Baylor College of Medicine

DEPARTMENT OF PEDIATRICS

Texas Children's Hospital®

Division of Infectious Diseases

Infection in Pediatric Solid Organ Transplants

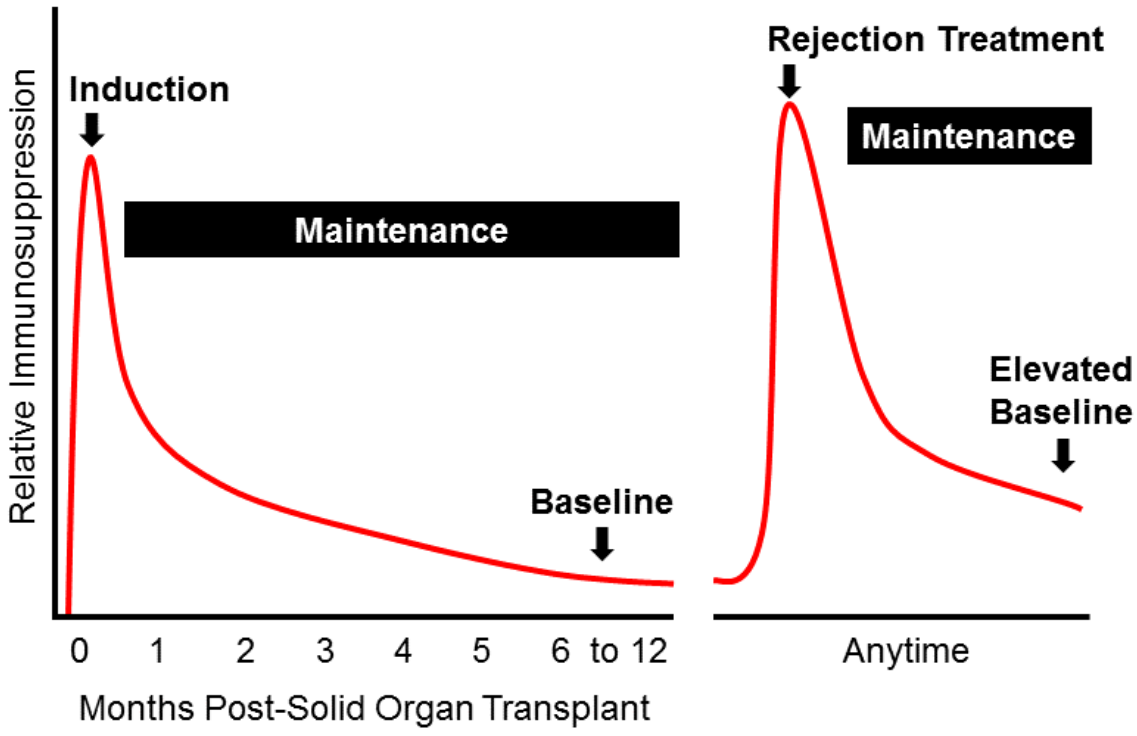
Elizabeth A. Moulton, MD, PhD

January 17th, 2025

Outline

- Immunosuppression & infection post-transplant
- Risk factors for multidrug resistant organisms (MDRO) in pediatric transplantation
- MRDO experience at Texas Children’s Hospital
- Challenging case

