LUNG TRANSPLANT APP ONBOARDING

Compiled by: Jessica Chance, NP & the Lung Txp APP Team

Meet the Team: APPs

- Jessica Chance
- Terra Davis
- Eddie Garcia
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- Dereck Wright



Meet the Team: Attendings

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Dr. Fernando Torres
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Dr. Adrian Lawrence
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Meet the Team

Pharmacy

- Jessica François Witt
- Van Ngo
- Mary Olumesi
- Raelene Trudeau
- Rachel Yue-Transition of care
- Marilyn Mootz Pitts- Transition of care
- Sandirai Musuka- Transition of care
- Inpatient Care Coordinators
 - Mona Jackson
 - Aneena Varghese
 - Debra Walker
- Outpatient Social Worker
 - Stacy Franz



Meet the Team

- Outpatient APP
 - Luke Mahan
- Outpatient Post Txp Coordinators
 - Preethi Alexander
 - Ann Cuddy
 - Siti Pearson
 - Juana Ramos
 - Cheryl Nava
- Outpatient Pre-Txp Coordinators
 - Kayla Bradford
 - Ashley Davis
 - Geno George
 - Jody Hernandez



A TYPICAL DAY IN THE LIFE OF A LUNG TXP APP

APP 24-Hour Coverage

- Floor team
 - Covers 7A-7P floor patients only
 - Some providers working 12h shifts (7a-7p) vs8 hr shifts (8-430P)
 - Typically 3-4 providers on weekdays and 1 provider on weekends

- ICU team
 - Day shift 1 provider
 - Cover7A-7PICU patients only
 - Fellow present Monday through Friday
 - Night shift 1 provider
 - Cover 7P-7A all floor and ICU patients providing cross coverage overnight for acute events and admissions

A Day in the Life

• Floor

- Arrive. Sign in as first call. Review overnight events. Receive any necessary signout. Chart review. Check in with nursing staff. Check in with care coordinators. Pre-round on patients. Develop and start initiating plans.
- Physician rounds typically 10A-2Pish depending on physician. Start with brief table rounds with whole team followed by walking rounds. Prioritize discharge patients with goal to discharge before noon. Transplant pharmacy joins MWF
- Remainder of day spent completing chart documentation and clinical plan
- $\circ~$ Sign out verbally and via signout form

ICU Dayshift

- Arrive. Sign in as first call. Receive signout from night APP. Monday-Friday discuss with fellow and split patients. Chart review. Check in with nursing staff. Pre-round on patients. Develop and start initiating plans.
- Physician rounds typically 10A-1P with attending, fellow, RN and RT. Time varies depending on physician and how active previous night was. Bedside bronchs usually happen in concurrence with rounding.
- Remainder of day spent completing chart documentation, clinical plan and procedures
- Signout to night shift APP
- ICU Nightshift
 - Arrive. Sign in as first call. Receive signout from fellow, ICU day APP and floor APP.
 - Typically less structured than dayshift with responsibilities including the following
 - Complete outstanding consents, complete follow up items from day shift, chart check, round on ICU patients and complete nightly rounding note, round on sick floor patients, respond to all rapid responses and codes for lung transplant patients, complete admissions

Plan/Assessment

- Summary of patient course/admission: keep to 1-3 sentences
- Chief complaint/issue: (i.e SOB/abdominal pain, etc)
- Lung txp: CXR, spirometry, DSA, oxygen requirement, last bronch/CT chest, previous rejection treatments.
- IS: List of regimen including goals. Last Cylex
- OIP: CMV status. Current medications. EBV/CMV latest results
- ID: Pertinent infection history and treatment.
- CVS: CAD history, arrhythmias/anticoagulation, medication, etc. Last ECHO
- GI: aspiration workup and any h/o major GI problems. Diet/NPO status
- Renal: Creatinine baseline
- Endocrine: Hx of DM
- HEME: any h/o cytopenia/anemia
- Neuro/Psych: delirium/depression/anxiety hx
- PT/OT/Deconditioning: PT/OT recs for discharge
- DVT/GI Prophylaxis: PPI, SQH/AC, SCDs, ambulation
- Social: List any SW orders, IV antibx, Inhaled antibx, PT/OT etc
- Dispo: ongoing issues/barriers to discharge/anticipate discharge date

Note Format



Meetings

• Daily:

• Care Coordination/Discharge Planning: On own time in AM

Tuesdays 7am -- 9am: Lung selection committee (Teams)
 Discussion of possible txp candidates, waitlist, post txp patients



• Thursdays 2pm – 2:30pm: multidisciplinary rounds on fresh txp patients

• Includes care coordinators, APPs, attendings, social work, pharmacists, dietician, speech, PT/OT, chaplain

The Care and Management of a

FRESH TRANSPLANT

Indications & Contraindications

- Clinically and physiologically advanced lung disease for which medical therapy is ineffective or unavailable
- High risk (>50%) of death from lung disease without transplant
- High likelihood (>80%) of surviving at least five years after lung transplant

- Active infection
- HIV with detectable viral load
- Malignancy with high risk of recurrence
- Significant dysfunction of other vital organs
 - GFR<40
 - AKI with rising creatinine
 - HD with low likelihood of recovery
 - Stroke within 30 days with cognitive impairment
 - Acute liver failure
 - Cirrhosis with portal hypertension or synthetic dysfunction
 - Acute coronary syndrome, MI within 30 days or significant coronary disease not amenable to revascularization
 - Untreatable hematologic disorders
- Active substance use
- Limited functional status
- Poor social support
- History of noncompliance
- High BMI (Goal <30kg/m2)

Pre-transplant Disease Processes

• Cystic Fibrosis

- Whole body disease. Not just respiratory illness.
- Respiratory
 - Optimize pulmonary toilet
 - High risk for multi-drug resistant infections
 - May need ID input
- Chronic sinusitis
 - Sinus hygiene
- Gl
 - Pancreatic enzymes
 - Bowel regimen (Avoid DIOS: distal intestinal obstruction syndrome)
 - CF diet order
- Diabetes
- Hyperkalemia

• IPF

- Keep on Cellcept if on pre-transplant
- Flare of underlying disease (i.e polymyositis)

• COVID ARDS

- Pulmonary Hypertension
 - Bilateral txp only
- COPD
 - If unilateral, may experience native lung hyperinflation requiring endobronchial valves
 - Continue Spiriva for native lung COPD

Brief highlight only. Further study required.

Anatomy of Lung Transplantation



Landing a Fresh Transplant

- Patients arrive directly from the OR. APP and attending receives patients and get sign-out from anesthesia and CVTS team.

- Usually a good idea to order "IP PULMONARY TEAM LUNG TRANSPLANT POST-OP" before patient arrives. Orders not included in the order set and needs to add separately on patient's arrival depending on what they are on: sedation, pressors and insulin gtt (if they are on epi)
- Vent: target Vt on the higher end 6L-8L/Kg and Peep ~8
- ABG on arrival and repeat every 12-24hrs and follow P/F ratio
- Hemodynamic goals: CVP 8-12, CI>2.2, SVR 800-1200, UOP>30 cc/hr and CT output <200cc/hr
- IS: OR medications: Imuran/Cellcept, Solumedrol and Simulect/FK gtt
- Antibiotics: Vanc/Zosyn/Levaquin. Inhaled Tobi and Ampho
- PPX: Gancyclovir and Bactrim (Usually not started for first few days in order to monitor renal function)

Things to think about when picking up a new transplant...

- Post-op complications?
- PGD & stage?
- Explant path
- Chest tubes?
- DSA? Order for POD#14
- When is the next bronch? How did the last one look?
- Date extubated
- Oxygen? Able to wean?
- What immunosuppression is patient on? Simulect given? And dates?
- CMV mismatch? When is Cytogam due? Pharmacist will usually update "pharmacy to provider" sticky note under "MD Kardex" with details of patient regimen
- High risk donor?
- Positive cultures? Antibiotic regimen?
- Post op arrhythmias? BB prophylaxis?
- CAD history?
- \circ Renal function
- Feeding plan? When is next MBSS if applicable? Is tube in place and post-pyloric?
- DVT prophylaxis/anticoagulation?
- Lines/tubes/drains?
- Therapy progress
- Home needs?

Post operative complications

- Primary graft dysfunction (PGD)
- \circ Rejection
- Airway
 - Bronchial stenosis
 - Bronchial dehiscence
- Hematologic
 - PE
 - Bleeding
- Pulmonary vascular stenosis
- Pleural
 - Hemothorax
 - Empyema

- \circ Infection
- Diaphragm dysfunction
- Renal dysfunction
- o Stroke
- o Delirium
- o PRES
- o Seizure
- o Arrhythmias
- Vasoplegia
- Wound dehiscence
- Surgical site infection

Delayed Chest Closure

- May opt for in cases of prolonged cardiopulmonary bypass time, prolonged ischemic time, coagulopathies or oversized donor lung grafts
- Increased risk of early post operative bleeding, infection and severe primary graft dysfunction
- Management:
 - Do not turn
 - NO CHEST COMPRESSIONS
 - Typically will diuresis for 2-3 days then return to OR for closure
 - Consider empiric Micafungin
 - Usually no major issues but remain mindful that patient's chest is open

Wound Dehiscence & Infection

- Occurs up to 2% of lung transplant recipients typically within first days-weeks but can be seen several months later
- Ensure that wound is assessed daily to every other day!
- $\,\circ\,$ Keep wound area clean and dry
 - $\,\circ\,$ For females, ensure surgical bra and interdry dressing is in place
 - $\,\circ\,$ Once able to shower, educate on avoiding direct water. NO BATHS
- Can be complicated by mediastinitis when there is direct extension of infection into the mediastinum
- Typically Candida infection isolated in cultures
- If dehiscence, purulent drainage or any significant concern for surgical site infection-> start Vanc/Zosyn/Micafungin, wound cultures if purulence present, order CT chest and notify CVTS
- May require surgical debridement, targeted antimicrobial therapy and wound vac placement

Fresh Txp: Home Care Needs

- If patient is CMV mismatch order:
 - Ganciclovir
 - Cytogam
- If the patient is NPO order:
 - Tube feeds
- If the patient is less than 30 days post transplant order:
 - Inhaled nebulizers
- If positive cultures or persistent secretions order:
 - IV antibiotics
- Review therapy notes for any DME orders or home health therapy services
- If PICC line needed, will also need Warfarin 1 mg while line is in place.



New Transplant Teaching

- Will need teaching prior to discharge from the following:
 - Transplant Coordinator (can be up to 2 hours)
 - Pharmacist (spread over a few days but will be a few hours on day of discharge to fill pill box)
 - Home health infusion company (if going home with IV/inhaled antibiotics)
 - Home health company (if going home with IV/inhaled medications or tube feeds)
 - Glucometer teaching (done by the nursing staff)
 - Dobhoff medication administration teaching (done by the nursing staff)
 - Dressing/drain care (usually done by nursing staff)

 Most patients and families are overwhelmed post transplant. Assess your patient and try to make sure teaching is not all at once right before discharge. Spread it out if possible and have the nurses start their part quickly after transfer to the floor.

Fresh Txp: 1 Month Workup

• If patient still admitted at 1 month post txp, make sure the following is done:

- Labs: CMV, EBV, Cylex, IgG, Copper, Mag, Phos, FK, CBC, CMP, LDH, INR, PFTs, HLA, HBV, HCV, HIV w/ NAT
- CT chest without contrast
- Bronchoscopy with biopsy

Lung Transplant Specific

PULMONARY

Table 1.

Glossary of Terms Related to Pulmonary Function Testing

Spirometric values

FEV₁: forced expiratory volume in one second; total volume of air a patient is able to exhale in the first second during maximal effort

FVC: forced vital capacity; total volume of air a patient is able to exhale for the total duration of the test during maximal effort.

