MTIS MIAMI TRANSPLANT INSTITUTE SYMPOSIUM 2026

Navigating the Storm: Sepsis in the Transplant Patient

Oveimar De La Cruz, MD, FIDSA.

Critical Care - Infectious Diseases

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@oveimarc_MD

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Objectives

- Overview of Sepsis Pathophysiology in the Transplant Recipient
- Identify Diagnostic Challenges
- Discuss Sepsis Management dilemmas in the Transplant Recipient

Why this matters?

- Immunosuppression blunts classic sepsis signs
- High exposure to MDR and opportunistic pathogens
- Delays in diagnosis/management cost lives and grafts

Case 1: Lung Transplant Recipient with Fever and Hypoxia

- 58-year-old male, bilateral lung transplant (8 months ago)
- Presents with low-grade fever, increased oxygen requirement, mild leukocytosis
- CXR: new right lower lobe infiltrate; CT chest: patchy consolidation
- Lung Transplant team requests a bronchoscopy for BAL

Case 1

What is the most likely cause of this patient's symptoms?

- A. Bacterial pneumonia
- B. Acute rejection
- C. Invasive pulmonary aspergillosis
- D. Cytomegalovirus pneumonitis
- E. Adenovirus pneumonia

Case 1: Lung Transplant - Invasive Aspergillosis - Clinical Summary

- 58M, bilateral lung transplant (8 months ago)
- Fever, increased O2 demand, mild leukocytosis
- CXR: new RLL infiltrate; CT chest: nodular patchy consolidation
- **BAL: positive for Aspergillus GM (> 1.0)**
- **TDM-guided voriconazole therapy started**

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Epidemiology

- Up to 50% of SOT recipients develop sepsis within 1 year
- Highest in lung and liver transplants
- Mortality 30–50%, higher with delayed recognition

Mehta Y et al. Am J Transplant, 2019; Sepsis epidemiology in SOT.

Mortality

- Case fatality rate: 30–50%
- Higher in MDR, oportunistic Pathogens, delayed diagnosis, lung transplant cases
- Requires early recognition and tailored treatment

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Wernly B et al. Eur J Clin Invest, 2017; Mortality in transplant-related sepsis.