Immunosuppression in Solid Organ Transplant

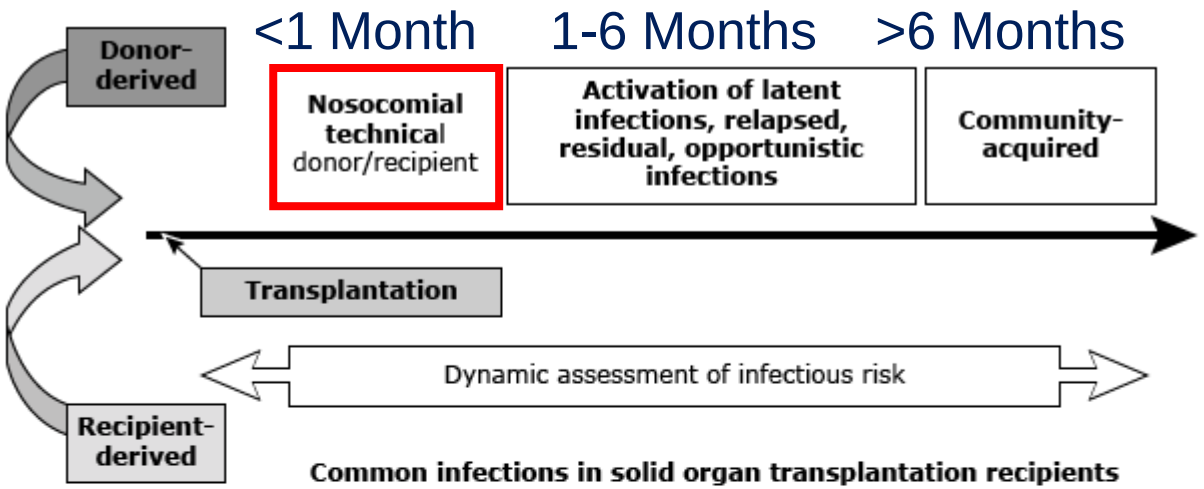


Net State of Immunosuppression

- Type, dose, duration, and temporal sequence of immunosuppression
- Underlying diseases or comorbid conditions
- Devitalized tissues or fluid collections
- Invasive devices: vascular access, urinary catheters, surgical drains, and ventricular assist devices
- Host factors: hypogammaglobulinemia, neutropenia, malnutrition, uremia, diabetes
- **Age, prior infection or immunization**
- Concomitant immunomodulating viruses CMV, EBV, HHV-6 and -7, SARS-CoV-2, HBV, and HCV

UpToDate Infection in the solid organ transplant recipient 2024
Fishman JA. Infection in solid-organ transplant recipients. N Engl J Med 2007; 357:2601.

Timeline of Infections in Solid Organ Transplant



Common infections in solid organ transplantation recipients

Antimicrobial-resistant species: • MRSA • VRE • *Candida* species (non-*albicans*) Aspiration Line infection Wound infection Anastamotic leaks/ischemia *Clostridium difficile* colitis	**With PCP and antiviral (CMV, HBV) prophylaxis:** • BK polyomavirus nephropathy • *Clostridium difficile* colitis • Hepatitis C virus • Adenovirus, influenza • *Cryptococcus neoformans* • *Mycobacterium tuberculosis* **Anastamotic complications**	**Community-acquired pneumonia, urinary tract infection:** *Aspergillus*, atypical molds, *Mucor* species *Nocardia*, *Rhodococcus* species Late viral: • CMV (colitis/retinitis) • Hepatitis (HBV, HCV) • HSV encephalitis • Community-acquired (SARS, West Nile) • JC polyomavirus (PML), skin cancer, lymphoma (PTLD)
Donor-derived (uncommon): HSV, LCMV, rabies, West Nile **Recipient-derived (colonization):** *Aspergillus*, *Pseudomonas*	**Without prophylaxis add:** *Pneumocystis* Herpes viruses (HSV, VZV, CMV, EBV) Hepatitis B virus *Listeria*, *Nocardia*, *Toxoplasma*, *Strongyloides*, *Leishmania*, *Trypanosoma cruzi*	

Surgical Site Infections

- Intestinal/Multivisceral 14-53%
- Liver 10-37%
- Lung 5-19%
- Heart 4-19%
- Kidney 3-11%

