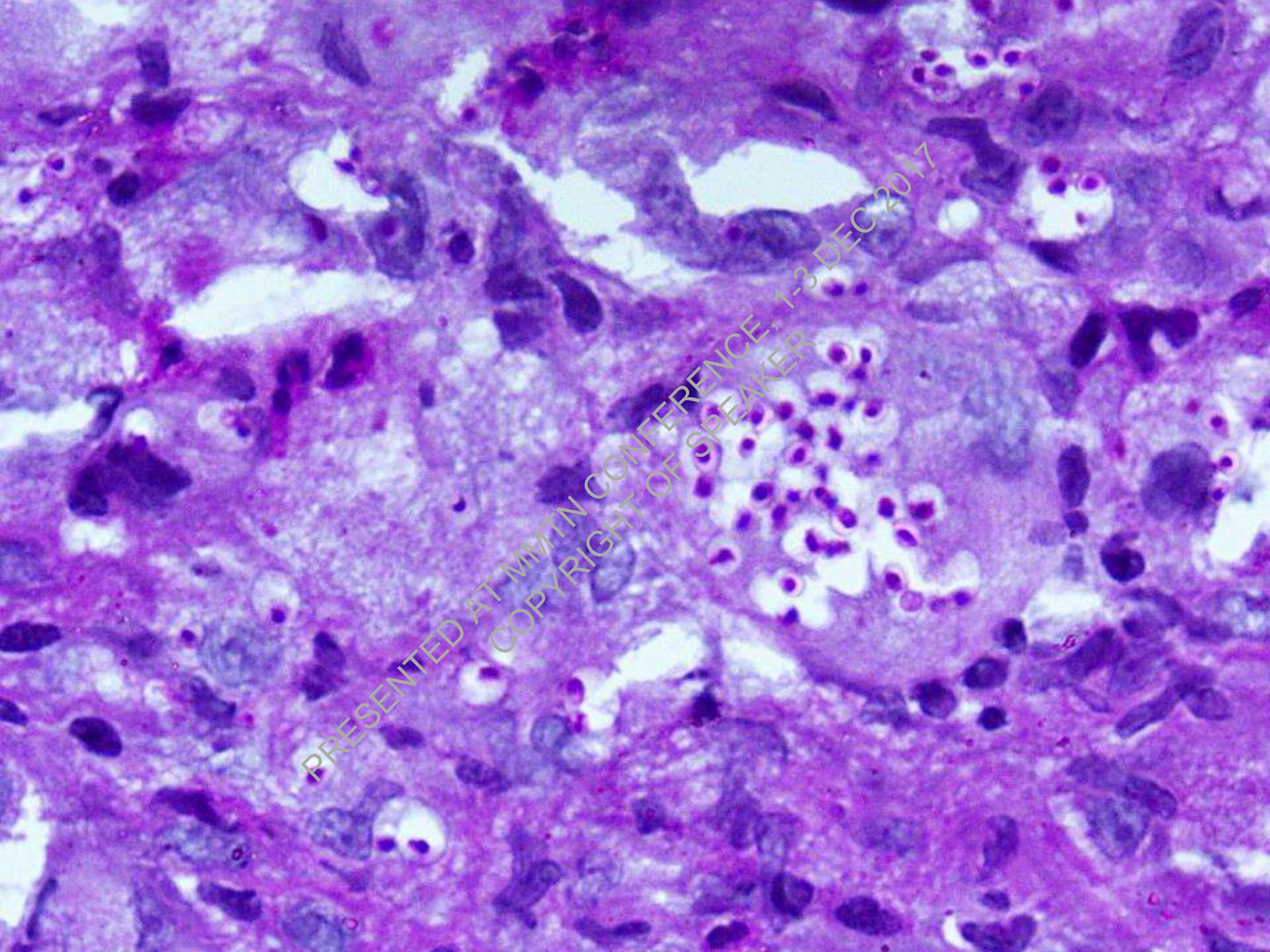


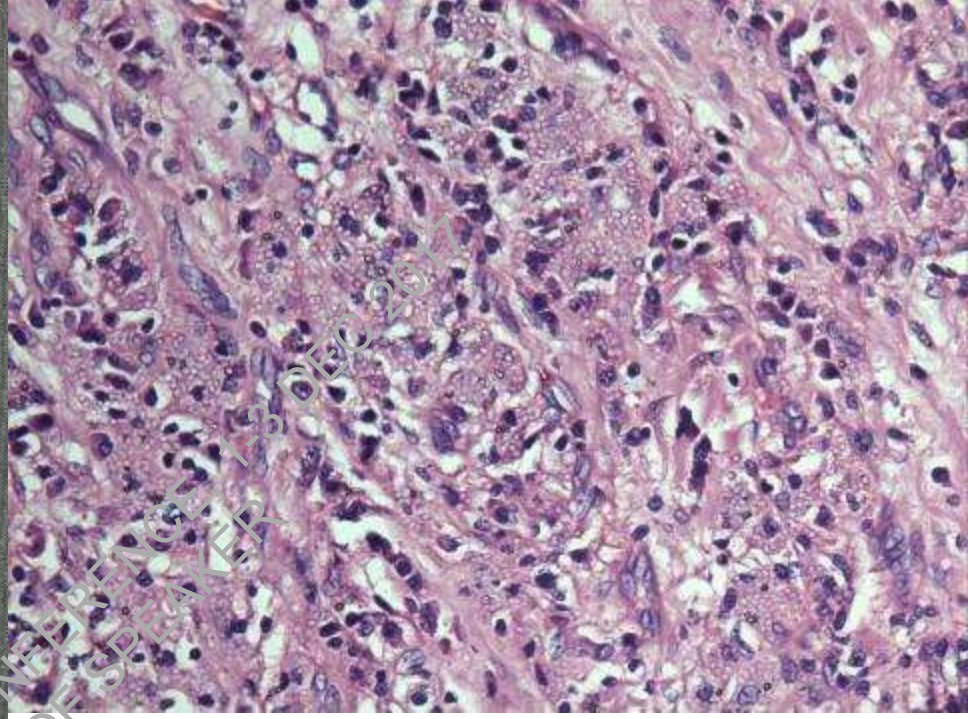


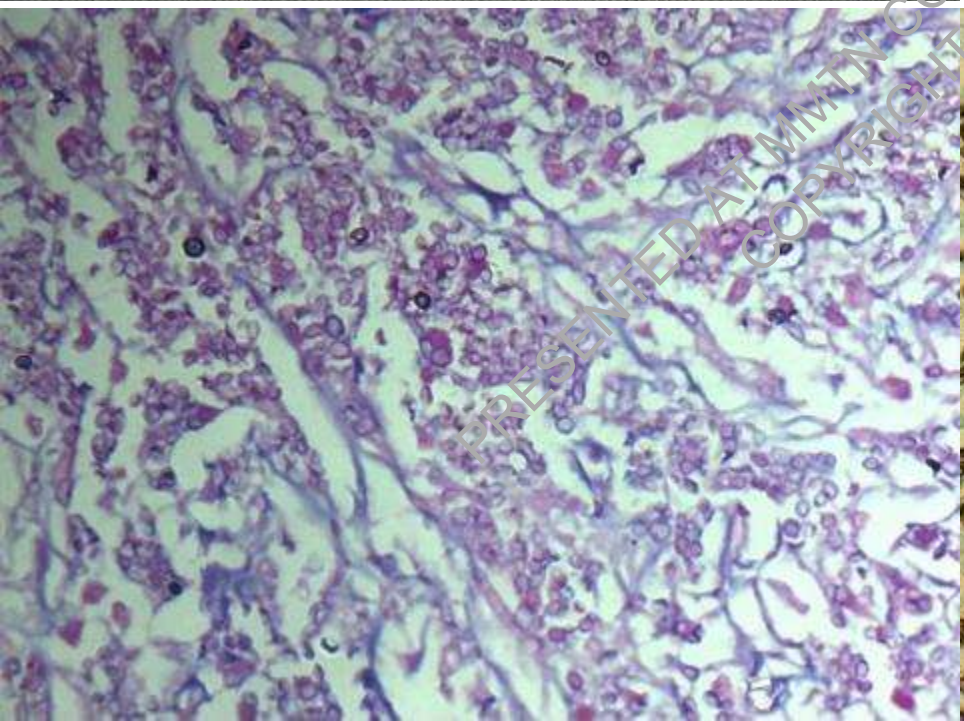


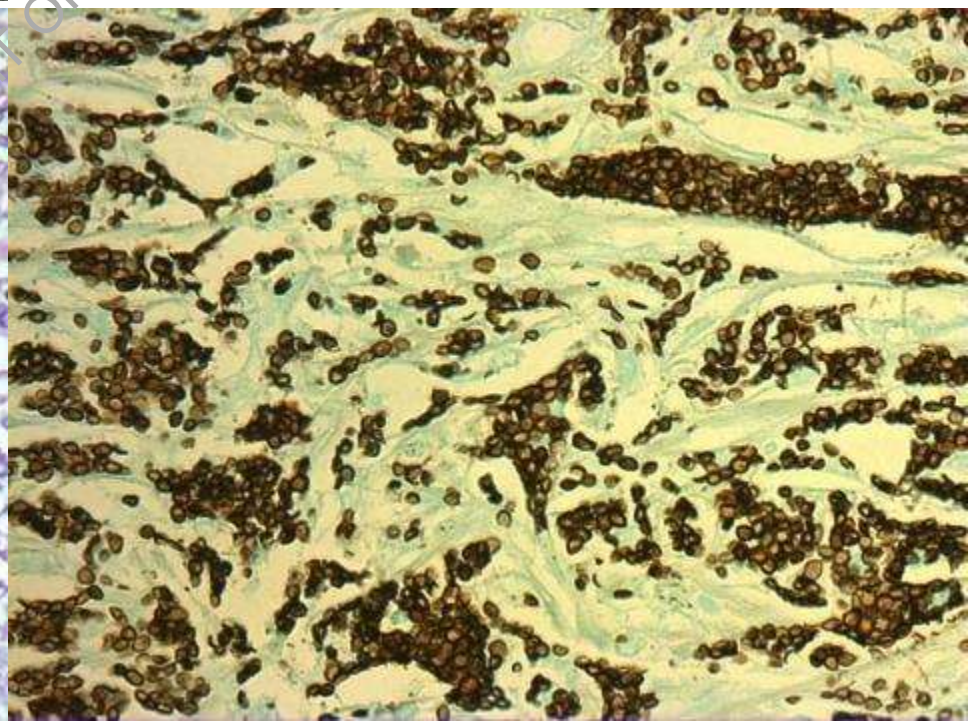


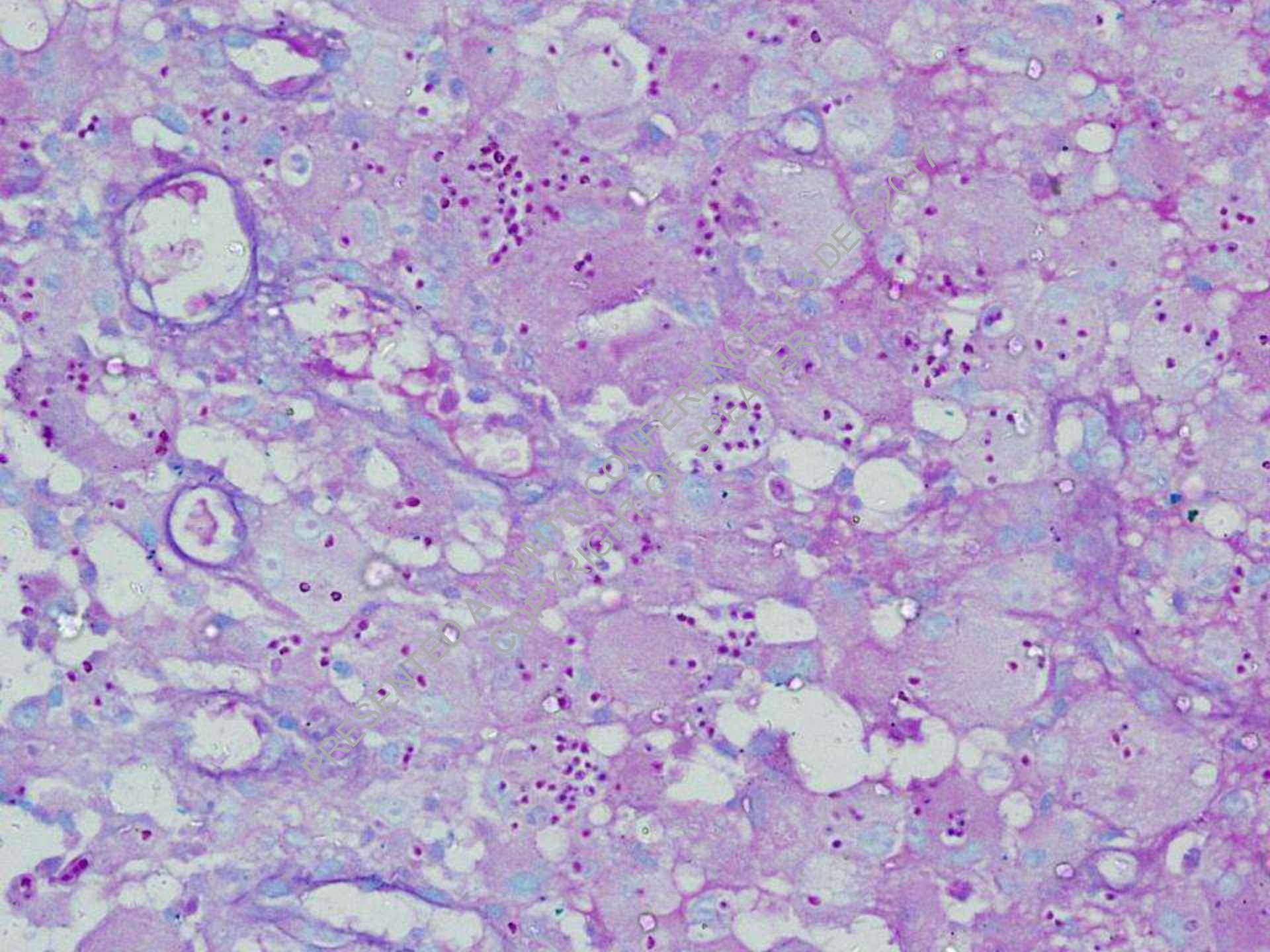


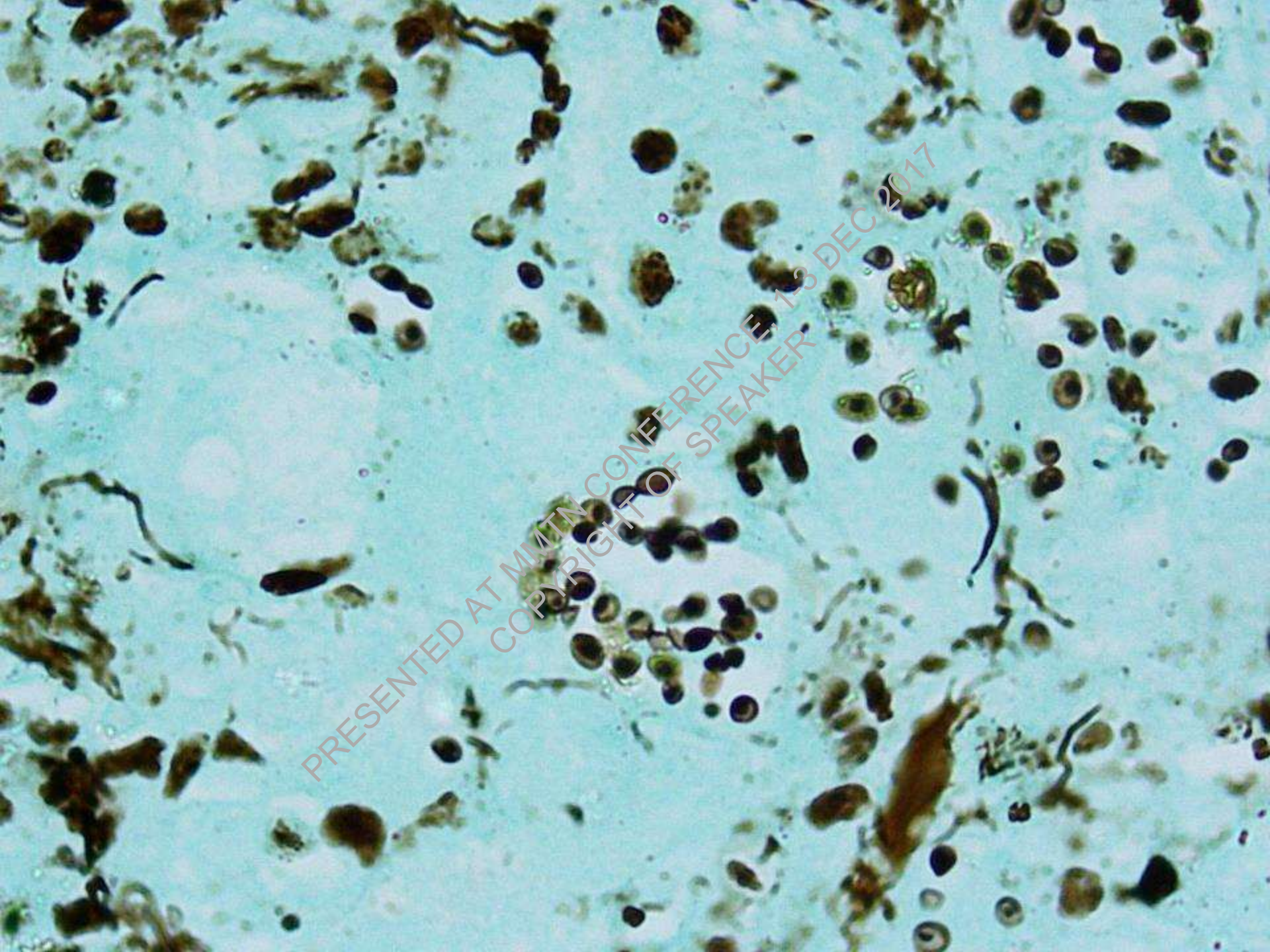