FEV1/FVC ratio: the percentage of the FVC expired in one second

FEV6: forced expiratory volume in six seconds

FEF_{25-75%} forced expiratory flow over the middle one-half of the FVC, the average flow from the point at which 25% of the FVC has been exhaled to the point at which 75% of the FVC has been exhaled

Other terms

DLCO: diffusing capacity of the lung for carbon monoxide

EIB: exercise-induced bronchoconstriction

LLN: lower limit of normal, defined as below the fifth percentile of spirometry data obtained from the Third National Health and Nutrition Examination Survey

TLC: total lung capacity; the volume of air in the lungs at maximal inflation

VC: vital capacity; the largest volume measured on complete exhalation after full inspiration

PFT Overview



ABG Review



ABG Interpretation





with partial respiratory compensation

Problem: too ittle metabolic base (HCO3-) Body's response: reduce respiratory acid (CO2)



Problem: too little respiratory acid (CO2) Body's response: reduce metabolic base (HCO3-)



with partial respiratory compensation

Problem: too much metabolic base (HCO3-) Body's response: Increase respiratory acid (CO2)

Respiratory ABG Abnormalities

Respiratory Acidosis

- PH < 7.35, PCO2 > 45, HCO3>30
- Etiology: Decreased alveolar ventilation, hypoventilation, lethargy/obtunded state, neuromuscular dysfunction
- Acute phase:
 - Sharp rise in pCO2 with only a small increase in HCO3
 - After 6-12 hours, the increase in CO2 will evoke the renal compensation but it will take several days to manifest
- Presentation: Somnolence, confusion, coma
- Management:
 - Improveventilation-BiPAP, intubation
 - Increase RR on vent
 - Minimize sedating medications
 - Narcan if applicable

• PH > 7.45

- Decreased CO2 secondary to hyperventilation
- Etiology: head injury, stroke, hyperthyroidism, anxiety, pain, fear, stress, drugs, PE, PTX, pneumonia

Respiratory Alkalosis

- Presentation: Lightheadedness, anxiety, stocking/glove tingling, hyperventilation
- Management:
 - Treat underlying cause
 - Have patient breathe into paper bag
 - Decrease RR on vent
 - Sedate patient
 - WARNING: Rapid correction may result in metabolic acidosis

Metabolic ABG Abnormalities

Metabolic Acidosis

- PH <7.35, HCO3 <22
 - Hallmark sign: Low serum bicarb
 - Anion gap can help evaluate the cause and aid with treatment decisions (High Anion Gap = more acidosis = more severe)
- High Anion Gap Acidosis
 - Causes: DKA, alcoholic ketosis, lactic acidosis, drug or chemical reaction
 - Treatment: Treat underlying disorder. Fluid resuscitation, HCO3 not indicated if due to DKA or hypoxia. HCO3 indicated with significant hyperkalemia
- Normal Anion Gap Acidosis (common in patients with renal failure)
 - Causes: Diarrhea (C.diff), Ileostomy, Renal tubular necrosis, recovery from DKA.
 - Treatment: Bicitra 10-30 ml with meals and HS, Sodium bicarb, HD

Metabolic Alkalosis

- PH >7.45, HCO3 >26
 - Characterized by high HCO3 and compensatory pCO2 rarely exceeds 55.
 - If pCO2 >55, superimposed respiratory acidosis is likely.
- Causes (Saline Responsive/Volume Contraction): Post-hypercaphia alkalosis, NGT suction, vomiting, loop or thiazide diuretics.
- Treatment: Correct volume deficit, correct electrolyte abnormalities, stop diuretics, PPI/H2 blockers for GI loss, Diamox.

Flexible Bronchoscopy

- Done bedside in ICU or in endoscopy suite for floor patients
- Can be done for airway clearance/BAL only or with biopsy (requires fluoroscopy in GI suite)
- Frequency
 - Initially every 1-3 days following transplant which will gradually spread out depending on airway findings
 - Perform prior to extubation and also prior to floor transfer if still needing airway clearance at that time
 - Completed again with surveillance biopsy at 1, 3, 6 and 12 months post op
 - Perform as needed for remainder of life
- If performing biopsy
 - Hold SQH morning of
 - $\,\circ\,$ INR < 1.5 if on anticoagulation
 - Post procedure CXR to assess for PTX
- NPO midnight prior
- Must have consent if on the floor

- ICU BAL orders:
 - Make sure to specify which lobe when ordering
 - NPO 2 hours postprocedure
 - Culture Respiratory (nonsputum) & ST- Bronch BAL
 - Culture Fungal -Bronch BAL
 - Culture AFB & Smear-Bronch BAL
 - Respiratory Viral Ags Screen

Occasionally MD will ask for special tests, place as requested

Respiratory Therapies Overview

$\circ\,$ Lung inflation

- Incentive spirometry
- IPPB if FEV1<1L or low lung volumes
- BiPAP
- Lung Clearance
 - Acapella-bedside flutter valve
 - CPT- percussor vs vest for high needs
 - Inhaled Mucomyst pre med with Albuterol for refractory secretions
- Metaneb: Positive pressure + oscillation
- Bronchodilators
 - Xopenex- preferred for tachycardia
 - Albuterol
 - Duoneb
- Inhaled antibiotics
 - Tobramycin, Caystin, Colistin, Vancomycin, Amphotericin
- Inhaled steroids: Pulmicort
 - Utilize for CLAD, airway inflammation

- Inhaled Nitric oxide (NO)- Vasodilator
 - Rescue therapy when standard therapy has failed in patients with severe acute hypoxemia or hemodynamic compromise
 - Improves V/Q matching
- Oxygen modalities
 - Nasal cannula-range from 1-6L
 - HFNC/oxymizer conserving device- NC that has a reservoir to allow for high percentage of oxygen delivery by increasing flow (6-15L)
 - Optiflow-Pressurized oxygen through a special NC that provides a specific FiO2 % and LPM. Positive pressure lost if mouth open
 - Non-rebreather-Rescue device 60-100% FiO2
- Diagnostics
 - Formal PFTs
 - Bedside spirometry
 - Walking oximetry
 - Nocturnal oximetry

Bipap

- Face mask that provides positive pressure as well as oxygenation.
- If on continuous BiPAP, patient will need to be monitored in ICU
- Used for hypercapnia, hypoxia, mucus plugging, pulmonary edema, prevention of atelectasis and sleep apnea
- Do not use if patient actively vomiting due to aspiration risk
- Used as a last resort prior to intubation
- Settings are usually comprised of:
 - Rate: Set minimum respiratory rate
 - IPAP: Inspiratory Pressure (driving pressure)
 - EPAP: Expiratory pressure (PEEP)
 - FiO2: Delivered oxygen percentage

- Management:
 - Management will vary depending on reason for use.
 - IPAP 10/ EPAP 5 with a rate of 12 is a good starting point
 - If patient is hypercaphic, will want higher IPAP (16-18) and lower EPAP (6-8).
 - For mucous plugging may need higher pressures as well.
 - Fluid overload/pulmonaryedema will need diuresis in addition to Bipap.
 - Lower settings can be used for atelectasis and sleep apnea.

Intubation/Ventilator Management

• Indications:

- Inability to protect airway- obtunded, post-ictal, esophageal varices rupture, profuse vomiting
- Poor gas exchange despite other therapies
- Complete respiratory failure

Types of Ventilation

• Invasive Ventilation (Intubation)

Modes of Mechanical Ventilation	Types of Breaths	Independent Variable	Dependent Variable	Notes	Mo
Volume Assist/Control	Assisted or Controlled	Preset Tidal Volume	PIP & Plateau Pressures	Control tidal volume Dung protective) Control of minute ventilation (RR & Vt)	CP
Pressure Assist/Control	Assisted or Controlled	Preset Pressure	Adequate Tidal Volumes (not feo high or low)	Patient comfort (decelerating flow), Control over delivered pressures (avoid barotrauma)	Bil
Pressure Support (PS)	Supported	Preset Pressure	Adequate Tidal Volumes (not too high or low)	Patient comfort Allows patient to maintain respiratory work effort	pre
Synchronized Intermittent Mandatory Ventilation (SIMV) + PS	Assisted, Controlled or Supported	PC-SIMV+Preset Pressure VC-SIMV+Preset Tidal Volume	PC- SIMV*Adequate Tidal Volumes (not too Ngh ar low) VC-SIMV-PIP & Plateau Pressures	Can get benefits of supported breaths (PS), but still ensure minimum number of mandatory breaths (controlled or casisted)	
Pressure Regulated Volume Control (PRVC)	Assisted or Controlled	Preset Tidal Volume	PIP & Plateau Pressures	Control Minute Ventilation Control Vt. Patient comfort (decelerating flow). Can limit high pressures (avoid barotrauma)	

Non-Invasive Ventilation (Mask)

Modes of NPPV	Description
CPAP (continuous positive airway pressure)	Set continuous pressure throughout respiratory cycle; patient initiates all breaths.
BiPAP (bilevel positive airway pressure)	Preset inspiratory and expiratory pressures; can set backup respiratory rate; patient initiates breaths.

Ventilator Terms/Abbreviations

Table 2. Abbreviations Associated With Mechanical Ventilation

AC	Volume control	Mode that delivers each breath with constant volume and flow.	
Auto- PEEP	Intrinsic PEEP	Positive end-expiratory pressure caused by inadequate expiratory time on a ventilator. Equals Total PEEP - Set PEEP.	
CPAP	Continuous positive sinway pressure	Constant pressure maintained at she airway opening throughout the breathing cycle. CPAP refers to PEEP during spontaneous breathing.	
E-Time	Expiratory flow	The period from the start of expiratory flow to the start of inspiratory flow. Controlled by patient. Remains constant only if patient is sedated or synchronous with ventilator.	
FIO,	Fraction of inspired oxygen	The percentage of oxygen delivered (21%-100%).	
I:E Ratio	Inspiration to expiration ratio	Time constant determined by total respiratory rate and inspiratory time.	
I-Time	Inspiratory time	The period from the start of inspiratory flow to the start of expiratory flow. This is a required setting on the ventilator.	
PBW	Predicted body weight	Males: 50 kg + 0.91 (Height in cm - 152.4) Females: 45.5 kg + 0.91 (Height in cm - 152.4)	

PC/AC	Pressure Mode that delivers each brea control a constant pressure.	
PEEP	Positive end- expiratory pressure	Positive pressure is held in the lungs during the exhalation phase of a mechanical breath.
PIP	Peak inspiratory pressure	Pressure recorded at end inspiration. Dependent on volume or pressure delivered and airway resistance.
Pplat	Plateau pressure The static transalveolar pres at end inspiration during ar inspiratory hold for an assis breath. Respiratory rate Number of preset mechanic breaths the patient will recomminute.	The static transalveolar pressure at end inspiration during an inspiratory hold for an assisted breath.
RR		Number of preset mechanical breaths the patient will receive per minute.
VE	Minute ventilation	The average volume of gas entering or leaving the lungs per minute (L/ min). Calculated by tidal volume x respiratory rate (VE = VT x RR).
VILI	Ventilator- induced lung injury	Lung injury resulting from barotrauma, volutrauma, atelectrauma, biotrauma, and oxygen toxicity in ventilated patients.
vt	Tidal volume	The volume of gas inhaled or exhaled during a breath.