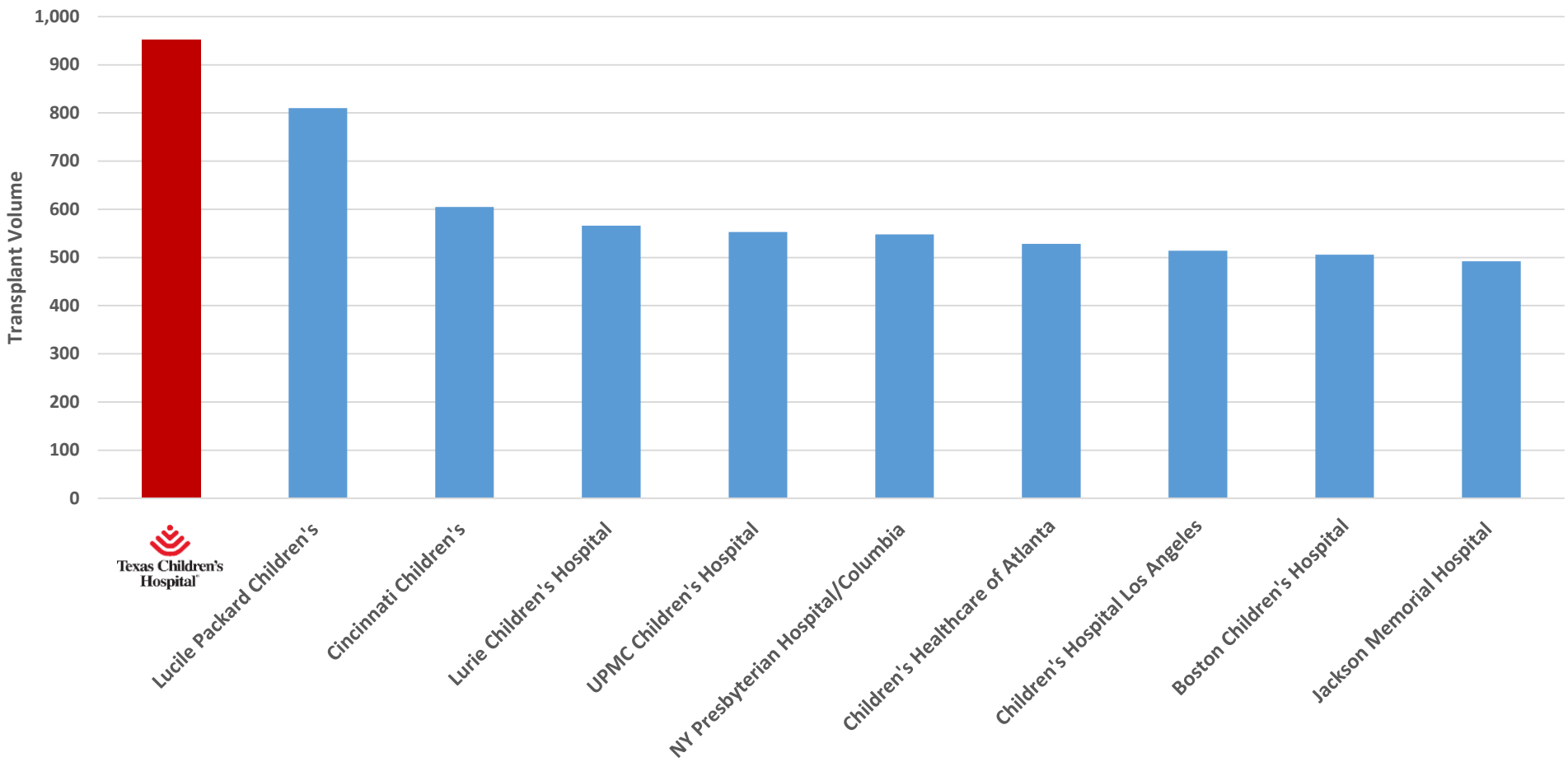
- Most commonly recipient's own flora but can be donor derived
  - Vancomycin-resistant *Enterococci*
  - Carbapenem-resistant *Enterobacterales*
  - Extended-spectrum beta-lactamase
  - Methicillin-resistant *Staphylococcus aureus*
  - Carbapenem resistant *Pseudomonas aeruginosa*

UpToDate Fishman JA. Infection in the solid organ transplant recipient 2024.
Abbo LM, Grossi PA. Surgical site infections: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant 2019;33(9):e13589.

Texas Children's has the Most Pediatric Transplants 2015-2024

#1 in volume
for last 7 years

Approximately
- 30% Heart
- 30% Liver
- 30% Kidney
- 10% Lungs



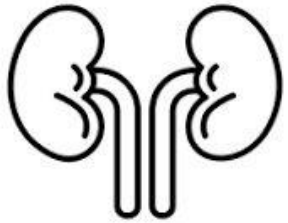
Baylor College of Medicine
DEPARTMENT OF PEDIATRICS

*Data from optn.transplant.hrsa.gov transplant volumes through December 2024, Slide courtesy of Diana Harter

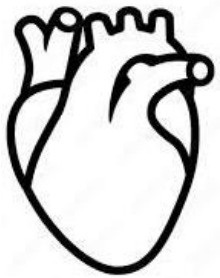
Texas Children's Hospital

Antibiotic Exposure & Risk Factors for Resistant Organisms

- Liver transplant: Biliary atresia
  - Recurrent cholangitis
  - Bile lakes
  - Prolonged antibiotics
  - Antibiotic prophylaxis



