Distance Learning and CME

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Associate Director, Division of Infectious Disease,
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Therapeutics,
Harvard University-Massachusetts Institute of Technology,
Division of Health Sciences & Technology
“Knowing is not enough, we must apply; willing is not enough, we must do.”

- Goethe
Medical Education: a lifelong obligation and privilege

• The pace of medical advances and basic science discoveries has never been greater.
• Traditional education initiatives are threatened
  – Cost
  – Conflict of interest concerns
  – Accountability
• The appearance of new diseases – from AIDS to SARS – and the difficulty in treating age-old pathogens like influenza and cholera remind us that we must think globally.
Wish List for Innovative Medical Education Efforts

• Broadly available ("a worldwide network")
• Can be accessed with available technology
• Can be utilized for a variety of purposes
  – “Primary learning” for students, trainees, (alternative or supplement to traditional lectures, journals, textbooks)
  – Continuing education for practitioners
  – Creation of networks of clinicians, researchers, and scholars that will share problems, ideas, and insights
  – Task forces for particular goals
    • Ethics
    • IRB and DSMB approaches
  – Rapid response needs
Requirements for Innovative Learning

- Interactive
- Self assessment
- Certification
- Deficits → special education
- Creation of communities of scholars, linked by distance learning approaches, and not limited by geographic barriers
Our Experience

• History of GCP project (cooperative effort – Silva, Rodriguez, and Rubin)
  – CITP program (produce clinical scientists)
  – CME efforts in Latin America
  – Distance learning experience
    • English, Spanish, Mandarin

• Approach to clinical problems
  – State of the art lectures
  – Annotated bibliography
  – Case studies (interactive)
  – E-conference room
This web course is made possible through an unrestricted educational grant from Roche Laboratories.
Welcome to this free Internet course on the diagnosis and treatment of Transplant Infectious Diseases.

Explore this online course module to discover the latest findings in the field:

- View video lectures given by world-renowned experts
- Work through interactive case studies to test your knowledge and patient management skills
- Browse our extensive Reference Library
- Receive consultation from field experts and exchange ideas in our eConference Room
- Earn CME credit

To begin, please register or go to the About page to learn more about the site.

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Welcome Melinda

The Study Guide will automatically track your progress through the case studies and lectures. Completion of all case studies is required for e-conference room membership. Lectures are not required for membership, but are highly recommended.

Key:   □ Not yet started  ☑ In-progress  ☑ Completed

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**IDT Lecture Index**

Our distinguished faculty review the essential principles of transplant infectious disease, concentrating on the latest approaches to diagnosis and treatment. Each lecture is closed captioned and divided into segments for convenient viewing and greater accessibility to specific topics of interest.

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**Software Requirements:** In order to view our lectures, you must have Flash version 6 or higher installed. Please install Flash by clicking on the install button or click help for more options.

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<td>This lecture offers an overview of organ transplantation and the infectious disease challenges facing the transplant recipient. Discussed in detail are patterns of illness (timetable of infection), the relation between the net state of immunosuppression and epidemiologic exposures in the causation of infection, and the most effective methods for preventing and treating infection. The concept of the therapeutic prescription (immunosuppressive and antimicrobial therapy) is emphasized.</td>
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## Case Studies:

Covering the major challenges faced in transplantation today, each case guides you through a real patient scenario, allowing you the opportunity to make decisions at critical junctures. To aid in your decisions, new information will be presented as you work through the case.

### Key:
- □ Not yet started
- ✗ In-progress
- ✔ Completed

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<td>Fever and Deteriorating Liver Function Tests 34 Days After Orthotopic Liver Transplant:</td>
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<td>Aspergillus respiratory tract colonization in a patient who had undergone bilateral lung transplantation:</td>
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<td>Recurrent Fever in a Liver Transplant Recipient: Author: Atul Humar, MD</td>
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<td>19 year old Woman with Fever and Malaise 111 Days Post-transplant:</td>
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Aspergillus respiratory tract colonization in a patient who had undergone bilateral lung transplantation

PRESENTING CONDITION

A 32 y.o. woman with cystic fibrosis underwent bilateral lung transplantation. Pre-transplant sputum cultures yielded three separate strains of Pseudomonas aeruginosa, each one resistant to either aminoglycosides or anti-pseudomonal beta-lactams. Perioperatively, she received imipenem, a lipid amphotericin formulation, and intravenous ganciclovir. Her immunosuppression consisted of tacrolimus 6 mg twice daily, prednisone 15 mg/day and mycophenolate 2 grams per day. After an initially stormy course (re-implantation reperfusion injury with prolonged intubation), the patient by the 4th week post-transplant was doing well. Routine surveillance bronchoscopy and sputum culture yielded Aspergillus fumigatus. Chest X-ray and CT were without evidence of invasive fungal infection.