Ventilator Troubleshooting

- High peak pressures:
 - Troubleshoot patient (suctioning, biting, coughing), ETT (kinking, clogged), circuit (water in circuit, kink in circuit) first.
 - If all clear, then evaluate for poor lung compliance (decreasing PEEP or TV, iNO, barotrauma)
- High plateau pressures:
 - Usually more indicative of poor lung compliance.
 - Interventions as above.
 - Breath hold technique to evaluate plateau pressures on the ventilator

- Auto-PEEP:
 - In COPD (pre-txp or in
 - native lung after single lung transplant) or other obstructive lung disease (ex. asthma).
 - Can check autoPEEP on the vent with preset calculator or by performing prolonged exhalation maneuver
 - Easiest temporary fix is temporarily disconnect vent from ETT and gently provide pressure to the chest to simulate exhalation.
 - Fixing underlying cause: breathing treatments (xopenex, albuterol, hour long neb).
 - If single lung transplant, may require double-lumen ETT to ventilate both lungs adequately.
Trach Management

- Tracheostomy placement is used when the patient does not tolerate extubation or rapid ventilator weaning and requires a slower/more controlled wean.
- Cuffed trach: can be used with ventilator and positive pressure ventilation (Bipap). Cuff must be deflated to use PMV. Watch cuff pressure to not cause tracheal breakdown.
- Cuffless trach: used during weaning, helpful with PMV, cannot be used with PPV.



Cuffed Trach



Cuffless Trach

Trach Management

- Weaning:
 - Full vent to CPAP/BiPAP to high flow via trach to TC trials +/- PMV trials to capping trials to decannulation.
 - Length of weaning depends on patient tolerance (oxygenation and oxygen requirements, positive pressure requirements, tiring, length of CPAP/capping).

• Vocab:

- TC (Trach Collar): Similar to simple mask, goes over trach and provides free flowing oxygen at a certain percentage.
- PMV (Passy Muir Valve): When placed on the hub of a tracheostomy tube or in-line with the ventilator circuit, it redirects airflow through the vocal folds, mouth, and nose, enabling voice and improved communication



Differentials for SOB/Decline in lung function

- Rejection
- Infection
- Pulmonary embolism
- Diaphragm dysfunction
- Aspiration
- Drug induced lung injury
- Pulmonary edema
- Heart failure
- Pericardial effusion

- Pneumothorax
- Pleural effusion
- Airway stenosis and malacia
- Atelectasis
- Neuromuscular dysfunction
- Deconditioning
- Underlying disease flare



Pleural effusion

- Etiology:
 - Infection
 - Rejection
 - Fluid overload
 - Trapped lung
 - Malignancy
 - Venous anastomosis stenosis or thrombosis
 - Hemothorax
 - Chylothorax-Pleural fluid triglyceride > 110mg/dL
- Diagnostics:
 - CXR
 - CT chest w/o contrast
 - Diagnostic thoracentesis
- Treatment:
 - Diuresis
 - Therapeutic thoracentesis
 - Pleurex/pigtail catheter
 - All empyemas require chest tube placement
 - tPA administration if loculated
 - Antibiotics if indicated
 - May require surgical decortication
 - Treat underlying cause
 - Treat early to avoid trapped lungs!



Pneumothorax

- Etiology:
 - Spontaneous
 - Post procedure (TBBx)
 - Presence of chest tube
 - Anastomotic dehiscence
 - Early post op may be due to undersized donor lung
- Diagnostics
 - \circ CXR
 - Mediastinal shift noted in tension PTX
 - Bronchoscopy for anastomosis assessment

• Treatment

- $\,\circ\,$ No intervention if small <20%
- High flow oxygen to aid re-expansion
- Chest tube placement if >20% or symptomatic
- Avoid positive pressure therapy (IPPB, BiPAP)
- Needle thoracostomy in emergent cases





Chest tube management

- Post operatively will have one mediastinal chest tube per lung
 - Transition to one Argyle and one blake drain per lung- "splitting tubes"
 - Follow chest tube output and call CVTS if > 200 ml/hr
 - Argyles will be removed first
 - Consider blake removal when output < 100 ml/day and lung remains well inflated
- Tubes also placed for pneumothorax and pleural effusion
- Chest tubes typically will start on -20 wall suction then transition to water seal and further to bulb suction.
- Can give tPA daily x 3 for loculated pleural effusions secondary to adhesions
 - Patient instructed to turn every 30-60 minutes for total of 4 hours
- Air leak: Continuous or intermittent bubbling present in the water chamber of the atrium. Indicates incomplete re-expansion of lung
- Accidental removal of tube: Place petroleum gauze and occlusive dressing over CT site.
- Always order STAT CXR and contact CVTS if following for any new onset or worsening air leak, subcutaneous emphysema, darkening and increasing chest tube output or tube malpositioning/removal
- CVTS will manage tubes if involved
- Patients can shower 24 hours after chest tubes are removed

Pulmonary Embolism

- Etiology: Migration of DVT
- Risk factors: recent surgery, trauma, immobilization, hormone therapy, malignancy, factor V Leiden
- Can result in lung infarction and cardiovascular compromise
- Presentation: Varies depending on clot burden but includes hypoxia, pleuritic chest pain, hemoptysis, hypotension, arrhythmias, syncope. May be asymptomatic.

• Diagnostics:

- Ventilation/perfusion scan
- CTA if renal function allows with appropriate IV hydration
- Venous dopplers (Upper and lower)
- Echo to look for right heart strain

Treatment

- Anticoagulation with Heparin gtt
 - Okay to start Warfarin transition after therapeutic Heparin levels x 2
- Mechanical thrombectomy
- Catheter directed vs systemic thrombolysis
- Consider IVC filter for significant lower extremity clot burden or inability to anticoagulated
- IVF should be limited as can worsen hemodynamics in setting of RV failure



Airway complications

- Anastomotic dehiscence
 - Typically occurs within first 5 weeks
 - Think about with presence of pneumothorax, subcutaneous emphysema, new/worsening hypoxia, inability to wean from vent
 - Assess with bronchoscopy
 - May require stent or surgical correction if severe
 - Can be life threatening!
- Bronchial stenosis
 - Typically within first 2-9 months
 - Narrowing of the airway causing atelectasis, dyspnea, wheezing, stridor, decline in lung function and post obstructive pneumonia
 - Assess with bronchoscopy
 - Clinically significant stenosis > 50% luminal narrowing
 - Management: IP bronchoscopy with balloon dilation, ablation, cryotherapy and/or stent placement

Pulmonary Vascular Complications

- Pulmonary venous stenosis and thrombosis
 - Typically occurs within first 24-48 hours following transplant
 - Clinical signs include pulmonary edema and venous congestion; can be unilateral or bilateral
 - Diagnostics: Cardiac CTA with special attention to suspected diagnosis or TEE as an alternative
- Pulmonary arterial stenosis
 - $\circ\,$ Typically within first 2 weeks following transplant
 - Clinical signs include hypoxia and pulmonary hypertension
 - Diagnostics: CTA
- Bronchovascular torsion
 - Typically occurs within first 4 days following transplant
 - Clinical signs include hypoxia, difficulty weaning ventilator and serosanguineous secretions on bronchoscopy
 - Diagnostics: Abnormal airway tract can be noted on CT without contrast as well as bronchoscopy
- Treatment will depend on severity of complication and will range from close monitoring to surgical correction

Diaphragm dysfunction

- Etiology:
 - Phrenic nerve injury during transplant surgery
 - Can be unilateral or bilateral
- Clinical presentation:
 - Can be asymptomatic or present with dyspnea, hypoxia, tachypnea, hypercapnia, paradoxical breathing
- Diagnosis:
 - Elevated diaphragm noted on CXR
 - Fluoroscopy "sniff test" to assess presence of paradoxical motion
 - Pulmonary function tests with MIP and MEP
- Treatment:
 - BiPAP; typically nocturnal but can be used throughout day if severe
 - Diaphragm plication if paradoxical motion present and symptomatic



Drug Induced Lung Injury

- Common culprits
 - Sirolimus
 - Pentamidine
 - Macrobid
 - Amiodarone
- Treatment
 - Stop offending drugs
 - High dose steroids
- Miscellaneous medications not used post transplant
 - Metformin lactic acidosis
 - ACE/ARB Minimize use due to renal injury risk
 - NSAIDS listed as an allergy for transplant patients; Aspirin okay
 - Heparin and Warfarin preferred over alternative anticoagulants due to risk of bleeding and reversal agents

PGD

- Severe lung injury that occurs within first 72 hours of lung transplant
- Based on presence of diffuse pulmonary opacities on imaging and hypoxemia without identifiable cause
- Histopathologic pattern: Diffuse alveolar damage (DAD)
- Assessed at start of reperfusion of second lung (T0) then at 24, 48 and 72 hours
- Etiology: multiple different types of injury that occur prior to or during harvesting including subsequent inflammation triggered by graft warming and reperfusion
- Diagnosis of exclusion: Assess volume status, CT chest, bronchoscopy, TTE, TEE if severe to assess pulmonary vein outflow
- Treatment: Manage like ARDS with lung protective ventilation: High PEEP, low TV; diuresis, inhaled NO and even ECMO if severe

Table 5. Recommendations for Grading of Primary Graft Dysfunction(PGD) Severity

		Radiographic infiltrates consistent with
Grade	Pao ₂ /Fio ₂	pulmonary edema
0	>300	Absent
1	>300	Present
2	200-300	Present
3	<200	Present

ARDS

- Patients typically present with dyspnea and a reduction in arterial oxygen saturation after 6 to 72 hours (or up to a week) following an inciting event.
- HALLMARK SIGN: Hypoxemia despite increasing supplemental oxygen
- Causes: Sepsis, infectious or aspiration pneumonia, TRALI, PGD, CT surgery, trauma and burns, inhalation injury, shock, drug toxicity (ex. Amiodarone)
- S/S: tachypnea, tachycardia, and diffuse crackles. AGITATION. When severe, acute confusion, respiratory distress, cyanosis, and diaphoresis may be evident. Cough, chest pain, wheeze, hemoptysis, and fever are inconsistent and mostly driven by the underlying etiology.

ARDS Diagnostic Criteria:

Clinical Diagnosis: All 4 must be met

- Respiratory symptoms must have begun within one week of a known clinical insult, or the patient must have new or worsening symptoms during the past week.
- Bilateral opacities must be present on a chest radiograph or computed tomographic (CT) scan. These opacities must not be fully explained by pleural effusions, lobar collapse, lung collapse, or pulmonary nodules
- The patient's respiratory failure must not be fully explained by cardiac failure or fluid overload. An objective assessment (eg, echocardiography) to exclude hydrostatic pulmonary edema is required if no risk factors for ARDS are present.
- A moderate to severe impairment of oxygenation must be present, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO2/FiO2)

The severity of the hypoxemia defines the severity of the ARDS:

Mild ARDS – The PaO2/FiO2 is >200 mmHg, but ≤300 mmHg, on ventilator settings that include positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm H2O.

Moderate ARDS – The PaO2/FiO2 is >100 mmHg, but ≤200 mmHg, on ventilator settings that include PEEP ≥5 cm H2O.

Severe ARDS – The PaO2/FiO2 is $\leq 100 \text{ mmHg}$ on ventilator settings that include PEEP $\geq 5 \text{ cm}$ H2O.

ARDS Treatment

- Treat the underlying cause.
- Supportive care.
- ARDS net protocol for ventilation (see next slide)
- Paralytic can be used to decrease the body's intrinsic oxygen demand
- Pronation increases the alveolar surface area by allowing the posterior portion of the lungs to fully expand without dependent weight.
- Inhaled Nitric/Veletri: A smooth muscle relaxant that, when inhaled, improves lung compliance by relaxing the smooth muscle of the lung.
- ECMO: In severe cases where maximum ventilator support are not successful, the patient may be placed on VV or VA ECMO (dependent on cardiac function).
- Ventilated patients are at increased for barotrauma due to poor lung compliance and high ventilator support required.



