



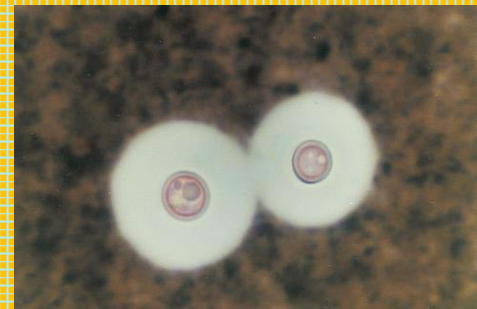
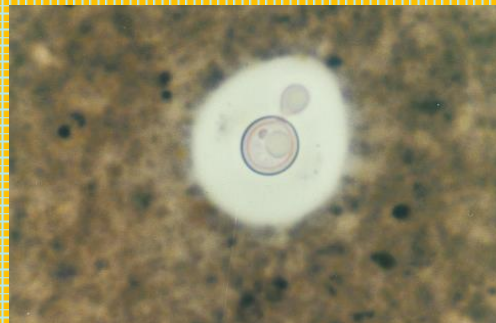
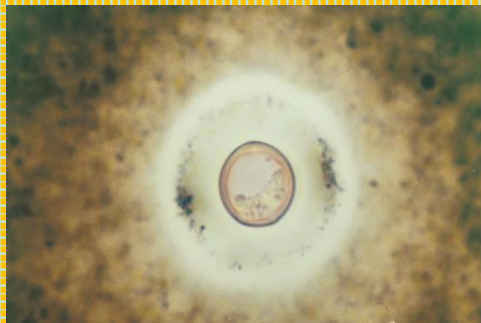
CRYPTOCOCCOSIS

Introduction

- A systemic mycotic disease caused by members of the genus *Cryptococcus*.
- Characterised by 'Cryptococcoma' in lungs and other organs
- **Synonyms** : Torulosis, Torula meningitis, European Blastomycosis, Busse-Buchke's disease

- **Sanfelice** isolated from peach juice
- **Busse and Buschke** isolated from tibail lesion
- **Von Hansemenn** presented first report of Cryptococcal meningitis
- An opportunistic pathogen as healthy humans have strong resistance to it and that frank infection occurs primarily in debilitated patients

- Asexual form is associated with human infection.
- Reproduces by budding.
- **Kwon-chung** named the sexual form as *Filobasidiella neofromans*.
- It is a Basidiomycete



Etiology

- *Cryptococcus neoformans* the major pathogenic member of this genus.

Kwon Chung <i>et al.</i> (1982) ¹	Franzot <i>et al.</i> (1999) ²	Boekhut <i>et al.</i> (2001) ³	Kwon Chung <i>et al.</i> (2002) ⁴ Currently Accepted
<i>C. n.</i> var. <i>neoformans</i> (serotypes A, D, AD)	<i>C. n.</i> var. <i>grubii</i> (serotype A)	<i>C. neoformans</i> (serotypes A, D, AD)	<i>C. n.</i> var. <i>grubii</i> (serotype A)
	<i>C. n.</i> var. <i>neoformans</i> (serotype D)		<i>C. n.</i> var. <i>neoformans</i> (serotype D)
<i>C. n.</i> var. <i>gattii</i> (serotypes B, C)	<i>C. n.</i> var. <i>gattii</i> (serotypes B, C)	<i>C. bacillissporus</i> (serotypes B, C)	<i>C. gattii</i> (serotypes B, C)

Epidemiology

- Widely distributed around the world
- Incidence has increased sharply since 1950 as the number of AIDS patients has increased
- One of the important pathogen in AIDS patient
- Others at risk are:
 - Prolonged steroid therapy
 - Organ transplantation
 - Malignancy
 - Immuno-suppressed



URBAN AREA

Cryptococcus neoformans

- Found in soil contaminated by bird droppings (Pigeons).
- Thrives on the nitrogenous compounds of avian guano
- Pigeons do not become infected. Inhibited by body temperature of $> 40^{\circ}\text{C}$.
- Serotype A: Worldwide esp. America
- Serotype D: European countries



Cryptococcus gattii

- Never cultured from bird guano
- Flowering -- river red gums (*Eucalyptus camaldulensis*) and forest red gums (*E. tereticornis*)
- Geographically restricted:
 - Australia, N. Africa and Mediterranean, SE Asia
 - Mexico, Brazil, Paraguay, California

In India

- Disease has been reported from almost all parts of the country.
- The annual incidence has increased 15 fold between 1970-82 and 1995-99 in Chandigarh.
- *C. neoformans* is predominantly found in clinical samples, while *C. gattii* infection has also been reported.
- Cryptococcosis occurs in ~ 3–30% of HIV patients.
-
- *C. neoformans* infection reported in immunocompetent adult male and females.

