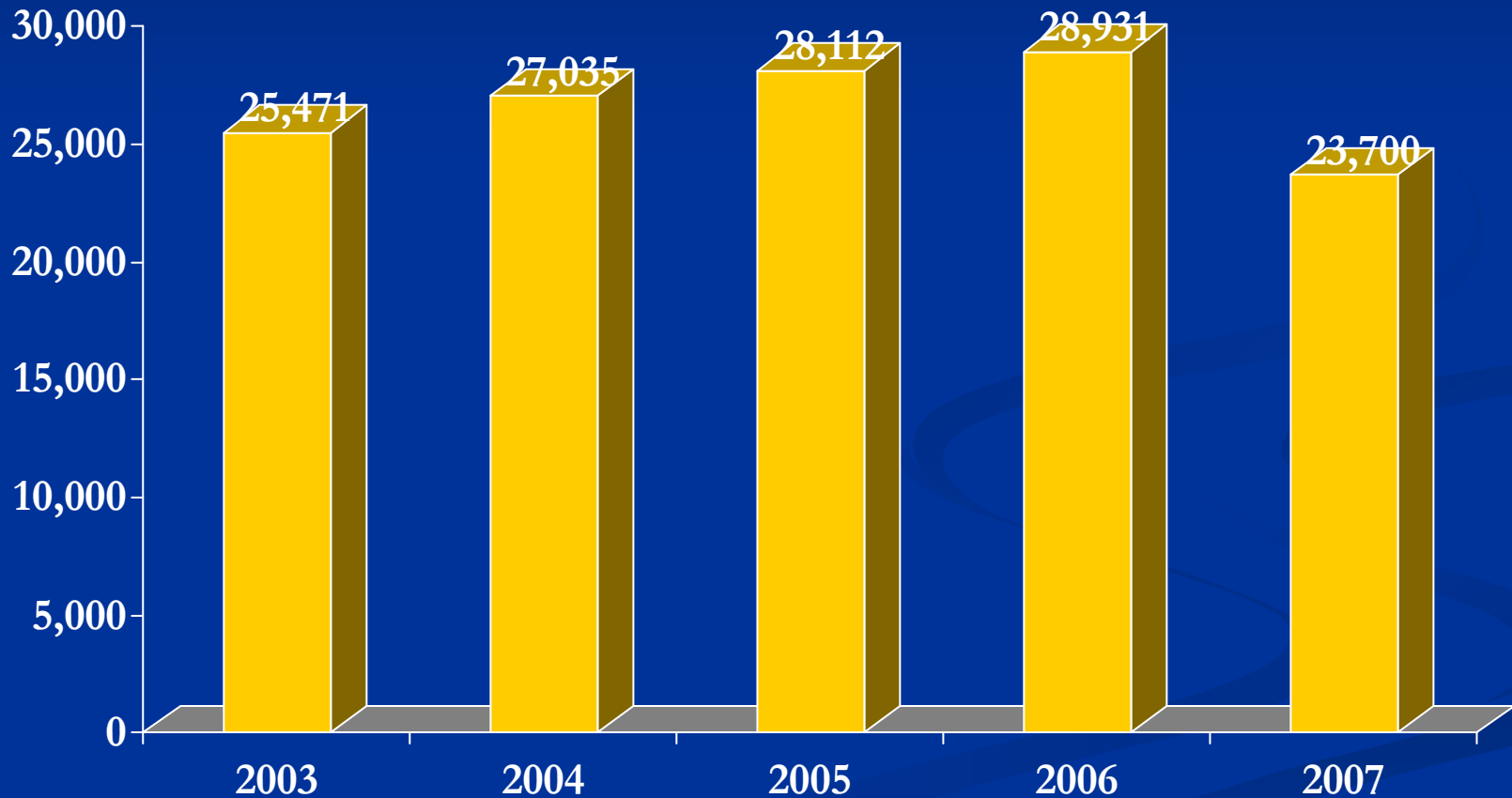




Difference in Invasive Aspergillosis in Solid Organ Transplant Recipients

Shahid Husain MD, MS
Assistant Professor in Medicine
Transplant Infectious Diseases
University of Pittsburgh

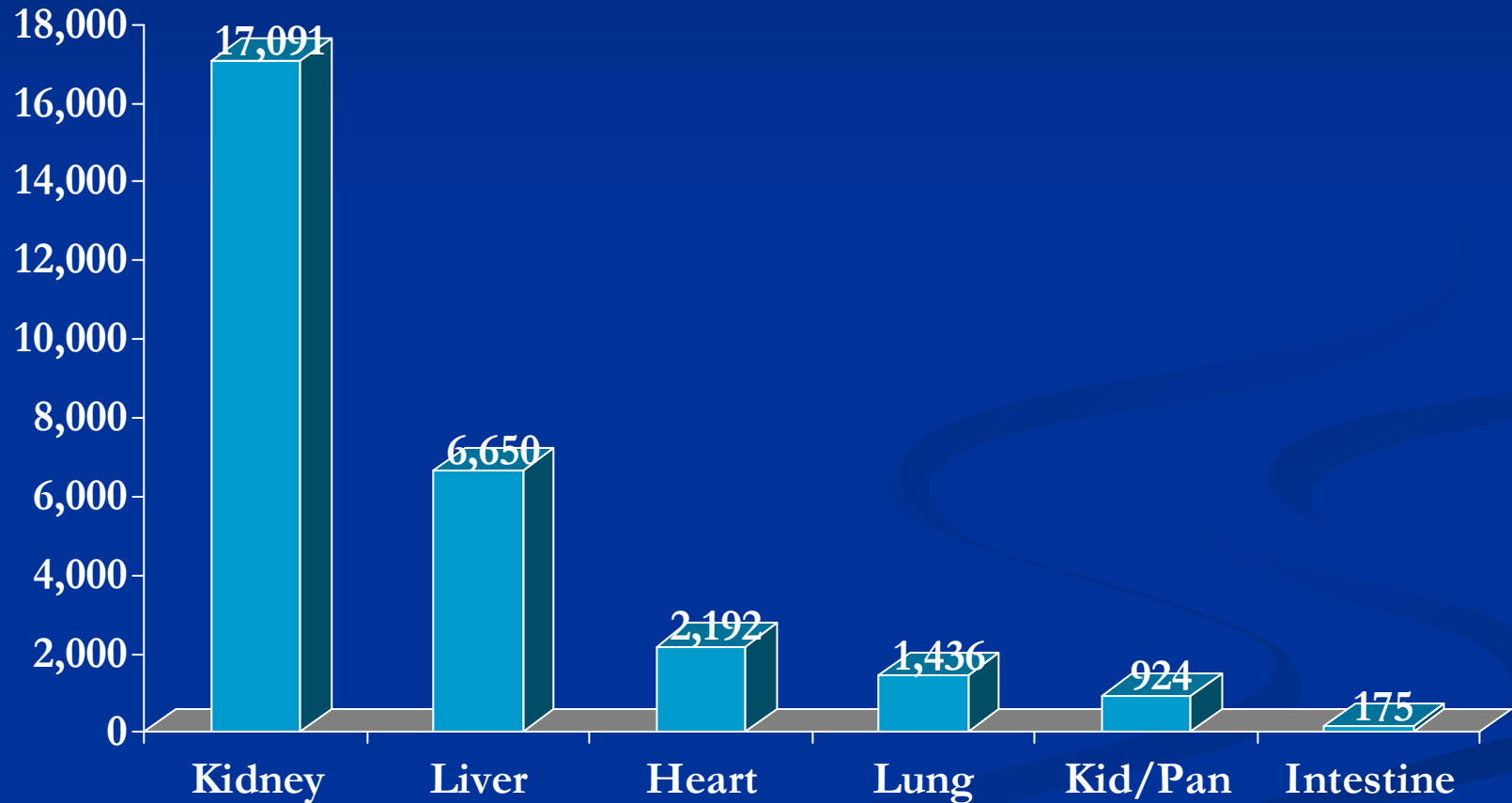
Solid Organ Transplants Performed in United States