NIH NHLBI ARDS Clinical Network Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

- PaO₂/FiO₂ ≤ 300 (corrected for altitude)
- Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
- 3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

- Calculate predicted body weight (PBW) Males = 50 + 2.3 [height (inches) - 60] Females = 45.5 + 2.3 [height (inches) - 60]
- 2. Select any ventilator mode
- 3. Set ventilator settings to achieve initial V₁ = 8 ml/kg PBW
- Reduce V_T by 1 ml/kg at intervals ≤ 2 hours until V_T = 6ml/kg PBW.
- Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
- Adjust V_t and RR to achieve pH and plateau pressure goals below.

OXYGENATI ON GOAL: PaO₂ 55-80 mmHg or SpO₂ 88-95%

Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/ higher FiO2

FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO ₂	0.7	0.8	0.9	0.9	0.9	1.0	
PEEP	14	14	14	16	18	18-24	

Higher PEEP/ lower FiO2

FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FIO ₂	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

PLATEAU PRESSURE GOAL: < 30 cm H₂O

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T .

If Pplat > 30 cm H₂O: decrease V_t by 1ml/kg steps (minimum = 4 ml/kg).

If Pplat < 25 cm H₂O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H₂O or V_T = 6 ml/kg.

If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains \leq 30 cm H₂O.

The Management of Lung Transplant

REJECTION

Lung Biopsy Pathology

Table 1 Semi-quantitative summary of the distinguishing features, in terms of sites of inflammation and the respective cell types involved, used to classify acute cellular rejection according to the International Society For Heart & Lung Transplantation (ISHLT) consensus document (1)



All images taken at 100× magnification and supplied courtesy of Institute for Pathology, Hannover Medical School, Hannover, Germany. LYM, lymphocytes; EOS, eosinophils; NEU, neutrophils.

Lung Biopsy Pathology

Table 2 Semi-quantitative summary of the distinguishing features, in terms of sites of inflammation and the respective cell types involved, used to classify lymphocytic bronchitis observed in transbronchial biopsies according to the International Society For Heart & Lung Transplantation (ISHLT) consensus document (1)

Variable				
Infiltration	B0: none	B1R: low grade	B2R: high grade	BX: ungraded
Cell lineage		LYM, EOS(-)	LYM, EOS(++), NEU(-)	Sampling artifact, infection
Sub-mucosal	-	+	++	
Intra-epithelial	-	1716	+	
Necrosis/exudates	2	121	-/+	

All images taken at 100× magnification and supplied courtesy of Institute for Pathology, Hannover Medical School, Hannover, Germany. B1R, Revised 2007 definition of B1; B2R, Revised 2007 definition of B2; LYM, lymphocytes; EOS, eosinoptablehils; NEU, neutrophils.

Pathology Grading for Rejection

- A. Acute vascular rejection (vascular rejection of any grade may occur with or without acute airway rejection)
 - AO: none
 - A1: minimal
 - A2: mild
 - A3: moderate
 - A4: severe
- B. Lymphocytic bronchiolitis B0: none
 - B1R: mild
 - B2R: severe
- C. Chronic airway rejection C1: bronchiolitis obliterans
- D. Chronic vascular rejection Accelerated graft vascular sclerosis

Adapted from Stewart S, Fishbein MC, Snell GI, et al. Revision of the 1996 working formulation for the standardization of nomenclature in the diagnosis of lung rejection. J Heart Lung Transplant. 2007;26:1229–42

Acute Cellular Rejection (ACR)

- "Acute cellular rejection is the predominant type of acute lung transplant rejection and is mediated by T lymphocyte recognition of foreign major histocompatibility complexes (MHC), also known as human leukocyte antigens (HLA) in humans, or other antigens" (Up to Date)
- Risk factors:
 - Medication non-compliance
 - Reduced immunosuppression regimen
 - Infection
 - Aspiration
 - Any injury could theoretically predispose patient to a rejection episode... always look for an inciting factor!

- Common chief complaints:
 - Shortness of breath
 - Cough
 - Hypoxia
 - Decline in spirometry
 - "Feel great" (incidental finding on surveillance bronchs)

ACR continued

Biopsy Rejection Grade Protocol:

- Grade A1 without clinical symptoms
 - 1. No treatment and continue to monitor spirometry and symptoms
- Grade A1 with clinical symptoms
 - 1. Methylprednisolone IV 10mg/kg daily x 3 days (pulse)
 - 2. Repeat biopsy in 4 weeks
- \circ Grade A2, A3 or A4
 - 1. Methylprednisolone IV 10mg/kg daily x 3 days
 - 2. If on azathioprine, switch to mycophenolate (start with 500 mg twice daily for one week then increase to 1000 mg twice daily as tolerated)
 - $\circ\,$ 4. If on cyclosporine, switch to tacrolimus
 - \circ 5. Repeat biopsy in 4 weeks



Orders:

- Solumedrol 10mg/kg every 24 hours x 3 doses
- Hold Prednisone until SM done
- Consider taper depending on presentation and pathology
- Consider diabeties consult if hyperglycemia or hx of uncontrolled diabetes
- Adjust immunosuppression switch Imuran to Cellcept; increase Cellcept dose; or if on CYA and can tolerate FK switch to that. Also may consider adding Rapamune. All of these decisions made with attending input

https://365utsouthwestern.sharepoint.com/sites/hsp_UHPolicies/Policies/Transplant%20Guidelines/Lung %20Transplant%20Treatment%20of%20%20Rejection%20.pdf

Refractory Rejection

- If patient continues to decline despite recent pulse steroids, consider Anti-thymocyte globulin (ATG)
- Pre-ATG workup
 - Baseline CD3, CMV, EBV, DSA, pan-cultures, dopplers, V/Q, echo, BNP, CT chest, bronchoscopy +/- biopsy
 - GES, EXR and MBSS to assess for aspiration but can be done after ATG initiation
- Thymoglobulin- Rabbit derived
 - Pre-medication: Tylenol 650 mg, Benadryl 25 mg and SM 20 mg IV 30 minutes prior to infusion
 - Can adjust steroid based on clinical presentation
 - Can re-dose pre-meds 4-6 hours into infusion especially during first few doses as they are the most difficult to tolerate. This typically manifests as flu-like symptoms.
 - Initial dose 0.5 mg/kg
 - Assess daily for ability to tolerate clinically and monitor blood counts carefully
 - Consider holding if WBC <3 or platelet count declines by 30-50%.
 - If okay to proceed then increase dose to 1 mg/kg
 - If continues to tolerate well, increase dose to 1.5 mg/kg which is max dosing
 - Continue to dose daily until goal 6-9 mg/kg reached
- Repeat CD3 and re-dose if absolute CD3 not at goal <25 https://365utsouthwestern.sharepoint.com/sites/hsp_UHPolicies/Policies/Iransplant%2 OGuidelines/Lung%20Transplant%20Treatment%20of%20%20Rejection%20.pdf



- ATGAM-Horse derived
 - May be used for patients who have received Thymoglobulin in the past
 - \circ Start with test dose
 - Dosing: 10 mg/kg daily for 10 days
 - Can extend by additional 3-5 doses if repeat CD3 not at goal
- Goal of therapy is for stabilization of lung function but lung function may worsen before it gets better and may take several weeks to see results

Post Thymo Prophylaxis:

- Ensure appropriate PJP and CMV prophylaxis
- Antifungal prophylaxis for 6 months
 - Posaconazole 300 mg daily preferred
 - Voriconazole: 200mg po BID alternative
 - Watch for hallucinations and need for FK adjustments
 - Send ASAP to pharmacy for PA/Price check upon starting

Antibody Mediated Rejection (AMR)

• Also known as humoral rejection

- "Mediated by antibodies directed against donor HLA or other epitopes. These antibodies may have been present in the recipient at a low level prior to transplant or may develop afterwards. Generally, if HLA antibodies are identified in the potential recipient, the corresponding HLA antigens are avoided in a donor (so-called virtual cross-match)." (UptoDate)
- Usually treated when MFI >4000; when in doubt, Dr. Kaza is contact person for DSA therapies



https://365utsouthwestern.sharepoint.com/sites/hsp_UHPolicies/Policies/Solid%20Organ%20Transplant%20Program%20and%20Clinics/Transplant%20Guidelines/Lung%20Transplant%20Transplant%20of%20%20Rejection%20.pdf

Stages of AMR



AMR continued

Patients with **Positive DSA and stable PFTs**

- DSA considered + if MFI >4000
- If ≤ 90 days of transplant, consider adjustment in IS and more frequent monitoring of DSA before treating
- Check total Immunoglobulins prior to first infusion
- If SCr > 2mg/dl or >30% from baseline, consider holding dose
- Immune globulin (10% sucrose free) 500 mg/kg
 - 1. Premedication: Acetaminophen 650 mg and diphenhydramine 25 mg orally
 - 2. Consider hydration with 500ml NS prior to infusion, if patient has symptoms
 - 3. Protocol dosing
 - A. Loading dose: Every other day for 4 doses (Can give daily if tolerating)
 - B. Weekly x 4 doses
 - C. Bi-weekly x 2 doses
 - D. Monthly x 6 doses
 - d. Consider giving a dose of Rituximab (Rituxan) 375 mg/m2 (rounded to nearest 10 mg).
 - $\,\circ\,$ e. Follow DSA and spirometry monthly x 3 years to monitor

AMR continued

Patients with **Positive DSA and acute declining PFTs and with or without positive C4d** (found on TBBx)

- Check total Immunoglobulins and IgG subtypes prior to first infusion
- If SCr > 2mg/dl or >30% from baseline, consider holding dose
- Discuss plan with attending and/or Dr. Kaza but could include the following:
- IVIG protocol
- Therapeutic Plasma Exchange (TPE)
 - $\circ~$ 1. TPE every other day for 5 treatments
 - $\,\circ\,$ 2. TPE will be followed by IVIG 100 mg/kg infusions after each session
 - 3. Then IVIG 500mg/kg x 3 more doses daily. Total dose to be given around the period of TPE is 2g/kg of IVIG
 - 4. Premeds prior to each dose of IVIG include acetaminophen 650 mg and diphenhydramine 25 mg orally
 - 5. Continue to follow remainder of IVIG protocol
 - To order TPE place order "Consult to Transfusion medicine;" then page #1 in "on call" system. Apheresis will send nurse to do vein assessment. Most likely patient will need dialysis catheter for PLEX place in IR or at bedside. If IR and poor access, request Trialysis catheter which gives extra lumen
- Rituximab (Rituxan) 375 mg/m2 (rounded to nearest 10mg) infusion
 - Must hav e chemotherapy consent
- Bortezomib (Velcade) alternative given SQ 1.3 mg/m2 on days 1, 4, 8 and 11
 - Must hav e chemotherapy consent
 - Hold dose if platelets <30,000 or ANC < 750
 - Side effects: Peripheral neuropathy

IVIG Mechanism in AMR



Therapeutic Plasma Exchange (TPE)

immunopaedia.org



- Watch clotting factors especially platelets and fibrinogen
 - PLEX team will draw labs every AM before PLEX
 - Replace with FFP if fibrinogen < 100
- Test fibrinogen levels before removing PLEX line. Goal > 150 prior to removal

Chronic Rejection



Chronic Rejection



BOS Classification

TABLE 1. BRONCHIOLITIS OBLITERANS SYNDROME CLASSIFICATION SYSTEM

	1993 Classification*	2003 Classification [†]
BOS 0	$FEV_1 > 80\%$ of baseline	$FEV_1 > 90\%$ of baseline and $FEV_{25,75} > 75\%$ of baseline
BOS 0 p		FEV ₁ 81–90% of baseline and/or FEV ₂₅₋₇₅ \leq 75% of baseline
BOS 1	FEV ₁ 66–80% of baseline	FEV ₁ 66–80% of baseline
BOS 2 BOS 3	$FEV_1 51-65\%$ of baseline $FEV_1 \leq 50\%$ of baseline	$FEV_1 51-65\%$ of baseline $FEV_1 \leq 50\%$ of baseline