In animals

- Can occur in all animals as a rare sporadic disease
- Some epizootic outbreaks of mastitis and pneumonia have been described in cattle, Sheep and goat
- The disease also described in goats, horses, sheep, dogs, cats and primates
- Birds – disease rare, carry and shed in feces
- Koala bears in Australia.

Mode of transmission

- Man and animals acquire infection by inhaling the aerosolized yeast forms.
- In avian nesting areas the yeast cells possess minimal capsules and hence the cells dry and easily aerosolized and can be inhaled reaching up to the level of alveoli.
- Infections is always exogenous and not between animal to animal or animal to man or man to man.

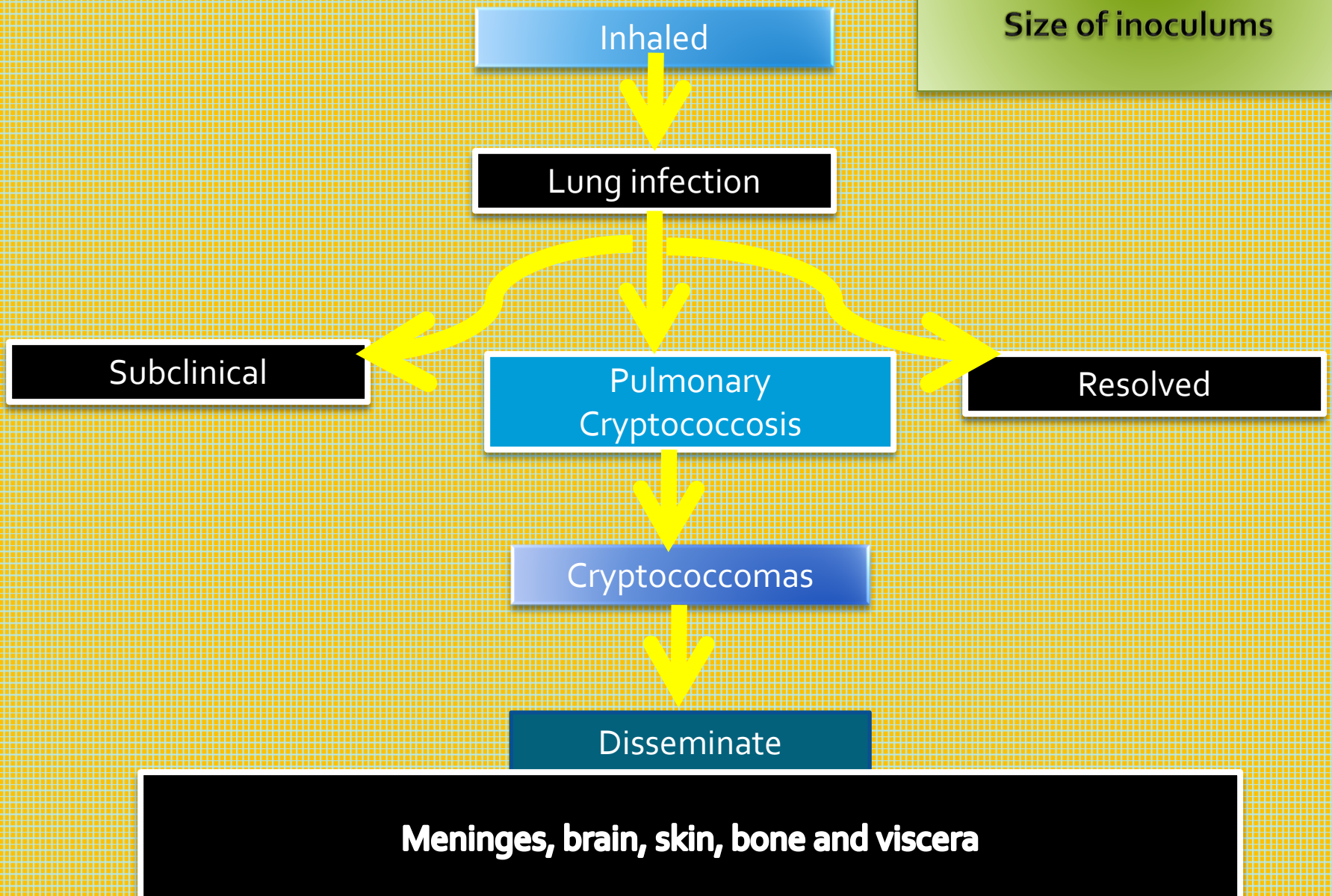
Virulence Factors

Capsule (CPS) – prevents effective opsonization, suppresses lymphocytes, survives within & toxic to macrophages, decreases inflammatory responses.