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Common Sources of Infection

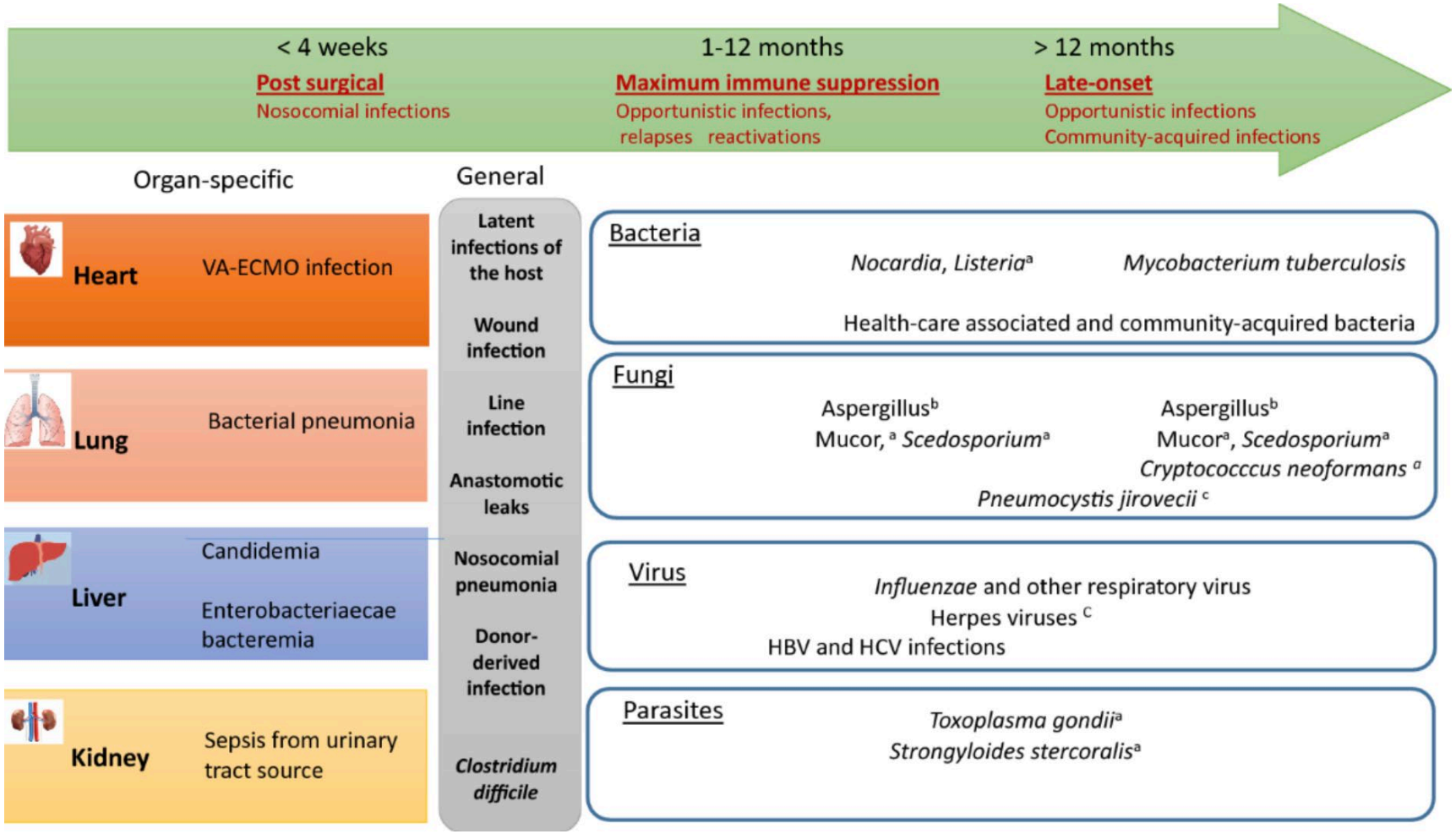
- Respiratory: 30–50%
- Urinary: 20–30%
- Bloodstream: 10–25%
- Also includes surgical sites, intra-abdominal abscesses

Pappas PG et al. Clin Infect Dis, 2010; Infection sites in transplant recipients.

Early vs. Late Infections

- Early (<30 days): Nosocomial, surgical site, catheter-associated
- Late (>30 days): Opportunistic fungi/viruses, community-acquired pathogens

Fishman JA. NEJM, 2007; Early vs. late infections in SOT.



Timsit, JF. *et al.* Diagnostic and therapeutic approach to infectious diseases in solid organ transplant recipients. *Intensive Care Med* **45**, 573–591 (2019)

Organ-Specific Infections

- Lung: Pneumonia, bronchial infections (Pseudomonas, Aspergillus) CARV, CMV, ADV
- Liver: Biliary/intra-abdominal infections (Enterococcus, Candida)
- Kidney: UTI, urosepsis (E. coli, Klebsiella)
- Heart: Bloodstream/device-related (S. aureus)
- Pancreas: Intra-abdominal abscesses

Fishman JA. NEJM, 2007; Site-specific infections.

Impact on Graft Function

- Sepsis triggers inflammation, ischemia, and rejection
- Lung: Chronic Lung Allograft Dysfunction
- Heart/Liver: cytokine damage, microcirculatory failure
- Kidney: AKI affects long-term graft survival

John GT, Oberbauer R. Transplantation, 2016; Graft dysfunction from sepsis.

Gregson A. CID 2016. Infectious Triggers of Chronic Allograft Dysfunction.

Case 2

- 65-year-old female, deceased donor kidney transplant (2 years ago)
- Brought to ED with confusion, hypotension, no fever
- Labs: WBC 4.3k, AKI (Cr 3.4 mg/dL), lactate 4.2, PCT mildly elevated

Case 2

Which is the most appropriate initial antibiotic therapy?