Question: What is the significance of the finding of Aspergillus fumigatus in the sputum of this patient?

Possible Answers:

a. [ ] Aspergillus species are frequent contaminants of sputum cultures, and have no significance in this setting.

b. [ ] Aspergillus in the sputum is a marker for an abnormal bronchial tree, particularly for chronic bronchitis and bronchiectasis, but is of little significance in terms of invasive disease.

c. [ ] A variety of clinical syndromes can be associated with the isolation of Aspergillus species in the sputum, each of which requires different management.

d. [ ] The finding of Aspergillus species in the sputum of an immunosuppressed patient with evidence of acute or subacute pulmonary disease should be regarded as significant.

e. [ ] Aspergillus colonization of the respiratory tract in transplant recipients is associated with an increased risk of invasive pulmonary disease.
Aspergillus respiratory tract colonization in a patient who had undergone bilateral lung transplantation

Go Back to the Beginning and Start Over

Aspergillus species are frequent contaminants of sputum cultures, and have no significance in this setting.

Incorrect. Although this statement has been made in the microbiology literature, it applies only to certain groups of patients. Patients with chronic lung disease, particularly those individuals with bronchiectasis and/or cavity formation, may indeed have colonization with Aspergillus species without evidence of invasive infection clinically. However, in a patient with a clinically compatible syndrome and x-ray, who is immunosuppressed, the isolation of Aspergillus species on sputum culture should be taken very seriously, with the expectation that invasive disease requiring treatment is present.

TRY AGAIN

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Aspergillus respiratory tract colonization in a patient who had undergone bilateral lung transplantation

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Aspergillus respiratory tract colonization in a patient who had undergone bilateral lung transplantation

A variety of clinical syndromes can be associated with the isolation of Aspergillus species in the sputum, each of which requires different management.

Correct. The clinical effects of Aspergillus species can be divided into five different categories:

1. **Colonization syndromes**: Aspergillus can colonize an abnormal bronchial tree and/or preexisting cavities- most commonly bronchiectasis and/or old tuberculosis. The usual effects of this are irritative- hemoptysis, increased sputum production, and cough.

2. **Allergic Syndromes**: Aspergillus can induce asthma, and can be a cause of hypersensitivity pneumonitis or extrinsic alveolitis. In this case, it is the host's response to organic antigens.

3. **Allergic Bronchopulmonary Aspergillosis**: This syndrome can be considered as being a combination of a colonization and an allergic syndrome. These patients have a functional defect in the bronchial tree such that colonization is maintained. The consequence of this is cough productive of sputum containing brown bits of Aspergillus, with fleeting infiltrates on chest x-ray and eosinophilia. The end result of untreated disease is central bronchiectasis.

4. **Invasive Aspergillosis**: Invasive aspergillosis is an angiovascual infection with three cardinal manifestations: infarction, hemorrhage, and metastases. *A. fumigatus* and, to a lesser extent, *A. flavus* account for the great majority of such infections, with the lungs being the primary portal of entry. Other primary sites of invasion include the nasal sinuses, and damaged skin. Invasive aspergillosis occurs in patients with severe neutropenia and/or impaired cell mediated immunity.

5. **Semi invasive Aspergillosis**: This is a slowly progressive, necrotizing infection seen in patients without clear cut immune deficits, but with such systemic conditions as diabetes, liver disease, systemic viral infection, etc. It is best treated with surgical excision.

In addition, there is the possibility of crossover syndromes. For example, 80% of patients with bronchopulmonary aspergillosis (#3 above) become symptom free and clear the Aspergillus on steroids; those that do not may develop invasive disease. Aspergillomas in a cavity may have some degree of local invasion, which can become clinically important if surgical manipulation is undertaken or if immunosuppression occurs. The advent of azole therapy for invasive aspergillosis, particularly voriconazole has permitted early and aggressive therapy (preemptive therapy) to prevent disseminated infection.
Aspergillus respiratory tract colonization in a patient who had undergone bilateral lung transplantation

**Main learning points for this case:**

**Clinical Course:** The patient was treated preemptively with voriconazole for 2 months, and cleared the *Aspergillus* colonization. The dose of tacrolimus was decreased to 1 mg twice daily (achieving the same therapeutic blood level as was observed on a 6 mg twice daily regimen), while on the voriconazole. On completion of the course of voriconazole, the dose of tacrolimus was returned to its previous level.