Estenne M et al. J Heart Lung Transplant 2002;21:297–310



- Chronic Lung Allograft Dysfunction: umbrella term for chronic rejection. Defined as decline in lung function beyond one year from transplant and persisting for more than 3 weeks
 - Two main types:
 - Bronchiolitis obliterans syndrome (BOS): progressive airway obstruction defined as a progressive decline in forced expiratory volume in one second (FEV₁)
 - Restrictive allograft syndrome (RAS): upper lobepredominant fibrotic changes and restrictive pulmonary function tests
- Risk factors:
 - PGD post op
 - Infections (specifically Aspergillus and Pseudomonas)
 - Acute rejections (cellular or antibody)
 - GERD
 - Single lung transplant

Chronic Rejection

- Common symptoms: declining spirometry despite multiple interventions, SOB, cough, changes on imaging.
- Before labeling chronic rejection: rule out all other causes for symptoms
 - Pulmonary embolism
 - Heart failure
 - Infection
 - Malignancy
- Treatment:
 - Prevention is best
 - Avoiding risk factors
 - Appropriate OIP
 - Azithromycin 250mg MWF
 - Singular 10mg daily in evening
 - Photophoresis (ECP) depends on patient location/insurance coverage. Set up outpatient
 - Consider Methotrexate 5-10 mg weekly
 - Last resort: Re-transplantation only select patients

https://www.uptodate.com/contents/chronic-lung-transplant-rejection-bronchiolitis-obliterans



Immune System Review



Immunosuppression Targets


Overview

• Most are on three drug regimen:

- Calcineurin inhibitor and/or MTor inhibitor
- Cell-cycle inhibitor (antimetabolite)

• Prednisone

 Occasionally patients will be on 2 or 4 drug regimen due to side effect profile

Newer trend: Belatacept



Calcineurin Inhibitors

Interfere with T cell activation, proliferation and differentiation

- Tacrolimus (Prograf/"FK")
 - Routes: oral capsule, oral suspension, sublingual, IV
 - Sublingual twice as potent as oral
 - IV is 3-4 times as potent as oral
 - Suspension hard to obtain, avoid if possible
 - Goal levels
 - 0-6 months: 10 15 (8 10 if age >65)
 - 6-12 months: 8 12
 - \circ >12 months: 5 10
 - Most common side effects: AKI, Tremors, PRES, MAHA
 - Infusion must be run through designated peripheral IV so as not to interact with levels
 - May run lower goal due to renal dysfunction or other side effects.
 - Needs to be scheduled at 0900/2100 for accurate trough levels
 - FK gtt starts in OR if Simulect not given. If Simulect is given, initiation deferred until 1-3 days post op for stabilization of renal function
 - Will need to decrease dose by half when starting azole therapy and increase dose when discontinuing therapy due to interaction

- Cyclosporine ("CYA")
 - Goal levels
 - > 12 months:150-200
 - Not commonly used unless intolerance to FK
 - Only mixed in certain juices
 - Given at 1300

Both meds need to have levels checked prior to AM dose



MTor inhibitors

Inhibits T cell proliferation



- Rapamune (Sirolimus)
 - Goal levels:
 - Rapamune only (6-10)
 - In conjunction with FK (4-8)
 - Given at 1300
 - Most common side effects
 - Lung toxicity
 - Peripheral edema
 - Proteinuria
 - Oral ulcers
 - Poor wound healing
 - \circ VTE
 - Common reason to use:
 - CKD
 - Cancer
 - Must be on 1 mg warfarin
 - Discontinue 4 weeks prior to surgery if able and hold at minimum for 4 weeks after

Cell-cycle Inhibitors

Suppresses proliferation of T and B lymphocytes

- Cellcept (Mycophenolate)
- Myfortic (Mycophenolate sodium): enteric coated
 - Not equivalent in dosages
 - Most common side effects
 - Gl issues (Myfortic better tolerated)
 - Bone marrow suppression
- Preferred agent if rejection history

- Imuran (Azathioprine)
 - Most common side effects
 - Transaminitis
 - Pancreatitis
 - Bone marrow suppression
- Preferred agent unless on Cellcept pre-txp
- Given on the floor within 30 minutes of posted OR time



Steroids

Decrease production of inflammatory cytokines and inhibition of t-cell activation process

- All patients are put on Prednisone post-transplant and will stay on for life
- Induction: 500 mg IV Solumedrol given in OR followed by 125 mg every 8 hours x6 followed by 0.25 mg/kg BID
- Weight-based regimen: divide in AM/PM if on high dose
 - 0-1 month: 0.5 mg/kg/day
 - 1-2 month: 0.4 mg/kg/day
 - 2-4 month: 0.3 mg/kg/day
 - 4-6 month: 0.2 mg/kg/day
 - 6-9 month: 0.15 mg/kg/day
 - 9-12 month & maintenance: 0.1 mg/kg/day
- Prednisone Tapers: acute viral illness, AFOP, rejection. Usually start at 40mg and taper every 3-7 days. Organizing pneumonia requires 1 mg/kg with longer taper
- Stress dose: IV Solumedrol 40-60 mg every 6-8 hours for patients with respiratory distress
- High dose steroids (aka PULSE): Rejection 10mg/kg Solumedrol x 3 days. Okay to resume home dose unless significant decline in lung function, abnormal lung pathology or persistent symptoms requiring Prednisone taper



Belatacept CD28 T-cell co-stimulation blocker

- Newer agent; monoclonal antibody
- Usually part of a 4 drug regimen
- When to use it:
 - Renal dysfunction
 - CNI intolerance
 - Antibody mediated rejection
- Must be EBV IgG serum positive with recent negative PCR due to high risk of PTLD.
- Quantiferon gold negative within past year.
- Do not start until approved by insurance
- Schedule:
 - 10 mg/kg IV on day 1, 5, week 2, 4, 8, 12
 - 5 mg/kg on week 16, and then every 4 weeks
- Dot phrase for consent: .TXPBELATACEPTPATIENTCOUNSELING

Simulect

IL-2 receptor antagonist

- Induction use only: 20 mg given in OR for patients with pulmonary hypertension or age >65
- Can be re-dosed on POD4 if unable to start Prograf due to renal dysfunction or if patient received a large amount of blood products in the intra-operative and immediate post-operative time frame





CMV

- CMV mismatch protocol for fresh transplants (donor +/ recipient -)
 - Ganciclovir IV for first month then transition to renally dosed Valcyte for life
 - Cytogam protocol
 - Note: Valcyclovir and Acyclovir do not cover CMV
- CMV non-mismatch (-/-, +/+, -/+)
 - Start with IV Ganciclovir x 14 days or until discharge (whichever comes first) then transition to lifelong Valcyte
 - Maintenance dose: adjust for creatinine clearance
 - > 60: 450mg PO BID
 - 40-59: 450mg PO daily
 - 25-39: 450mg PO every other day
 - 10-24: 450mg PO Mon & Thurs
 - Common Side Effects
 - Renal dysfunction
 - Leukopenia
 - Hold when WBC < 3.5 with plan to restart when WBC > 4
 - If underdosed, risk for drug resistance
 - Can substitute Letermovir 480 mg daily for those with refractory leukopenia.
 - $\,\circ\,$ Will need Valtrex 500 mg twice daily for HSV/VZV coverage





PJP (pneumocystis carinii pneumonia)

- Bactrim SS 400/80mg daily 1st line (also covers Nocardia)
 - Watch out for hyperkalemia, renal dysfunction, leukopenia
- \circ If unable to use Bactrim due to allergy or side effect
 - Toxoplasma D+/R-
 - Atovaquone 1500mg daily
 - can be expensive send to pharmacy to check co-pays
 - Otherwise
 - Pentamidine 300 mg inhaled monthly
 - Watch for possible bronchospasm; pre-medicate with albuterol
 - Will need home care coordination order
 - Dapsone 100mg daily
 - Check G6PD once cannot use if low
 - Watch for methemaglobinemia, leukopenia
 - Atovaquone (Mepron)



Post operative Bacterial Prophylaxis

- IV antibiotics: 7 days total for patients without complications or airway secretions
 - Vancomycin 1 g every 12 hours (Pharmacy to follow for dosing)
 - Zosyn 3.375 g every 8 hours (run over 4 hours)
 - Transitioned to every 6 hours with each dose over 30 minutes at home
 - Aztreonam 2g IV every 8 hours alternative for those with allergy
 - Levaquin 750 mg daily
 - Alternative regimen may be utilized for any pretransplant infections
- Will need targeted 14 day therapy for any positive lower respiratory tract cultures

Inhaled antibiotics: 30 days total

- Tobramycin 300 mg twice daily
 - Alternatives:
 - Inhaled Colistin 150 mg BID
 - PO Augmentin 875-125 mg BID x 14 days
 - PO Levaquin 750 mg daily x 14



Fungal Prophylaxis

- Inhaled Amphotericin B Liposomal 25 mg every Monday, Wednesday and Friday for 30 days
- Fluconazole 400 mg daily for 90 days
 - 200 mg daily for GFR < 40
 - Transition to Nystatin QID until Prednisone 10mg or less
 - $\,\circ\,$ Swish and spit for patients who are NPO
 - Swish and swallow for all others
 - Mycelex troche 10 mg PO QID alternative
- Post Thymoglobulin
 - Posaconazole 300 mg daily for 6 months
 - Liquid 200 mg TID only if patient has feeding tube
 - Alternatives
 - Voriconazole 200 mg BID
 - Itraconazole 200 mg BID
 - Watch FK levels when starting and stopping!
 - Send to pharmacy for cost assessment ASAP!



The Management of

INFECTION

in Lung Transplant

Timeline of Post-Transplant Infections



Fishman JA. N Eng J Med. 2007;357:2601-2614.