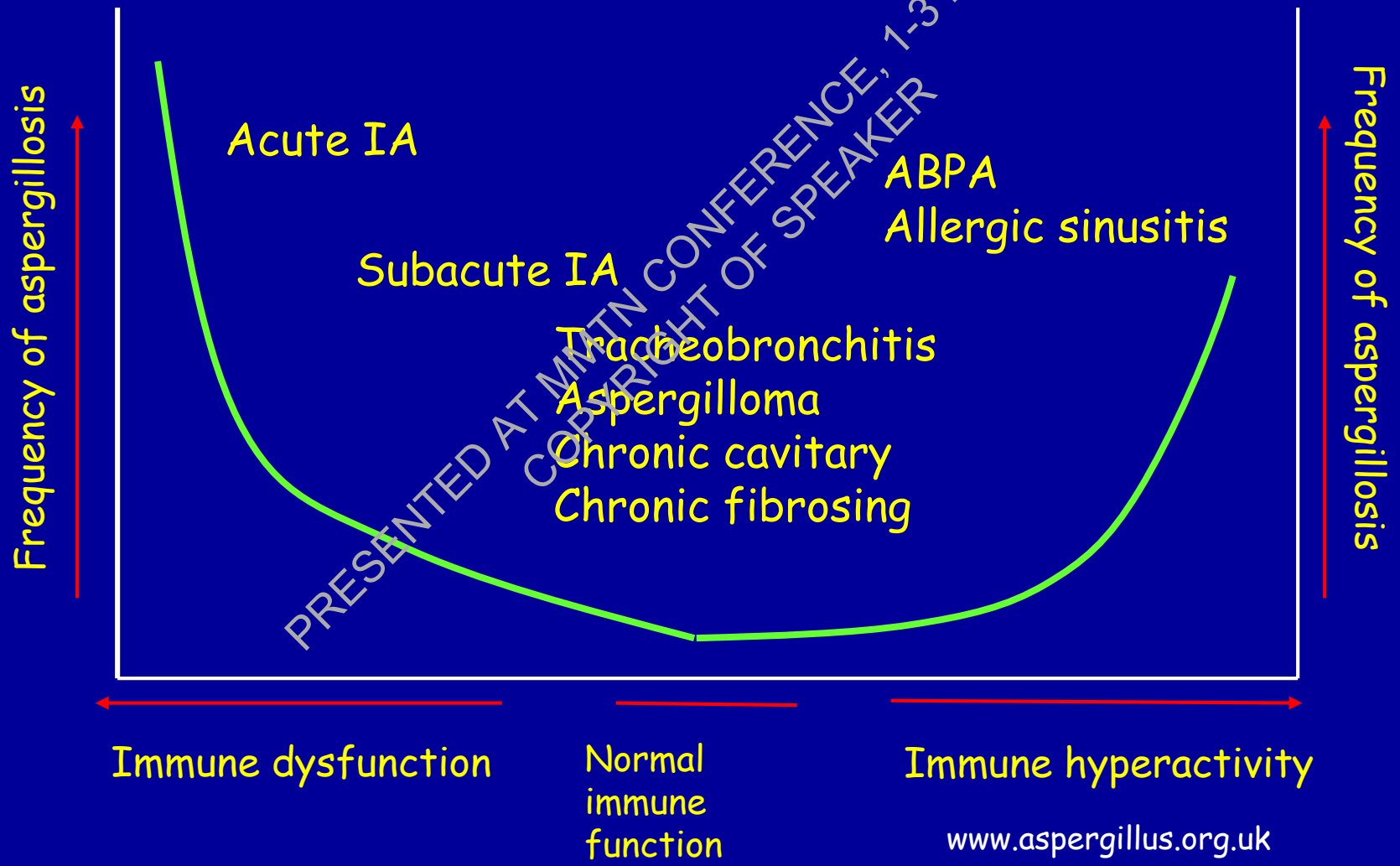






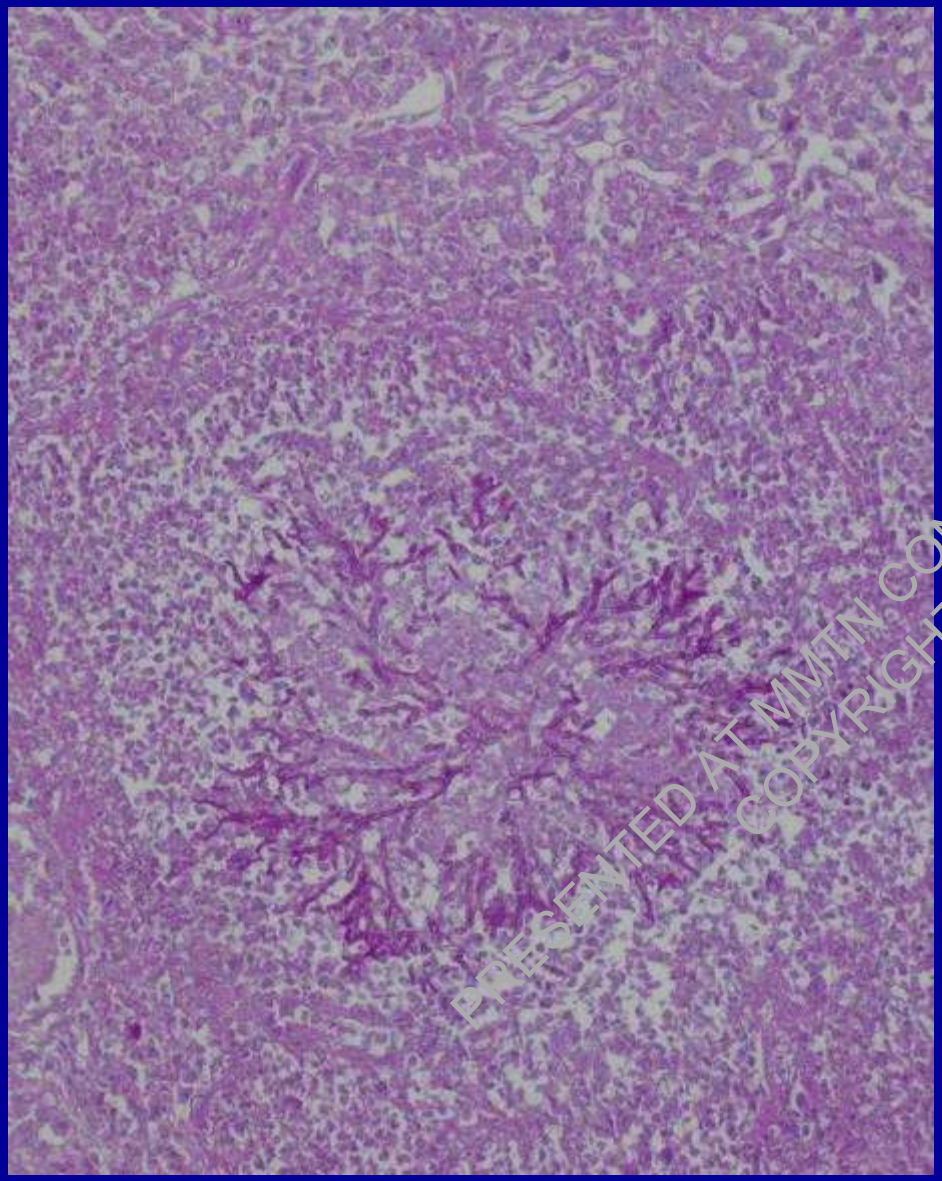


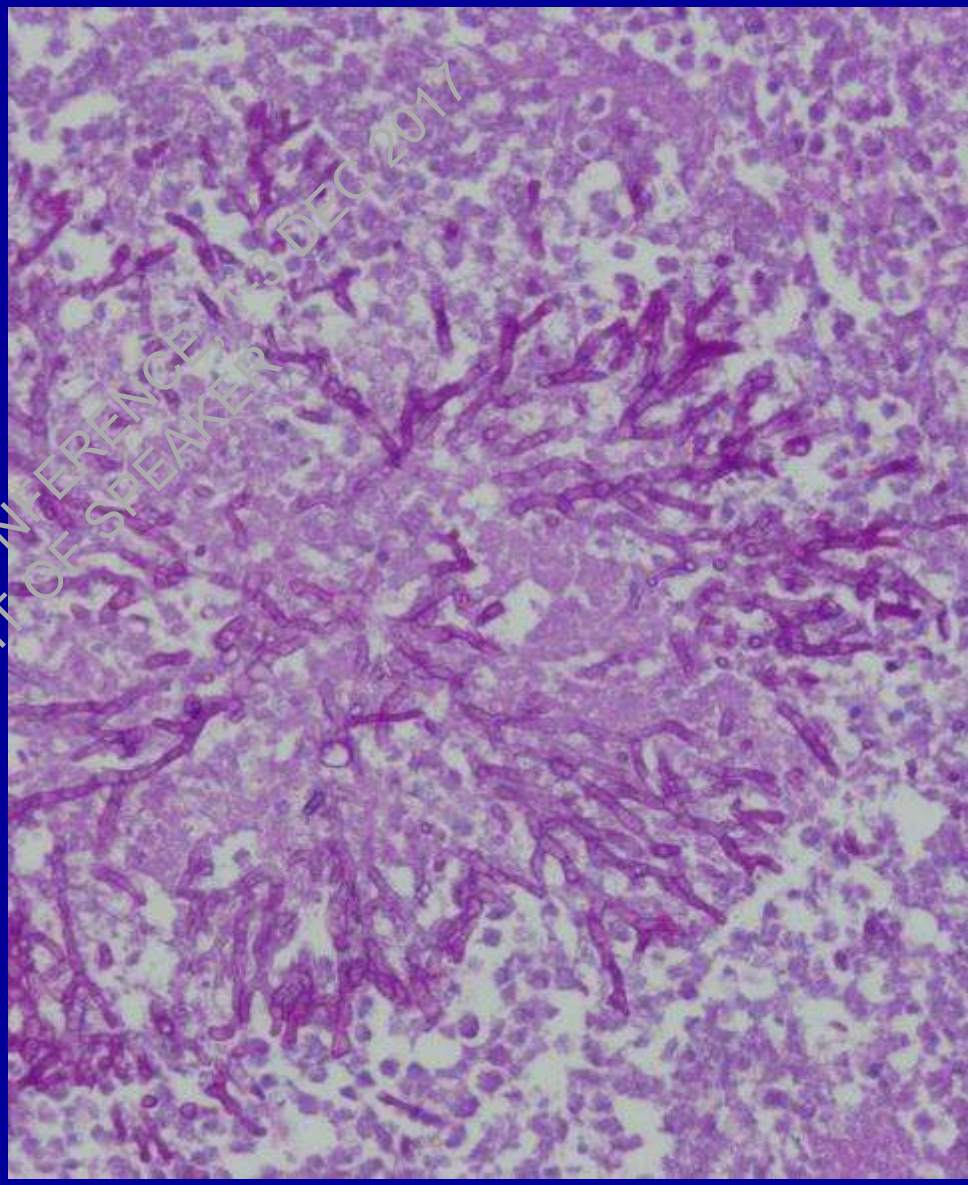
Interaction of *Aspergillus* with host

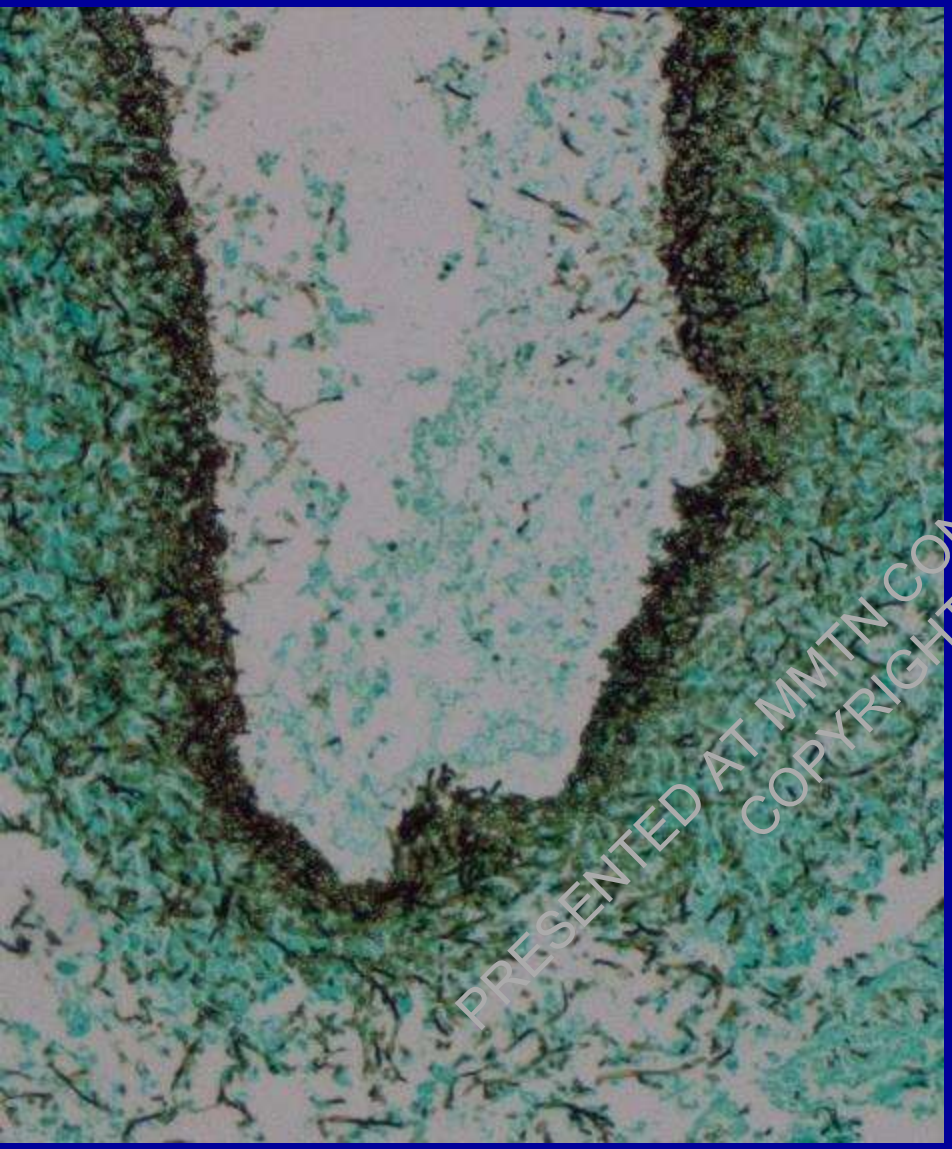


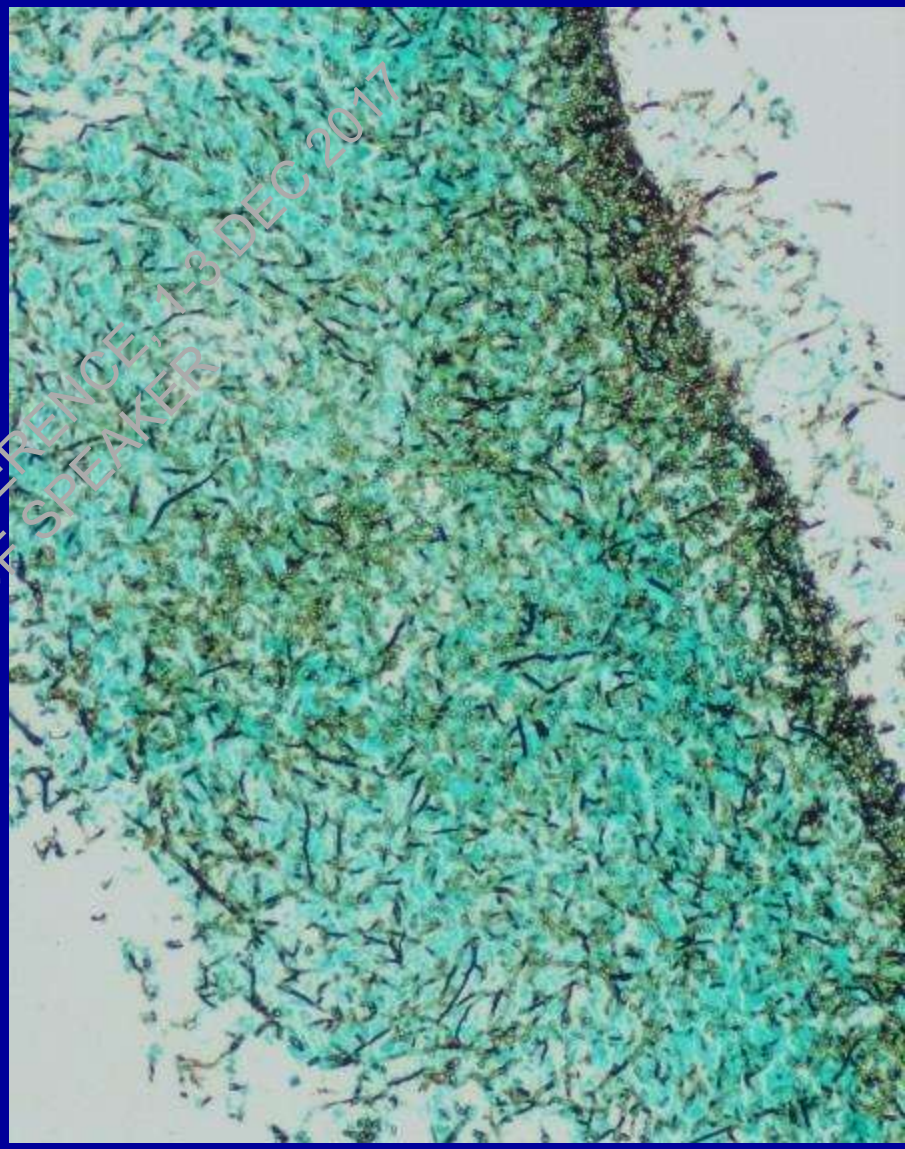
Acute invasive aspergillosis


