Invasive Mycoses: Current Trends & Challenges

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Mycoses

- Superficial/Deep/Systemic
- Localized/Spreading

Invasive Mycoses

- Endemic: exogenous agents
- Opportunistic: exogenous & endogenous
Increase in Cases of Invasive Mycoses Worldwide
Contributing Factors

- Increase in population at risk and longer survival:
  - Malignancies
  - Transplants
  - Extremes of age
  - Major surgery
  - HIV

- Increased exposure to endemic fungal infections:
  - Travel
  - Climate
  - Shifting population
Candidiasis

- Invasive candidiasis: >1996 to 2003 Europe, USA, Canada

- Candida species: Fourth leading cause of nosocomial blood stream infection (BSI)

- Temporal & geographical variation in species distribution, resistance

- M.A. Pfaller  D.J. Diekema  Epidemiology of invasive candidiasis: A persistent public health problem Clinical Microbiology Reviews 2007 20(1) 133–163
Invasive Mycoses: Impact

- Increasing demand for laboratory support
- Increase in use of antifungals
- Formulation of new and more effective antifungal agents
- Research & documentation
- Improved understanding of fungal pathogenesis
Increase in Types of Fungal Species Implicated
Opportunistic Mycoses: Etiology

Past
- Candida, Aspergillus, Cryptococcus
- *Pneumocystis jiroveci*

Current
- Additional, previously unrecognized opportunistic pathogens
- Yeasts, other than candida
- Nondematiaeous/hyaline molds
- Pigmented or dematiaceous molds
- Dermatophytes
Endemic Mycoses: Etiology

- *Histoplasma capsulatum*
- *Blastomyces dermatitidis*
- *Paracoccidioides brasiliensis*
- *Coccidioides immitis*
- *Penicillium marneffii*
Diagnosis of Fungal Infections

- Clinical examination
- Skin tests
- Radiology
- Histopathology
- Microbiology
- Serology
- Molecular & genetic methods
Diagnostic Mycology Service

Level & type of diagnostic service

- Assessment of institutional needs
- Assessment of type of practice & patient population

Antigen/Antibody Detection

- Systemic fungal infections: Beta D glucan
- Cryptococcus neoformans: antigen & antibody to capsular antigen
- Candida: antigen & antibody to mannan
- Aspergillus: Galactomannan
Molecular Methods

Sequencing

Identification of:
- Yeasts
- Filamentous fungi
- Dermatophytes

Detection of resistance genes
Yeast, yeast like fungus in tissue
- Blastomyces
- Cryptococcus
- Histoplasma
- Coccidioido immitis
- Candida

Hyphae in tissue
- Aspergillus, mucor fusarium
- Bipolaris/curvularia
- Dermatophytes
Histopathology: Current Techniques

- Histochemical staining
- Immunohistochemistry
- In situ hybridization
- PCR–Based Methods
- Laser based micro dissection

Radiological diagnosis

Advances in diagnostic & treatment radiology

Greater ability to collect tissue biopsy material for laboratory investigation.
Increase in Number and Use of Antifungal Agents
Antifungal agents

- Allylamines: Terbinafinedine
- Antimetabolites: Flucytosine
- Azoles: Clotrimazole, Fluconazole, Ketoconazole, Itraconazole, Voriconazole
- Echinocandins
- Polyenes: Amphotericin B, Nystatin
- Others: Griseofulvin, Tolnaftate, etc.
Antifungal Sensitivity Testing

- Recently developed & standardized
- Performed in referral centres & special laboratories
- Expensive
- Not routine in small labs

How do doctors select antifungal agents for treatment?
Empirical Antifungals

Early treatment:
Better prognosis, chance of recovery

Improved diagnostic techniques
- Rapid, accurate diagnosis
- Antifungal sensitivity testing
- Need for empirical antifungal therapy?


Management of fungal infections: The way forward
Role of Laboratory

- Mycology consultation service
- Advice on antifungal therapy
- Rapid, accurate diagnosis
- Team Work
- Follow up on outcome
- Research & training
Role of Clinician

- Utilization of new diagnostic tools
- Communication with laboratory staff
- Development of consensus guidelines
- Implementation of the above
Improved Understanding of Fungal Pathogenesis
Fungal Vaccines?

- Limitations of antifungal therapy
- Resistance of emerging fungal pathogens to existing agents
- Difficulty in rapid and accurate diagnosis

Antonio Cassone  Fungal Vaccines: Real progress from real challenges Lancet Infectious Disease 2008; 8: 114–124
References

- John R. Perfect Fungal Diagnosis: how do we do it and can we do it better Current Medical Research and Opinion 2013 29(4) 3–11
- M.A.Pfaller D.J. Diekema Epidemiology of invasive candidiasis: A persistent public health problem Clinical Microbiology Reviews 2007 20(1) 133–163
- Antonio Cassone Fungal Vaccines: real progress from real challenges Lancet Infectious Disease 2008; 8: 114–124