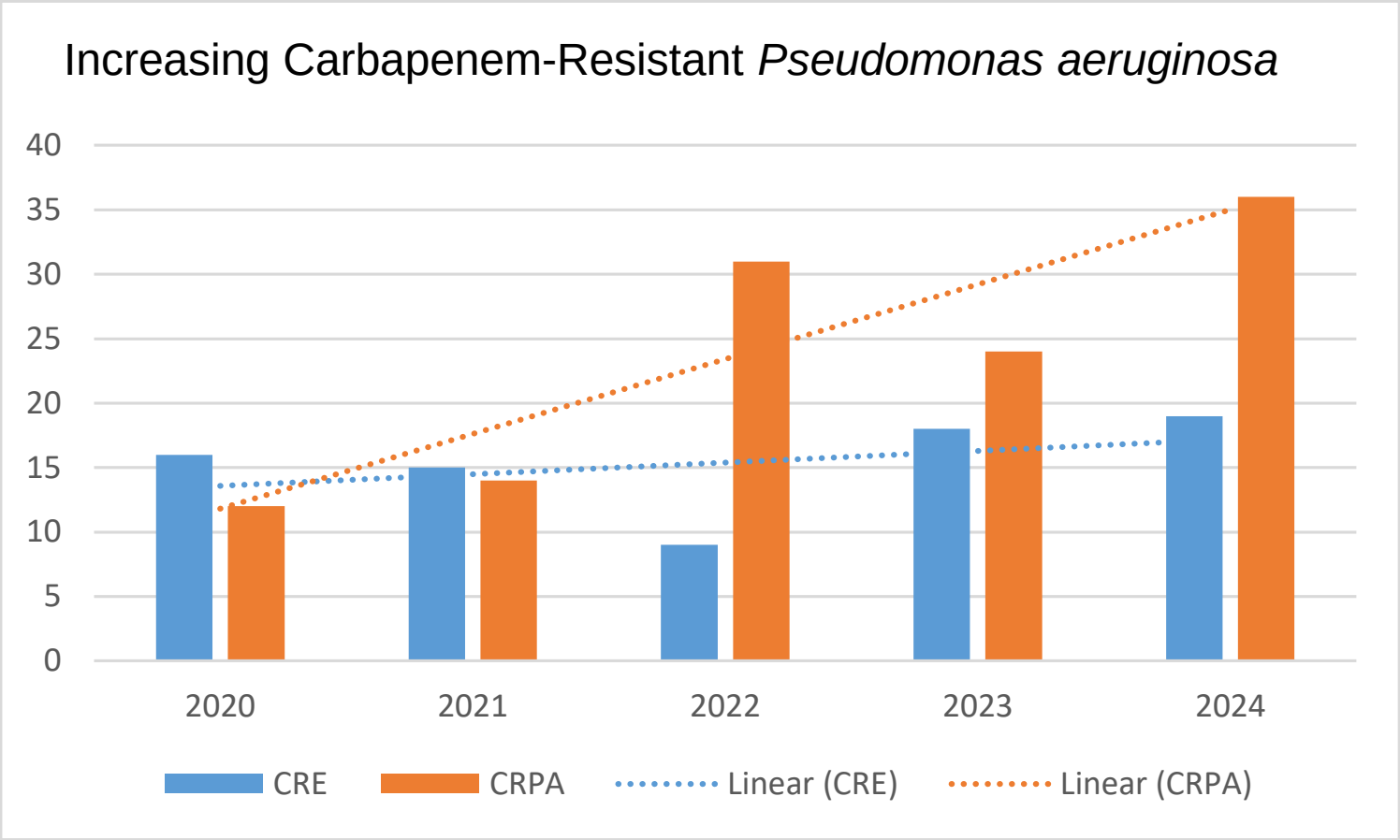
- Kidney transplant: Anatomic issues
  - Recurrent urinary tract infections
  - Intermittent catheterization
  - Antibiotic prophylaxis
  - Dialysis