Infection Initial Workup

- Respiratory PCR viral panel
- Cultures
 - Urine
 - Blood
 - Fungal
 - AFB
 - Sputum
- Lab work
 - Lactate
 - CMV
 - EBV
 - IgG
 - Disease specific labs
- Bronch (if needed)
 - Variety of cultures can be sent



- Imaging (dependent on presentation)
 - \circ CXR
 - \circ KUB
 - CT scans
 - Chest
 - Abdomen/pelvis
 - Head
 - TEE if persistent positive blood cultures or concern for endocarditis
- Meds
 - Empiric antibiotics (typically Vanc/Zosyn -/+ Levaquin)
- Important Note: Check patient's infectious history (Epic: Summary tab → micro reports).
 Often will give clues on what current issue is

- Respiratory Syncytial Virus (RSV)/Parainfluenza (PIV)/Human Metapneumovirus (hMPV)
 - Inhaled Ribavirin (if lower respiratory tract infection present or inability to tolerate PO due to renal function or blood counts)
 - 2g every 8 hours x 9 doses; can extend an additional 6 doses if not improved by end of initial course
 - Can transition to PO Ribavirin for additional 5 days which is weight based and renally dosed
 - Pulse steroids
 - Synagis 7.5 mg/kg given for RSV
 - Empiric antibiotics
 - Supportive care
- Influenza
 - Tamiflu 75 mg PO BID x 5 days; can extend to 10 days if still symptomatic. Adjust for renal function
 - Exposure prophylaxis: 75 mg PO daily for 10 days
 - Prednisone taper
 - Empiric PO antibiotics
- Adenovirus
 - Cidofovir 1 mg/kg TIW x 3 weeks or until cleared
 - Probenicid 2g 3 hours prior to dose, 1 g at 2 and 8 hours after completion
 - 1L NS infusion 1-2 hours pre and post infusion
- Rhinovirus/coronavirus (NOT COVID corona)
 - Prednisone taper
 - Empiric PO antibiotics

Respiratory Viruses

Community Acquired Respiratory Viruses (CARV)



- Notes:
 - Detected via respiratory viral panel (nasal swab) or can be seen in BAL respiratory viral AGS screen
 - **Usually** do **not** bronch when patient + for respiratory virus in order to avoid introducing virus deeper into the lungs and because we have a cause for symptoms
 - High risk for bacterial infection and/or rejection post viral infections
 - Association with long term chronic rejection
 - Always check IgG and replete with 500 mg/kg IVIG if low <550
 - Inhaled Ribavirin therapy
 - Negative pressure rooms needed
 - No pregnant or lactating females allowed to enter room

COVID-19 Treatment



- Patients will be admitted to COVID floor and under our service
- We follow a protocol specific to our patients
- Currently, we are trying to admit patients before they become severely ill; some patients will get outpatient Remdesivir infusions

in UTSW Lung Transplant patients

- Current Lab Studies
 - On admission: troponin, ECG, CRP, ferritin, D-dimer IgG, MRSA, DSA, COVID spike IgG, COVID spike IgM, COVID IgG NC semiquant
 - Daily: CBC, CMP, Ferritin, Troponin, CRP, D-dimer, LDH
- Other Tests: CXR, CT dependent on clinical situation
- Current Treatments:
 - Prednisone 60 mg daily followed by taper
 - Escalate to pulse steroids if hypoxia or infiltrates noted
 - Remdesivir for 5-10 days dependent on imaging/severity of symptoms/hypoxia
 - $\circ~$ 1. Discontinue if LFTs x10 ULN
 - 2. Avoid if GFR <30
 - Empiric Antibiotics
 - Supportive care/symptom management
 - Elevated Ddimer: Lovenox 40 mg daily (avoid if GFR<50) for 30 days from onset of symptoms
 - Warfarin can be alternative

CMV infection

- Second most common infection in lung transplant following bacterial pneumonia
- Highest risk population: CMV mismatch D+/R-
- Presentation:
 - Fever, malaise, myalgias, arthralgias, leukopenia, thrombocytopenia
 - End organ manifestations:
 - Pneumonia, encephalitis, retinitis, hepatitis, colitis
- Diagnostics:
 - CMV PCR- Blood
 - Follow positive CMV PCR weekly
 - CMV Quant BAL
 - Pathology
 - CMV genotype
 - $\,\circ\,$ do not send if PCR <1000



o Treatment

- o CMV viremia < 3000 IU/ml
 - Treatment dose Valcyte
- CMV viremia >3000 IU/mI/Enteritis/Pneumonitis
 - Ganciclovir (GCV) 5 mg/kg IV BID renally dosed
 - Cytogam 150 mg/kg IV BIW for those with end organ or refractory disease
 - Can transition to treatment dose Valcyte once viremia and end organ disease improves
 - Treat for minimum of 3 weeks or until CMV PCR negative x 2 done 1 week apart
 - Presence of end organ disease requires 4 6 weeks of treatment minimum
- $\circ~$ GCV resistance and refractory CMV
 - Presence of mutation on genotype or failure to decrease > 1log10 of CMV PCR titer in a week
 - Typically will involve ID
 - Consider Maribavir
 - Cidofovir Do not use with UL54 mutation
 - o Foscarnet
 - High dose GCV 10 mg/kg

EBV infection

- $\circ\,$ High risk for PTLD
- \circ EBV reactivation defined as two consecutive PCR's > 10,000 IU/ml
- Presentation:
 - LAD, fever, night sweats, hepatosplenomegaly, mass lesion, abdominal pain
- Diagnostics:
 - EBV PCR-blood
- Treatment:
 - $\circ\,$ Reduce IS
 - Consider Rituxan 375 mg/m2

Bacterial Infections

- Stenotrophomonas Maltophila
 - MDR gram bacillus
 - Closely related to pseudomonas
 - Treatment options: Bactrim/Levaquin/Ceftazidine/Minocycline
- Pseudomonas
 - Gram negative aerobic bacilli
 - Follow sensitivities: start w/ Zosyn and Levaquin as well as inhaled Tobramycin or Colistin
 - Typically treat for 3 week course if recurrent
- Klebsiella
 - Gram non-motile, rod shaped
 - Treatment: dependent on area of infection/susceptibilities

- Enterococcus
 - Gram + cocci, often in pairs & short chains
 - Faecalis more virulent than faecium
 - Treatment: depends on where infection is located and sensitivities
- Staph Aureus
 - Gram + cocci
 - Endocarditis w/u if bacteremia
 - Vanc (if MRSA)/if mSSA, de-escalate
- Nocardia
 - Gram + Actinomycetes
 - Can spread to central nervous system
 - Alwaysget a CT head WO!
 - Treatment: Bactrim, Imipenem, Merrem, Minocycline typically under ID guidance for 6-12 months



Bacterial infections cont.

- Neisseria
 - Gram negative
 - Meningitidis, gonorrhoae
 - Susceptibilities for treatment
- C difficile
 - Spore-forming gram + bacillus
 - Typically associated with antibiotic use
 - Presentation: Diarrhea, abdominal pain, abdominal distention, fever, hypovolemic state, hypotension if severe
 - Diagnostics:
 - C diff stool testing
 - Active disease noted when toxin +
 - CT A/P if concerned about colitis
 - Concern for megacolon if large bowel dilation >7cm
 - Treatment:
 - PO Vancomycin 125 mg QID x 2 weeks
 - Severe disease 250 mg QID
 - Recurrent infection requires prolonged taper
 - +/- Flagyl or Dificid for severe disease
 - Avoid Imodium!

• Of note:

- Not a comprehensive list just the most commonly seen
- Dependent on infection patient may need home IV antibiotics
 - Clarify meds, duration of therapy with physician before placing orders
 - Consult PICC line order
 - If renal function low or INR high, need to place specific comment that is cleared by MD to place
 - Will need 1 mg Warfarin while line in place
 - Home Discharge IV medication order



Fungal Infections

- Diagnostics:
 - Labs: fungal blood cultures, serum/BALA. Galactomannan, serum/BAL fungitell, serum Blastomyces Ab, Urine Blasto Ag, serum Coccidioides Ab, serum/CSF Cryptococcal Ag, serum/urine histo galactomannan
 - CT chest for thoracic infections
 - Findings may include consolidation, cavitary lesions and nodular/mass like lesions
 - Bronchoscopy with fungal cultures/TBBx
- Aspergillus- Most common fungal infection
 - $\,\circ\,\,$ Can be angioinvasive so patients may present with hemoptysis or sanguineous BAL
 - Treatment: Voriconazole, Posaconazole
- Scedosporium
 - Can see disseminated disease including skin lesions
 - Treatment: Voriconazole
- Candida
 - Types: albicans, glabrata (fluc resistant), parpsilosis, tropicalis, krusei (fluc resistant)
 - Treatment: Micafugin, Fluconazole, inhaled ampho B
- Histoplasmosis
 - Endemic in Midwest-Ohio and Mississippi river valleys
 - Treatment: Itraconazole

- Cryptococcus
 - Typically presents as meningitis or pneumonia
 - Requires lumbar puncture if meningeal signs present
 - Treatment: Fluconazole, Posa, Vori, Itraconazole
- Coccidioidomycosis
 - Endemic in Southwest-Arizona, Southern California
 - Treatment: Fluconazole, Itraconazole
- Mucor
 - Common species seen: Rhizopus and Mucor
 - $^\circ$ $\,$ Can see infarction and necrosis of host tissues due to v asculature invasion
 - High mortality
 - Treatment: IV Ampho B followed by Posaconazole
 - ID involvement suggested
- Pneumocystis jirovecci
 - Can present as severe inflammatory pneumonia
 - Presentation: Fever, cough, dyspnea, chest pain, night sweats, weight loss, hypoxia
 - Diagnostics:
 - Elevated LDH and beta-D-glucan
 - CXR- diffuse bilateral infiltrates.
 - CT chest may include nodules, hilar LAD, bilateral assymetric patchy mosaic "crazy paving" GGO
 - Bronchoscopy PCP BAL studies
 - Treatment: IV Bactrim treatment of choice

Mycobacterium infections

- Nontuberculous mycobacteria (NTM) most common
- Common species: M. Abscessus and Avium
- Typically occurs several years post transplant
- May develop disseminated infection including skin lesions
- Presentation:
 - Low grade fever, weight loss, night sweats, chronic cough, sputum production, dyspnea, hemoptysis, skin lesions

- Diagnostics:
 - AFB blood cultures
 - CT chest for pulmonary disease may reveal nodules, infiltrates, abscesses and cavitating nodules
 - Bronchoscopy AFB cultures
 - Lung or skin biopsy
- Treatment:
 - Typically will monitor for isolated airway cultures without CT evidence of active infection
 - If requiring treatment; multidrug regimen is utilized for 6-12 months under ID guidance
 - Common agents: Zithromax, Imipenem, Rifabutin, Ethambutol, Rifampin, Moxifloxacin, INH, Zyvox, Tigecycline

Parasites

- Toxoplasmosis
 - Treatment: Pyrimethamine + sulfadiazine + leucovorin calcium generally for 6 weeks
- Strongyloidiasis
 - Presentation: GI symptoms, cough, dyspnea
 - $\,\circ\,$ Look for eosinophila and/or high IgE
 - Test: strongyloides Ab IgG
 - Treatment: Ivermectin



*Lung Transplant Specific *

CARDIAC COMPLICATIONS

Post operative Troponin elevation

Related to surgery

- Troponin typically will continue to rise in the hours after surgery then will plateau and start to decrease
- Correlate with EKG for ST-elevation
- If not decreasing after 3-4 days, then investigate further

Atrial Arrhythmias

- Atrial flutter/fibrillation
 - Most common arrhythmia we see post-op
- Questions to Ask:
 - Hx of cardiac issues?
 - Hx of arrhythmias?
 - Fluid status?
 - o Stable/unstable?
 - Could this be something other than post op complication? (i.e pericardial hemorrhage? Bleeding elsewhere?)
- Orders
 - EKG
 - Evaluate meds (On beta blocker? Antiarrhythmic?)
 - Electrolytes
 - Fluid status
 - ECHO for structural defects
 - Consult EP for refractory



- Common treatments:
 - First line: Beta blockers (Metoprolol) and Calcium channel blockers (Diltiazem)
 - AFwRVR:
 - IV Metoprolol 5 mg every 2-3 times if pressure stable
 - Start Dilt gtt if above unsuccessful cannot titrate on the floor
 - Bedside cardioversion in ICU only if AFwRVR refractory to above interventions and patient unstable
 - Advanced agents for refractory arrhythmias include Rythmol, Tikosyn, Sotalol guided by EP
 - Scheduled cardioversion (DCCV) with EP
 - Ablation (fresh post-op NO left side for 90 days, right side may be ok – situation dependent)
 - EKGs daily or post meds (i.e Sotolol)
 - Anticoagulation
- Of note: We use a lot of QTc prolonging meds (i.e. Azithromycin/SSRIs/Seroquel/antifungals) – be aware when any others are ordered

Heart Failure



- Differential under shortness of breath
- InitialTests
 - BNP
 - ECHO
 - Physical Exam- JVD, lower extremity edema
- Orders
 - Sodium and fluid restrictions
 - Telemetry
 - Strict I/O
 - Weight daily
 - Right heart cath (**Occasionally to assess volume status)
- Treatment
 - Diuretics
 - Watch kidney function**
 - Adjustment of medications
 - Prevention of relapse
 - Usually do not consult HF unless severe case



Basic Hemodynamics

- <u>SVO2</u>: SvO2 is the percentage of oxygen attached to the hemoglobin in the blood leaving the right ventricle. Therefore, SvO2 can be used to determine if CO and oxygen delivery is sufficient for the patient.
 - Low SvO2 indicates that either body tissues are taking more oxygen from the blood as compensation for increased oxygen needs or are not receiving enough oxygen to begin with (CO is not high enough to meet the body's demand).
- <u>Stroke Volume (SV)</u>: the volume of blood pumped out of the left ventricle of the heart during each systolic cardiac contraction
- <u>Stroke Index (SVI)</u>: the v olume of blood pumped by the heart with each beat (in milliliters) divided by the body surface area (square meters). This allows direct comparison of the stroke v olume index of large and small patients.
- <u>Cardiac Output (CO)</u>: CO is the amount of blood pumped by the heart each minute and is simply heart rate multiplied by stroke volume (the amount of blood ejected with each beat).
- <u>Cardiac Index (CI)</u>: CI is merely CO with consideration of the patient's body surface area (BSA), and is, therefore, more accurate for clinical decision making
- <u>Mean Arterial Pressure (MAP)</u>: the average arterial pressure throughout one cardiac cycle, systole, and diastole.

