International Society for Heart and Lung Transplantation (ISHLT)

Lung Transplantation Core Competency Curriculum

(ISHLT LTx CCC)

Draft Document by

The Educational Workforce of the
ISHLT Pulmonary Council

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Selected references and resources

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Minimum Experience Requirement
Selected references and resources

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Minimum Experience Requirement
Selected references and resources
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Minimum Experience Requirement
Selected references and resources

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Minimum Experience Requirement
Selected references and resources

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Minimum Experience Requirement
Selected references and resources
INTRODUCTION

The purpose of this compendium is to provide a curriculum of core competencies in lung transplantation. The ISHLT Academy provides a concise synopsis of clinical knowledge and associated essential professional skills to facilitate the mastery of all surgical and medical aspects involved in the care of patients receiving lung transplantation.

This compendium does not replace a textbook, but intends to provide an outline of essential topics and aims to assist with detailed review. This should be of benefit for both seasoned clinicians and current trainees. The former may find selective revision of complimentary areas in lung transplantation useful, whereas the latter may benefit from a more complete review of all topics during fellowship or other subspecialty training in lung transplantation.

Inevitably, some overlap of clinically related aspects may have occurred. Extensive referencing should assist selective review of published evidence for each topic.

This document also includes active hyperlinks and related multi-media resources. These should be considered during individual study to develop competency in various aspects of lung transplantation.

The core curriculum should also serve programs providing lung transplantation with a tool to review their standards of care, develop protocols and implement guidelines established in lung transplantation.

Wherever possible, specific learning objectives have been defined. Minimal recommended clinical experience has been proposed with the awareness that this may be variable dependent on individual professional background and regional program limitations. The outlines will also serve as a template for a post-graduate course curriculum to be provided by the ISHLT academy at future annual meetings.

The educational workforce of the Pulmonary Council of ISHLT hopes that this compendium will prove to be useful. We would welcome constructive feedback to further develop its scope and accuracy.

On behalf of the Pulmonary Council of ISHLT,

Chris Wigfield MD FRCS
Chicago, IL.
March 2010
I. INTRODUCTION TO LUNG TRANSPLANTATION: BACKGROUND AND ISHLT REGISTRY

((C H WIGFIELD MD))

Learning Objectives

1) To develop context and historic background for lung transplantation.
2) To understand indications and expected outcomes in lung transplantation.
3) To appreciate current challenges and limitations associated.
4) Review the registry report and ISHLT resources.

1. Background

   Historical Context
   First Lung Transplants
   Advent of Immunosuppression

2. Outcomes in Lung Transplantation

   Current expected survival rates
   Comparative survival
   Conditional survival after 1 year
   Outcomes dependent on native pulmonary disease process

3. Challenges in Lung Transplantation

   Donor Scarcity
   Waiting List mortality
   Bronchiolitis Obliterans

4. Lung Transplantation Databases and ISHLT Registry

   Data Access
   Statistics available
   Data submission
Selected hyperlinks for the Background to Lung Transplantation

http://www.ishlt.org/meetings/ishltAcademy.asp

Overall Lung and Adult Lung Transplantation Statistics

Pediatric Lung Transplantation Statistics

All Heart/Lung Transplantation Statistics

http://www.ishlt.org/registries/quarterlyDataReport.asp

www.jhiltonline.org

Scientific Registry of the International Society for Heart and Lung Transplantation: Introduction to the 2005 Annual Reports

http://www.optn.org (the unified transplant network established by the United States Congress under the National Organ Transplant Act (NOTA) of 1984)

www.eurotransplant.nl

http://www.transplant-observatory.org/C18/National%20Transplant%20Organizati/default.aspx (international data on transplantation and multiple links)
II. EVALUATION AND MANAGEMENT OF THE LUNG TRANSPLANT CANDIDATE

(K M Chan MD)

Learning Objectives

5. Understand general and disease specific considerations for lung transplant referral
6. Review appropriate and cost effective testing, cancer screening, vaccination, consultation and multidisciplinary support of the lung transplant candidate
7. Understand the importance of “waitlist” management for the transplant candidate
8. Understand the importance of informed consent for transplantation, high risk donor acceptance and research participation
9. Discuss and review risks associated with anti-HLA antibodies, elevated panel reactive antibody screens and desensitization therapies
10. Understand lung donor allocation schemes and the relationship to the urgent inpatient lung transplant evaluation

1. Indications for lung transplant referral
   a. General considerations
      i. End stage lung disease
      ii. Ambulatory
      iii. Maximal medical management
      iv. Minimal or no co-morbid illness
      v. Tobacco cessation
      vi. Strong psychosocial support
      vii. Physiologic age considerations
      viii. Previous or current malignancy
ix. Systemic disease

x. Body Mass Index (BMI) considerations

xi. Colonization with highly resistant organisms (e.g. *Burkholderia cepacia genomovar III*, *M chelonae abscessus*)

xii. Mechanical ventilation

b. **Disease specific listing considerations** (including single or double LTx listing)
   i. IPAH
   ii. Emphysema
   iii. CF
   iv. IPF
   v. Other