PRESENTED AT MMTN CONFERENCE, 1-3 DEC 2017
COPYRIGHT OF SEER
AFIP M-20705

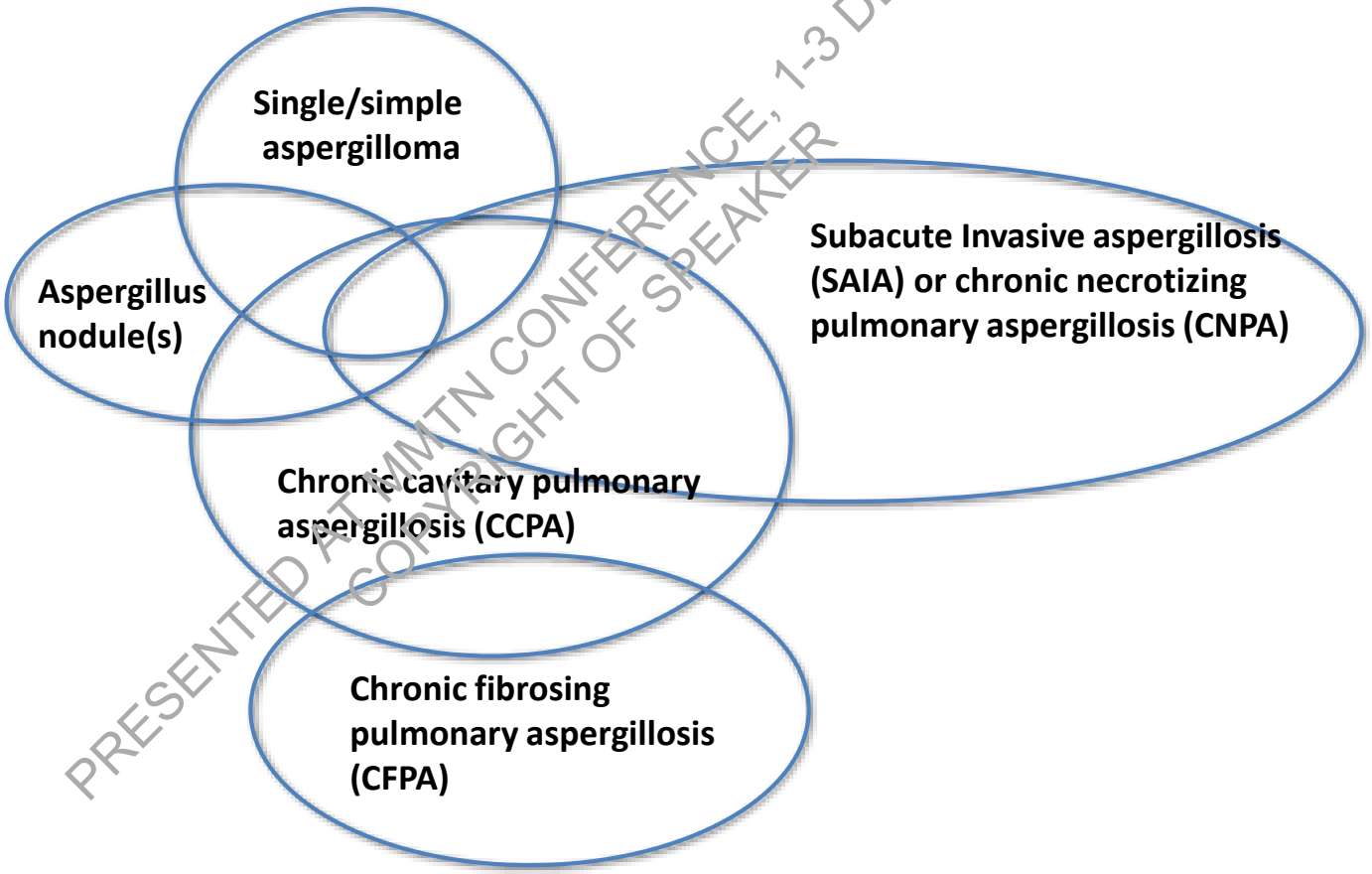






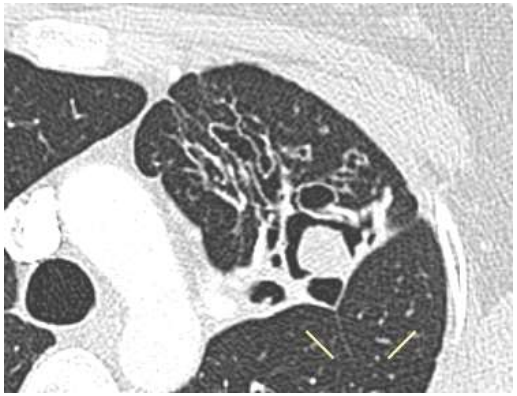


Clinical phenotypes of chronic aspergillosis



Denning et al. Eur Respir J 2016; 47: 45