A. Vancomycin

B. Ceftriaxone

C. Meropenem

D. Linezolid

E. Bactrim

Case 2: Kidney Transplant - ESBL Sepsis -

- 65F, deceased donor kidney transplant (2 years ago)
- Presents with confusion, hypotension, no fever
- Labs: Cr 3.4, lactate 4.2, WBC 5.6
- **Blood cultures: Extended-Spectrum Beta-Lactamase E. coli**
- **Started on meropenem**
- **Immunosuppression adjusted**

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Diagnostic Difficulties: Uncommon Clinical Manifestations

- Suppressed cytokine responses from CNIs/steroids obscure sepsis signs
- Differentiating septic AKI vs. calcineurin nephrotoxicity vs. rejection
- Immunosuppression blunts leukocytosis, fever, CRP response
- **Diagnostic inertia due to overlapping SIRS-negative clinical profiles**

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Kalil AC, Dakroub H, Freifeld AG. Sepsis and solid organ transplantation. Curr Drug Targets. 2007

Sepsis scores (like SOFA, qSOFA, MEWS) frequently fall short on IC hosts

- Blunted inflammatory response
- qSOFA may overlook early sepsis due to late-presenting symptoms in immunocompromised hosts
- Pre-existing allograft dysfunction can artificially raise SOFA scores
- Certain opportunistic infections linked to sepsis may need tailored scoring systems.

King, J. et al. (2023). Early Recognition and Initial Management of Sepsis. NCBI.
Sanguanwit, P. et al. (2023). Comparison of qSOFA, SIRS, NEWS and REWS scores. PMC. Laterre, F. (2018). MEETING ABSTRACTS. Springer.
Friol, A. et al. (2025). Prediction of Invasive Pulmonary Aspergillosis. Springer.

Antimicrobial Resistance

- MDR gram-negatives: Pseudomonas, Acinetobacter, CRE
- Gram-positives: MRSA, VRE
- Drivers: hospital stays, broad-spectrum use, invasive procedures

van Duin D, Pinski KS. Curr Opin Infect Dis, 2018; AMR in SOT.

Clinical Red Flags Everyone Should Know

- New oxygen requirement
- Altered mental status
- Rising creatinine or LFTs
- Hypotension or tachycardia
- “Something feels off”

Biomarkers

- Procalcitonin: influenced by immunosuppression
- CRP: non-specific, useful with trends
- Use serial levels for monitoring

Schuetz P et al. Clin Infect Dis, 2012; Procalcitonin utility.
Jerome E et al. Transplant Immunology 2022. Systematic review of diagnostic accuracy of procalcitonin for post-op sepsis/infection in liver transplantation

Emerging Diagnostics

- **16S rRNA:** culture-negative infections. Broad - spectrum PCR
- **MicroGenDx:** qPCR + extGen Sequencing (any sample)
- **GenMark ePlex:** Syndromic Multiplex PCR
- **Karius:** cfDNA sequencing (blood, BAL)
- **T2MR:** Rapid fungal/bacterial ID (DNA + hypermagnetic nanoparticles)

*Novel diagnostics can be expensive

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Blauwkamp TA et al. Nat Microbiol, 2019; Emerging diagnostics.

Schmitz J et al. Future Microbiol. 2018

Why They Matter?

- Faster organism identification
- Earlier de-escalation
- Less unnecessary antimicrobial exposure

Empiric Therapy Principles

- Time-critical initiation of broad-spectrum antibiotics (<1 hour)
- Incorporate host factors: neutropenia, colonization history, recent pathogens

Kumar A et al. Crit Care Med, 2006; Importance of early antibiotic therapy.

Empiric Therapy Principles

- Empirically cover for MDR pathogens when indicated,
- Consider donor-derived organisms early post-transplant
- Adjust dosing for altered PK/PD in ECMO, CRRT, and hypoalbuminemia

Kumar A et al. Crit Care Med, 2006; Importance of early antibiotic therapy.