2. **Transplant Candidate Evaluation and Ongoing Management**
   a. Respirologist/pulmonologist
   b. Thoracic Surgeon
   c. Social Worker
   d. Psychiatrist/Psychologist
   e. Pre Transplant coordinator
   f. Financial coordinator
   g. Pharmacist
   h. Nutritionist
   i. Pre transplant education/Patient Support groups
   j. Pulmonary Rehabilitation
k. Testing

i. Pulmonary
   1. Pulmonary function tests including ABG
   2. 6MW/Shuttle test
   3. Cardiopulmonary exercise test (CPET)

ii. Radiographic
   1. High Resolution CT of the chest (HRCT)
   2. Perfusion (V/Q) scan
   3. Esophagram
   4. Bone densitometry

iii. Cardiac
   1. EKG
   2. Echocardiogram
   3. Cardiac stress test
   4. Cardiac catheterization
      a. Right
      b. Left

iv. Gastrointestinal
   1. EGD, PEG tube placement
   2. Colonoscopy
3. 24 hour pH probe and manometry

v. **Health Care Screening**
   1. Dental examination
   2. Colon
   3. Skin
   4. Prostate
   5. Breast
   6. Cervical/Ovarian

vi. **Vaccines**
   1. Hepatitis B
   2. Pneumococcal/Influenza
   3. Tetanus etc.

vii. **Laboratories and serology**
   1. Basic labs
      a. Comprehensive panel
      b. CBC
      c. 24 hour creatinine clearance
      d. A1AT level
      e. ACE level
      f. Nicotine/toxicology screen

   2. Infectious Serology
a. EBV, CMV, HSV, VZV, HIV
b. Toxoplasma, RPR
c. Hepatitis A, B, C

3. Blood typing and HLA
   a. PRA

4. Other
   a. PPD skin test or quantiferon testing

viii. Additional referrals as necessary
   1. Cardiology
      a. Coronary artery disease
   2. Infectious Disease
   3. Gastroenterology
      a. A1AT deficiency (hepatology)
      b. CF (liver disease, DIOS etc)

I. Special considerations including informed consent
   i. Hepatitis B or C
   ii. HIV
   iii. Acceptance of high risk donor
   iv. Research participation
m. Special considerations: high panel reactive antibody screen
   i. Desensitization therapy
   ii. Prospective and retrospective crossmatching

n. Urgent inpatient evaluation
   i. Mechanical ventilation
   ii. ECMO
   iii. Deconditioning

3. Lung Allocation Systems
   a. United States
      i. Lung Allocation Score
   b. Europe
      i. Eurotransplant allocation
   c. UK
      i. Lung allocation
   d. Australia
      i. Lung Allocation
   e. Other Countries
      i. Lung Allocation
Minimum Experience Requirement:

(Modified from UNOS Membership Criteria)

Participate in the care of 15 or more lung transplant candidates for a minimum of 3 months from the time of referral to the time of listing and/or transplantation.

Participate in the care of 3 or more lung transplant candidates with an elevated PRA of > 25% from the time of patient referral to the time of transplantation incorporating desensitization procedures.

Participate in the care of 3 or more lung transplant candidates undergoing urgent in-hospital evaluation for lung transplantation.

Selected references for Evaluation and Management of the Lung Transplant Candidate:

Candidate Selection:


Urgent Transplant Evaluation:


Informed Consent


Sensitized Patient:


Lung Allocation:


Selected hyperlinks for Evaluation and Management of the Lung Transplant Candidate:


International Guidelines for the Selection of Lung Transplant Candidates. The International Society for Heart and Lung Transplantation, the American Thoracic Society, the American Society of Transplant Physicians, the European Respiratory Society.

2009 ESC/ERS Guidelines on the Diagnosis and Treatment of Pulmonary Hypertension
III. **LUNG ALLOGRAFT DONATION AND PROCUREMENT**

(C H Wigfield MD)

**Learning Objectives**

11) To develop a clinically relevant understanding of donor brain death, the basic pathophysiology and donor certification issues
12) To differentiate types of donors as relevant to lung transplantation
13) Knowledge of waiting list and donor availability concerns
14) Lung allograft matching criteria
15) Procurement, procedure and understanding of possible adverse advents
16) To develop insight into possible donor management and allograft of optimization
17) Develop a basic insight to future directions in lung allograft procurement

1. **Historical Notes and Background**

   a. **General considerations**

      i. Overview and historical Perspective

      ii. Brain Death Definition and Criteria

      iii. Definitions of Donors (DDND v DDCD)

      iv. Donor Scarcity and Waiting List

      v. Definition of Standard v Extended Criteria Donors in LTx

         (SCD v ECD)