- <u>Central Venous Pressure (CVP)</u>: CVP is a representation of RV preload and pressure. Best snapshot of fluid status
- <u>Pulmonary Artery Pressure (PAP)</u>: PAP is a reflection of cardiac heart pressures and is read as a systolic and diastolic number.
 - Pulmonary artery systolic pressure (PASP) is the pressure exerted by the right ventricle (RV) during systole on the PA.
 - Pulmonary artery diastolic pressure (PADP) is a measurement of the pressure in the PA during RV diastole. This is a continuous waveform measurement
- <u>Pulmonary Artery Wedge Pressure (PAWP)</u>: A measurement of left v entricular end-diastolic pressure. Basically, this is a measurement of preload, or filling v olume, to the left v entricle (LV)
- <u>Stroke Volume Resistance (SVR)</u>: Also known as total peripheral resistance (TPR), is the amount of force exerted on circulating blood by the vasculature of the body.
 - Best snapshot of fluid status or pressor effect
 - High SVR may mean that the patient is dry or that we are clamping too much with pressors.
 - Low SVR can mean shock state or fluids overload. Correlate clinically.

Normal Hemodynamic Values

Normal Hemodynamic Values

SVO2	60-75%					
Stroke volume	50-100 mL					
Stroke index	25-45 mL/M ²					
Cardiac output	4-8 L/min					
Cardiac index	2.5-4.0 L/min/M ²					
МАР	60-100 mm Hg					
CVP	2-6 mm Hg 20-30 mm Hg					
PAP systolic						
PAP diastolic	5-15 mm Hg					
PAOP (wedge)	8-12 mm Hg					
SVR	900-1300 dynes·sec·cm ⁻⁵					

Types of Shock

Cardiogenic Shock

- A loss of effective cardiac contractile function that results in impaired CO, impaired O2 delivery, and reduced tissue perfusion
- Causes: Acute MI (most common), dysrhythmia, pericardial tamponade, hypoxemia, pulmonary edema, PAH, acute valvular regurgitation, acute VSD.
- Treatment: Initial CAREFUL IVF administration (you need enough fluid to move the pressors), Vasopressors/inotropes , Nitroglycerin if concern for ischemia, IABP, Impella, VA ECMO (bridge to VAD or bridge to heart transplant).

Hypovolemic Shock

 Results from a loss of >20% of circulating volume (dehydration or hemorrhagic)

 Causes: Internal/external bleeding, DKA/HHNK, severe dehydration

 Treatment: Fluid resuscitation, PRBCs if hemorrhagic, vasopressors if needed

Obstructive Shock

- Inadequate cardiac output as a result of impaired ventricular filling (blockage in PA, severe PTE).
- Causes: Massive pulmonary embolism (most common), tension ptx, acute cardiac tamponade, obstructed valvular disease, disease of the pulmonary vasculature (PAH).
- Treatment: Maintain BP while treating the underlying cause. IVF and Vasopressors. VV/VAV ECMO in severe cases

Types of Shock

Distributive Shock: Three forms of shock characterized by vasodilation, decreased intravascular volume, reduced peripheral vascular resistance, and loss of capillary integrity

Neurogenic Shock

- Loss of peripheral vasomotor tone as a result of spinal cord injury or regional anesthesia.
- Management: Maintain airway, IVF, vasopressors as needed.
- Sometimes emptying the bladder with a foley catheter or promoting a BM can help with relieving spinal cord pressure and can improve symptoms

Anaphylactic Shock

- IgE mediated reaction that occurs shortly after an exposure to an allergen.
- S/S: Hives, SOB, oral/airway edema, hypotension, cardiac arrest
- Treatment: Maintain airway (always secure airway before any other treatment measures), Benadryl (for hives), Epinephrine SQ/IM (respiratory distress, wheezing, or stridor), IVF, IV steroids, H2 antagonists, Inhaled beta agonist for bronchospasm (Albuterol)

Septic Shock

- Caused by infectious organisms
- S/S: hypotension, the ONLY shock with increased CO/CI.
- Treatment: Fluid resuscitation, Vasopressors. Upon diagnosis, antibiotics should be started within 1 hour

Shock Treatment

- Initial treatment should always be fluid resuscitation.
- Most require Vasopressors/Inotropes which are listed in this chart -->
- Other treatments include treating the underlying cause which is outlined in the previous slides.



Effects of Shock on Hemodynamic Parameters											
Туре	HR	Pulse Pressure	BP	SVR	PVR	CVP	PAP	PAWP	со	SVO ₂ /ScVO ₂	
Cardiogenic Shock	1	\downarrow	\checkmark	\uparrow	Ŷ	\uparrow	\uparrow	1	\checkmark	\downarrow	
Hypovolemic Shock	Ŷ	\downarrow	\checkmark	\uparrow	↑	\downarrow	\checkmark	\checkmark	\checkmark	\downarrow	
Distributive Shock		2550	85.74			11.25					
Neurogenic Shock	\downarrow	4	\checkmark	\downarrow	~	\checkmark	\checkmark	\checkmark	\downarrow	\downarrow	
Anaphylactic Shock	Ŷ	\downarrow	\checkmark	\downarrow	~个	\checkmark	\downarrow	\checkmark	\checkmark	\downarrow	
Septic Shock	1	¥	\checkmark	\downarrow	~↑	\checkmark	1~↓	\checkmark	^~↓	^~↓	
Obstructive Shock	Ŷ	\downarrow	\checkmark	\downarrow	\uparrow	\uparrow	^~↓	^~↓	\downarrow	\downarrow	

Note: Hemodynamic effects in some illnesses are highly variable

Key: ↓, decrease; ↑, increase; ~, no change

BP, Blood pressure; CO, cardiac output; CVP, central venous pressure; HR, heart rate; PAP, pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; *ScVO*₂, central venous oxygen saturation; *SVO*₂, mixed venous oxygen saturation; *SVR*, systemic vascular resistance.


• Questions to Ask:

- Fluid intake?
- Recent change in FK dose?
- Urine output?
- Flank pain?
- $\circ~$ Hx of UTI's

• Differential Diagnosis:

- Medication related
 - FK
 - Antibiotics
 - Diuretics
 - Contrast induced

• Hypovolemia:

- Dehydration
- Blood loss
- GI loss
- Hypotension
- Infection
- Hydronephrosis





- Orders:
 - Urine studies (UA, urine cx, urine sodium, urine creatinine)
 - Urine FENA need urine sodium/creatinine
 - Urine FeUREA (if on diuretics) need urine creatinine/urea
 - Hold nephrotoxic meds
 - Fluids dependent on cause
 - Allow fuller SBP ~ 130-140mmHg
 - Renal ultrasound if needed or persistent elevation creatinine
 - PVR if history concerning for retention
 - Nephro consult if no improvement w/ first line measures (consult "renal txp" d/t lung txp)

Electrolyte Management

• Potassium (3.5-5.0)

- Hyper:
 - Most common in transplant patients
 - Usually don't treat until 5.5 or above unless symptomatic
 - Can be medication/disease related
 - Bactrim
 - FK
 - \circ CF
 - Renal
 - Order set in epic ("Hyperkalemia")
 - Common orders:
 - EKG
 - Kayexalate
 - Lokelma
 - D50/insulin/Lasix
 - Calcium Gluconate if EKG changes
- Hypo:
 - Seen with diarrhea/nutritional deficiencies, diuretic use
 - If critically low IV replacement
 - Pay attention to route/formulation when ordering
 - Usually do NOT schedule daily potassium except for specific cases
 - If hx of arrhythmias target 4.0 or above
 - What is magnesium level? Potassium won't stay in range if mag is low.

- Magnesium (1.6-2.6)
 - Hyper: not often seen
 - Hypo: common
 - Target 2.0 or above to prevent arrhythmias
 - Correct both Mag and potassium
 - Most patients on supplements post txp
 - Supplements can interfere w/ FK absorption
 - May need IV replacement inpatient
- Phosphorus (3.5-4.0)
 - Hyper: Common with CKD
 - May need phos binder
 - Hypo:
 - IV if 2.0 or less
 - PO if 2.1 or more

Electrolyte Management: Sodium (135-145)

- Hypernatremia
 - Sodium imbalances can be complicated
 - Common in txp patients
 - Think: fluid balance, medications, hormones, renal disease
 - Don't correct too quickly!
 - Correct for hyperglycemia
 - <u>Sodium Correction for Hyperglycemia MDCalc</u> <u>www.mdcalc.com</u> (
 helpful sodium calculators!)

Image via: <u>hypernatremia - UpToDate</u> (swmed.edu)



Electrolyte Management: Sodium (135-145))

• Hyponatremia

- Tests:
 - Serum/urine osmolality
 - Serum/urine sodium
- Evaluate for medication culprits
 - SIADH common!
 - Hold Bactrim and SSRI if severe
 - Fluid restrict
- Correct for hyperglycemia!
 - <u>Sodium Correction for Hyperglycemia MDCalc –</u> <u>www.mdcalc.com</u> (
- Watch trends! Chronically mildly low? Or acute decline?
- Don't correct too quickly!



 Image via: <u>https://www-uptodate-</u> com.foyer.swmed.edu/contents/images/NEPH/101823/Apprdetermincausehy pntrm.aif

IV Fluids



Image via: www.bmj.com Intravenous Fluid therapy in adult inpatients



Images via: healthandwillness.org

Continuous Renal Replacement Therapy (CRRT) • Citrate: The pre-filter and that keeps the filter from the meniter inpired only

- 24-hour dialysis therapy used for patients with AKI and fluid overload
- Useful in hemodynamically unstable patients on pressors to decreased the strain on the heart from large volume removal in a shortened timeframe (HD)
- Consult Nephrology for initiation and management

- Citrate: The pre-filter anti-coagulation that keeps the filter from clotting. Have to monitor ionized calcium.
 - Not all patients are on this
- Bath: The dialysate fluid that coats the filter that facilitates the transfusion of electrolytes across the membrane and stabilized electrolyte imbalances in the patient
 - 4K bath: Filters potassium to keep patients level at 4
 - 2K bath: Used to pull more potassium out of the body in severely hyperkalemic patients
- Post-filter bicarb: Used after the filter as a bicarb infusion for patients with continued acidosis despite CRRT
- Net even: You are dialyzing off the same amount of fluid per hour that you are giving to the patient
- Net negative: You are dialyzing off more fluid than you are giving to the patient
- "Pulling 0" No fluid removal; filtration only

Lung Transplant Specific

GIISSUES

- Some of our lung patients are semipermanent/permanent NPO status (can be during acute course or implemented w/ chronic decline)
 - Common reasons:
 - Proven aspiration
 - Esophageal dysmotility
 - Scleroderma
 - Severe reflux waiting on Nissen
 - Severe gastric distention/gastroparesis
 - Severe deconditioning
- Review chart/ask patient when on admission to avoid putting in diet orders inaccurately
- If fresh transplant, there should be a consent note in the chart if conversation has been had about being a "tube feeding transplant" which means patient WILL NOT need MBSS and will be tube feed dependent.
 - Eventual PEG/J will be placed ~3 months post transplant

NPO Status



- Compliance is an issue with NPO status. Need to verify with patients if they are only doing tube feeds or if they have been eating as well.
- Tolerance to tube feeds can be challenging due to frequent/chronic diarrhea. Always get c.diff before prescribing Imodium!