- **Phenol oxidase and melanin production** - antioxidant
- **Phospholipase and proteinases** – needed for invasion from respiratory tract into CNS

Pathogenesis

Determined by
Immune status of host
Virulence of the strain
Size of inoculums



- After dissemination infection localizes in the meninges, spreading to the brain.
- Characteristic lesion in the brain comprises of groups of fungal cysts without inflammation
- The obvious sign is headache and visual disturbances.
- Confusion, personality changes, agitation and lethargy.
- Meningoencephalitis is always fatal if not treated.

Clinical Manifestations

- Pulmonary cryptococcosis

- Asymptomatic carriage may occur in healthy people as well as those with chronic lung disease
- May experience a self limited pneumonia
- Invasive chronic pulmonary disease may occur

- CNS disease

- Meningitis (85%), meningoencephalitis, Cryptococcoma
- Generally symptoms more insidious .
- Higher burden of organisms in AIDS, with variable inflammatory response

- Cutaneous cryptococcosis

- Papule and abscess and subsequent ulceration
- Nodular lesions and Cellulitis



- Bone and joint disease

- Lytic lesions

- Ocular cryptococcosis

- Occurs in 45% of all patients with meningitis
- Manifested as ocular palsies to retinal involvement.
- Chances of visual loss.

- Genitourinary disease

- Prostate acts as a site of localization.
- There may not be prostatitis yet the yeast can be isolated
- Penile ulcers and vulvar lesion

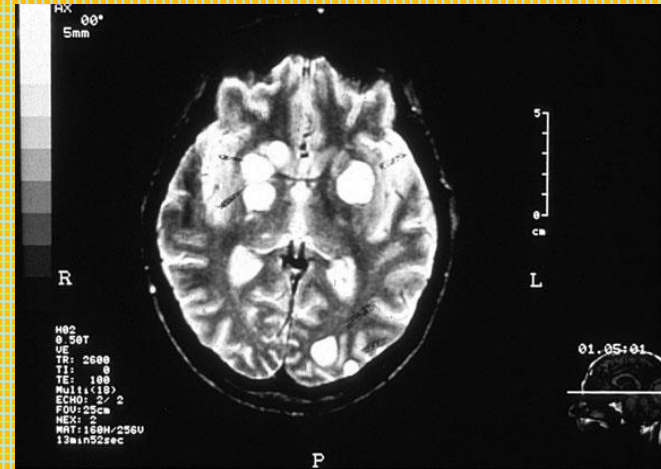
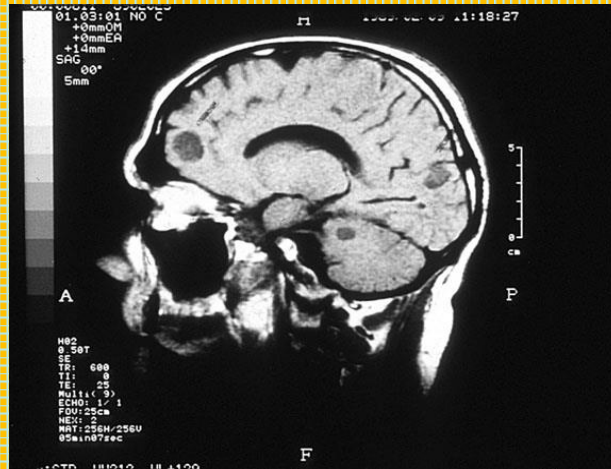
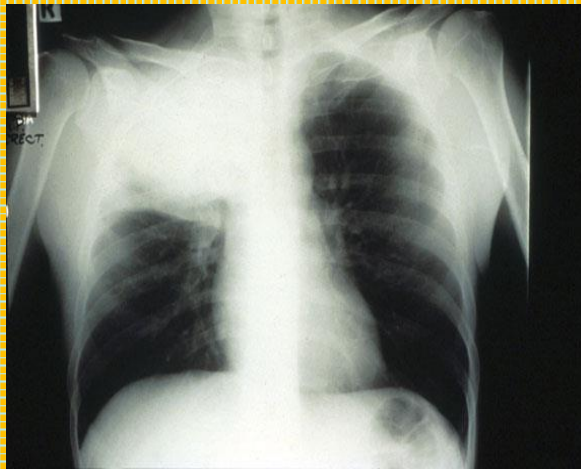


FIGURE 22.25

Cryptococcosis. A late disseminated case of cutaneous cryptococcosis in which fungal growth produces a gelatinous exudate. The texture is due to the capsules surrounding the yeast cells.