2. **Donor Offer and Evaluation Process**

   a. **Matching Criteria in Lung Transplantation**

      i. Serology confirmation
ii. Size matching

iii. Laterality Issues

iv. Organ Procurement Consent

v. Allocation Scores and recipient matching

b. Evaluation Process

i. Procurement Offer

ii. Provisional Acceptance

iii. Logistics and Confirmed Acceptance

iv. Donor Net systems/ IT technology

v. Etiology of Donor Lung Injury:
   a Neuroendocrine Dysregulation,
   b Permeability and Pulmonary Edema
   c Airway, Pulmonary and Pleural Trauma,
   d Aspiration Pneumonitis
   e Respiratory Infections,
   f Ventilation related Issues,

vi. Modified Evaluation process:
   a High Risk Donors
   b Donor type related (DDND v DDCD)
   c Pediatric Donor
c. **Donor Assessment**
   - i. Donor Information and Evidence Review
   - ii. Verification of Brain Death Certification
   - iii. UNOS donor Criteria
   - iv. Bronchoscopy of Donor Lungs
   - v. Visualization of Donor Lungs
   - vi. Additional Investigations
   - vii. Dialogue with Recipient Surgeon’s Team
   - viii. Multiorgan Procurement Communication

d. **Donor Management and Optimization**
   - i. Options for Allograft improvement in situ
   - ii. Fluid Management and Re-evaluation
   - iii. Extended Criteria Donors

3. **Lung Allograft Procurement**
   a. **Lung Procurement**
      - i. Preparations and Dissection (with/ without Cardiac procurement)
      - ii. Antegrade Pulmoplegia Principles
      - iii. En Bloc Excision of Allografts: Essentials and Pitfalls
      - iv. Backbench Assessment and Retrograde Pulmoplegia
      - v. Lung Separation
vi. Transport Requirements

b. Planned Ischemia and Reperfusion Preparation
   i. Allograft Ischemia Basics
   ii. Preparation of Donor Lung for Anastomoses
   iii. Re-warming, Re-perfusion and Re-ventilation

4. Additional Lung Allograft Options and Future Directions
   a. Additional Lung Allograft Sources
      i. Living Related Lung Donation
      ii. Split Lung Allografts
      iii. DDCD Lung Allografts
   b. Future Directions
      i. Ex Vivo Lung Perfusion
      ii. Xenografts in Lung Transplantation

Minimum Experience Requirement:

For recommendations see UNOS Statements on Lung Transplant Surgeon Certification Process: UNOS appendix B; Attachment I—XIII 73 pp.

Reasonable Minimum experience: “10 or more Lung Allograft Procurements as Primary Surgeon under supervision of qualified lung transplant surgeon”. Case must be documented with Donor UNOS (or equivalent ID Number).
Selected references for Lung Donation and Procurement:


Weill D et al Donor Criteria in Lung Transplantation An Issue Revisited CHEST 2002; 121:2029– 2031


Wigfield CH et al Organ Procurement Data Evaluation of Rejected Marginal Donors in Lung Transplantation Chest 2006 130 (4): 152S


**Mason, DP** Should lung transplantation be performed using donation after cardiac death? The United States experience J Thorac Cardiovasc Surg 2008;136:1061-1066

**Mallory G B. et al** Management of the pediatric organ donor to optimize lung donation Pediatric Pulmonology Vol 44 Issue 6, Pages 536 - 546 2009


**Selected hyperlinks for Lung Donation and Procurement:**

- **A Review of Lung Transplant Donor Acceptability Criteria (a consensus report of the ISHLT Pulmonary Council)**
- **Primary Lung Graft Dysfunction Part III: Donor Related Risk Factors and Markers**
- **Donor Lung Procurement** Cliff K. Choong, MD, Bryan F. Meyers, MD and G. Alexander Patterson, MD
- **Report of the Xenotransplantation Advisory Committee of the International Society for Heart and Lung Transplantation: the Present Status of Xenotransplantation and its Potential Role in the Treatment of End-Stage Cardiac and Pulmonary Diseases**
- **www.donoraction.org** (organ donation information in Europe)
- **www.organdonor.gov** (U.S. government organ donation information site)
IV. LUNG TRANSPLANTATION: SURGICAL AND POST-OPERATIVE MANAGEMENT

(DAVID MASON MD)

