Chronic lung transplant rejection
Bronchiolitis obliterans

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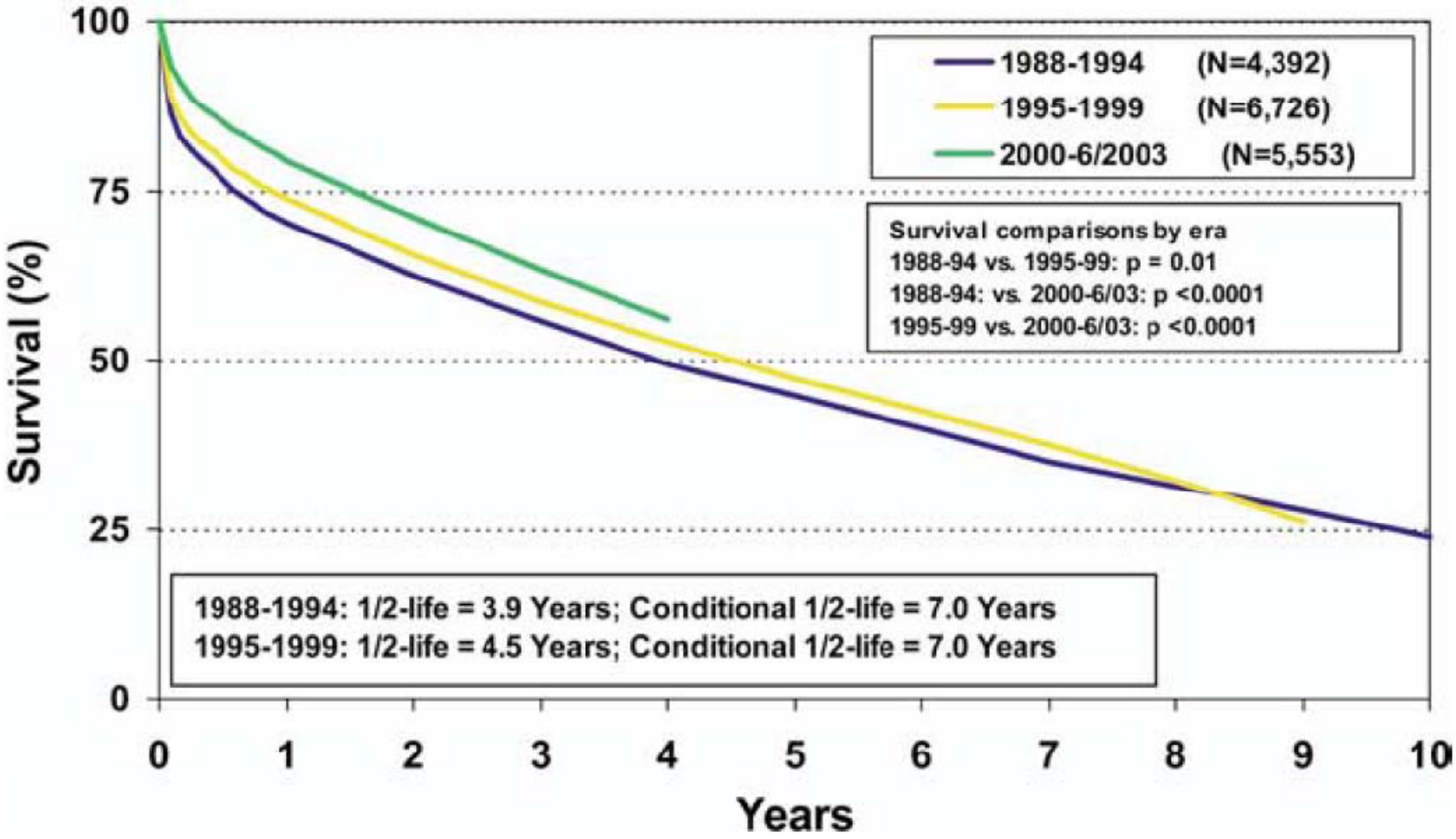
International Society for Heart and Lung Transplantation (ISHLT)