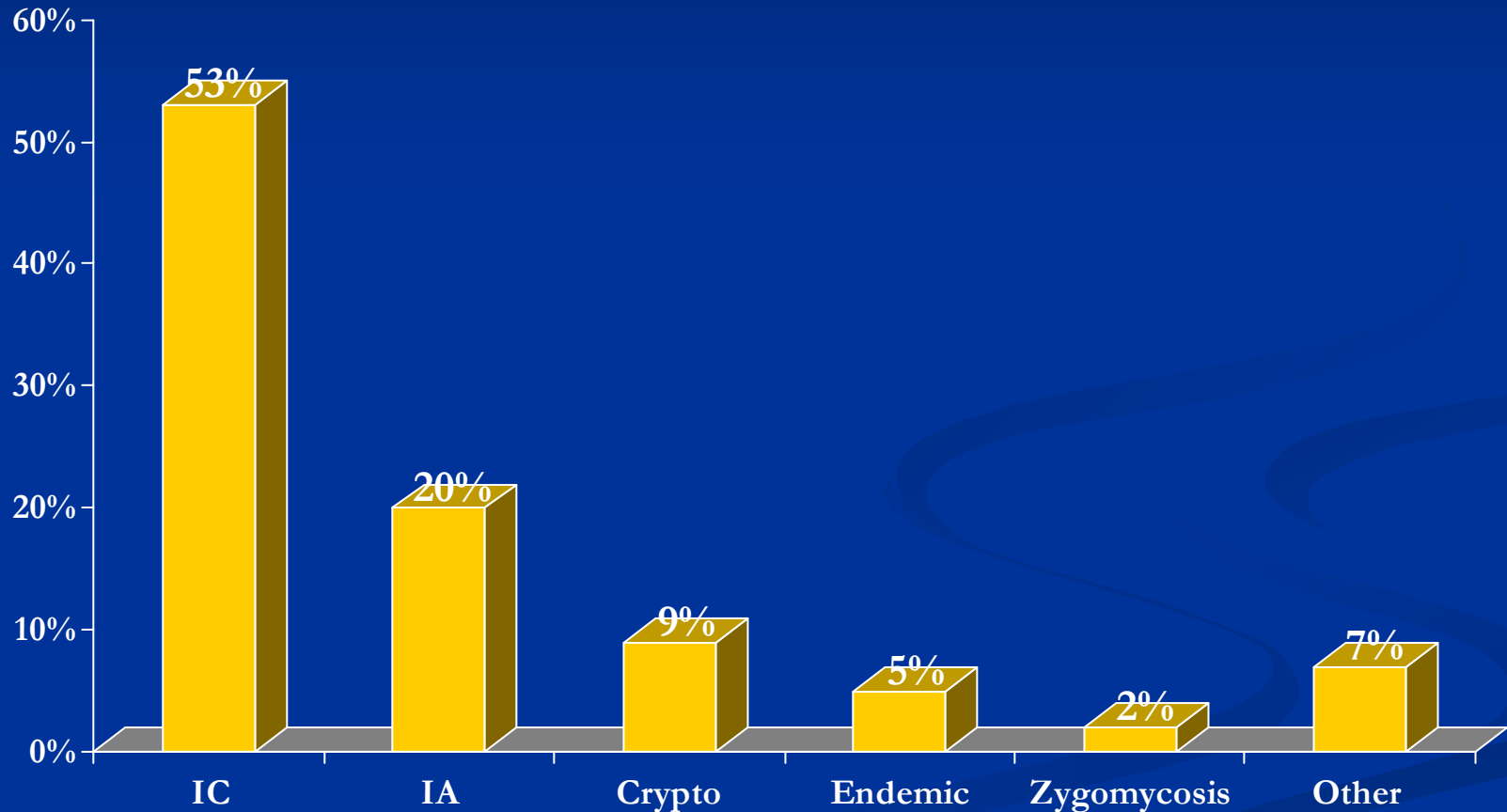
Data for 2007 is until October 2007

UNOS

Solid Organ Transplants Performed in USA in 2006



TRANSNET Data :1073 IFIs

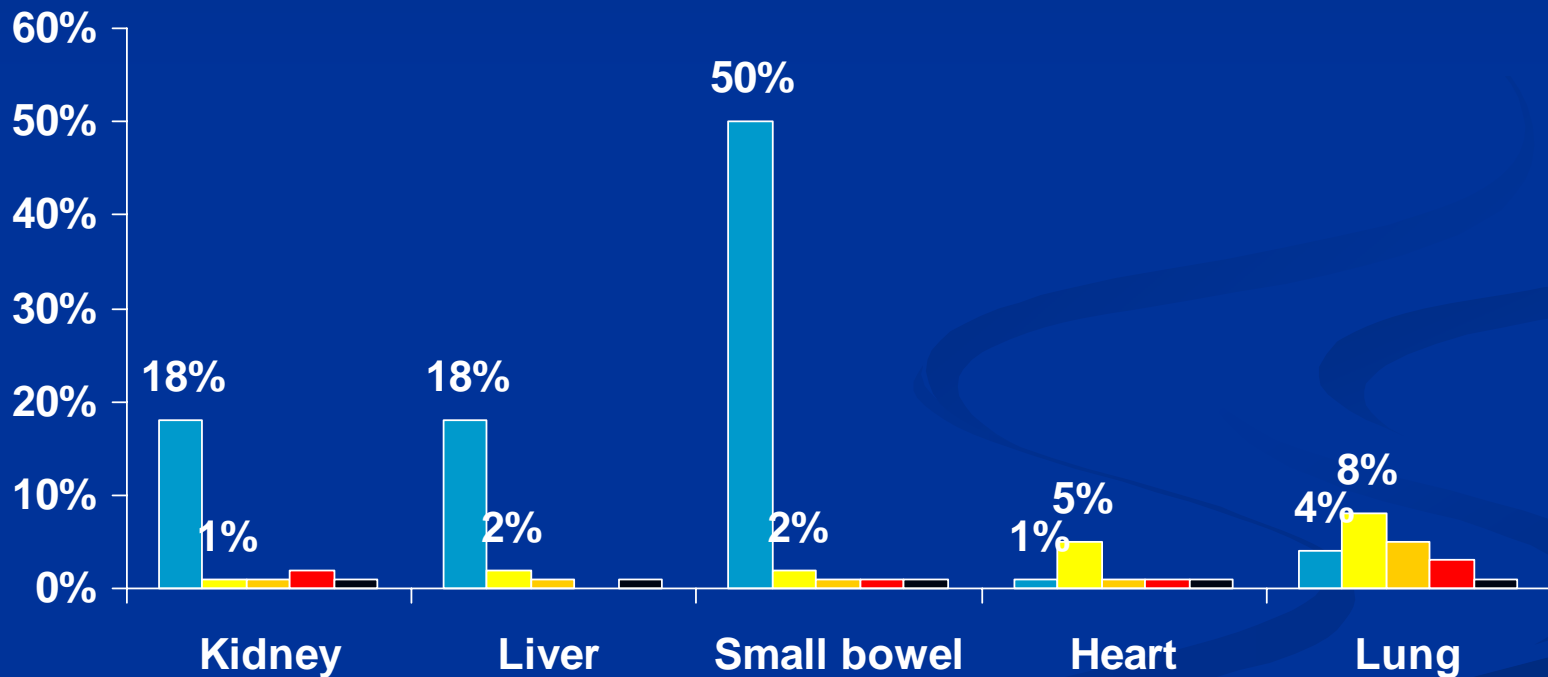


March 2001-October 2006

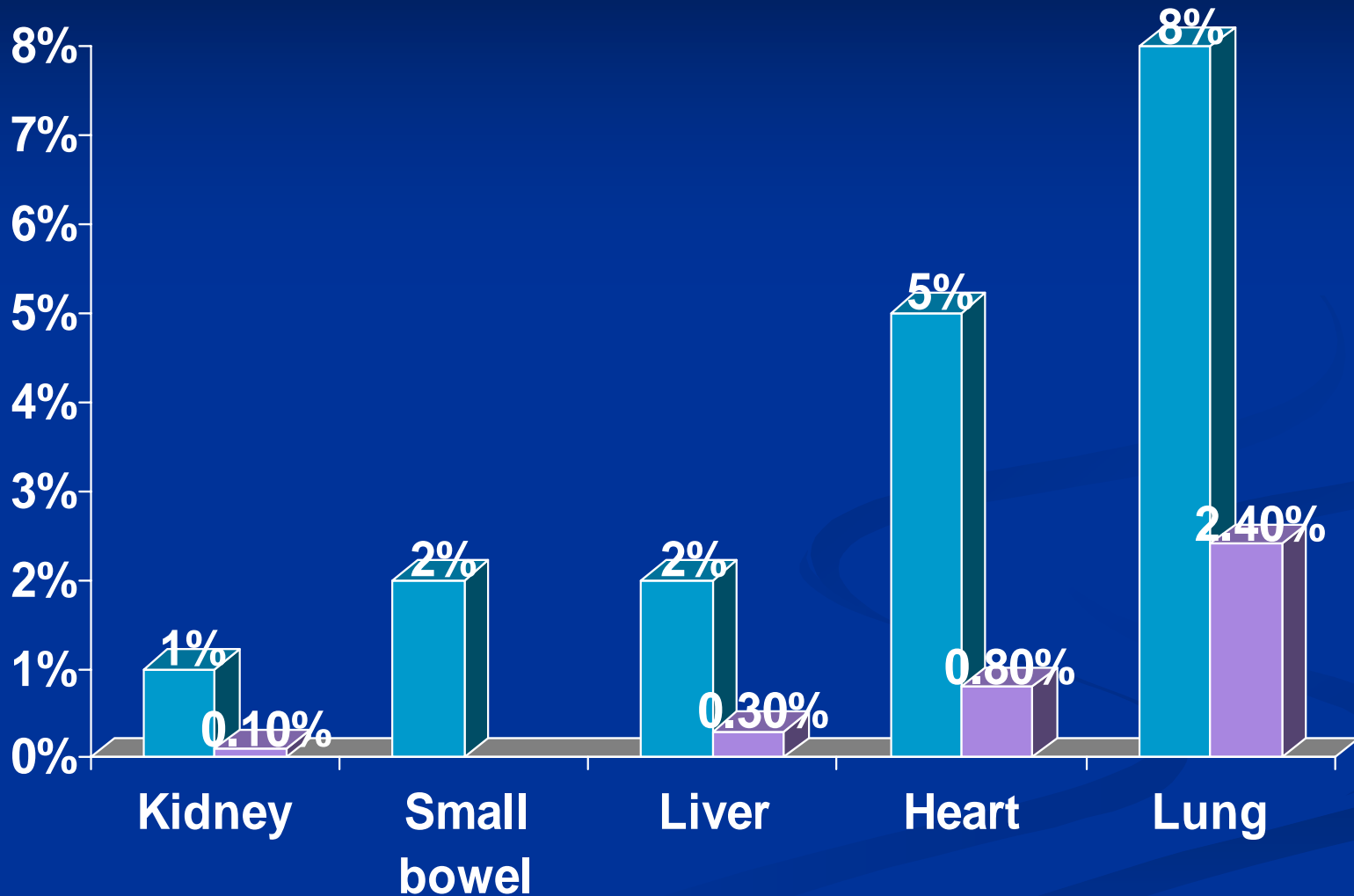
Pappas PG ICAAC 2007-M1195

Distribution of Fungal Infections in SOT

■ *Candida* spp. ■ *Aspergillus* spp. ■ *Cryptococcus* ■ Endemic Mycoses ■ Others