Learning Objectives

18) Understand the principles and practice of size matching between donor and recipient
19) Review the differential diagnosis and treatment strategies for graft failure in the early postoperative period
20) Discuss the management of pleural complications after lung transplantation
21) Understand the diagnostic and treatment strategies of bronchial, pulmonary artery and pulmonary venous complications
22) Understand the indications for, management of and contraindications to extracorporeal mechanical support after lung transplantation

a Immediate Post Transplant Management

1. Surgical Complications of Lung Transplant
2. Medical Complications post Lung Transplantation
3. Prophylactic Regimen (antibiotics, anti-fungal and anti-viral)

b Surgical Conduct

Size matching between donor and recipient
Single versus double lung transplant
Coordinating the timing of surgery
Technical aspects of pneumonectomy
Choice of incision- median sternotomy, bilateral anterior thoracotomy, clamshell, anterior vs posterolateral thoracotomy
Use of cardiopulmonary bypass and intraoperative ECMO- disease specific, PAH Anastomotic techniques- running, interrupted, suture choice
c **Postoperative Complications**

Graft dysfunction- differential diagnosis and treatment (NO)

Anastomotic

   Airway- dehiscence, stenosis, bronchovascular fistula, stents

   Vascular- pulmonary vein and artery stenosis

Pleural – acute and chronic effusions; empyema

Renal Failure – prevention and treatment


d **Special Considerations**

Preoperative ECMO- VA vs VV. Criteria for listing and delisting, status 7.

Postoperative ECMO- separation/weaning

Combined cardiac surgery and lung transplantation. Stents vs CABG

**Minimum Experience Requirement:**

UNOS Certification criteria for lung transplantation

Participate in the matching of 15 or more lung transplant donors to recipients
Participate in 15 or more operative and postoperative lung transplant managements.
Selected references for Lung Transplantation: Surgical and Post-Operative Management

TBC

Selected hyperlinks for Lung Transplantation: Surgical and Post-Operative Management

http://www.ctsnet.org/sections/clinicalresources/videos/media-90.html
Cliff K. Choong, MD, Bryan F. Meyers, MD and G. Alexander Patterson, MD

http://www.ctsnet.org/sections/clinicalresources/videos/media-80.html
Cliff K. Choong, MD, Bryan F. Meyers, MD and G. Alexander Patterson, MD

http://mmcts.ctsnetjournals.org/cgi/content/abstract/2005/0809/mmcts.2004.000984
Split lung transplantation with intraoperative extracorporeal membrane oxygenation (ECMO) support
Gabriel Mihai Marta, Clemens Aigner and Walter Klepetko

Primary Lung Graft Dysfunction Part I: Introduction and Methods

Primary Lung Graft Dysfunction Part II: Definition. A Consensus Statement of the International Society for Heart and Lung Transplantation

Primary Lung Graft Dysfunction Part III: Donor Related Risk Factors and Markers

Primary Lung Graft Dysfunction Part IV: Recipient-Related Risk Factors and Markers

Primary Lung Graft Dysfunction Part V: Predictors and Outcomes

Primary Lung Graft Dysfunction Part VI: Treatment
V. IMMUNOLOGY AND REJECTION AFTER LUNG TRANSPLANTATION AND IMMUNOSUPPRESSION PROTOCOLS

(D J LEVINE MD)

Learning Objectives for Immunologic Concepts in Lung Transplantation

23) Review the general concepts and definitions of Basic Immunology
24) Recognize the roles of lymphocytes responsible for immune responses (B vs T cells)
25) Discuss the different types of rejection and each of their proposed mechanisms
26) List the causes of HLA allo-immunization
27) Understand the differences in the tests involved in the evaluation of the immune work up prior to transplantation

Immunologic Concepts in Lung Transplantation

A. Definitions

B. Normal Immune Response
   1. Innate vs Adaptive Immune System
   2. Molecules and cells of the immune system
      T cells
      B cells
      NK cells

3. Response to foreign antigen

C. Immune response to allograft
   1. Mechanism of allore cognition
   2. Humoral vs Cellular Rejection
   3. Proposed mechanism of each type of allograft rejection:
      a. Hyperacute rejection
      b. Acute rejection
      c. Chronic rejection
      d. Humoral rejection

D. Tolerance
   Definition
   Mechanisms
   Clinical Implications

E. Immunogenetics
1. ABO Blood System
2. Major Histocompatibility Complex I and II
   A. HLA Nomenclature and HLA genetics
   B. Causes of HLA-specific alloimmunization
   C. HLA Antigen Matching in Lung Transplantation
3. Methods used to detect anti-HLA antibodies
   A. Calculated PRA (c-PRA), Virtual Crossmatch
   B. Detection of presence of anti-HLA antibodies
   C. Panel reactive antibodies
   D. Complement Dependent Cytotoxicity (CDC)
   E. Flow Cytometry
   G. Solid Phase Assays
      1. Luminex
      2. Flow Cytometry
      3. ELISA
   H. Screening strategies

F. Non-HLA Antigens

G. Clinical applications of transplant immunology and typing

Experience Requirement:

Participate in evaluation of the immunologic work up along with immunologist of 15 patients being evaluated for transplantation.