**Summary and Conclusions:**

A patient with end stage pulmonary disease due to cystic fibrosis underwent bilateral lung transplantation. This patient developed colonization of the respiratory tract with *Aspergillus fumigatus*. Because of the risk of subsequent invasion, he was treated with preemptive voriconazole, which eliminated the fungus. In transplant patients such as this, the addition of voriconazole to the therapeutic regimen mandates a decrease in the dosage of tacrolimus or cyclosporine, because of the down regulation of the metabolism of these drugs by hepatic cytochrome P450 enzymes caused by the azoles. As in this case, the dose of the calcineurin inhibitors must be decreased with the initiation of voriconazole, and then increased when the voriconazole is discontinued.

Please return to your study guide to continue the course.

**REFERENCES:**

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Reference Library

The IDT Reference Library is a:
- Repository of over 1000 relevant journal articles
- Powerful search engine to find specific information within the site

Searching by keyword or browsing by medical topic, you will generate a page listing all site references and related articles by author, title, publication, and date.

Search Items by Keyword: [ ] in [All Categories]

Or Browse by Medical Topic:
Click on the arrow to expand each topic category. Click on the actual topic name to go to search results for that topic.

Filter Contents By:
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1 Basic Principles of Transplant Infectious Disease
2 Clinical Management
3 Antimicrobial Drugs of Special Importance
4 Clinical Syndromes Produced by Invasive Microorganisms
5 Microbial Etiology of Infectious Disease Syndromes
6 Drug and Radiation-induced Adverse Events
7 Parasites
8 Transplant Type

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1 Basic Principles of Transplant Infectious Disease
   * Survival of a patient transplanted with a kidney infected with Cryptococcus neoformans. : Ooi BS, Chen BT, Lim CH, Khoo OT, Chan DT.
   1.1 Impact of Immunosuppressive Therapy
   1.2 Risk of Infection
   1.3 Principles of antimicrobial therapy

2 Clinical Management
   * Salmonellosis: Microbiologic, Pathologic and Clinical Features. : Rubin R, Weinstein L.
   * Infectious disease problems. : Rubin R.
   * Radiation reaction in the lung: Report of a fatal case in a patient with carcinoma of the lung, with studies of pulmonary function before and during prednisone therapy. : Rodman T, Karr S, Close HP.
   * The Nisbet Symposium: Hodgkin's disease--Radiological aspects of the disease. : Martin JJ.
   * Lung function in patients receiving busulphan. : Littler WA, Ogilvie C.
   * Pulmonary infiltrates associated with leukoagglutinin transfusion reactions. : Ward HN.
   * Pulmonary
   * Pulmonary disease in the immunocompromised host. : Rosenow EC III, Wilson WR, Cockerill FR III.
   * Pneumonia in febrile neutropenic patients and in bone marrow and blood stem-cell transplant recipients: use of high resolution computed tomography. : Heussel CP, Kauczer HU, Heussel GE, et al.
   * Predictors of mortality in the immunocompromised patient with pulmonary infiltrates. : Poe RH, Wahl GW, Qazi R, et al.
   * Pulmonary infections in immunocompromised patients who do not have acquired immunodeficiency syndrome: a systematic approach. : Conces DJ Jr.
   * Infectious disease complications of renal transplantation. : Rubin RH.
   * Advances in preventing nosocomial pneumonia. : Failing LJ.
   * Effect of cimetidine on gastric bacterial flora. : Ruddell WSJ, Axon ATR, Finlay JM, et al.
   * Enteral nutrition in patients receiving mechanical ventilation: Multiple sources of tracheal colonization include the stomach. : Pingleton SK, Hinthorn DR, Liu C.
   2.1 Temporal Sequence of Infection (Timetable)
   2.2 Antimicrobial treatment design
   2.3 Hierarchy of diagnostic interventions
   2.4 Linkage of diagnostics and therapeutics
   2.5 Proven empiric strategies
Title: Pulmonary infections in immunocompromised patients who do not have acquired immunodeficiency syndrome: a systematic approach.

Author(s): Conces DJ Jr.


Date: 1998-00-00


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Lessons from Initial Experience

- Active vs passive learning
- Fungal infection
- Transplant Infectious Disease
- Statistics
- Study Design
- Clinical Pharmacology
- Case Studies in Biomedical Ethics
“Our heads are round so that our thinking can change direction.”

- Francis Picabo

“Many people say that it is the intellect which makes a great scientist. They are wrong; it is character.”

- Albert Einstein

“This is not the beginning of the end; it is the end of the beginning.”

- Winston Churchill