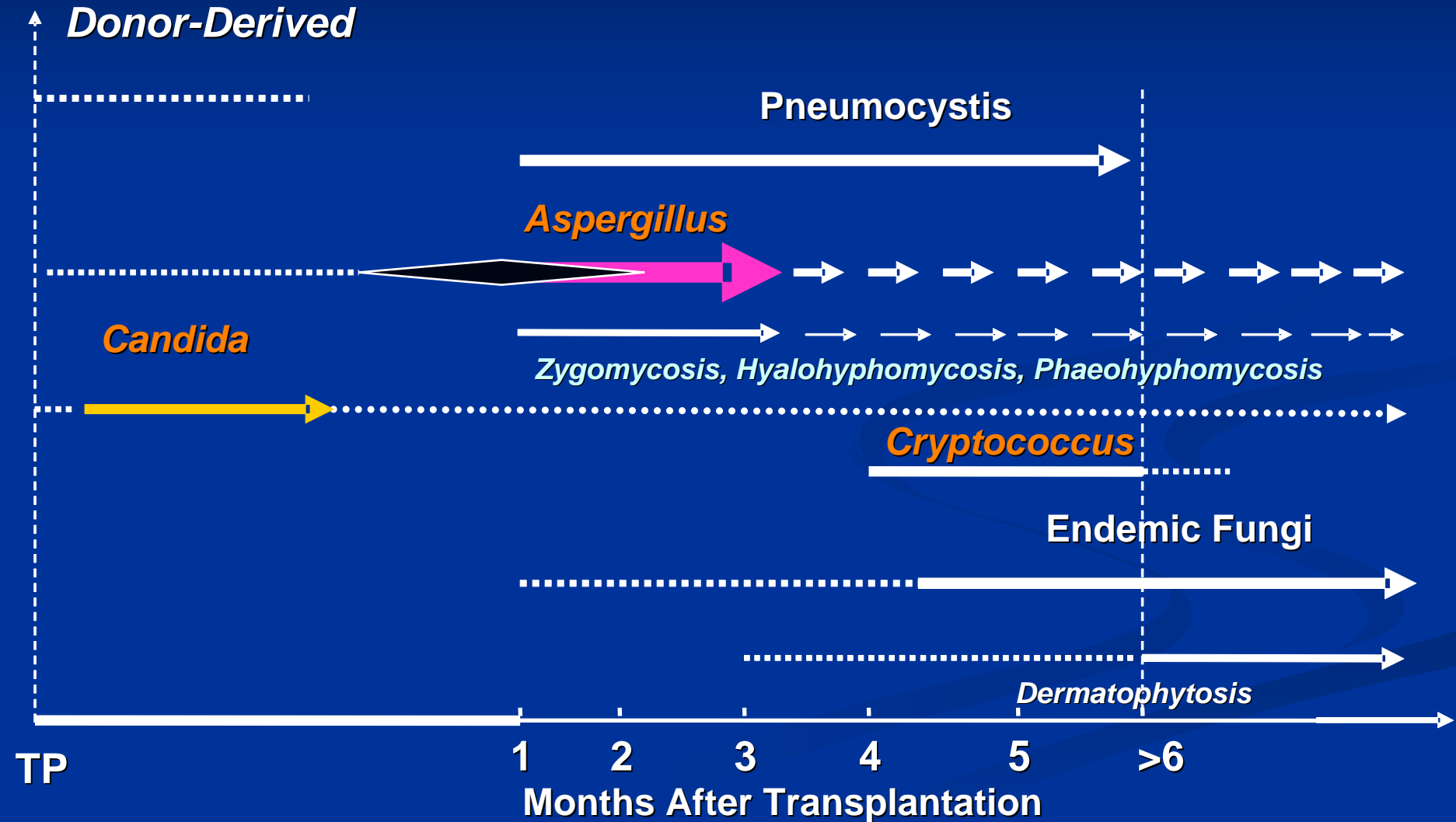


Invasive Aspergillosis in SOT

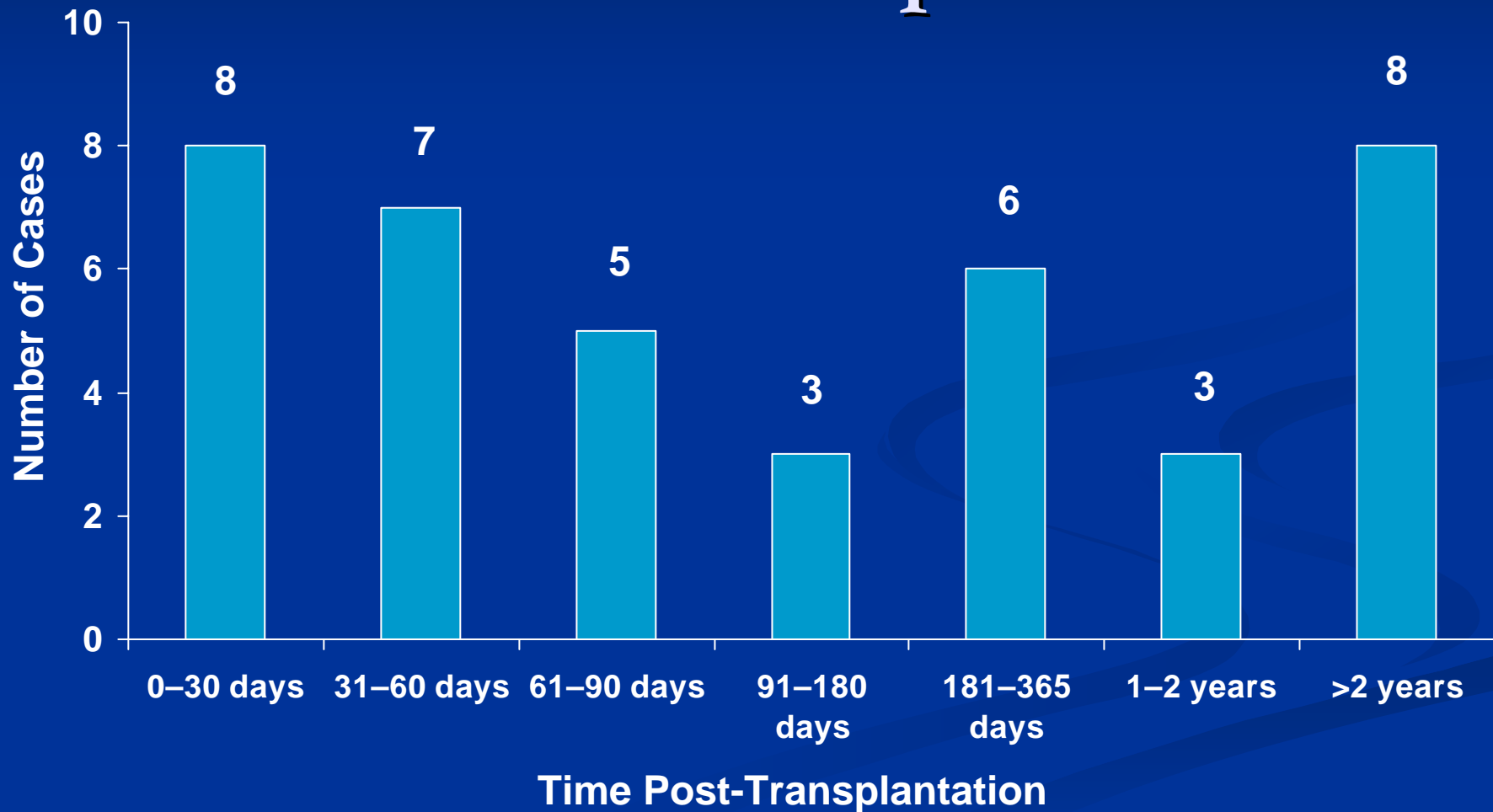


Singh N 2005, Morgan J 2005

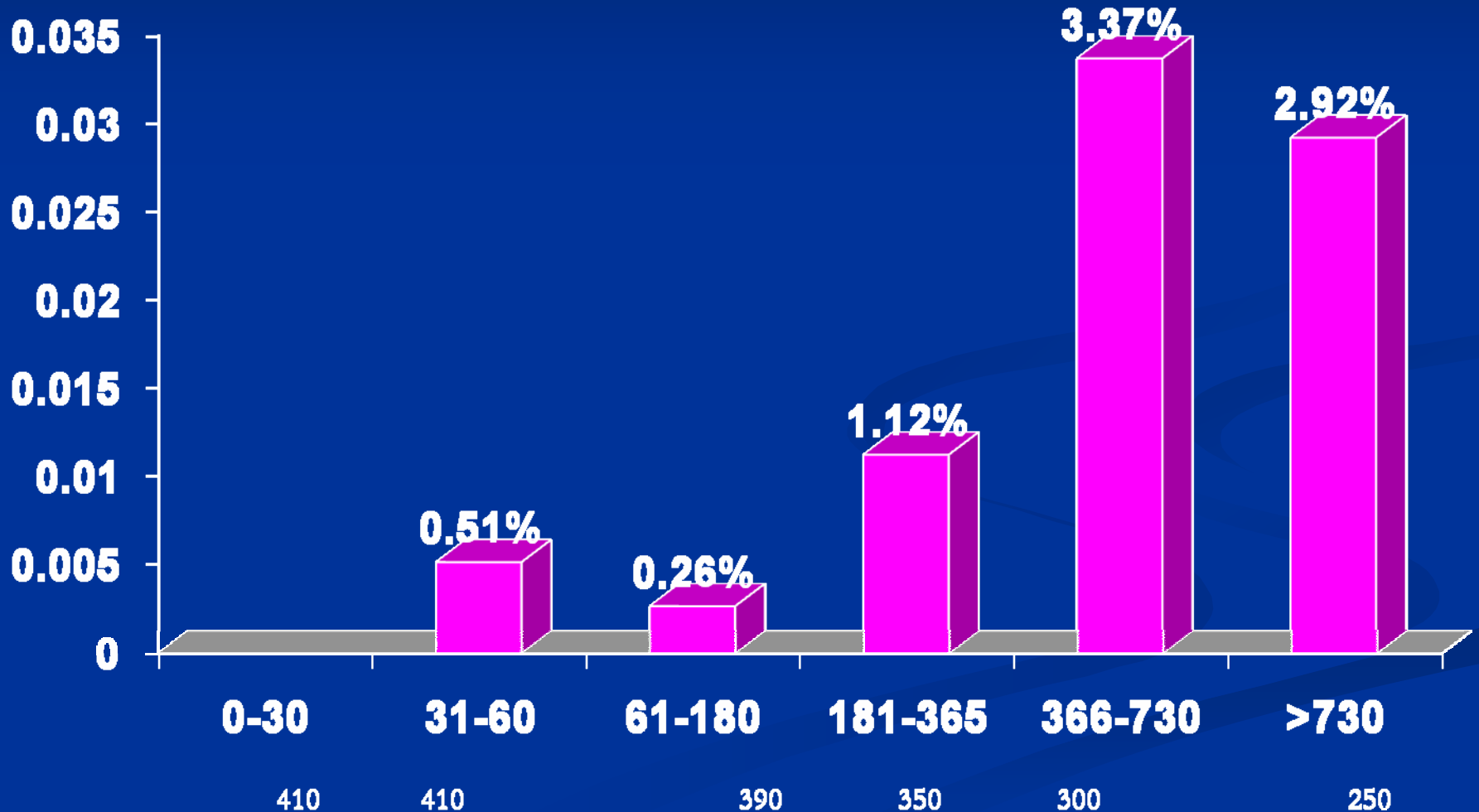
Old Timeline of Post-Transplant Fungal Infection