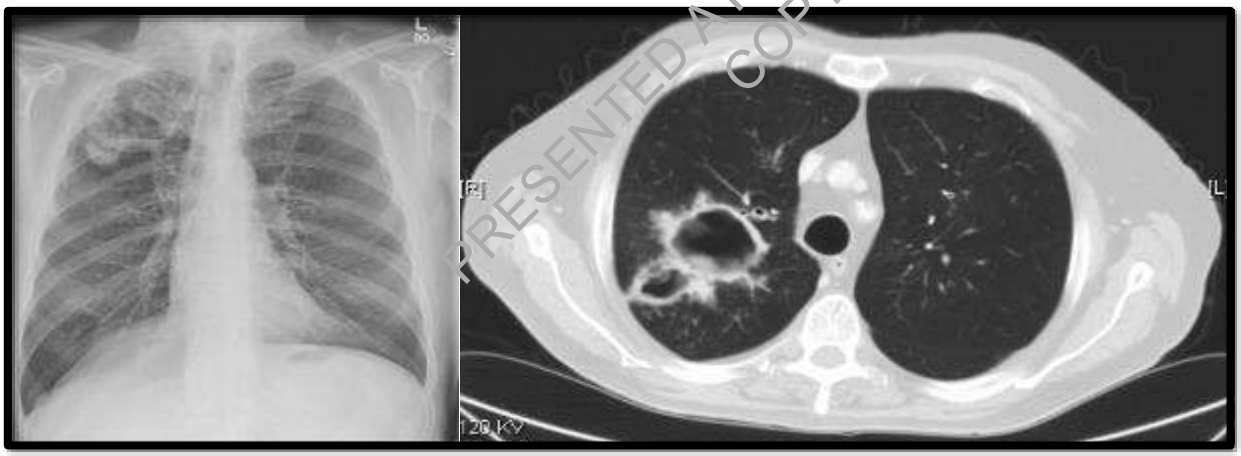
Chronic pulmonary aspergillosis



Aspergilloma

CCPA

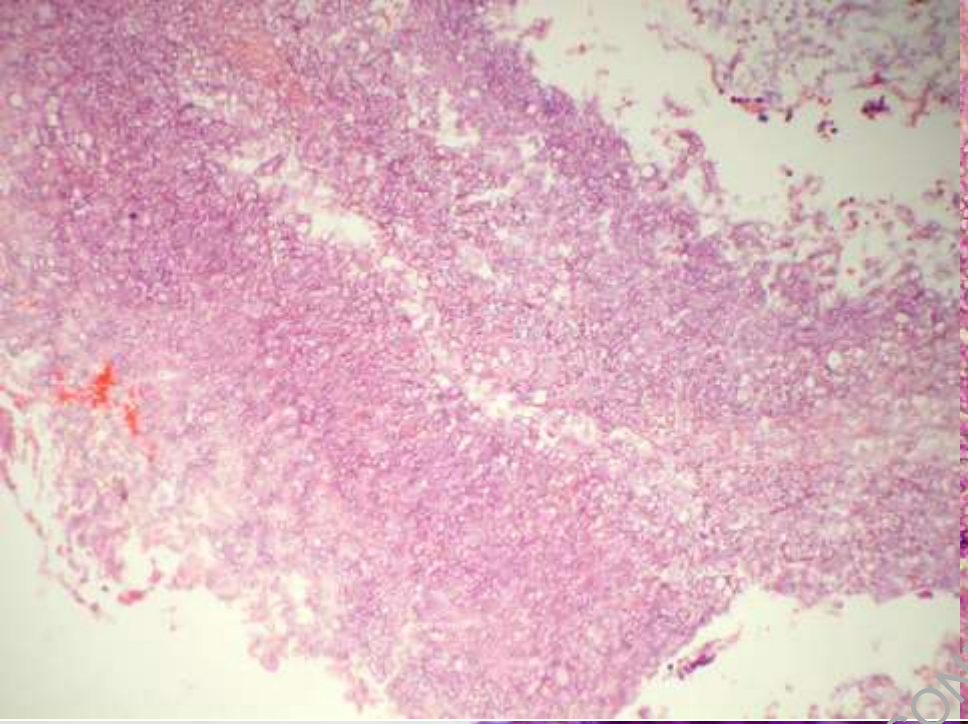
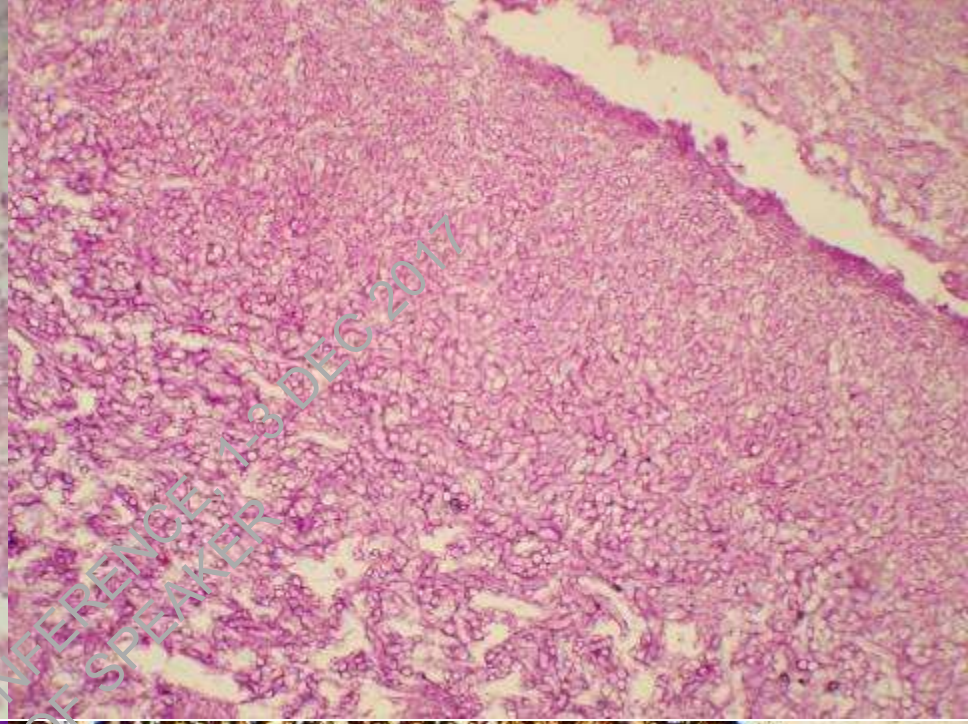
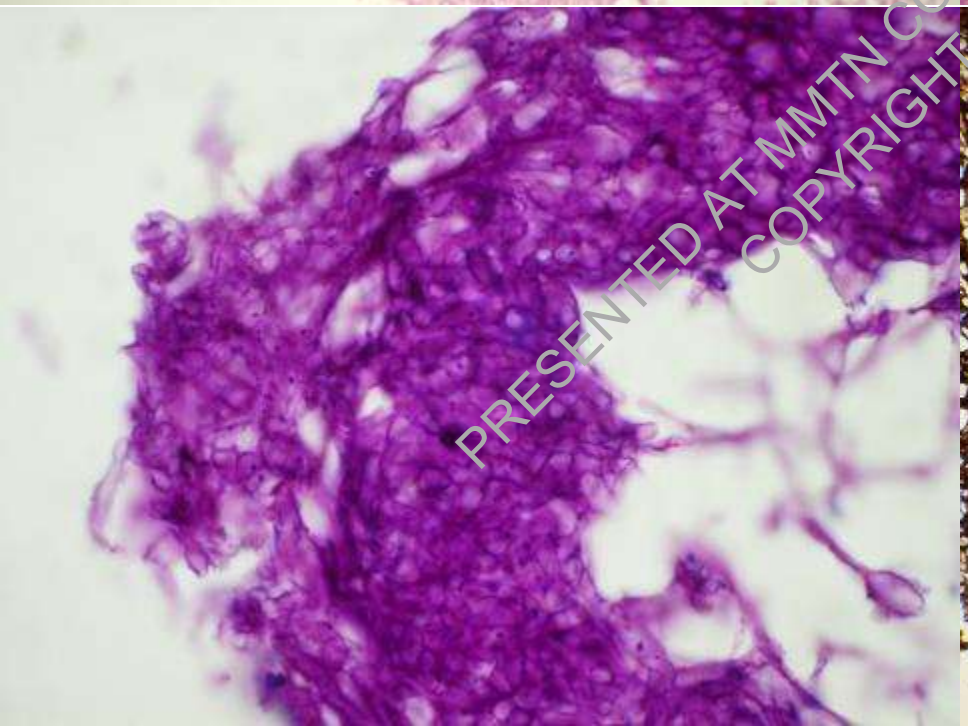
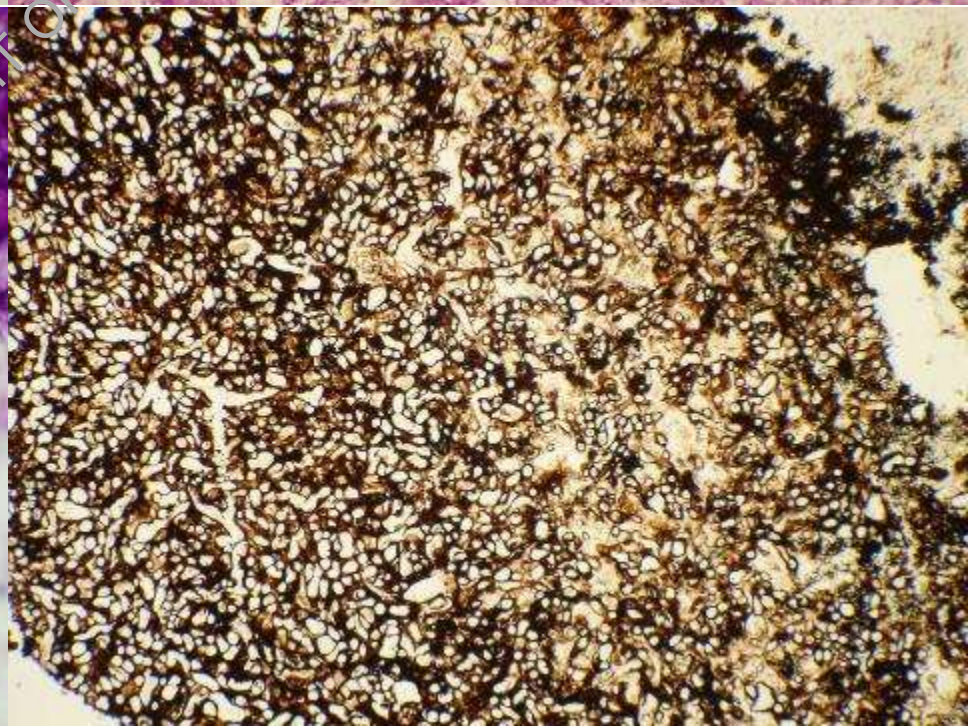
CFPA