Literature Review for Transplant Immunology

Rejection in the Lung Transplant Recipient

1. Hyperacute Rejection
   A. Definition
   B. Mechanism
   C. Pathology
   C. Treatment

2. Acute Cellular Rejection
   A. Definition-(ISHLT guidelines)
   C. Detection, Evaluation and Diagnosis
      a. Surveillance bronchoscopy
         1. Pros and Cons
         2. Table of possible surveillance schedules
      b. Monitoring
         1. Spirometry
         2. Clinical status
         3. Bronchoscopy
         4. Radiographic changes
   D. Grading of acute cellular rejection
      a. ISHLT Pathologic grading
   E. Type of ACR
      a. Recurrent
      b. Refractory
      c. Lymphocytic bronchiolitis
   F. Treatment Options
      a. Modified immunosuppression regimen
         1. Steroid pulse and taper
         2. Change calcineurin inhibitor
         3. Alemtuzumab, antithymocyte globulin, ECP,
         4. Others
   G. Outcomes
   H. Clinical Implications
   I. Risk Factors

3. Bronchiolitis Obliterans Syndrome (Chronic Rejection)
   A. Definition (ISHLT guidelines)
   B. Evaluation and Diagnosis
      1. Spirometric Diagnosis
      2. Pathologic diagnosis
      3. Radiographic findings
      4. Clinical findings
      5. Grading (ISHLT guidelines)
   C. Monitoring
D. Treatment Options
   1. Photophoresis
   2. Azithromycin
   3. Augment or change immunosuppression
   4. Re-transplantation

E. Risk Factors
   1. Acute cellular rejection (ACR)
   2. Lymphocytic bronchitis/bronchiolitis (LB)
   3. Organizing pneumonia
   4. HLA mismatch
   5. GERD
   6. CMV/respiratory viruses
   7. Primary Graft Dysfunction (PGD)

1. Humoral or Antibody-Mediated Rejection

A. Definition

B. Evaluation, Screening and Diagnosis
   a. Serologic
   b. Pathologic
   c. Immunologic

C. Monitoring
   1. Donor specific antibodies
   2. C4d monitoring

D. Treatment Options
E. Outcomes
F. Risk Factors

2. The Sensitized Recipient

A. Screening
   1. Types of screening pre-transplant
      i. PRA
      ii. V-PRA
   2. Issues of the sensitized patient
   3. Treatment and monitoring prior to transplantation
   4. Treatment and monitoring peri-operatively and post transplant
   5. Risks
Learning objectives of Rejection in the Lung Transplant Recipient

28) Define the different types of lung transplant rejection
29) Discuss the diagnostic approaches to evaluation for each of the different types of rejection post-transplant
30) Discuss surveillance bronchoscopy and pros and cons
31) Define acute cellular rejection per the ISHLT guidelines
32) List the risk factors and outcomes for BOS (chronic rejection)
33) Outline the timeline each type of rejection
34) Understand significance of the sensitized patient
35) Review the histological differences between acute and chronic rejection
36) Explain the treatment options for patients with BOS

Experience Requirement for Rejection in the Lung Transplant Recipient

1. Review the slides of at least 10 patients with pathologist with acute cellular rejection.

2. Diagnose and treat at least 10 patients with acute cellular rejection, humoral rejection and bronchiolitis obliterans syndrome (BOS).

3. Perform at least 10 bronchoscopies post transplant to evaluate for ACR.
Literature Review for Lung Transplant Rejection


Immunosuppression for Lung Transplantation

Learning Objectives for Immunosuppression post Lung Transplantation

37) Discuss the triple agent immunosuppression protocol and which types of agents are typically used
38) Understand the side effects of each of the drug classes
39) Describe the monitoring of levels of the calcineurin inhibitors and what range of levels is appropriate
40) List the possible complications of induction therapy
41) Discuss the laboratory tests to order to evaluate toxicity from the different classes of drugs
42) Discuss drug-drug interactions with the calcineurin inhibitors

I. Overview of Immunosuppressive Agents

II. A. Immunosuppressant Action and the Immune Cascade (how all of the agents relate within the cascade where the agent affects the immunologic process).
B. Induction Agents
C. Primary Immunosuppressants
D. Adjuvant agents

E. Induction
   a. Pro versus con of induction
   b. Risks and Benefits
   c. Agents (For all agents: target, indication, dose, administration, adverse events, monitoring)
      i. Similect (Basiliximab)
      ii. Campath (Anti CD-52)
      iii. Thymoglobulin (rATG)
      iv. OKT3 (anti-Cd-3)

F. Maintenance
   a. Triple Agent Immunosuppression Regimen
b. Corticosteroids
   i. Mechanism of action
   ii. Pharmacokinetics, dosing and drug monitoring
   iii. Side effects
   iv. Drug-drug interactions

c. Calcineurin Inhibitors
   (Cyclosporine and Tacrolimus)
   i. Mechanism of action
   ii. Pharmacokinetics, dosing and drug monitoring
   iii. Side effects
   iv. Drug-drug interactions

d. Anti-proliferative agents
   (Azathioprine and Mycophenolic acid (MMF))
   i. Mechanism of action
   ii. Pharmacokinetics, dosing and drug monitoring
   iii. Side effects
   iv. Drug-drug interactions

e. TOR inhibitors
   (Sirolimus and Everolimus)
   i. Mechanism of action
   ii. Pharmacokinetics, dosing and drug monitoring
   iii. Side effects
   iv. Drug-drug interactions