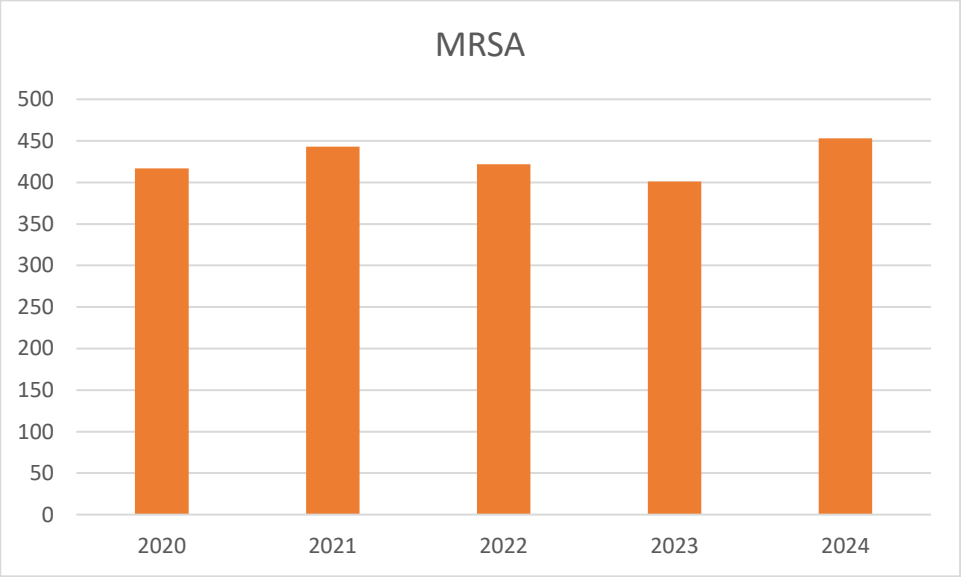


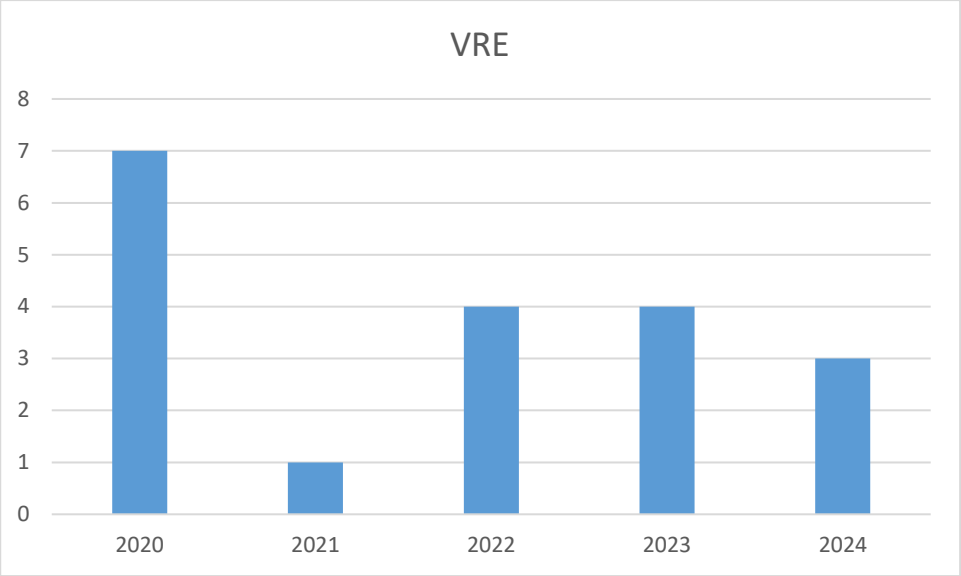
- Heart transplant: Congenital heart disease, cardiomyopathy
  - Surgery
  - Prolonged hospitalizations
  - Central line dependent
  - Mechanical circulatory support (ventricular assist device (VAD), extracorporeal membrane oxygenation (ECMO))

- Lung transplant: Cystic fibrosis, bronchiolitis obliterans, surfactant deficiency, pulmonary hypertension
  - Frequent pneumonia/antibiotics
  - Poor airway clearance
  - Tracheostomy dependence
  - Ventilator dependence
  - ECMO