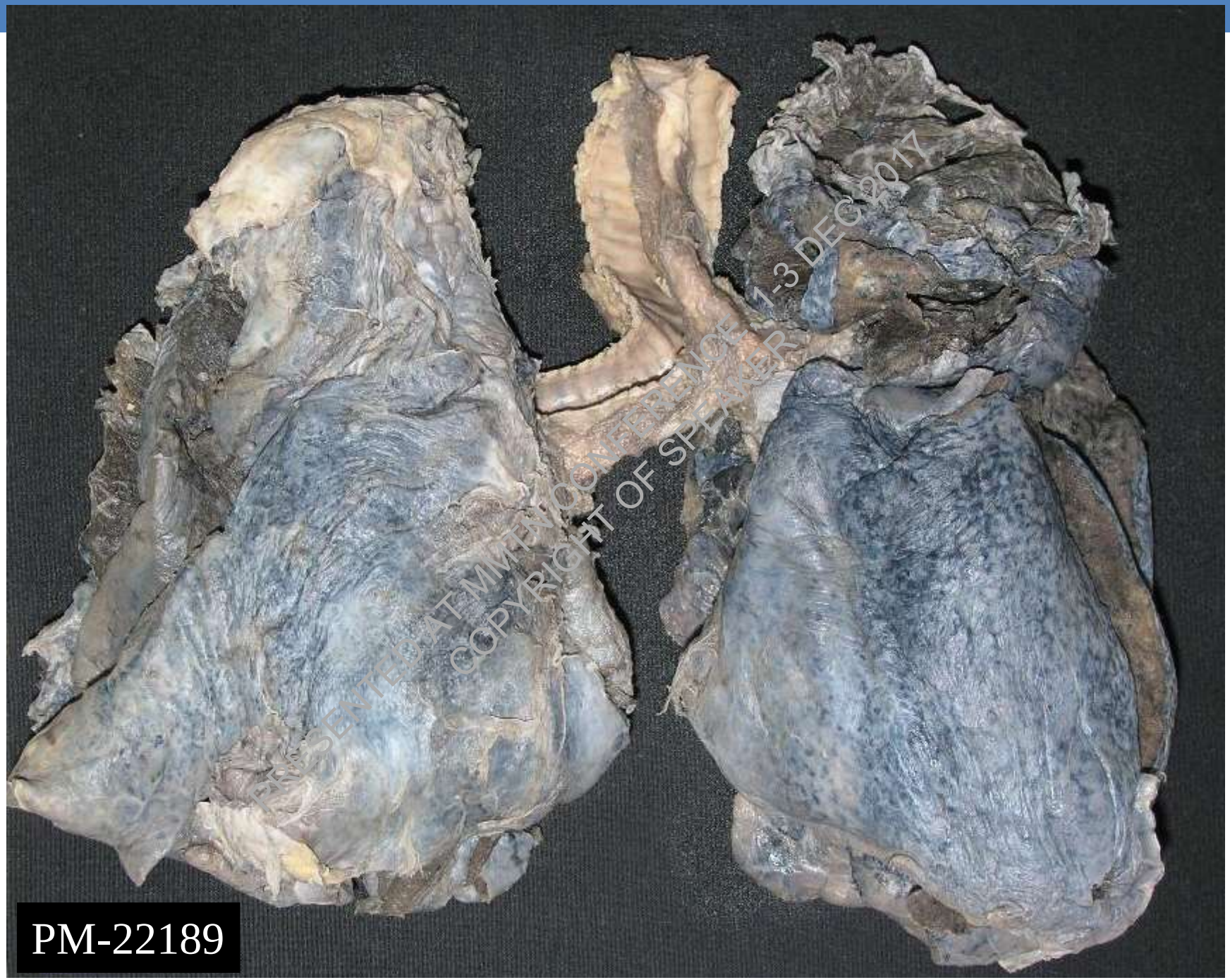
Sub-acute invasive aspergillosis

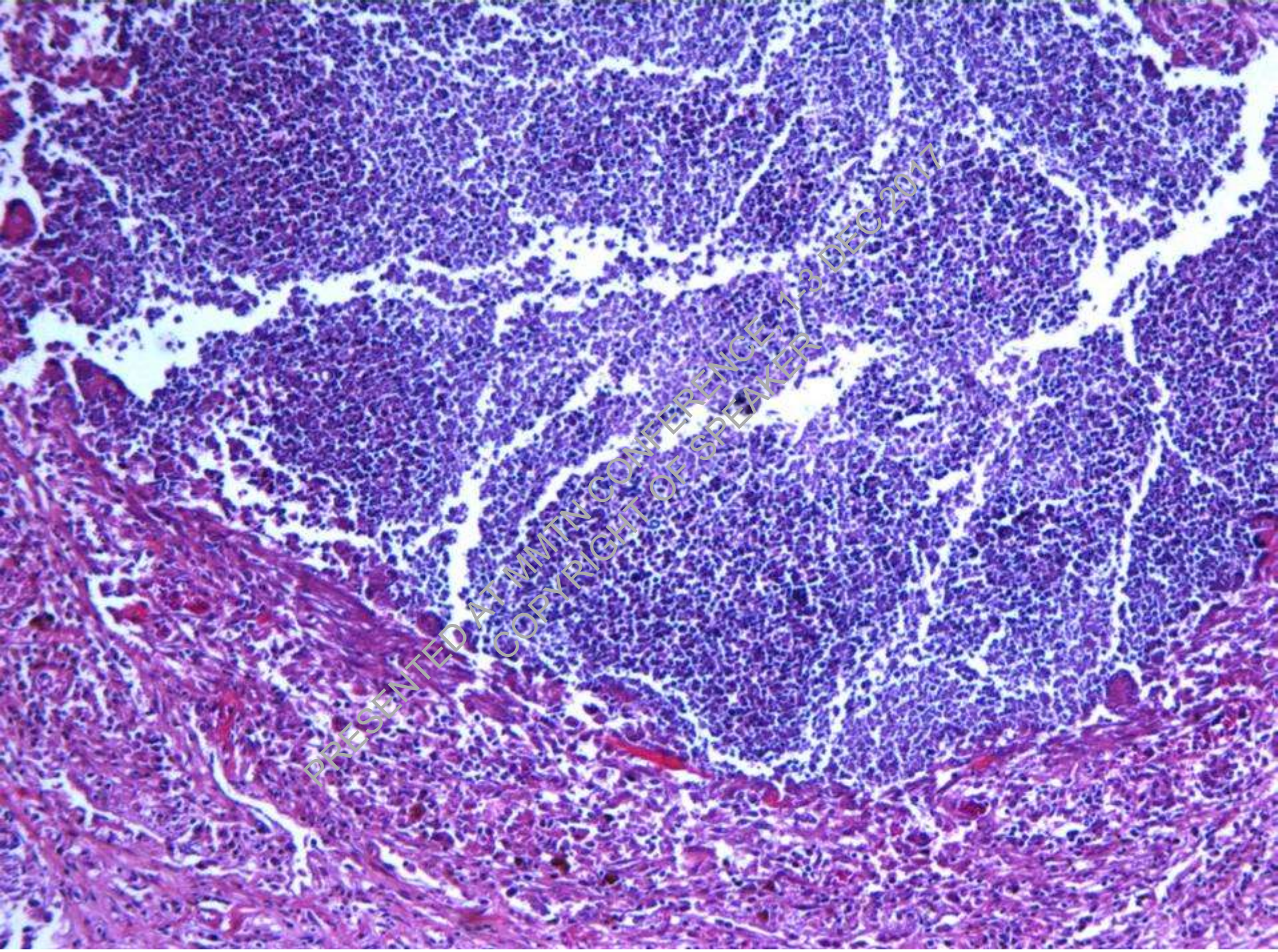
Aspergillus nodule

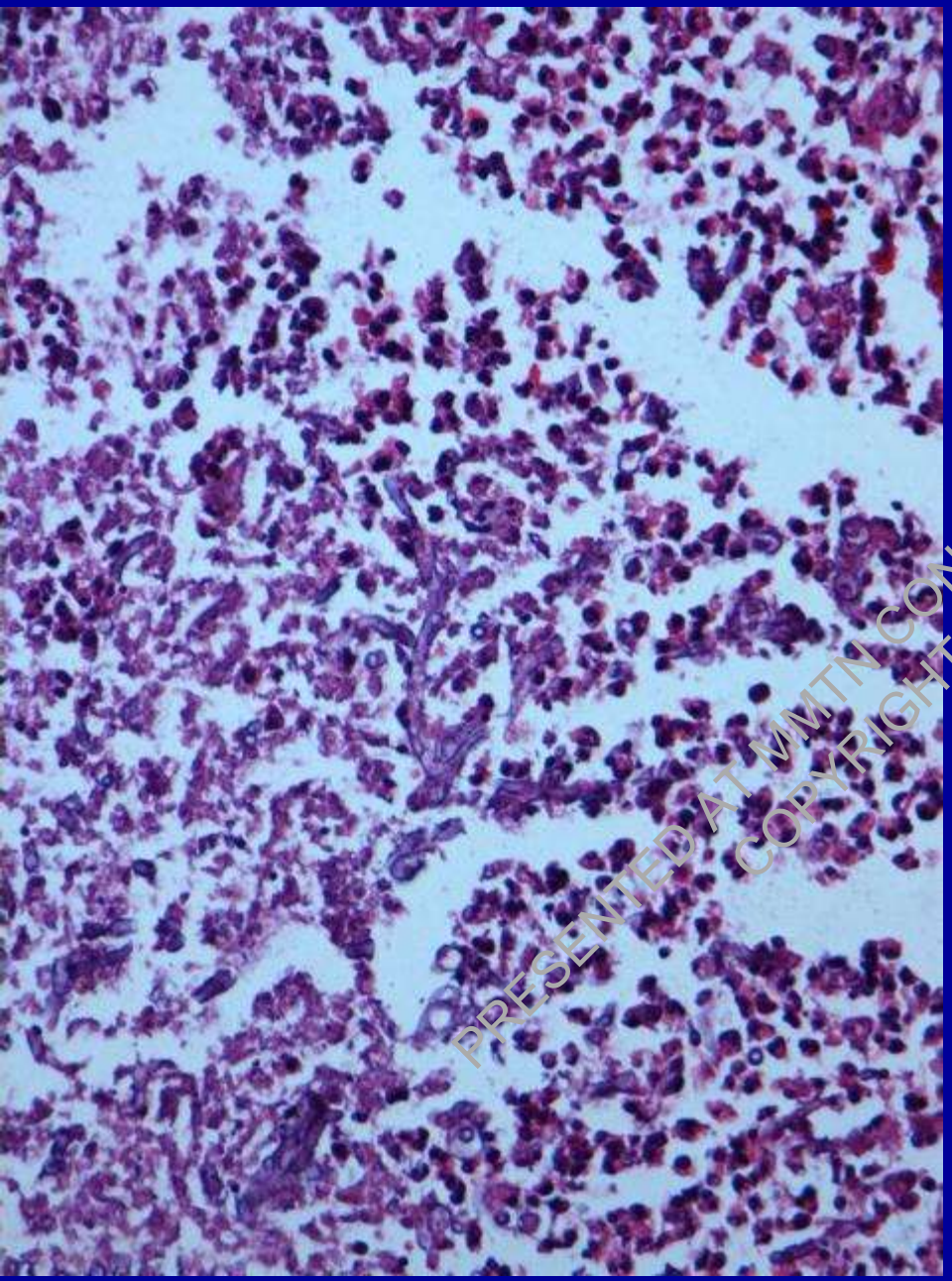