G. Rejection
   a. Acute Rejection
      i. Augmentation of Maintenance Therapy
      ii. Adjustment of Maintenance Therapy
   b. Chronic Rejection (BOS)
      i. Augmentation of Maintenance Therapy
      ii. Adjustment of Maintenance Therapy
      iii. Azithromycin
   c. Humoral Rejection
      i. Plasmapheresis
      ii. IVIG
      iii. Rituximab
      iv. Velcaide

H. Trends and Issues in Immunosuppression

I. Salvage Therapy for Chronic Rejection
   a. Total lymphoid Irradiation (TLI)
   b. Extracorporeal Photopheresis (ECP)
J. Desensitization
   i. Plasmaphoresis
   ii. IVIG
   iii. Rituximab
   iv. Velcaide

Experience Required for Immunosuppression post Lung Transplantation.

1. Treat 15 patients with immunosuppression post lung transplant and adjust changes and following for side effects or drug drug interactions.

Literature Review of Immunosuppressants post lung transplantation.

Hyperlinks:

- Generic Drug Immunosuppression in Thoracic Transplantation: An ISHLT Educational Advisory (pdf)

Hematologic Disorders Post Lung Transplantation

Learning Objectives for Hematologic Disorders post lung transplantation.

43) List the major causes of leukopenia post lung transplantation
44) Understand treatment options for drug-induced penias
45) Discuss the reasons for anemia post lung transplantation

1. Thrombocytopenia
   a. Evaluation and Diagnostic work up
   b. Drug reactions
      i. Immunosuppressive
      ii. Antibiotics
   c. Infection
   d. Treatment options

2. Anemia
   a. Evaluation and Diagnostic Work up
   b. Drug Reaction
      i. Immunosuppressive
      ii. Antibiotics
   c. Infection
   d. Iron deficiency
   e. HUS
   f. Treatment options
3. Leukopenia or Leukocytosis

  a. Evaluation and Diagnostic Work up
  b. Drug Reaction
     i. Immunosuppressives
     ii. Antibiotics
  c. Infection
  d. Treatment Options

Experience Requirements for Hematologic Disorders post lung transplantation

Evaluate, monitor and treat 10 patients with leukopenia, thrombocytopenia or anemia post transplant.
Non-Pulmonary Medical Complications and Issue Post Lung Transplantation

I. Gastrointestinal Issues Post Lung Transplantation

Learning Objectives for Gastrointestinal Issues Post Lung Transplantation

46) Discuss the risk factors for bowel perforation post lung transplantation
47) Understand the significance of GERD in lung transplantat recipients and its association with BOS (chronic rejection)
48) Identify the gastrointestinal issues that are important to Cystic Fibrosis patients have who undergo lung transplantation
49) Understand the etiologies behind the common gastrointestinal symptoms patient have post lung transplantation
50) Discuss the different anti-infective and immunosuppressive agents that typically are associated with gastrointestinal side effects and liver toxicity

A. Frequent Problems and their possible etiologies

1. Nausea/Vomiting
   a. Medications
   b. Infection
   c. Gastroparesis/delayed gastric emptying
   d. Small bowel obstruction or ileus
   e. GERD

2. Diarrhea
   a. Medications
   b. Infection: C.difficile, protozoa, viral, bacterial
   c. CMV Colitis
   d. Ischemic Colitis
   e. Prior co-morbidities

3. Abdominal Pain

B. Colonic Issues

1. Bowel Perforation: multiple risks and etiologies
2. Diverticulitis/diverticulosis
3. PTLD/Malignancy
4. Colitis (viral, fungal or ischemic)
5. Pseudoomembranous colitis and C. Diff
C. Small bowel obstruction
   a. Gastroparesis
   b. PTLD
   c. Constipation

D. Upper Gastrointestinal Issues
   1. Gastroparesis
   2. Esophagitis
   3. PUD
   4. GERD

E. GERD and BOS

F. GI Bleed
   1. Peptic Ulcer Disease
   2. Esophagitis
      a. Candidiasis or fungal
      b. Malignancy
      c. CMV or viral

G. Biliary Disease
   1. Cholelithiasis pre-transplant
      a. Timing for cholecystectomy
   2. Cholecystitis

H. Pancreatitis
   1. Infection
   2. Medication: Cyclosporine, Azithiprine, Prednisone

I. GI Complications of Cystic Fibrosis Patients
   1. DIOS
   2. Pancreatitis
   3. Cholecystitis
   4. Bowel obstruction