Resistance at Texas Children's Hospital



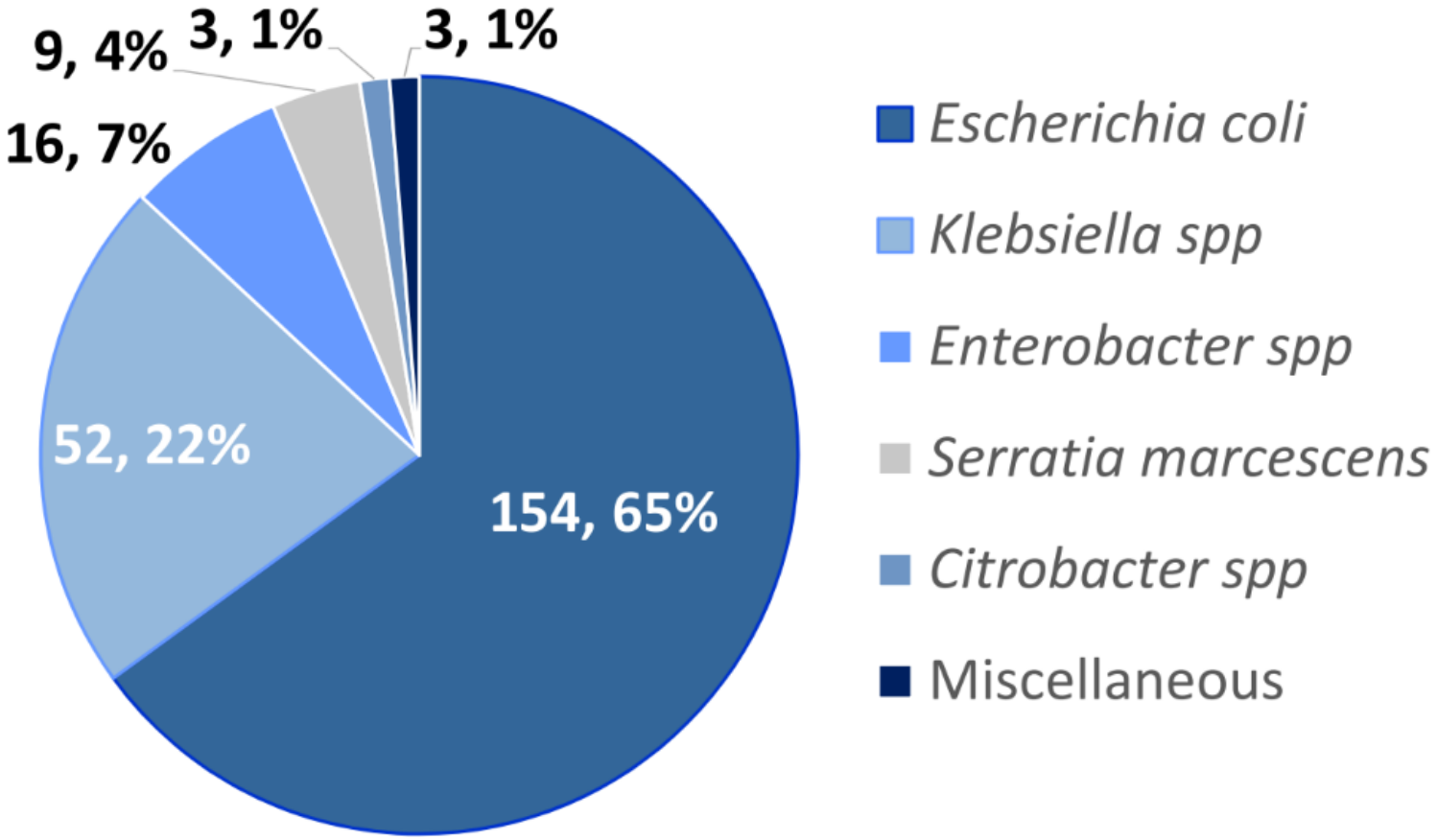




Slide courtesy of Denver Niles MD, D(ABMM)

Distribution of Multidrug-Resistant Gram-Negatives at TCH

- Infectious episodes in 2022 from any site
  - *P. aeruginosa* excluded
- Carbapenem treatment in 32% (75/237)
- ~10% in transplant



Aarika Young, MPH, CIC *et al*. Risk Factors for Multidrug-Resistant Gram-negative Infections across a Pediatric Hospital System. Poster SHEA 2024. Slide courtesy of Catherine Foster, MD.

MDR Infections in My Last 2 Weeks on Transplant Service

ESBL *E. coli*

- Liver abscess/bilomas with biliary stricture and percutaneous drain
- Asymptomatic bactiuria in a heart-kidney transplant
- Bacteremia pre-transplant, then post-transplant ESBL *E. coli* and *Enterobacter* bacteremia, peritonitis and hepatic artery thrombosis 7 days after liver transplant
- VRE peritonitis in infant 4 days after liver transplant

Carbapenem-Resistant *Pseudomonas*

- UTI 5 days after renal transplant
- Bacteremia and biloma 24 days after split liver transplant
- Bacteremia & UTI in distant renal transplant recipient on VV-ECMO for parainfluenza
- Nearly pan-resistant PA VAD infection on chronic Imipenem-Cilastatin-Relebactam with new candidemia
- MRSA pneumonia in VAD patient on VA-ECMO