Immunosuppression Adjustment

- Risk of rejection vs. infection control
- Taper steroids if needed
- Decrease or hold antimetabolite immunosuppression
- Monitor for CNI toxicity or interactions
- Discuss with Transplant, Pharmacy, and ID Teams

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Wernly B et al. Eur J Clin Invest, 2017; Immunosuppressive therapy considerations.

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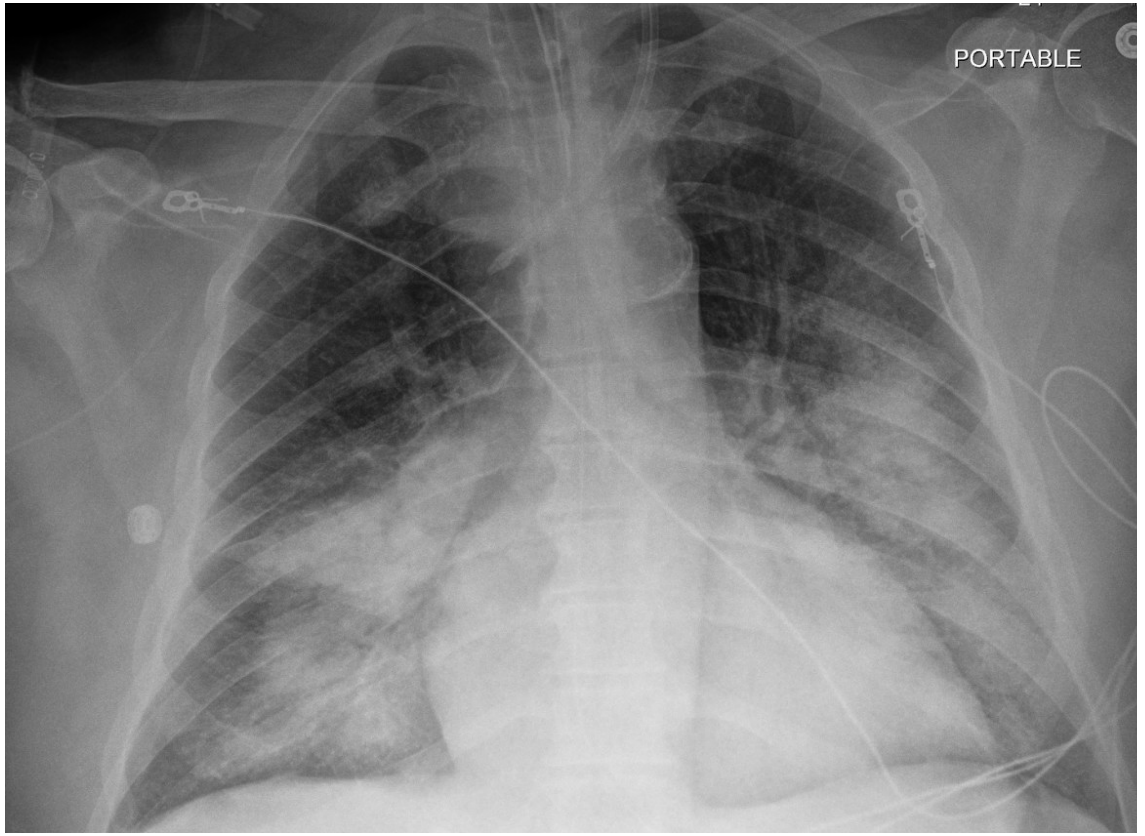
Case 3:

- 60M with ESRD from nephrolithiasis and T2DM
- S/p DDKT in March of 2025 with delayed graft function (DGF)
- Presented 1 mo post-transplant with cough, flu-like symptoms
- CXR: Perihilar dense airspace disease → transferred to Jackson
- Started on empiric antibiotics (Cefepime/Vanc)

Case 3: Day 1

- Admitted to IMCU → upgraded to SICU for respiratory failure and hypotension

- Required levo @10 mcg/min, HFNC, CVVHD → intubated on arrival to SICU



Interdisciplinary Assessment: Nursing, RT, PharmD and Provider's input.