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Chronic rejection

- **Chronic vascular rejection**

  the less common, atherosclerosis

  developing in the pulmonary vasculature

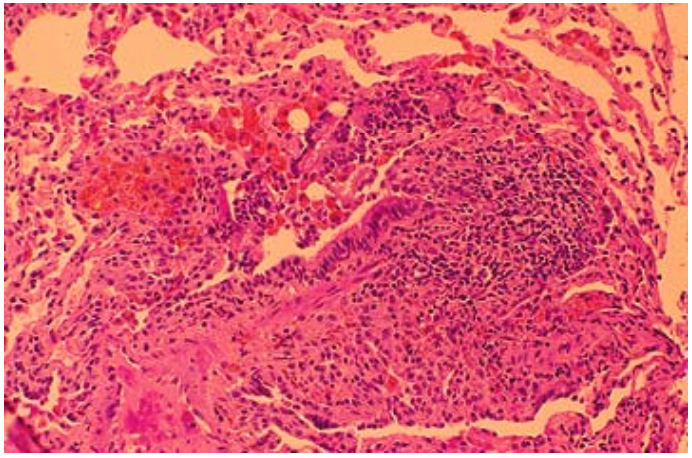
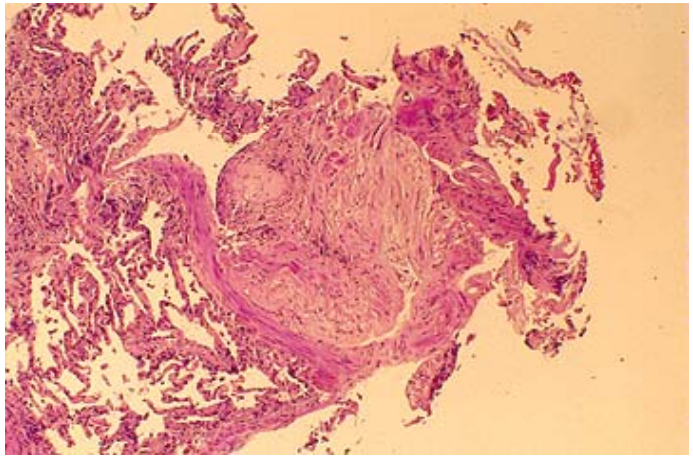
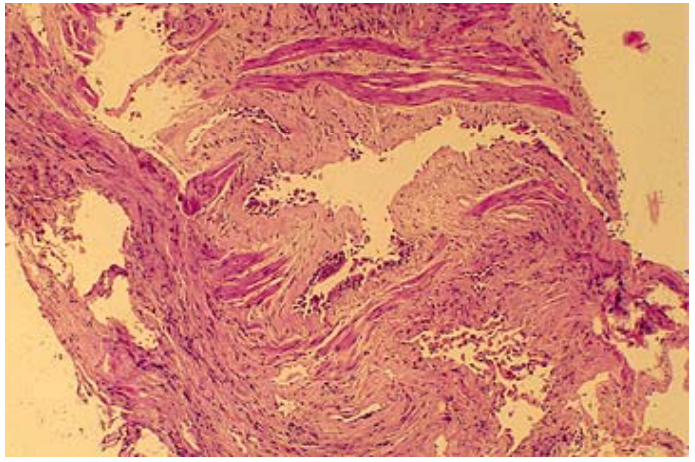
- **Chronic airway rejection**

  the more common and morbid

  the presence of bronchiolitis obliterans,

Pathology of BO

- Inflammation and disruption of epithelium
- ingrowth of fibromyxoid granulation tissue
- fibrosis

Classification and grading of pulmonary allograft rejection

A. Acute rejection		**B. Airway inflammation-lymphocytic bronchitis/bronchiolitis**
Grade 0: None Grade 1: Minimal Grade 2: Mild Grade 3: Moderate Grade 4: Severe	with/ without	Grade X: Ungradeable Grade 0: None Grade 1R: Low grade Grade 2R: High grade
C: Chronic airway rejection: bronchiolitis obliterans		
0: Absent 1: Present		
D: Chronic vascular rejection: accelerated graft vascular sclerosis		

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J Heart Lung Transplant 2007; 26:1229.

Etiology of BO

- Acute rejection
- Chronic rejection
- CMV infection
- Primary graft dysfunction
- Gastroesophageal reflux
- Transplant type (single LT vs double LT)
- Autoimmunity

Risk factors for BO

Probable

Acute rejection

Lymphocytic bronchitis/bronchiolitis

CMV pneumonitis

Medication noncompliance

Primary graft dysfunction

Potential

CMV infection (without pneumonitis)

Organizing pneumonia

Recurrent infection other than CMV

Older donor age

Prolonged allograft ischemia

Donor antigen-specific reactivity

Hypothetical

Underlying cause of lung disease

HLA-mismatching

Gastroesophageal reflux with aspiration

J Heart Lung Transplant 2002; 21:297

Clinical presentation

“Nonspecific and indolent”

	Early	Late
Symptoms	Nonproductive cough; dyspnea on exertion	Productive cough; dyspnea at rest
Physical examination	Clear chest	"Pops and squeaks"
Chest radiograph	Clear	Bronchiectasis, hyperinflation
Pulmonary function tests	Obstruction; most marked in mid flows (FEF (25-75)	Severe obstruction
Sputum culture	Negative	Pseudomonas

Diagnosis

- **Bronchiolitis obliterans syndrome**

  graft deterioration secondary to progressive airways disease for which there is no other cause, in the absence of histologic evidence of BO

Diagnosis

- **Classifications of BOS**

Current proposition	
BOS 0	FEV_1 > 90 percent of baseline and FEF_{25-75} > 75 percent of baseline
BOS 0-p	FEV_1 81 to 90 percent of baseline and/or FEF_{25-75} < 75 percent of baseline
BOS 1	FEV_1 66 to 80 percent of baseline
BOS 2	FEV_1 51 to 65 percent of baseline
BOS 3	FEV_1 50 percent or less of baseline

J Heart Lung Transplant 2002; 21:297.