Timing of Post-Transplant Invasive Aspergillosis (IA) in Liver Transplant

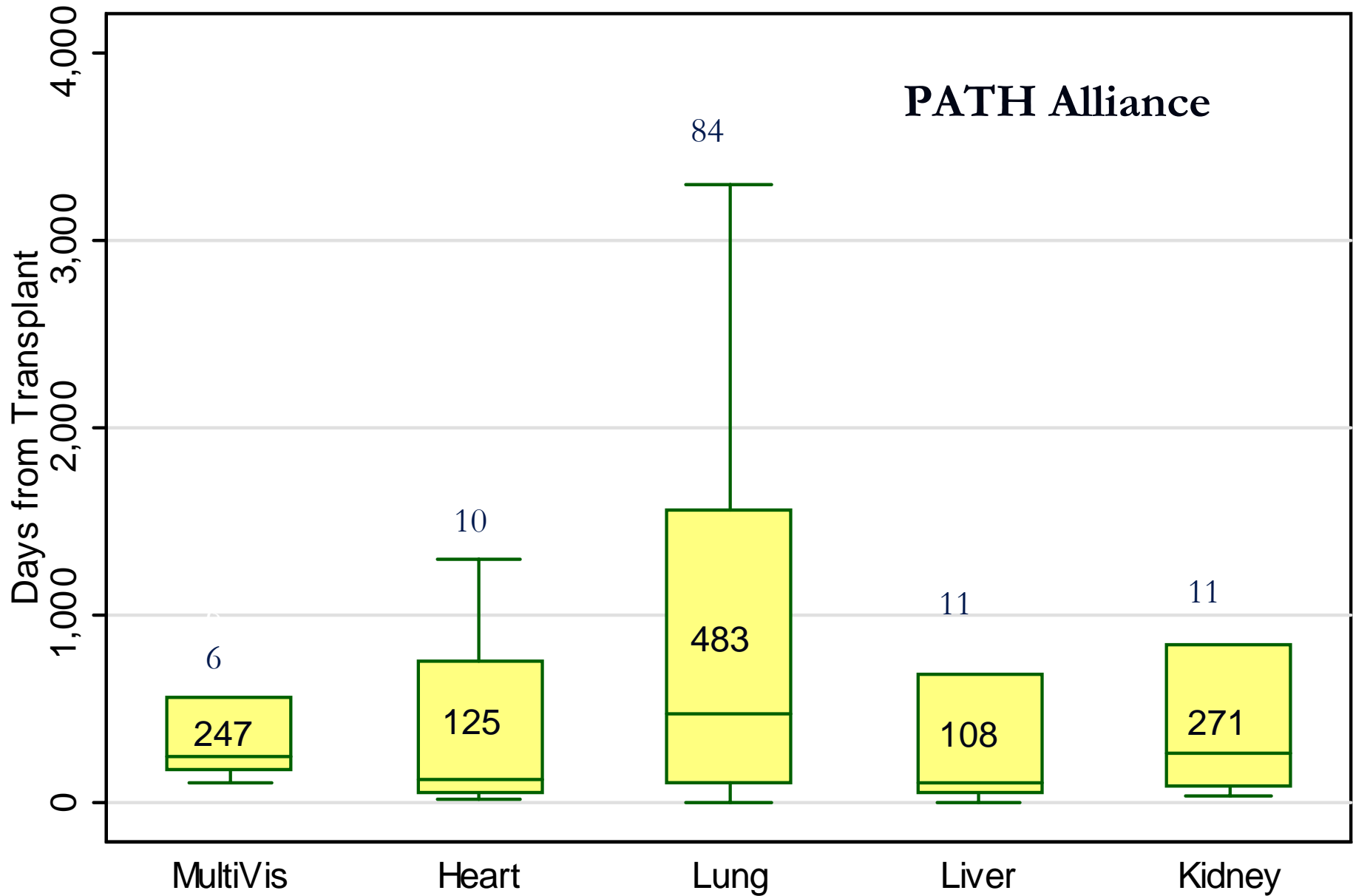


UPMC :Timing of Post-Transplant IA in Lung Transplant



Husain S (unpublished data).

Time to Onset to IA in SOT



excludes outside values

Reasons for Increase Time to Onset of IA

- Increased survival
- Improved surgical techniques
- Immunosuppression
- Late occurrence CMV infection or disease
- Use of antifungal prophylaxis

PATH Alliance: Clinical Presentation

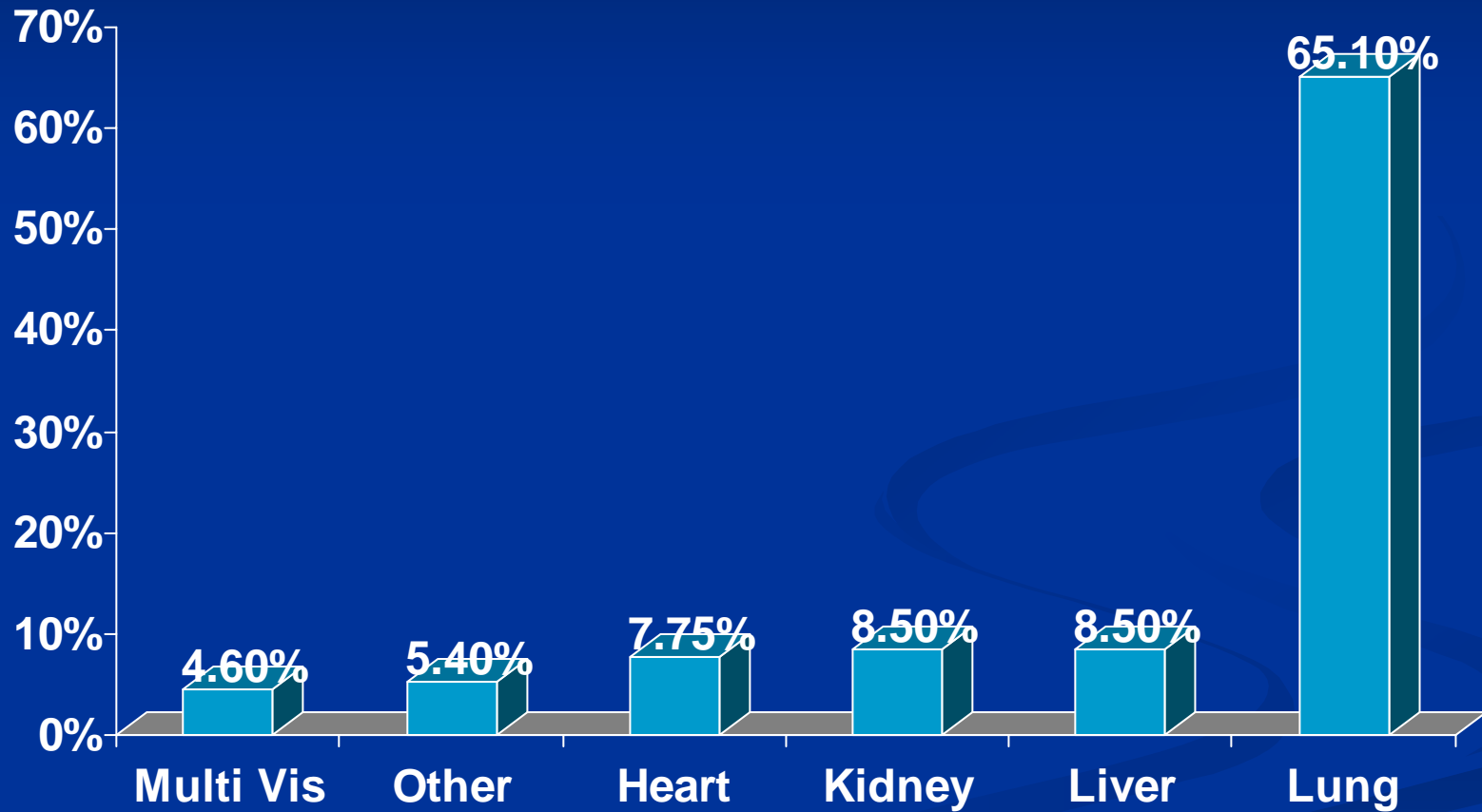
- SOT recipients from 7/04 to 12/07 were included
- 129 adult solid organ transplant recipients had 146 reported episodes of *Aspergillus* infection
- The data reported is on initial episode of *Aspergillus* infection



List of Centers in PATH Alliance

Center	Number of Patients
Duke University Medical Center	21
Emory University	2
Massachusetts General Hospital	10
Mount Sinai School of Medicine	4
Oregon Health Sciences University	1
University of Arkansas	2
University of Michigan	11
University of Minnesota	3
University of Nebraska	2
University of Pittsburgh	25
University of Washington	27
University of Wisconsin	20
Washington Hospital Center	1