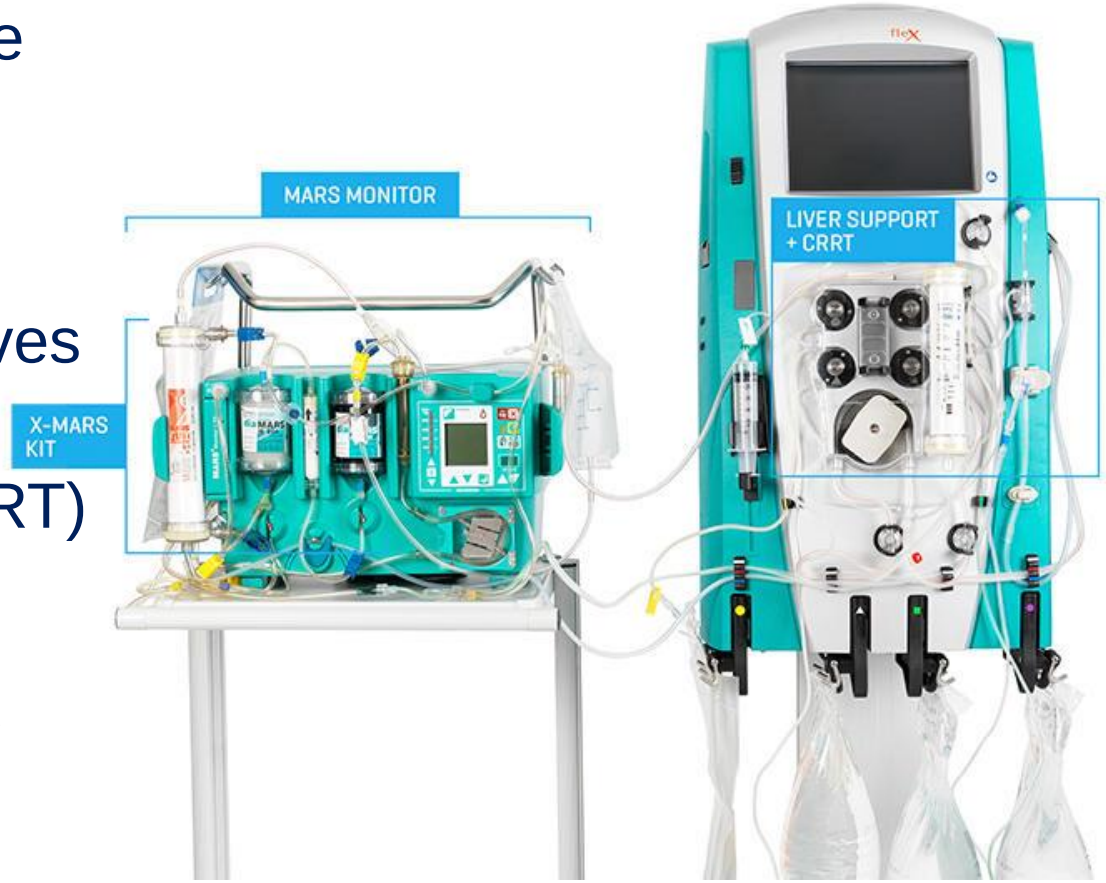
Risk Factors for MDRO Infections

- Biliary leaks, split liver grafts
- Biliary strictures & stents
- Hepatic artery thrombosis & necrosis
- Bleeding (intrabdominal, pulmonary)
- Urinary colonization
- Urinary stent & catheters
- Mechanical circulatory support ECMO/VAD
- Central lines
- MDRO colonization
- Prolonged ICU hospitalization
- Antibiotic exposure

Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice: MDR Gram-negative, MRSA, and VRE infections in solid organ transplant recipients. Clin Transplant 2019.