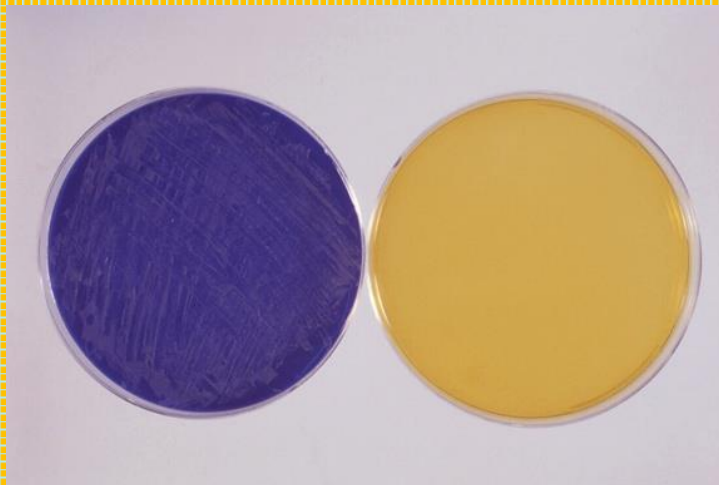
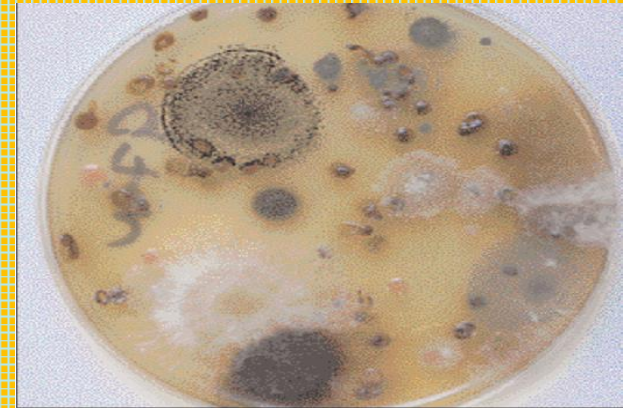
Diagnosis

- Direct microscopic examination
 - CSF, tissue, sputum and respiratory samples biopsies examined using India ink preparation
 - Tissues – mucicarmine staining.
- Radiology
 - Radiography , CT and magnetic resonance (MR) for menngitis.



• Culture

- Can be isolated in routine mycological media
- Supplemented with Cycloheximide.
- All are non-fermentative and produce urease
- *C. neoformans* can grow at 37° C
- And produce phenol oxidase (brown/ black pigment in bird seed agar)
- To differentiate growth on CGB agar.



CANAVANINE-GLYCINE-BROMOTHYMOL BLUE

C. neoformans (medium remains yellow) from *C. gattii* (medium turns a deep blue in 2-3 days)

- Serology

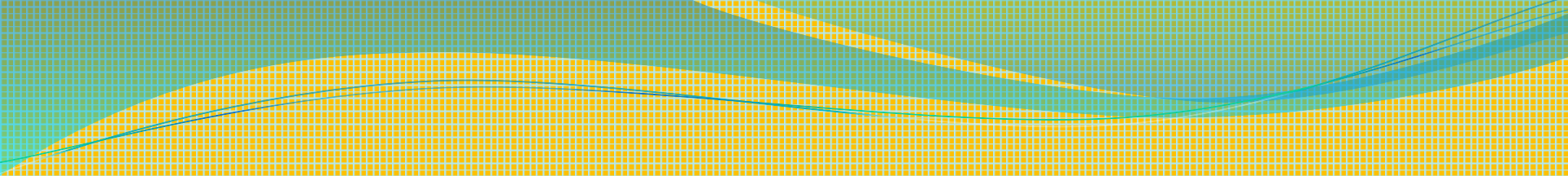
- Detection of CPS antigen using rabbit anti-*C. neoformans* antisera.
- Latex agglutination test (CSF, serum, urine)
- Enzyme immuno assay to detect Ag or Ab
- Ab --- not detected during active infection as CPS combines and inhibits its synthesis.

- Molecular detection

- Used to identify varieties, serotypes.
- Species specific primers developed.
- Strain identification by RFLP/RAPD analysis of genomic or mitochondrial DNA

Treatment

- The drugs of choice for treatment are Amphotericin B and Flucytosine in combination
- Fluconazole and itraconazole also used.



Thanks !!!