- Subtle respiratory or mental status changes
- Declining urine output
- Increasing pressor needs
- "Gut feeling" matters in transplant patients

Interdisciplinary Assessment: PT, OT, Dietitians & Social Work Matter

- PT/OT: sudden loss of endurance
- Dietitians: feed intolerance, poor absorption
- Social work/Case Management: access barriers, adherence issues, family dynamics
- Logistics delays worsen outcomes

Case 3:

What is the most appropriate next diagnostic step to identify the etiology of sepsis in this immunocompromised patient?

A. Repeat CXR after intubation

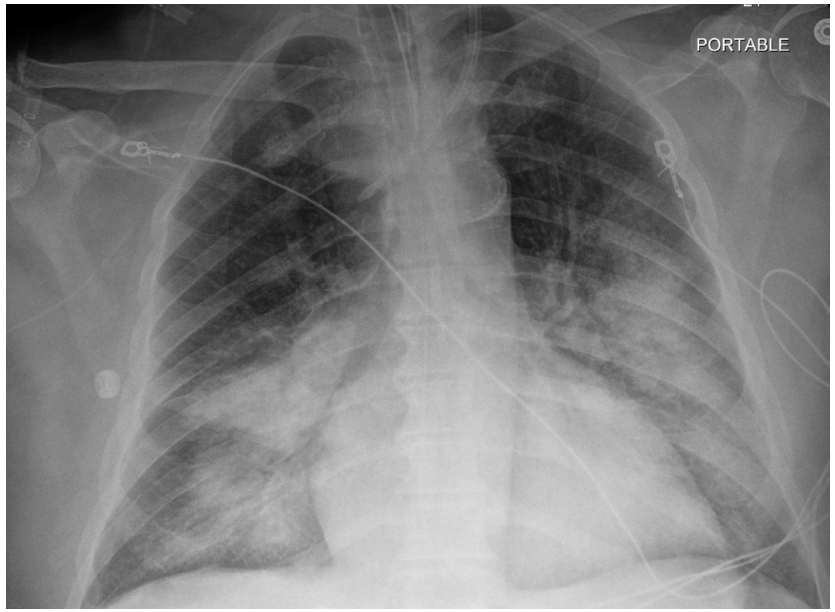
B. Empiric antifungal therapy without diagnostics

C. Bronchoscopy with BAL and multiplex PCR

D. Withhold all further diagnostics until hemodynamically stable

Case 3: Day 3

CXR



- WBC: 0.9. **BCX (2 sets) + K. pneumoniae, BAL culture + K. pneumoniae**, UA shows 8 WBC, LE++, Glucose 1000.
- Increased vasoactive requirements:
- Levo at 20, Epi at 10, Vaso at 0.1, Phenylephrine at 250.
- **Lactic acid levels reached 14.**
- **Shock Team consultation requested**.

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- "Despite maximal support, the patient continued to deteriorate, prompting multidisciplinary discussion about advanced **Mechanical Circulatory Support**."

Sepsis & ECMO

25–40% incidence in SOT on ECMO

ECMO alters antibiotic levels – adjust dosing

Device mimics sepsis signs, delays diagnosis

Sharma A et al. Clin Transplant, 2020; Sepsis with ECMO.

Protocol-Driven Management

- Implement Sepsis-3 bundle: MAP >65, lactate clearance, early source control
- Use rapid diagnostics (PCR, NGS, T2MR) to guide prompt pathogen identification and antimicrobial de-escalation
- Coordinate with Transplant, Pharmacy, and ID teams on immunosuppression modulation.
- Target antimicrobial stewardship through daily ID rounds

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Singer M et al. JAMA, 2016; Sepsis-3 guidelines.