Challenges of Dosing Antimicrobials for MDROs in Pediatrics

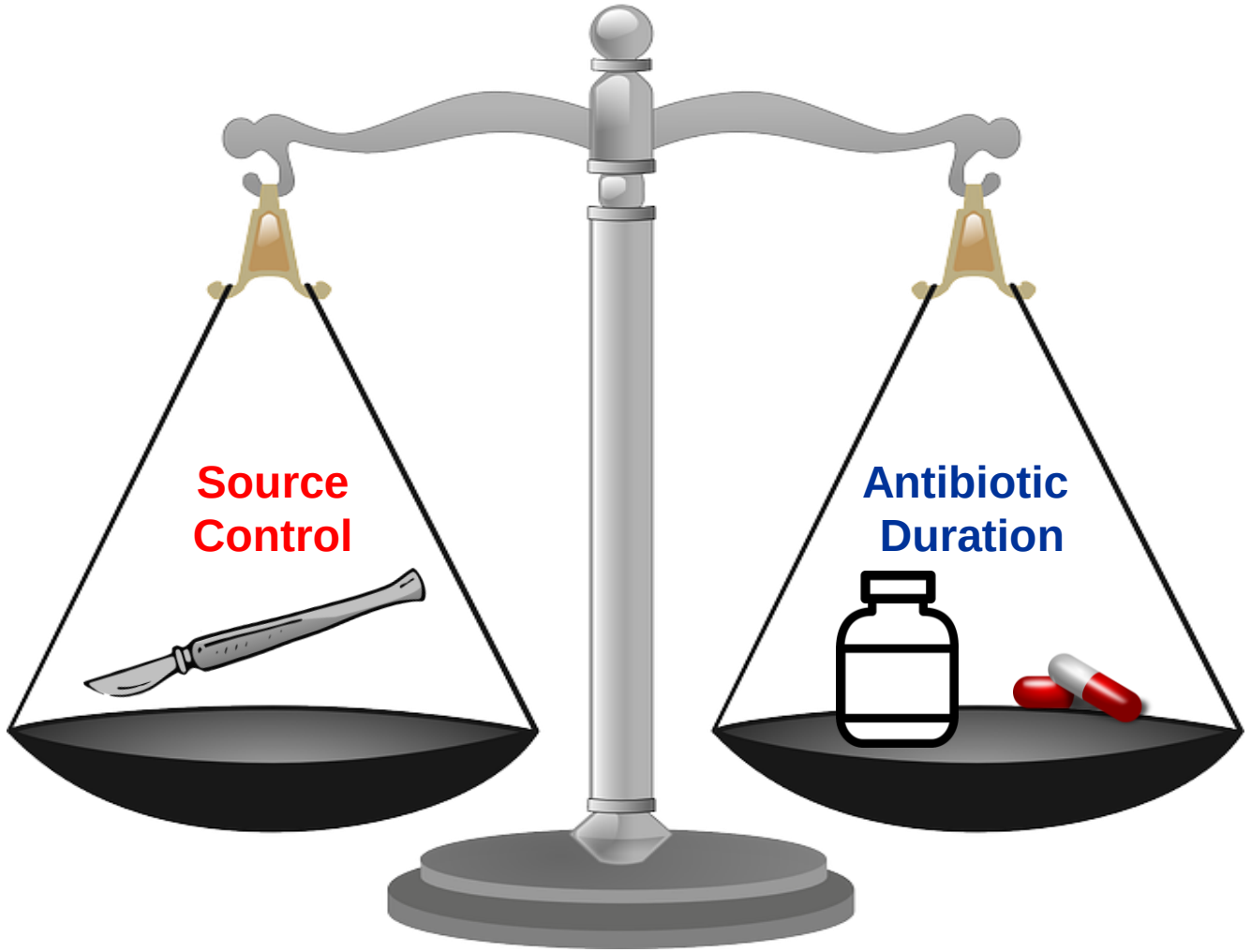
- **Lack of dosing guidance!**
- Often patients have abnormal clearance due organ dysfunction and support systems
- MARS (Molecular Adsorbent Recirculation Support) uses dialysis against albumin to remove toxins in liver failure, but also removes protein-bound drugs
- Continuous renal replacement therapy (CRRT) with supraphysiologic clearance to remove ammonia
  - 4-5 x physiologic clearance (2000 ml/hr/1.73 m^2)
- Extracorporeal membrane oxygenation (ECMO)



Good Source Control vs. Prolonged Duration of Antibiotics

Risks

- Perforations/ damage
- Bleeding
- Thrombosis
  - Hepatic artery
- New infections



Risks

- Antimicrobial resistance
- Fungal infections
- *C. difficile* infection

- Toxicity
  - Renal
  - Hepatic
  - Bone marrow

Take Home Points

- MDRO are a growing problem in transplantation and in pediatrics
- Limited dosing data for new antibiotics in pediatrics or with abnormal clearance
- Good source control is essential for MDRO infections, but it is more challenging/limited options in smaller patients
- Successful treatment requires multidisciplinary team: pharmacy, microbiology, medical teams, interventional radiology, surgery, and ID experts across the world.

Thank You

emoulton@bcm.edu

832-824-4330

Baylor College of Medicine

DEPARTMENT OF PEDIATRICS

Texas Children's Hospital