Aspergilloma

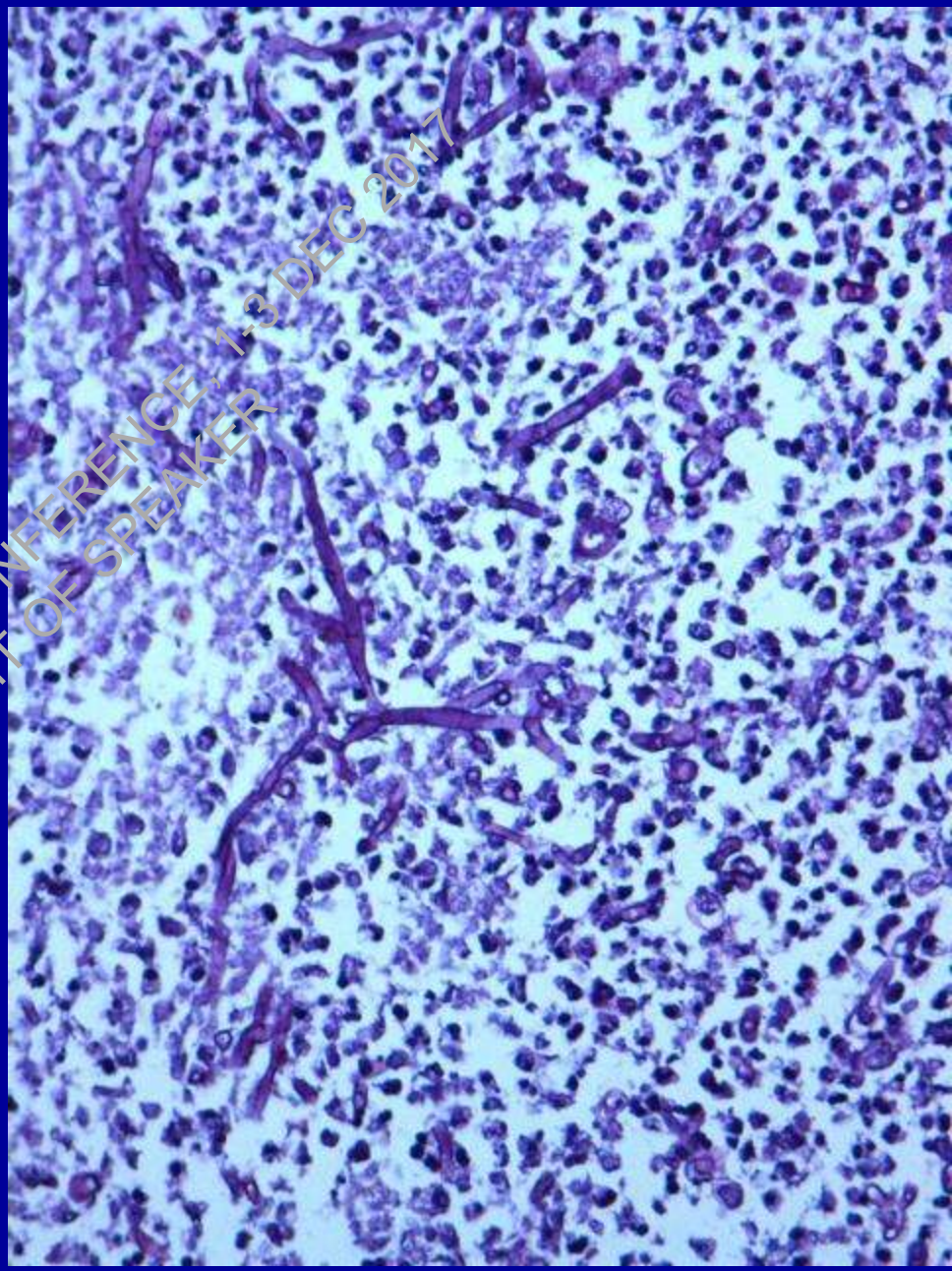





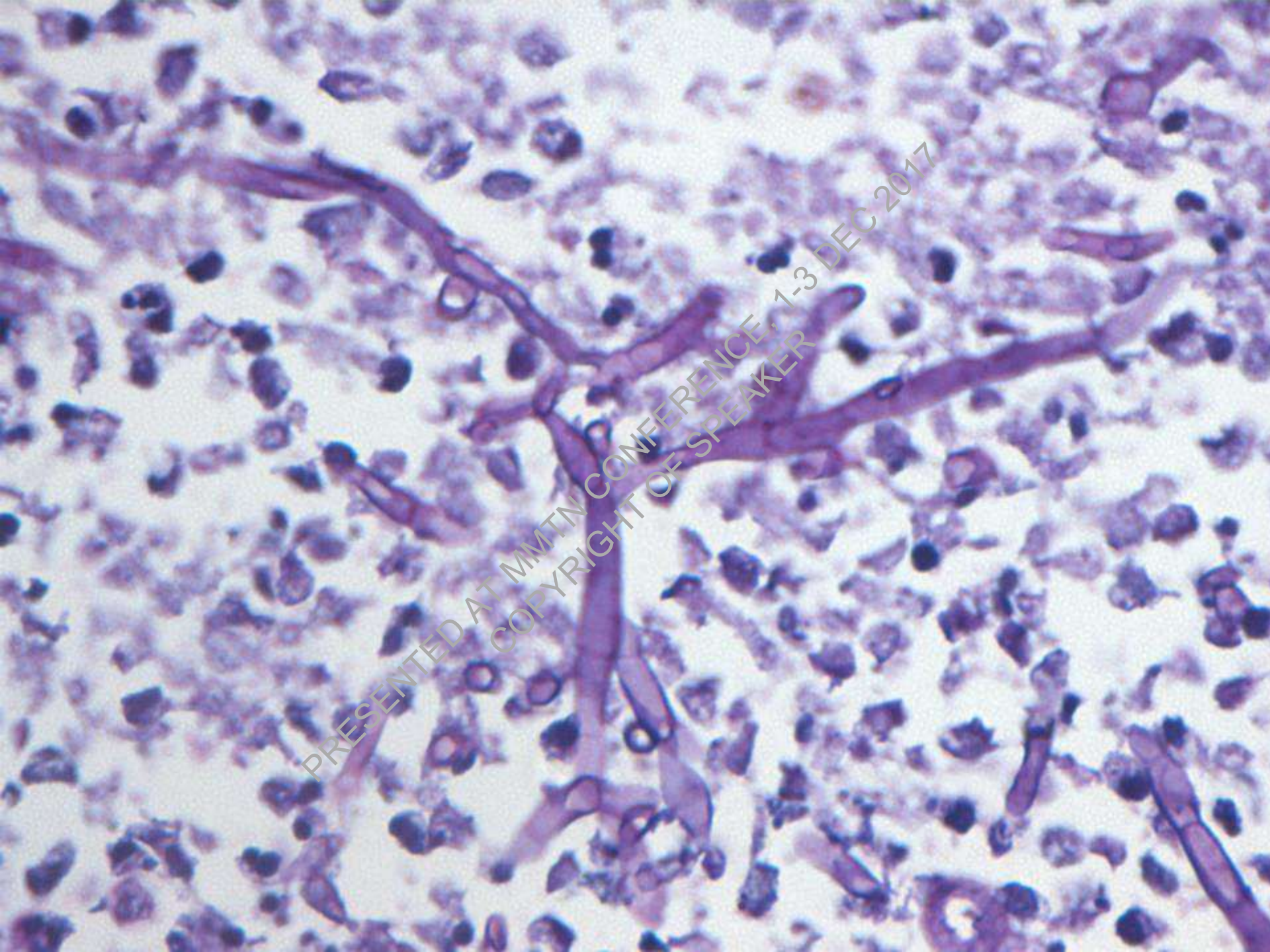
Chronic necrotizing pulmonary aspergillosis