PATH alliance : Type of SOT with IA 129 Patients



No. of Patients 67

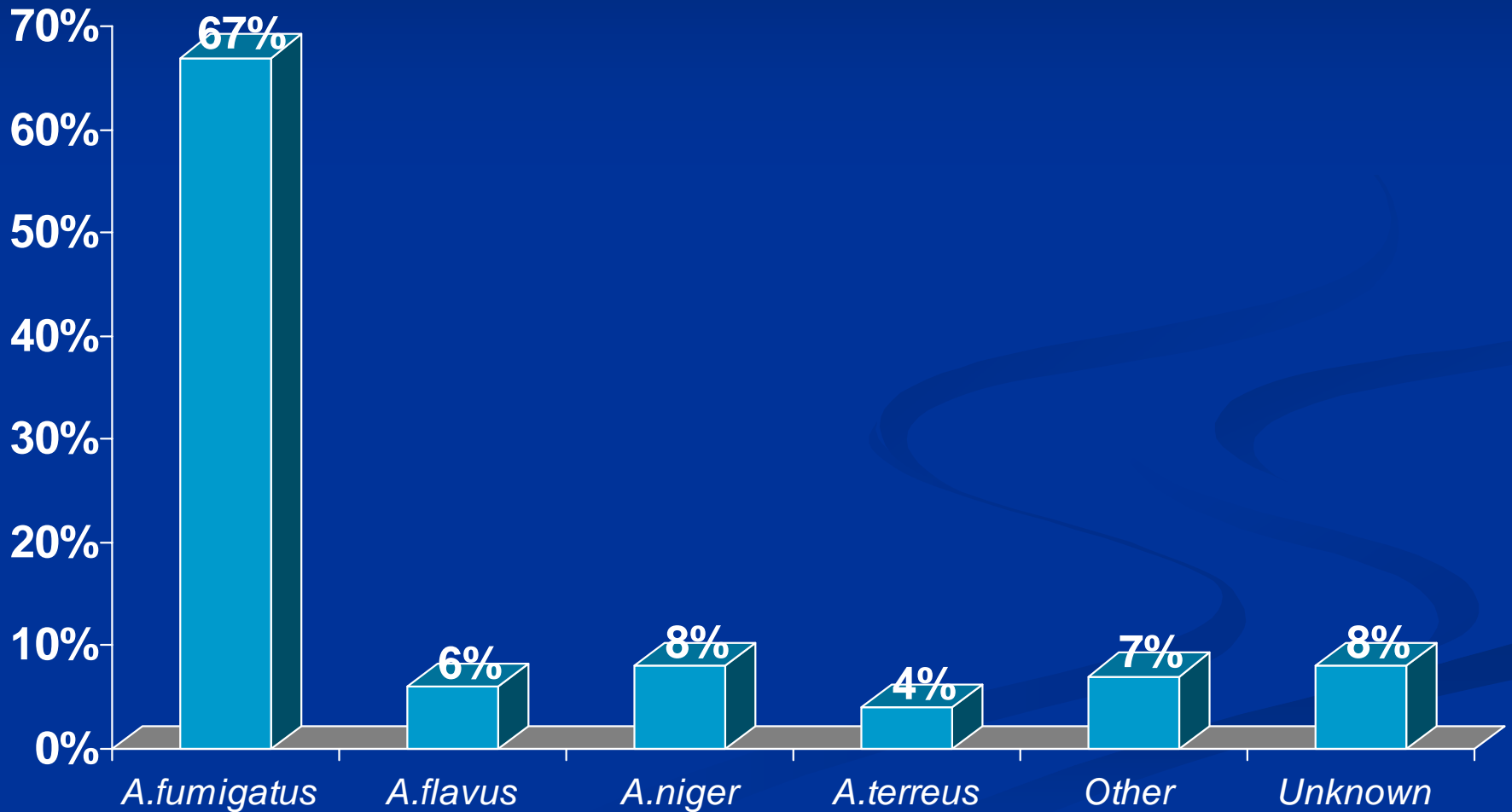
10

11

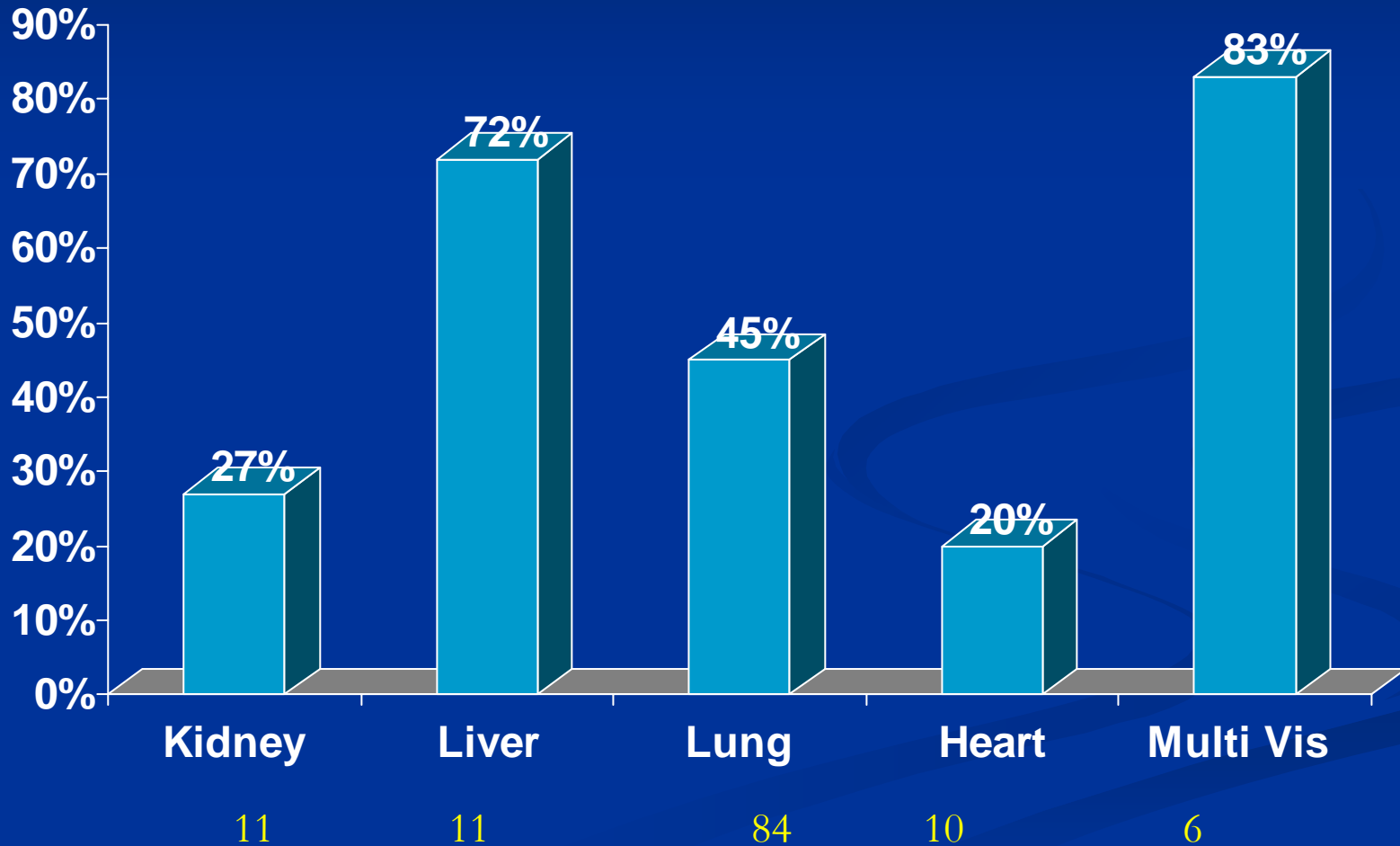
11

84

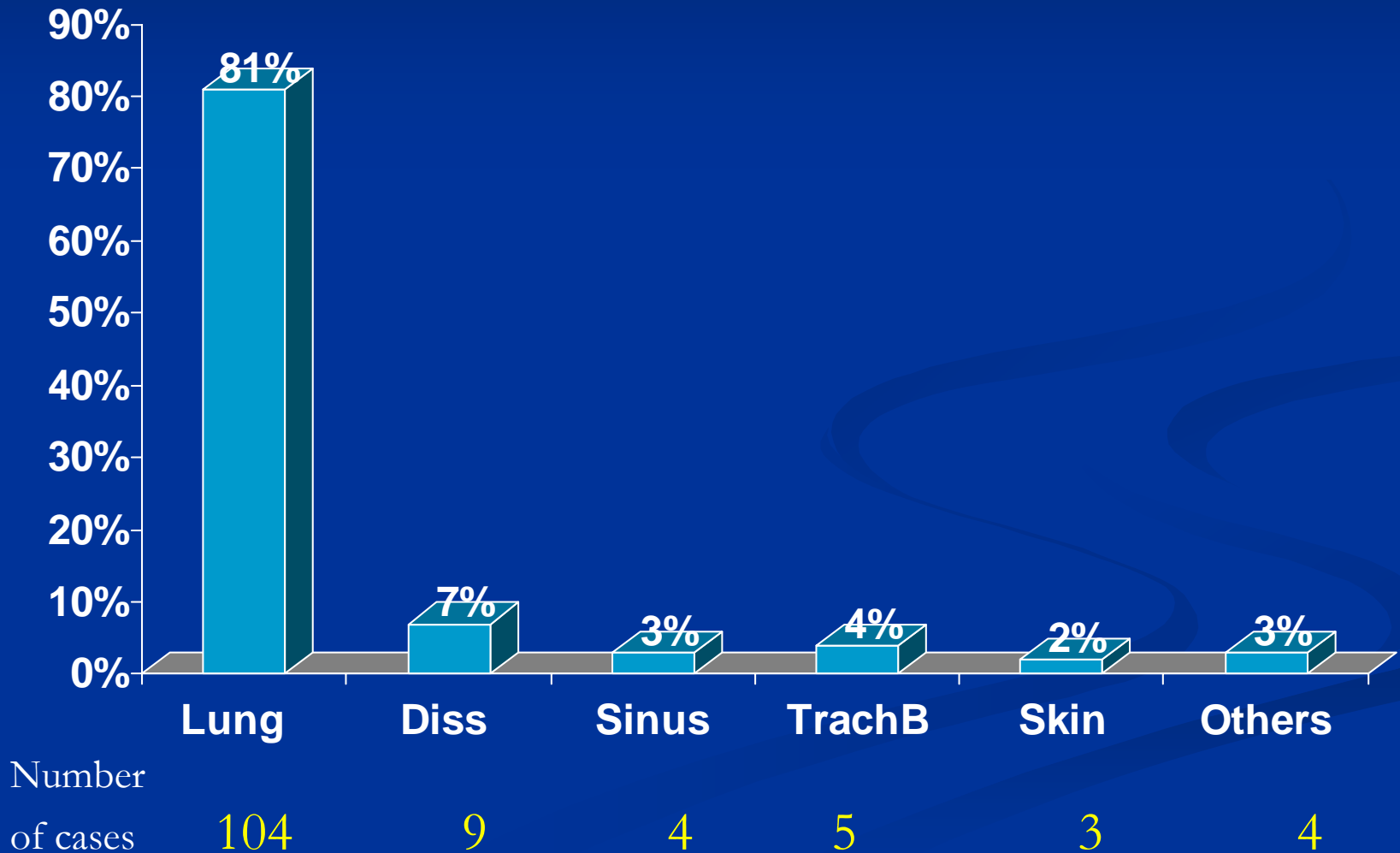
PATH Alliance : Distribution of *Aspergillus* species