J. Hepatic toxicity secondary to medication.

K. Hyperammonemia
References Gastrointestinal Issues Post Lung Transplantation


VI. **LUNG TRANSPLANTATION PATHOLOGY**  
(G BERRY MD)

**Learning Objectives**

51) To recognize the common indications and histopathological patterns in combined heart-lung, single lung and double lung transplantation  
52) To understand the common pathological complications utilizing a temporal approach  
53) To recognize the histopathological grades of acute cellular rejection  
54) To understand the current diagnostic challenges of acute antibody mediated rejection  
55) To describe the patterns and causes of airway inflammation  
56) To recognize the histopathological findings in chronic airway and vascular rejection  
57) To outline the pulmonary diseases that can recur in the lung allograft

1. **Pathology of Common Indications for Thoracic Transplantation**

   a. Congenital Heart Disease/Eisenmenger’s Syndrome  
   b. Cystic Fibrosis  
   c. Primary Pulmonary Hypertension  
   d. Chronic Obstructive Lung Disease  
   e. Idiopathic Pulmonary Fibrosis

2. **Specimen Adequacy and Handling**

   a. Transbronchial Biopsy  
      i. Number of Tissue Samples for Adequacy  
      ii. Tissue Handling and Fixation  
      iii. Processing of Urgent vs. Routine Biopsy  
      iv. Basic/Routine Staining  
      v. Immunohistochemical/Molecular Studies  
   b. Bronchioloalveolar Lavage  
   c. Endobronchial Biopsy  
   d. Video-Assisted Thoracoscopic Biopsy (VATS)
3. Post-Operative and Immediate Post-Transplant Graft Dysfunction
(Within 7 days)

a. Definition
b. Surgical Technical Complications
   i. Arterial/Venous Obstruction
   ii. Airway Dehiscence/Obstruction
c. Preservation Injury/Reimplantation Response
   i. Definition
   ii. Histopathological Findings
d. Hyperacute Rejection
   i. Definition
   ii. Histopathological Findings
   iii. Immunohistochemical/Immunofluorescent Findings
e. Infection
   i. Bacterial
   ii. Viral
   iii. Fungal
   iv. Other

4. Early Complications Following Lung Transplantation
(1 week – 6 months)

a. Definitions
b. Classification
c. Diagnostic Techniques

5. Acute Cellular Rejection (ACR)

a. Definition
b. Grading of ACR
   i. Minimal
   ii. Mild
   iii. Moderate
   iv. Severe
c. Morphological Mimics of ACR
   i. Bronchial-Associated Lymphoid Tissue (BALT)
   ii. Infection
   iii. Post-Transplant Lymphoproliferative Disorder
6. Infections in Lung Allograft
   a. Bacterial
   b. Viral
   c. Fungal
   d. Parasitic/Protozoan

7. Acute Antibody Mediated/Humoral Rejection (AMR)
   a. Definitions
   b. Histopathological Findings
   c. Immunohistochemical/Immunofluorescent Findings
   d. Ongoing Issues and Controversies

8. Airway Inflammation/Lymphocytic Bronchitis/Bronchiolitis
   a. Definition
   b. Histopathological features
   c. Grading of Acute Airway Rejection
      i. Low Grade
      ii. High Grade
   d. Morphological Mimics
      i. Airway Inflammation Associated with AMR
      ii. Bronchus-Associated Lymphoid Tissue (BALT)
      iii. Prior Biopsy Site
      iv. Ischemic Injury/Organizing Pneumonia
      v. Aspiration Injury
      vi. Infection

9. Post-Transplant Lymphoproliferative Disorder (PTLD)
   a. Definition
   b. Histopathological Patterns
   c. Immunohistochemical/Molecular Markers
   d. Role of EBV Infection
   e. Other EBV-associated Proliferations

10. Late Complications
    (Beyond 6 months)
    a. Definition
    b. Classification
    c. Diagnostic Techniques
11. Chronic Airway Rejection (CAR)
   a. Definition
   b. Histopathological Findings
   c. Grading of CAR
   d. Role of Transbronchial Biopsy
   e. Differential Diagnosis
      i. Organizing Pneumonia
      ii. Prior Biopsy Site
      iii. Aspiration

12. Chronic Vascular Rejection (CVR)
   a. Definition
   b. Histopathological Findings

13. Recurrence of Native/Primary Lung Disease
   a. Sarcoidosis
   b. Lymphangioleiomyomatosis (LAM)
   c. Diffuse Panbronchiolitis
   d. Giant Cell Interstitial Pneumonia (GIP)
   e. Desquamative Interstitial Pneumonia (DIP)
   f. Langerhans-Cell Histiocytosis
   g. Bronchioloalveolar Carcinoma

Minimum Experience Requirement:

TBC
Selected references for Lung Transplant Pathology


Selected hyperlinks for Lung Transplant Pathology

TBC
Learning Objectives

58) To define the cell populations and humoral/complement components integral to the host immune response to infection.