Team-Based Sepsis Care in Transplant Patients

- Everyone owns early recognition
- Escalation is a strength—not a failure
- Early coordination with Transplant Teams and Consulting Services
- No unilateral changes to immunosuppression
- Daily reassessment with intentional de-escalation

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Summary

- Transplant recipients are high-risk for sepsis and often do not present typically
- Fever and leukocytosis may be absent—subtle changes matter
- Early recognition and rapid escalation save lives *and grafts*
- Diagnostics and treatment are complex and require coordination
- Interdisciplinary communication is essential

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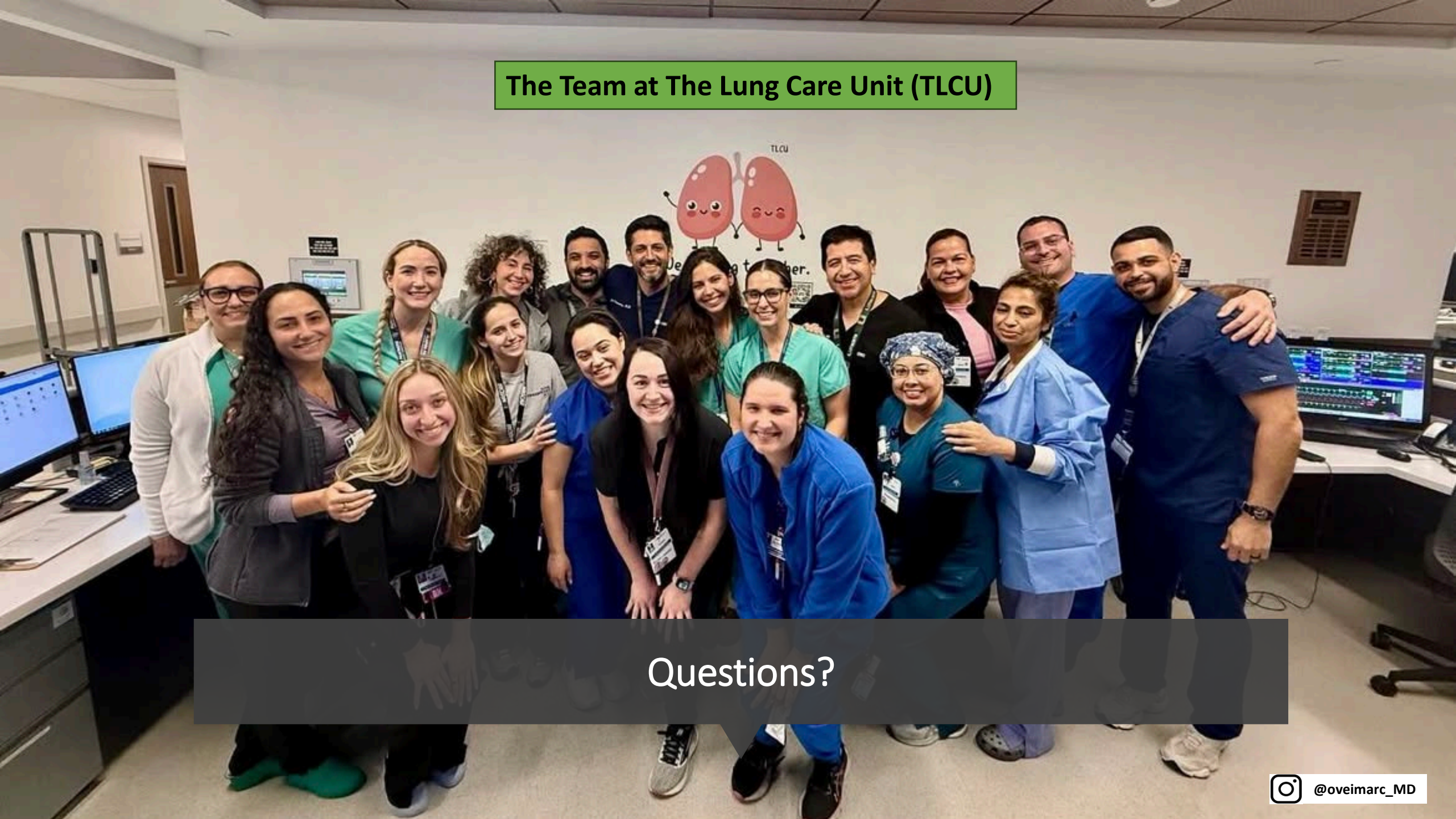
The Team at The Lung Care Unit (TLCU)



Questions?

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