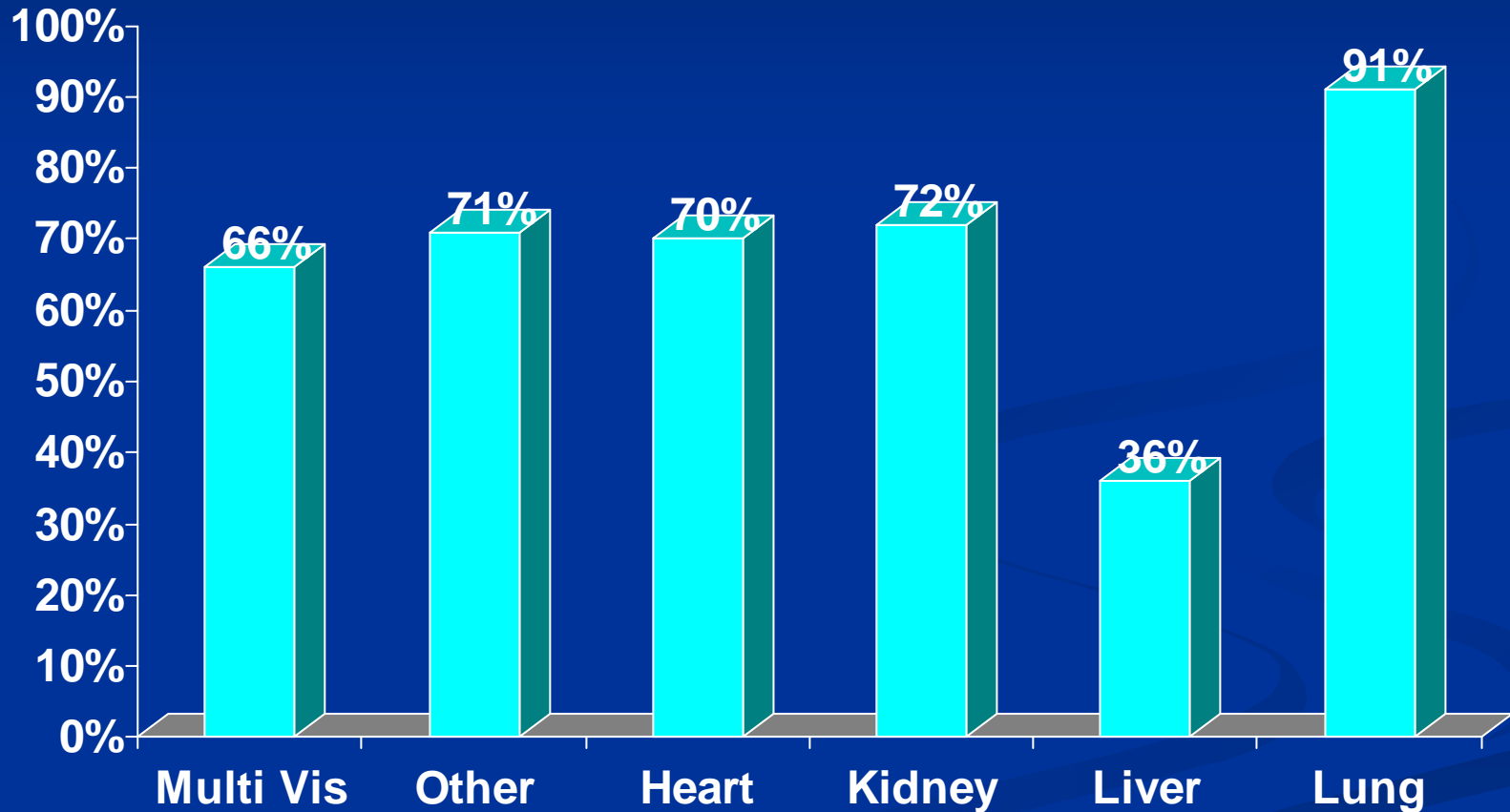
PATH Alliance : Proven cases in SOT



PATH Alliance: Distribution of Organ Involvement in IA

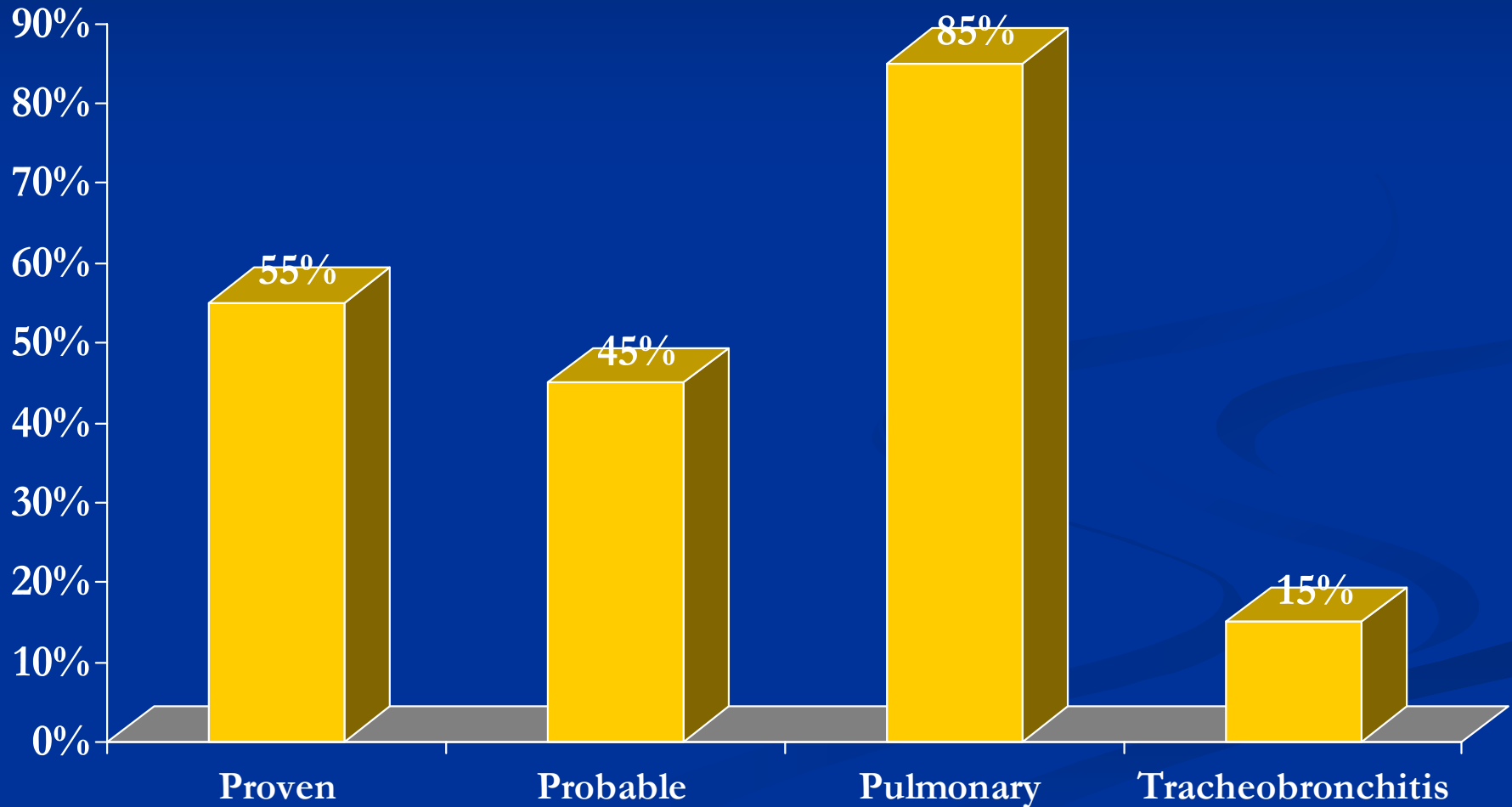


PATH Alliance: Distribution of Pulmonary IA among SOT

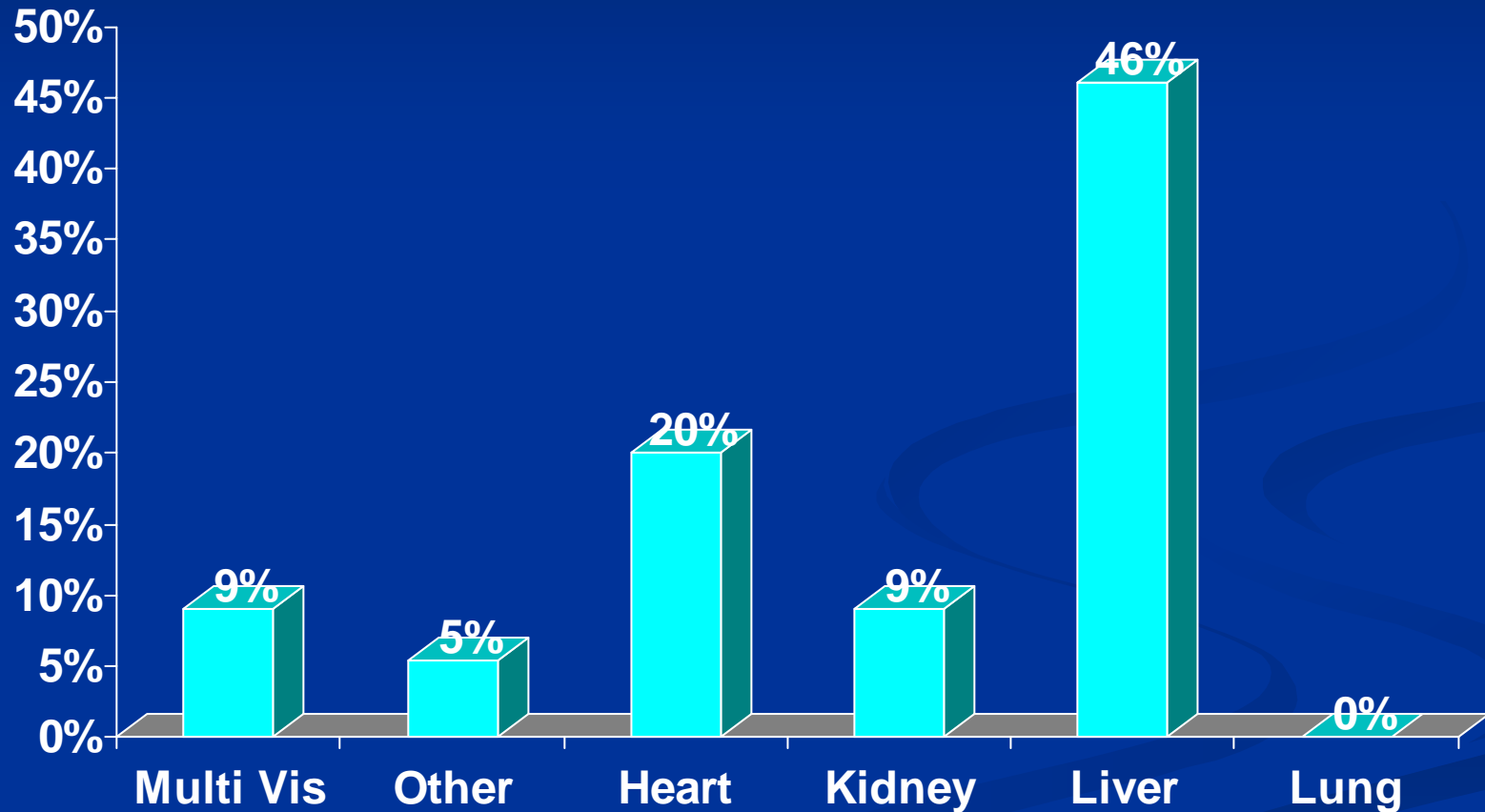


No. of Patients 6 7 10 11 11 84

UPMC :Categories of Pulmonary Infections in Lung Transplants

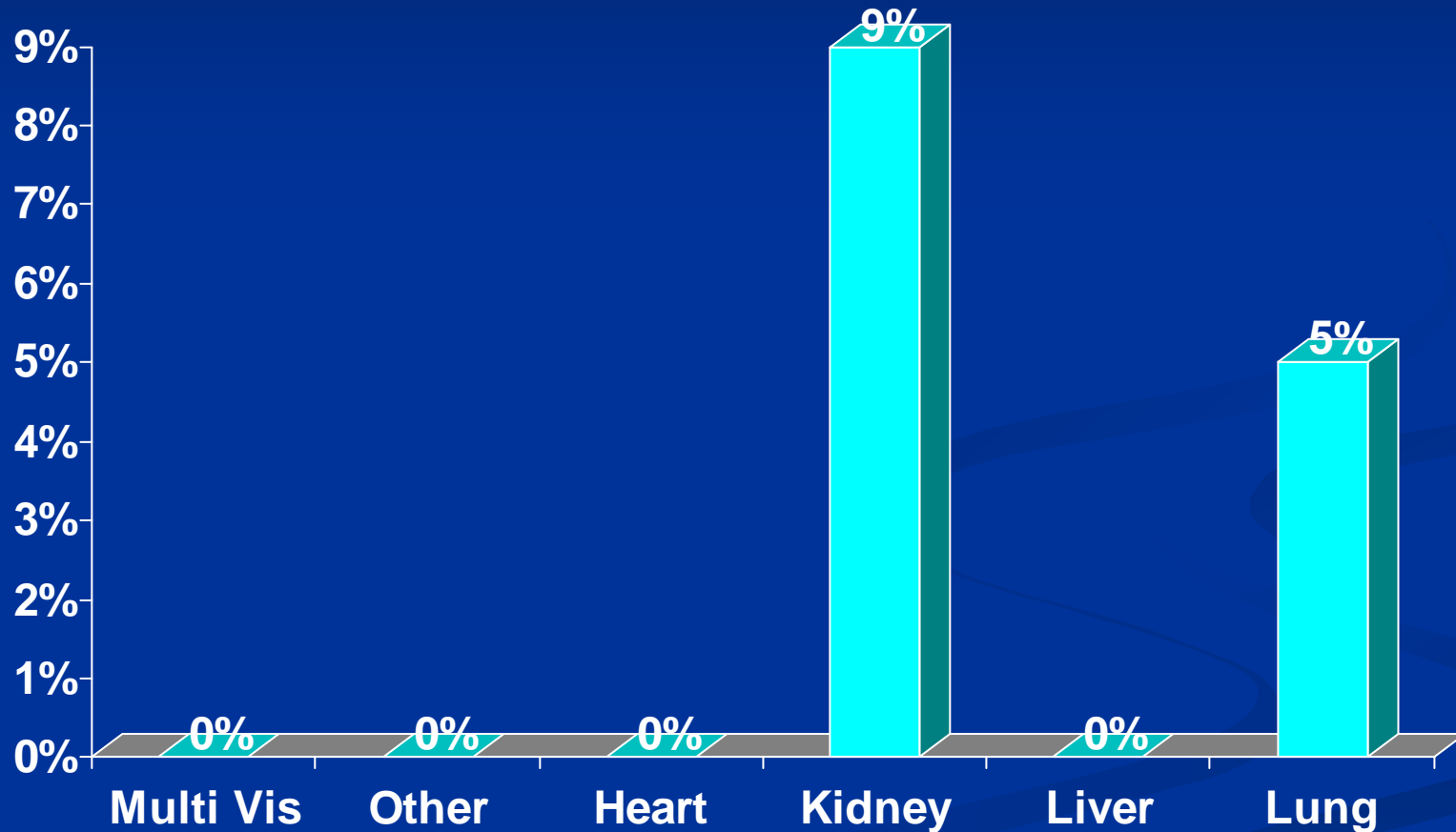


PATH Alliance : Disseminated Disease in SOT



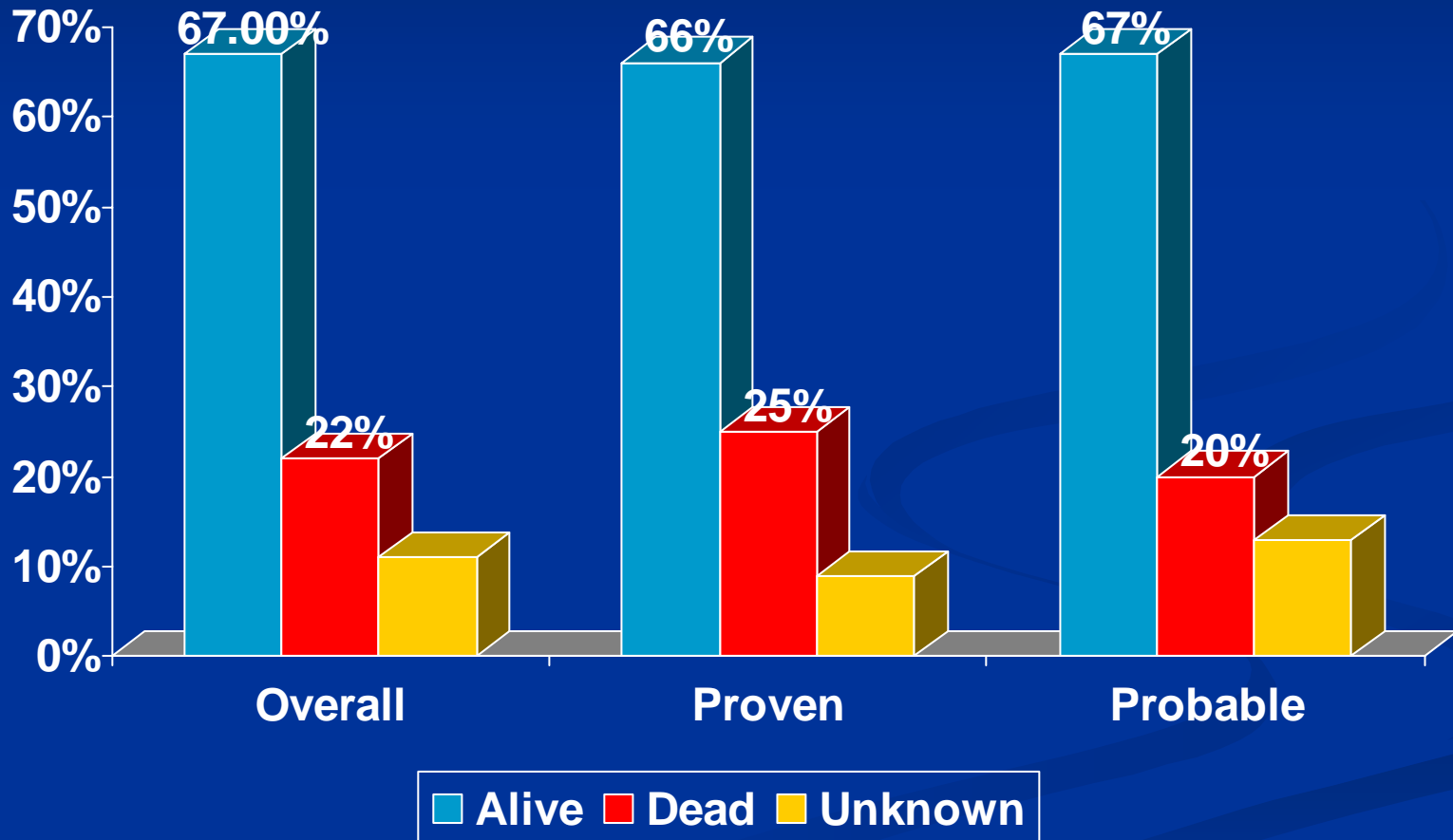
No. of Patients 6 7 10 11 11 84

PATH Alliance : Sinus Involvement

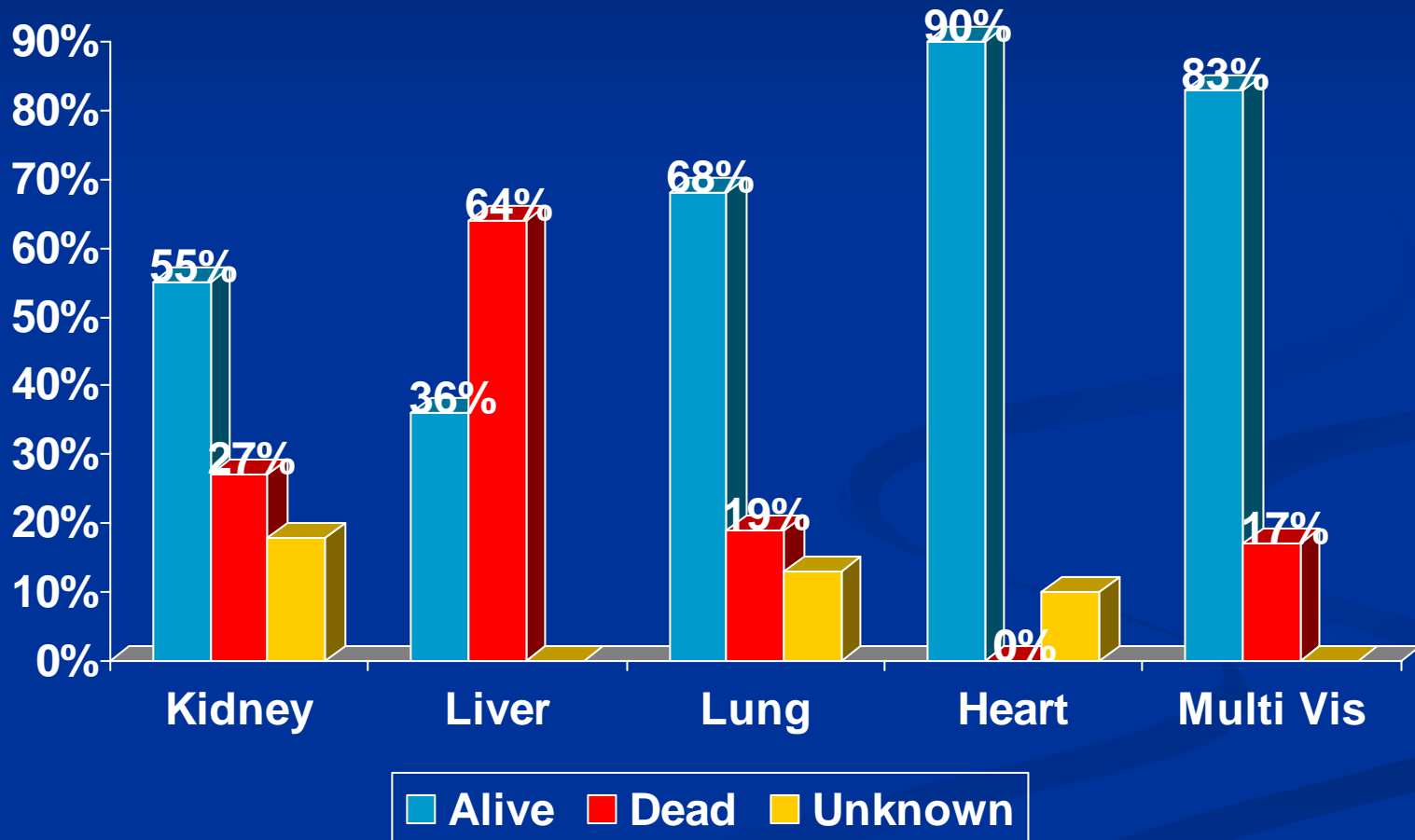


No. of Patients 6 7 10 11 11 84

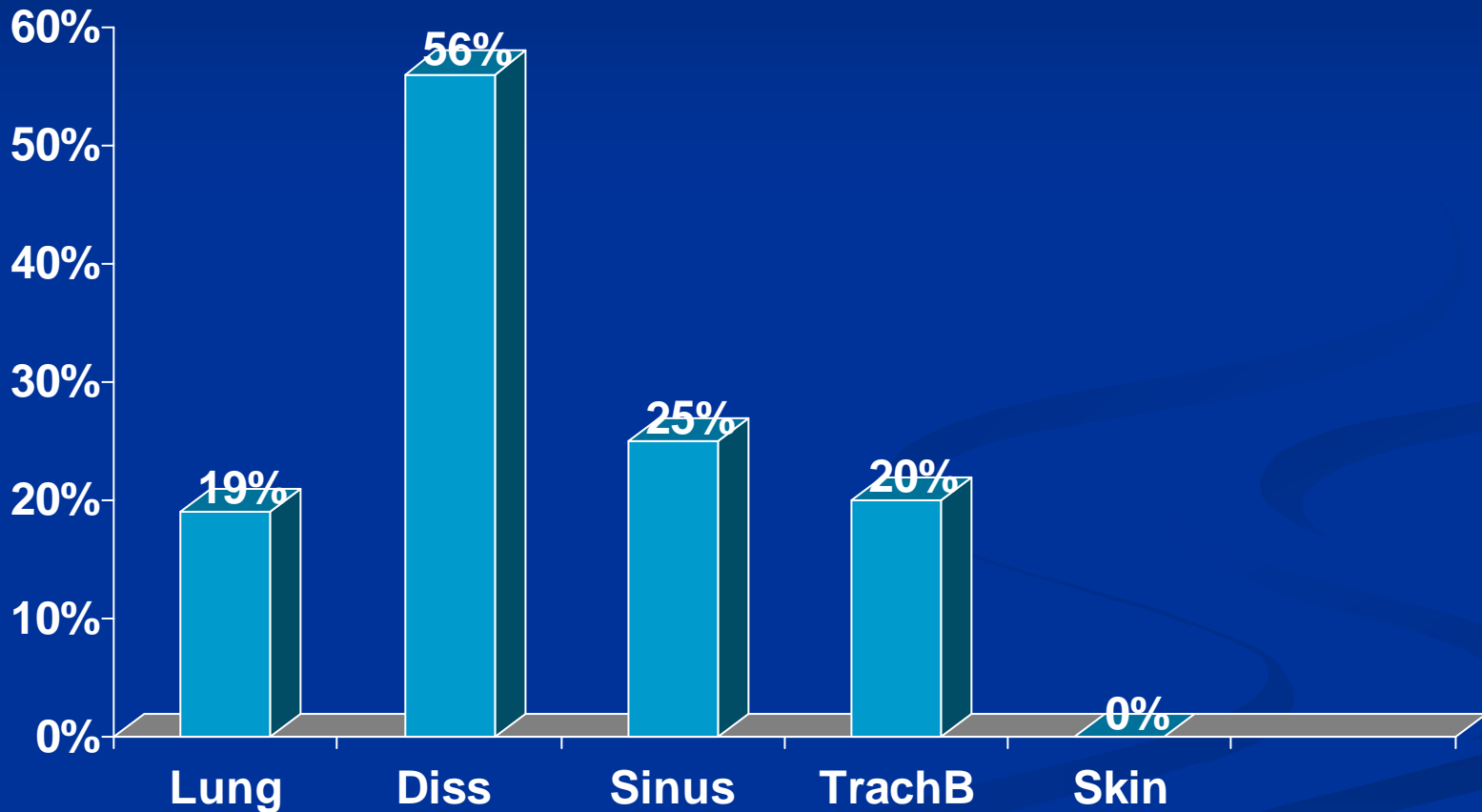
PATH Alliance : Overall Outcome at 12 Weeks



PATH Alliance : Outcome at 12 weeks



PATH Alliance : 12 Weeks Mortality by Organ Involvement