59) To highlight the specific components of innate and alloimmunity unique to the response to infection in the lung.

60) To list the aspects of the host immune response specific to viruses, bacteria, fungi, and parasites.

61) To understand the impact of corticosteroids, calcineurin inhibitors, cell cycle inhibitors, and T-cell depleting agents on specific components of the host immune response to infection in the lung allograft.

62) To outline the appropriate methods for evaluating the lung transplant candidate’s immunity to infection.

63) To describe the comprehensive approach to evaluating pulmonary and non-pulmonary infections in the lung transplant candidate.

64) To discuss the significance and evaluation of infections in the lung donor.

65) To demonstrate the impact of the surgical disruption of the normal pathways of innate lung immunity on the development of infection in the lung transplant recipient.

66) To describe the timeline, diagnostic methods, prophylaxis, and management of specific early and late post-transplant infections.

67) To list the potential non-infectious allograft sequelae resulting from infectious pathogens.

68) To discuss the utility of immunosuppressive drug levels, immune function assays, and viral DNA measurements in assessing the lung transplant candidate’s susceptibility to infections.
3 Immune Response to Infection

a. Components of the Immune Response to Infection
   i. Cell Types
   ii. Antibodies
   iii. Complement
   iv. T cell receptors and MHC molecules

b. Components specific to immune response to infection in the lung
   i. Innate Immunity
   ii. Cellular Immunity
   iii. Humoral Immunity

c. Immunity Against Specific Infectious Agents
   i. Immunity to Viruses
   ii. Immunity to Bacteria
   iii. Immunity to Fungi
   iv. Immunity to Parasites

d. Impact of Immunosuppression on Immune Response to Infection
   i. Corticosteroids
   ii. Calcineurens Inhibitors
   iii. Cell Cycle Inhibitors
   iv. T-Cell Depleting Agents

4 Evaluation of Infection in the Pre-Transplant Candidate

e. Evaluation of Immunity to Infection
   i. History of Infections
ii. Serologic Testing

iii. Immunoglobulin Testing

iv. Vaccinations

f. Approach to Evaluation of Airway Colonization/Infection

   i. History of Infection

   ii. Diagnostic Modalities

      1. Computed Tomography

      2. Sputum vs BAL

      3. Use of Synergy and Multiple Antibiotic Sensitivity Testing

   iii. Specific Pathogens

      1. Gram Negative Bacteria

      2. Fungi

      3. Mycobacteria

      4. Burkholderia Cepacia

g. Evaluation for Non-Pulmonary Infections

   i. Hepatitis B and C

   ii. HIV

5 Significance of Infections in the Donor

h. Diagnostic Approach

   i. History

   ii. Serologic Testing

   iii. BAL Gram Stain
i. Impact of Donor Infections on Early Allograft Function
   i. Bacterial and fungal pathogens
   ii. Viral pathogens
      1. CMV
      2. EBV
      3. Community acquired viruses

j. Impact of Donor Infections on Allograft Prophylaxis Strategies

6 Impaired Physiologic Mechanisms in the Allograft and Impact on Infection

k. Donor-specific Mechanisms
   i. Neurogenic edema
   ii. Ischemic Injury
   iii. Reperfusion Injury

l. Surgical Disruption of Normal Pathways of Innate Immunity
   i. Lymphatic Drainage
   ii. Atelectasis
   iii. Surfactant Depletion
   iv. Mucociliary Apparatus
   v. Airway Neural Denervation/ Loss of Cough Reflex

7 Overview and Timeline of Infections Following Lung Transplantation
8 Diagnosis, Prophylaxis, and Management of Early Post-Transplant Infections

m. Overview

n. Prophylaxis and Treatment of Bacterial Pneumonia

o. Anti-Fungal Prophylaxis

p. Utility of Inhaled Agents in the Post-Operative Period

q. CMV Prophylaxis

9 Diagnosis, Prophylaxis, and Management of Later Infections

r. Overview

s. Bacterial Pneumonia

t. Fungal Infections

u. Community Acquired Viral Pneumonia

v. CMV

w. PCP

x. Nocardiosis

y. Atypical Mycobacteria (MAC, M. Abscessus, etc.)

10 Non-Infectious Allograft Sequelae of Infectious Pathogens

z. EBV and the Development of PTLD

aa. CMV and the Development of BOS

bb. Community Acquired Respiratory Viruses and the Development of Acute Rejection and BOS

cc. Fungal and Bacterial Infections and Anastomotic Complications
11 Immune Monitoring and Infection

dd. IS Drug Levels

ee. Immune Function Assays

ff. Viral DNA
   i. EBV
   ii. CMV

Minimum Experience Requirement:

TBC

Selected references for the Diagnosis and Management of Infections Following Lung Transplantation

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ADDENDUM

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