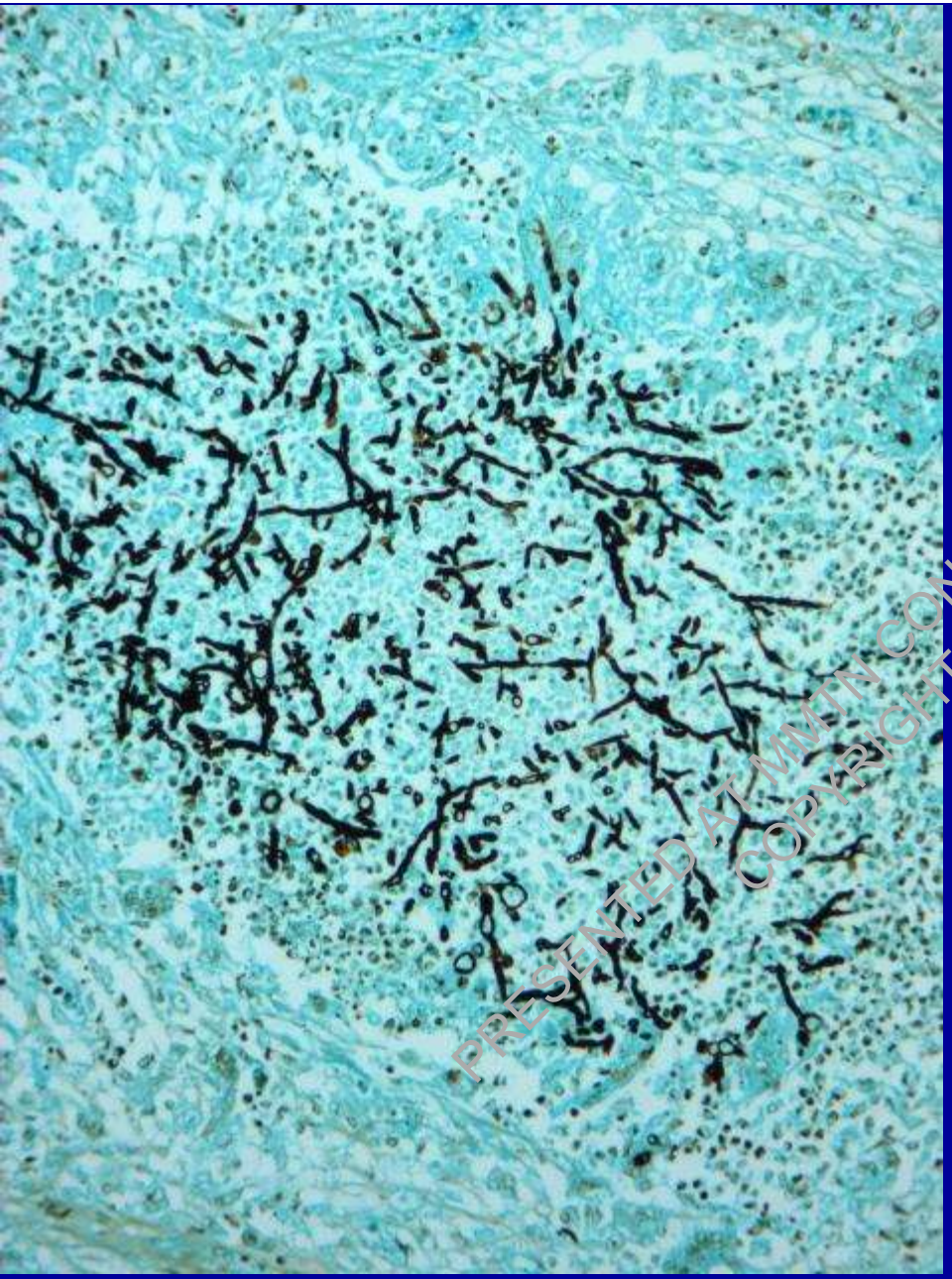


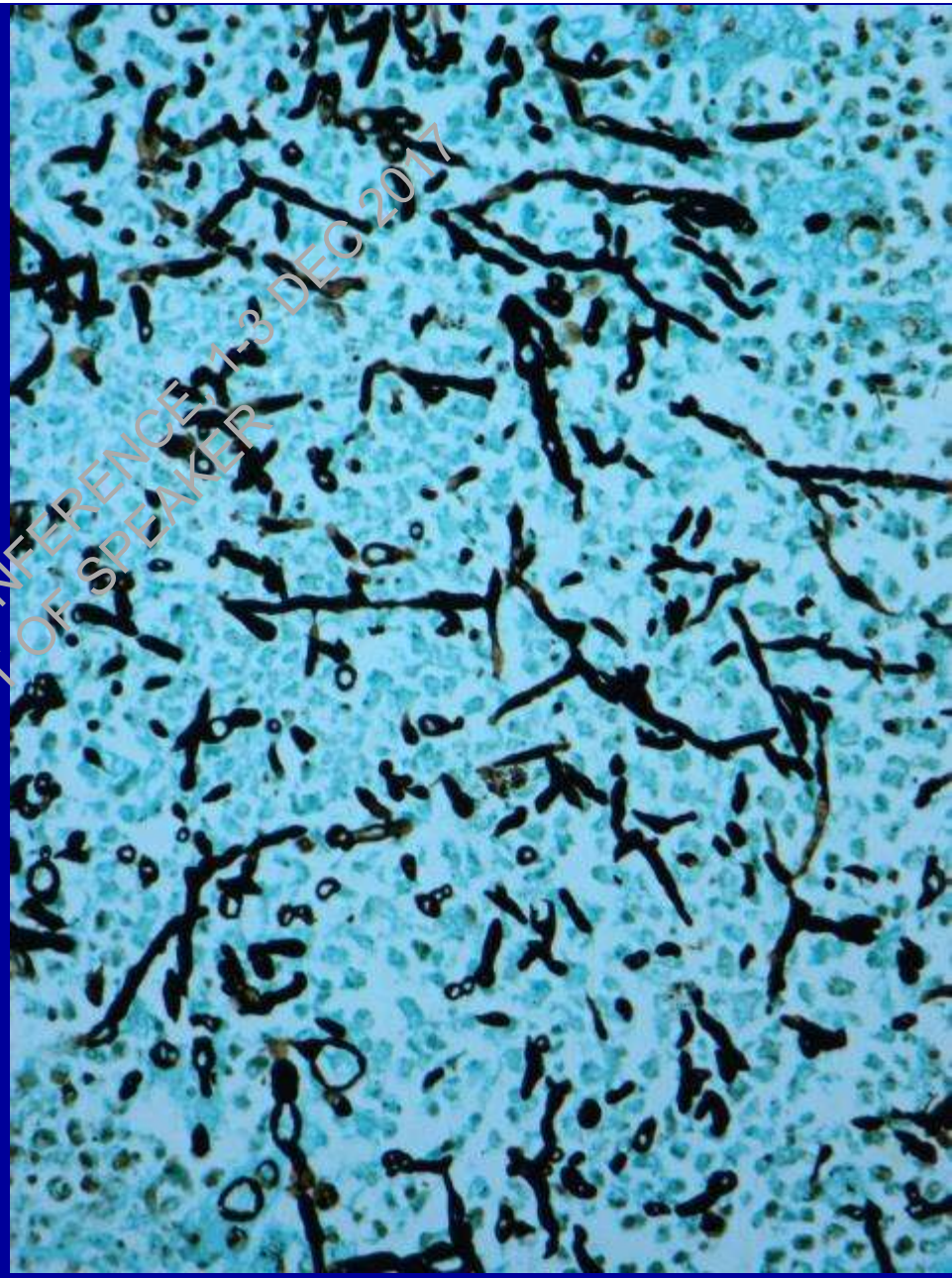








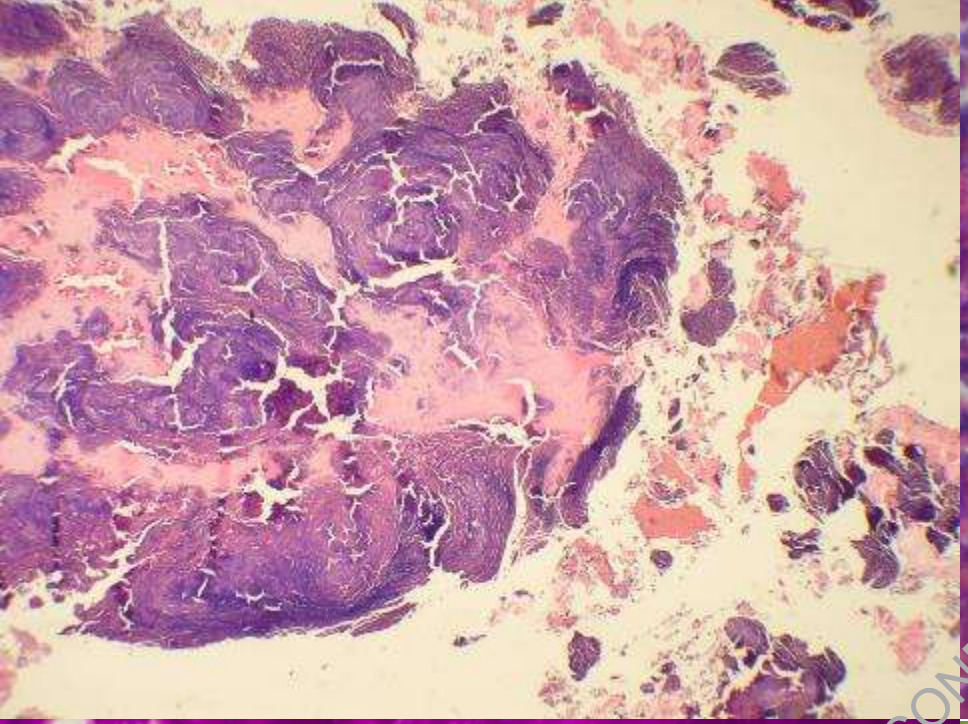


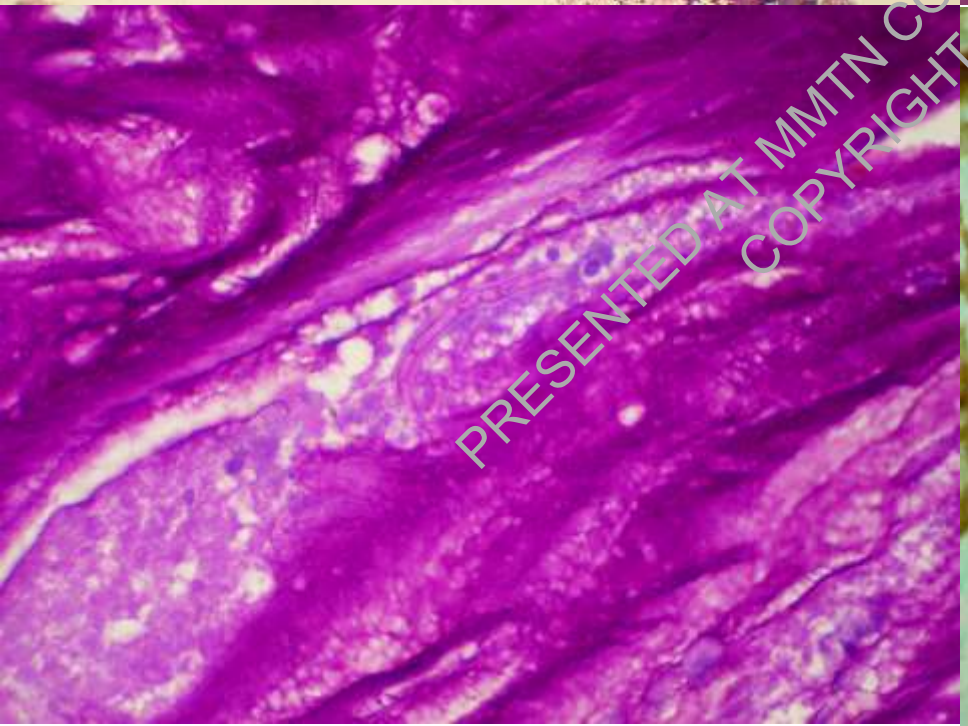


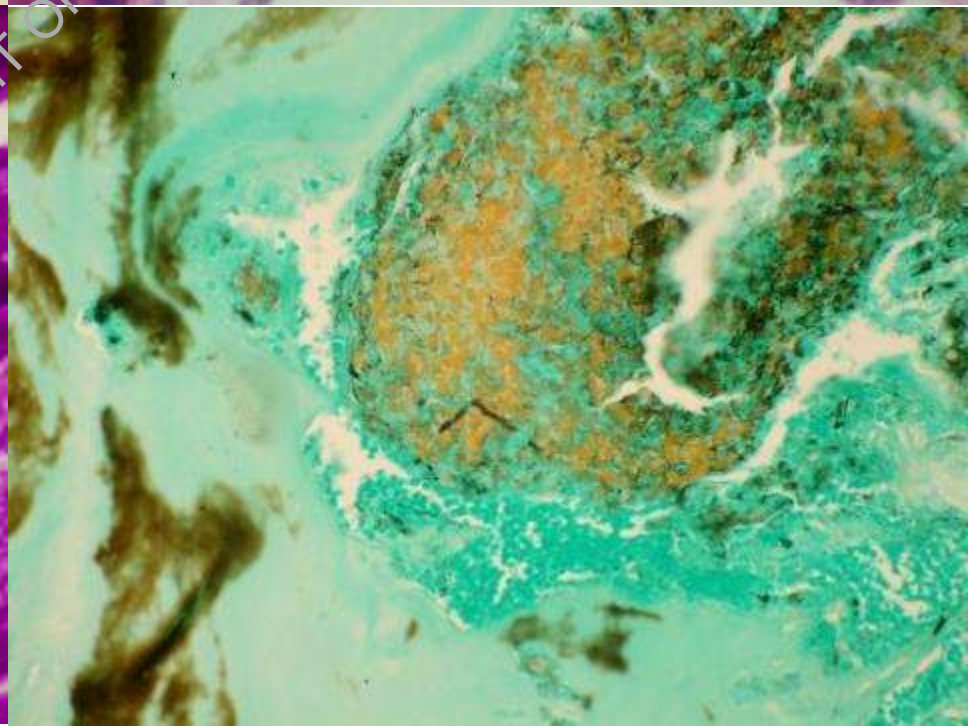
Allergic aspergillosis

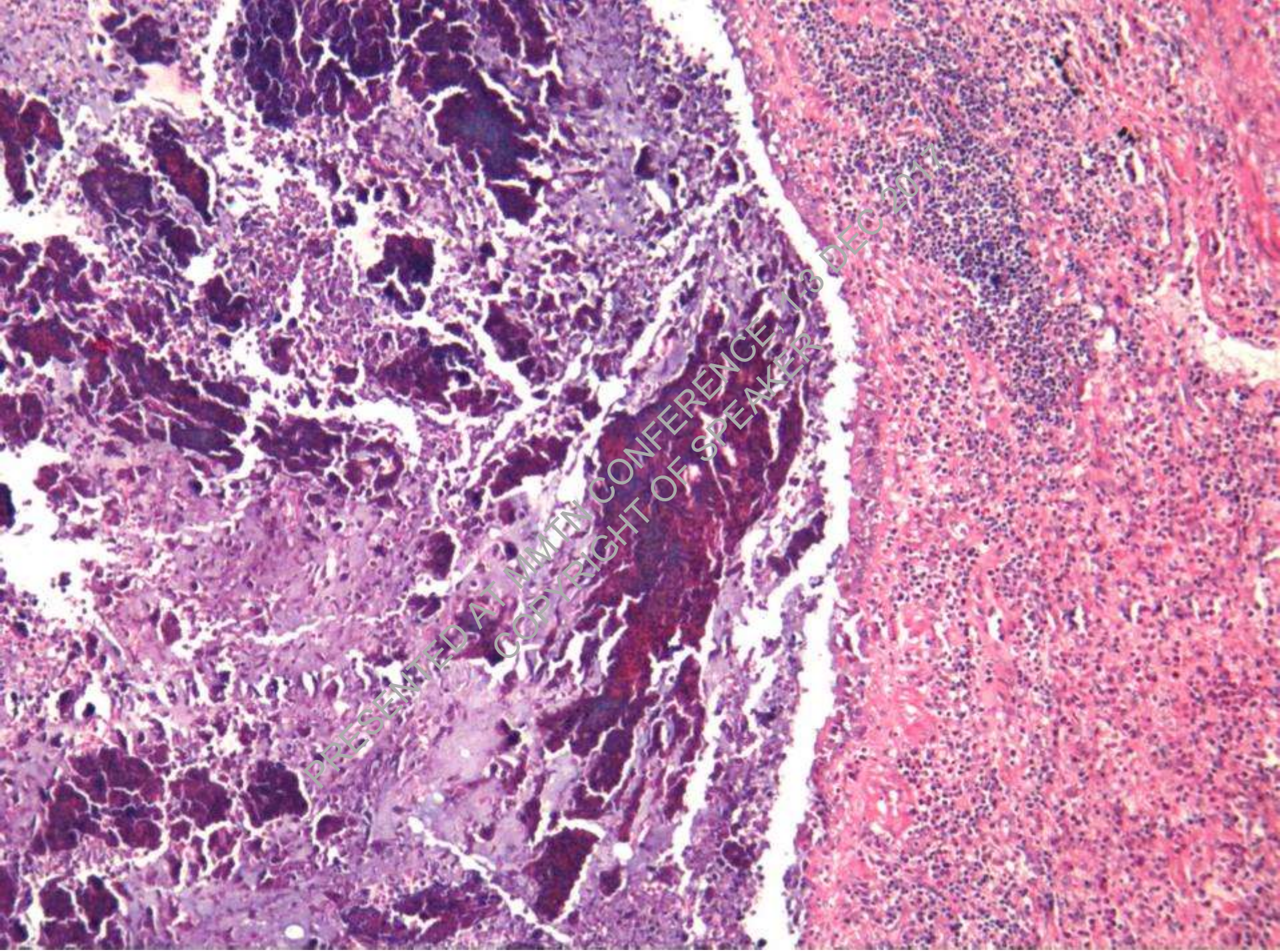