Higher state of immunosuppression

Denervation

Continuous contact with pathogens

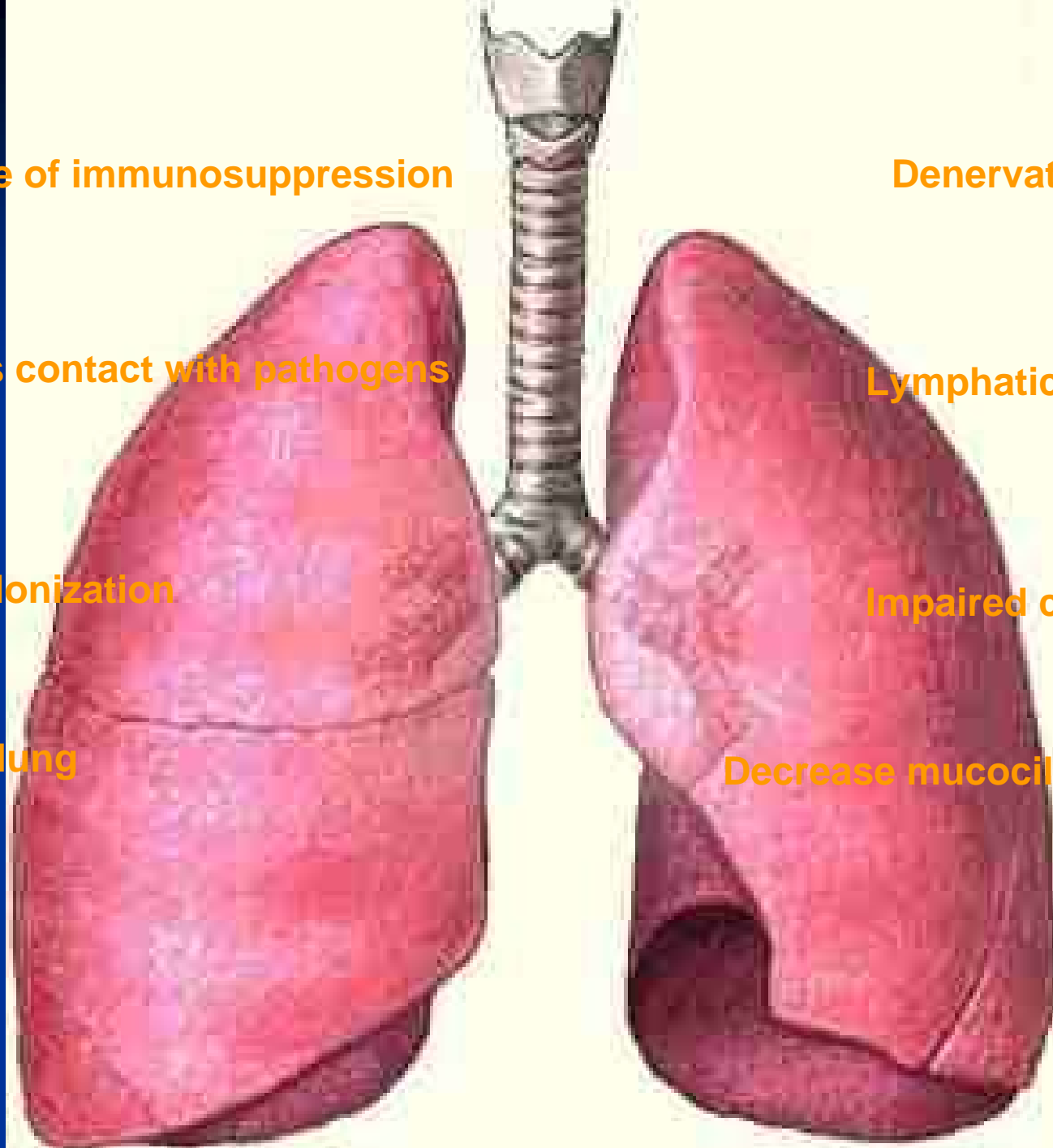
Lymphatic disruption

Airways colonization

Impaired cough reflex

The Native lung

Decrease mucociliary clearance



Higher Risk of Dissemination in Liver Transplant

- Earlier Onset
- Immunosuppression cyclosporin vs tacrolimus
- Iron Overload
- Th1/Th 2 Imbalance
 - IL 10, IL 4
 - IFN γ , TNF α , IL12, GM-CSF
- Role of other cytokines
 - CXCL2, CCL4 ,CCL3, IL 1 β
- TLR?

Brandhagen DJ Hepatology 2000, Alexander J Liver Trans 2006,
Roilides E JID 2001, Cortez KJ Infect Immun 2006, Balloy V Infect imm 2005

Summary

- Time to onset of IA in SOT is increasing with 50% of the cases occurring after 6 months
- Lung transplant recipients have the highest risk of IA in SOT
- Pulmonary aspergillosis is the most common presentation of IA in current cohort of lung transplants

Summary

- Liver transplants are uniquely susceptible to disseminated disease
- Highest mortality is noted in disseminated disease and lowest in isolated skin disease
- Pulmonary disease and tracheobronchitis had similar mortality

Implications

- The follow-up period of current prospective surveillance studies in SOT should be extended to capture the incidence of late onset invasive aspergillosis
- The dearth of human data to determine the biological markers for development and spread of invasive diseases necessitates incorporation of biological markers in clinical studies

- Stay Alert!
 - To believe is very dull.
 - To doubt is intensely engrossing.
- Oscar Wilde