Diagnosis

- **Role of transbronchial biopsy**
  - histologic diagnosis can be difficult
  - yield of the diagnosis is variable
- **Surrogate markers**
  - IL-12 in BAL fluid
  - exhaled NO
  - air trapping on chest CT

Natural history

- Rapid, relentless decline after onset
- Initial rapid deterioration followed by stabilization
- Subtle onset and slow, relentless progression

Treatment

"no well-established protocol"

- Immunosuppressant substitution
  - cyclosporine ► tacrolimus or MMF
  - azathioprine ► sirolimus
- Photopheresis
- Prolonged oral azithromycin therapy

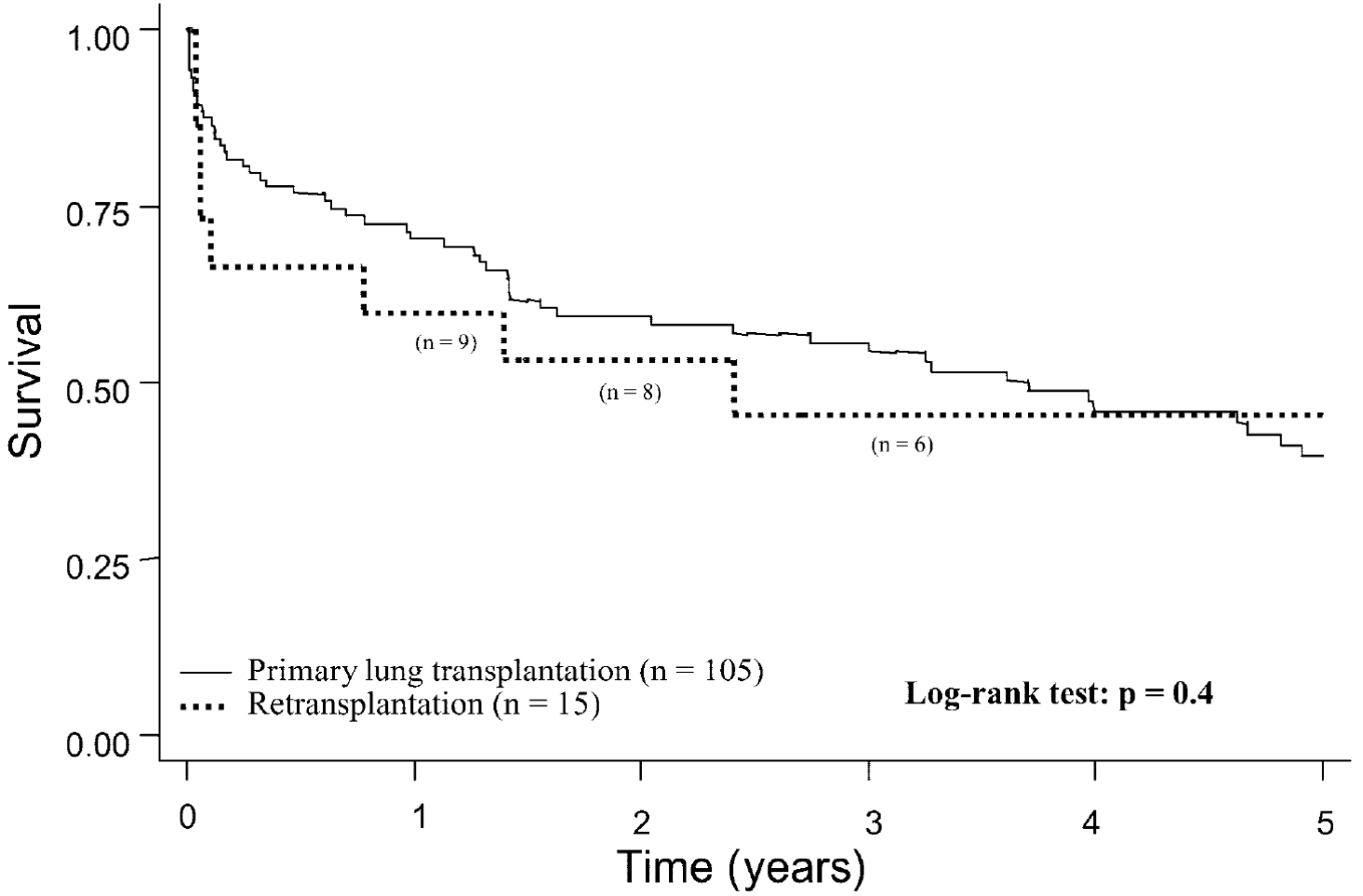
Treatment

- Anti-CD52 antibody Alemtuzumab
- High-dose inhaled glucocorticoids are not effective

- Retransplantation : *“controversial”*
  - BO tends to recur in an accelerated fashion ?

Treatment

- Survival following single-lung retransplantation and primary single lung transplantation



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