- allergic fungal rhinosinusitis

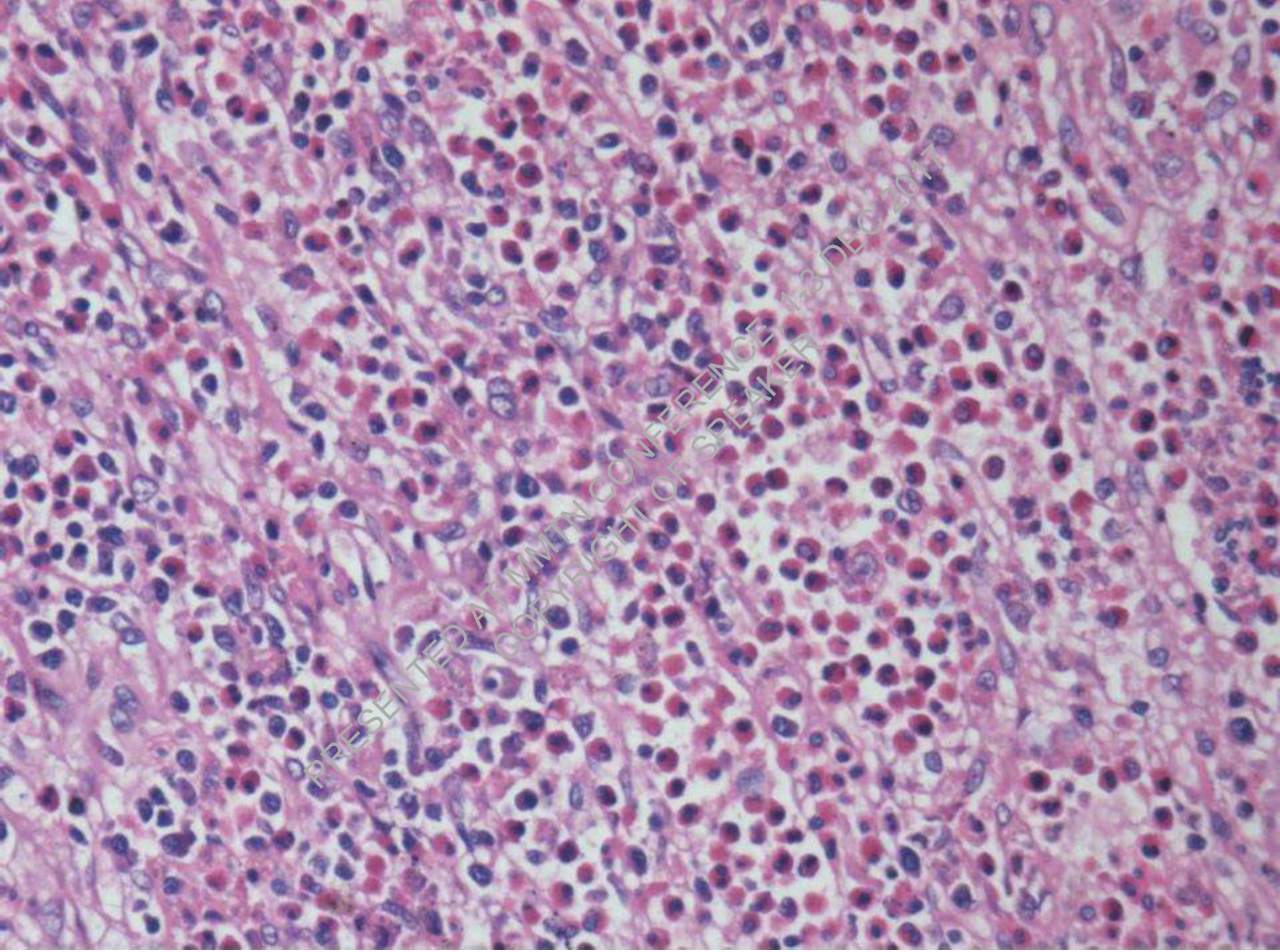
- allergic bronchopulmonary aspergillosis (ABPA)

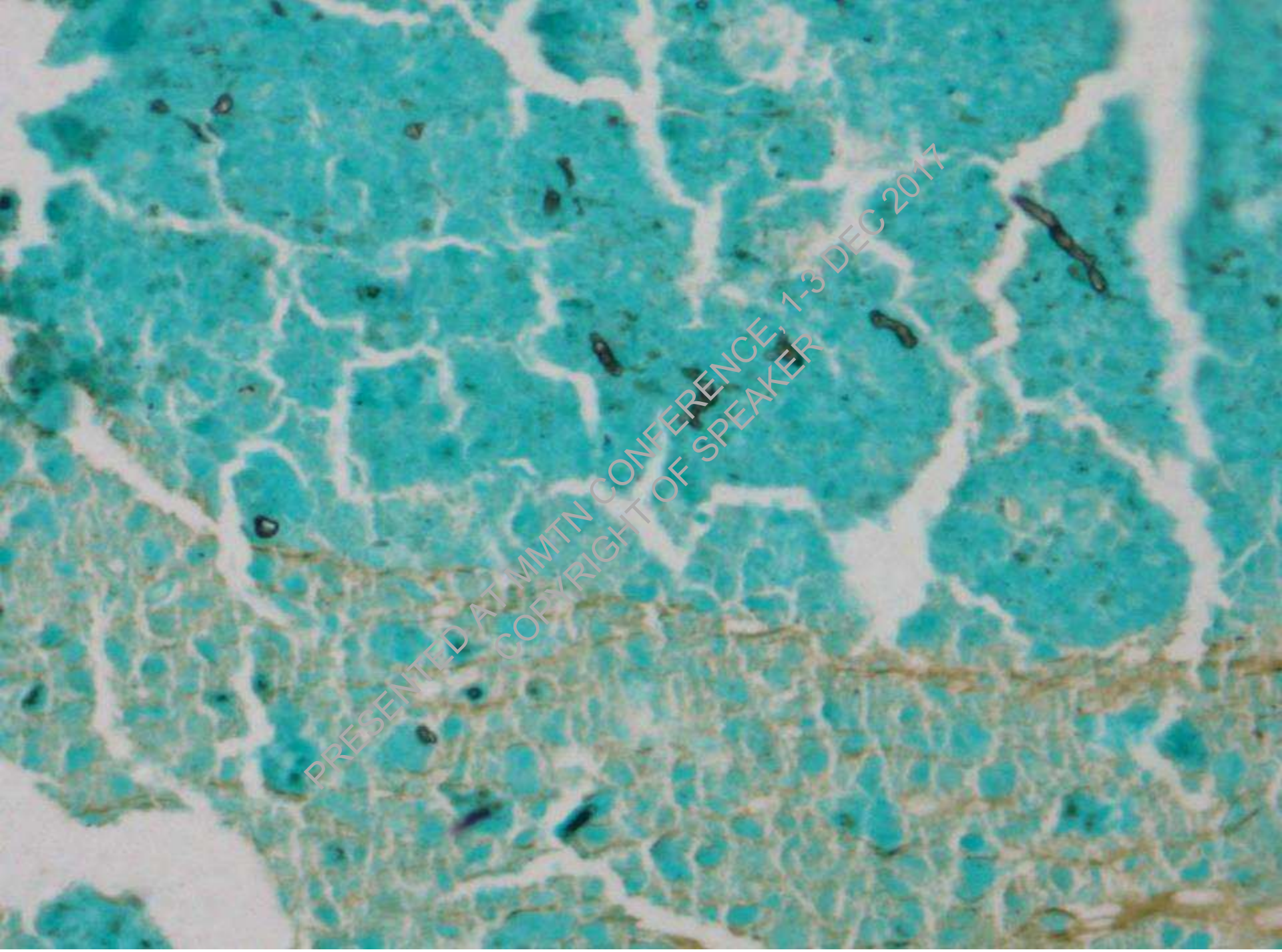




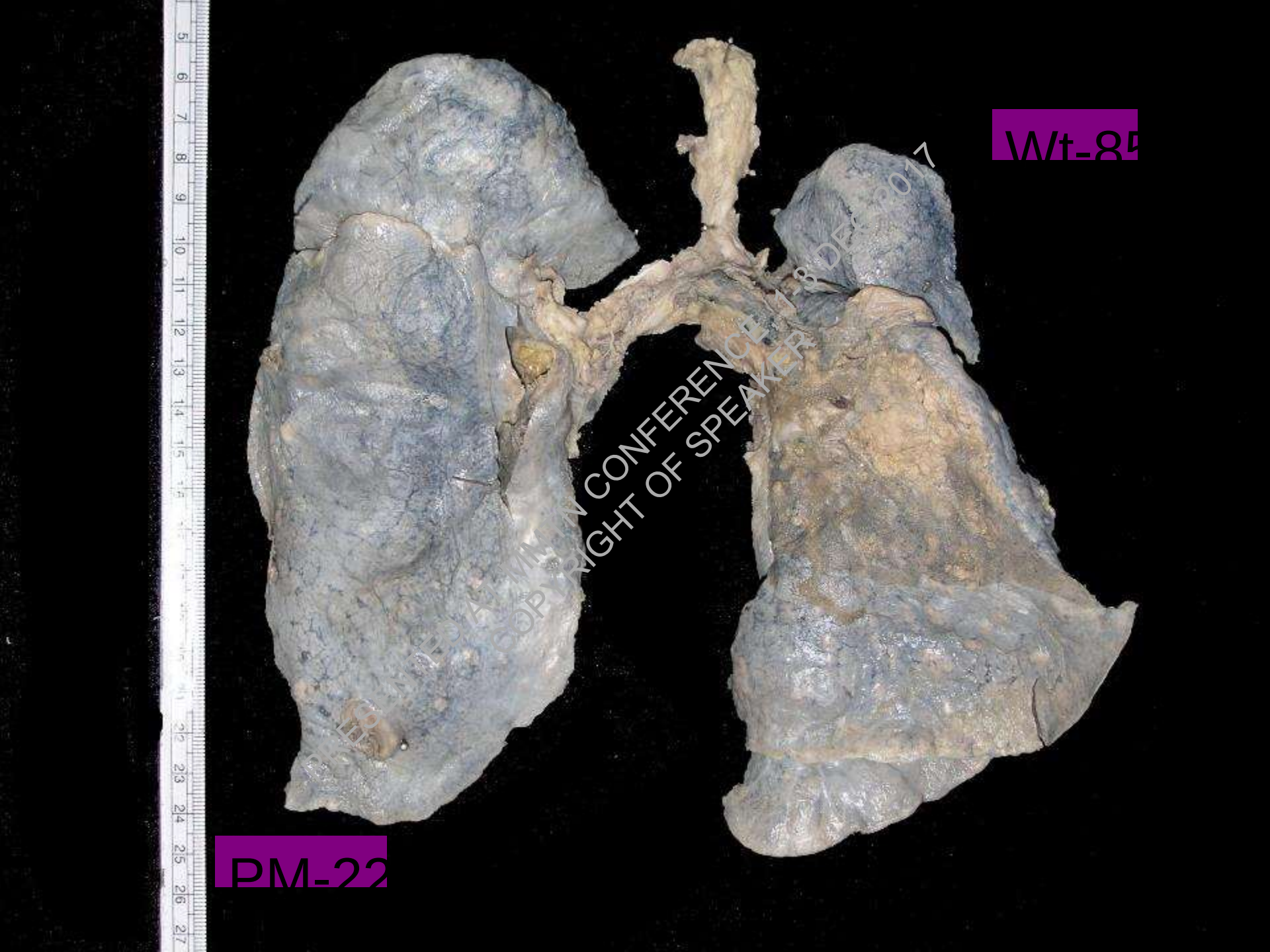








Pneumocystosis


Wt-85
PM-22
FILE NEONATAL MRI IN CONFERENCE 13 DEC 2017
COPYRIGHT OF SPEAKER