All About Dobhoffs

- 12 French
- Stocked in both supply rooms
- Post pyloric
 - Rare exceptions when pt does not need post pyloric; if long-term feeding, we want post pyloric to decrease aspiration risk
 - Placed by APP/RN/or GI team with EGD (if unsuccessful at bedside)
 - Place order for "stat" KUB post-placement
 - Place order for "tube cleared for use"; note dobhoff in comments once tube post-pyloric
 - If unable to get post-pyloric and waiting on GI, usually ok to do <u>daytime</u> tube feeds in meantime. Can trial Reglan in interim
 - Tubes bridled into place once post-pyloric (Can be done by nursing staff)

- Easily clogged
- Methods of "declogging":
 - Flushing with warm water/baking soda/co as directed by clinic team
 - Clog Zapper (in our 10B supply room)
 - Viokace and Sodium bicarb (smart text .dhtclog)



- Declogging machine (in conference room)
- Last resort: replacement look at hx did they need GI to place before?
- Prevention of clogs:
 - MANUAL flushes every 4 hours w/ warm water (place order under "water flush" and note "MANUAL" so it shows up on MAR)
 - Making sure all meds are crushed well and mixed well with water
 - Flushing the tube manually after any pause in tube feeds

*Eventually discussion may be had concerning permanent feeding tube placement; we prefer **GJ tubes** so that J can be for tube feeding and G can be for meds.

Aspiration Workup

- Some workup done prior to transplant to decide whether patient will need feeding tube post-transplant or Nissen
 - If severe reflux, patient will need Nissen three months post-transplant. Will be NPO w/ DHT until then.
- Post-op issues that necessitate further workup:
 - Decline in spirometry without clear cause
 - Right lung infiltrate
 - Aspiration on biopsy
 - Symptoms: "pills getting stuck" "choke when I drink liquids," reflux complaints



- MBSS (Orders: MBSS speech therapy & XR MBSS)
- Esophagram (Order: XR Esophagram
 - may need NPO 4-6 hrs prior)
- Gastric Emptying Study (Order: NM Gastric Emptying)
 - Will need to be NPO at midnight night prior
 - Place PRN order to d/c NPO for procedure or you will be paged
- PH/manometry studies may be warranted but can only be done outpatient.
- If needed: GI or IR to place GJ tube, will need DHT or NGT before the procedure

• Some Questions to Ask:

- Abdominal pain? Type?
- Sick contacts?
- Recent med changes?
- Keeping down IS meds?
- Change in food/diet/ eating out/raw foods?
- Change in respiratory status/spiro? (concern for aspiration if severe vomiting)
- Common differentials:
 - Medications
 - Tube feedings
 - Viral illness
 - Gastroparesis

Nausea/Vomiting

- Orders:
 - KUB or CT A/P
 - HOLD non-essential medications
 - HOLD Cellcept if recently started (big culprit)
 - Change PO meds to IV for acute phase
 - Anti-emetics (start w/Zofran; beware of easily sedated patients before Phenergan/ Compazine)
 - Fluids (dependent on length of illness/kidney function/cardiac hx)
 - Bland diet or clear liquids until acute phase ends
 - Check prior GI workup: any hx of reflux, gastroparesis? May need gastric emptying study (see aspiration workup)
- Discharge Planning:
 - If any IS meds are going to be changed d/t nausea/vomiting – send ahead to pharmacy



Diarrhea 4

- Questions to ask:
 - How long? How many BMs a day?
 - Sick contacts?
 - Type, amount, consistency?
 - Associated symptoms?
 - Med changes?
- Common Diagnosis:
 - Medications antibiotics, Reglan, Cellcept
 - C.diff
 - Viral illness (common or more rare type)
 - $\circ\,$ Tube feeding (especially at the beginning)

- Orders:
 - C.Diff
 - CMV PCR, Adenovirus PCR
 - GI pathogen panel/WBC stool/O&P stool
 - Hold any possible offending meds
 - Fluids (dependent on length of illness/kidney function/cardiac hx)
 - Start Lactobacillus daily
 - Do NOT order imodium until cdiff comes back negative. This goes for all patients with loose stools.
 - If cdiff neg, Imodium not working Iomotil is next choice. Can try scheduling if PRN not working or not consistently given.
- Discharge Planning
 - Send any medication changes on IS meds to pharmacy

Abdominal Pain

Right		Left
Gallstones Stomach Ulcer Pancreatitis	Stomach Ulicer Heartburn/ Indigestion Pancreatitis, Gallstoner Epigastric hernia	Stomach Uteur Duer Dierr Billiary Golie Palaceeattur
Kidney stones Urine Infection Constipation Lumbar hernia	Pancreatitis Early Aligendicitis Stotmat Dicer Influententory Howed Small forward Umbilical formula	Ridney Strines Diverticular Disease Constipation Inflammatory bowel disease
Appendicitis Constipation Paivic Pairi (Gyna Groin Pairi (Inguinal Hernia	Drine Infection Appendicitis e) Diverticular disease Inflammatory howel Petvic pain (Gynae)	Diverticular Disease Peters (sam (Genus) Gront Paul (Ingunal Degnis)

- Orders:
 - KUB
 - UA/culture
 - Lipase/LFTs/Lactate
 - CT scan w/ PO contrast dependent on hx and symptoms
 - Symptomatic treatment
 - Hold non-essential meds
 - Fluids if needed
 - Clear liquid diet or NPO

- Questions to ask:
 - Length of time? Location? Duration? Type? Precipitating factors? Alleviating factors?
 - Last BM?
 - Associated symptoms?
 - Hx of abdominal issues? (review in chart as well)
 - Med changes/diet changes
 - Sick contacts?
- Common Diagnoses:
 - Kidney stones
 - Diverticulitis
 - UTIs
 - Pancreatitis
 - Medications
 - Constipation
 - Hernia
 - Cholecystitis
 - Pneumatosis
 - DIOS (CF patient)
 - Rule out PTLD

lleus/SBO

- Prolonged absence of bowel function
- Etiology:
 - Intestinal manipulation, surgical anesthesia, narcotics, non-ambulatory state, mass lesion, constipation, adhesions
- Presentation:
 - SBO: Abdominal cramping, nausea, vomiting, abdominal distention, abdominal tenderness, inability to pass gas/stool
- Diagnostics:
 - Monitor with serial KUBs
- Treatment
 - Minimize narcotics
 - Encourage ambulation
 - Bowel regimen
 - NGT to LIWS if severe or N/V present
 - Consult surgery if concern for complete bowel obstruction



Pancreatitis

 Inflammation of the pancreas due to escape of pancreatic enzymes into the surrounding tissue causing autodigestion of the pancreas

• Etiology:

 Gallbladder disease, ETOH use, hypercalcemia, HLD, trauma, medications (Imuran, Bactrim, Lasix, Thiazides)

• Presentation:

- Nausea, vomiting, epigastric pain that radiates to back, abdominal distention, pain on palpation, fever, tachycardia, jaundice, hypotension
- Flank and umbilical discoloration in hemorrhagic pancreatitis

• Diagnostics:

- Trend Lipase and LFTs
- CRP
- CT A/P
- Treatment:
 - NPO
 - IVF
 - $\circ~$ NGT to LIWS
 - Pain control
 - May require antibiotics if severe or necrosis present
 - May require further intervention if fluid collections, significant necrosis or gallbladder pathology are present

Ranson Criteria

Admission

- Age > 55
- WBC > 16,000
- Glucose > 200
- LDH > 350
- AST > 250
- 5% mortality <u>risk</u> with <2 signs 15-20% mortality <u>risk</u> with 3-4 signs 40% mortality <u>risk</u> with 5-6 signs 99% mortality <u>risk</u> with >7 signs

During first 48 hours

- Hematocrit drop > 10%
- Serum calcium < 8
- Base deficit > 4.0
- Increase in BUN > 5
- Fluid sequestration > 6L
- Arterial PO2 < 60

GI Bleed

- Upper GI bleed
 - Etiology:
 - Peptic or esophageal ulcer, gastritis, esophagitis, esophageal varices, portal hypertension gastropathy, Mallory Weiss tear, malignancy, anticoagulation
- Lower GI bleed
 - Etiology:
 - Hemorrhoids, diverticulosis, infection, malignancy, inflammatory bowel disease, ischemia, angiodysplasia, radiation-induced
- Presentation
 - Hematemesis (UGIB), Melena (UGIB), Hematochezia (LGIB or brisk UGIB), hypotension, tachycardia, orthostasis, dizziness, confusion, angina, palpitations, cold/clammy extremities if severe

- Diagnostics:
 - Check coags
 - Trend H/H
 - Lactate
 - $\,\circ\,$ Type and screen
- Treatment:
 - Consult GI for EGD/colonoscopy
 - $\circ~$ Protonix infusion
 - Octreotide
 - \circ IVF
 - Blood transfusion as needed
 - Anticoagulation reversal
 - Intubation if needed for airway protection

Acute Liver Injury

• Etiology:

- Medication induced (Azoles, Imuran, antibiotics, Tylenol, statins), viral infection, ischemia, gallbladder pathology, muscle injury, malignancy
- Isolated ALP- think bone injury
- Presentation
 - Asymptomatic, RUQ pain, nausea, fever, jaundice, hypotension, AMS

- Diagnostics
 - \circ LFTs
 - Identify hepatocellular vs cholestatic pattern
 - Bilirubin- fractionate if elevated
 - GGT
 - Hepatitis panel
 - CMV, EBV, HSV, Adenovirus, Parvo, VZV
 - INR
 - CBC
 - Ammonia
 - $\circ~\mbox{Liver US}$
- Treatment
 - Treat underlying condition
 - Hold hepatotoxic medications

Lung Transplant Specific

HEME/ONC

Leukopenia

Most frequently seen hematologic disorder w/ txp

• Common Causes:

- Medications!!! (most common culprits: Cellcept, Imuran, Valcyte, Bactrim)
- Copper or Zinc deficiency
- Fungal infection
- Parvo viral infection
- Myelodysplastic syndrome (MDS)
- Short Telomere syndrome
- Bone marrow over suppression (check cylex)

• Orders:

- Zinc, copper, fungal blood culture, parvo IgG/IgM
- Hold possible offending meds
- Watch ANC: Neupogen/Zarixo when ANC <500; unless infection then <1000
- If persistent even w/ holding meds, consider heme consult and potential bone marrow biopsy



Anticoagulation

- Transplant patients with increased risk for blood clots
- Most common reasons for AC:
 - DVT: recheck after 3-6 months of AC therapy
 - PE: usually requires lifelong AC
 - Afib/Aflutter
 - Sometimes ask EP to weigh in on whether AC is required
- Preferred anticoagulant is Warfarin
 - Reversible w/ vitamin K
 - Lower renal risk
- Usually require heparin bridge to therapeutic INR 2-3
 - Lovenox 0.7 mg/kg BID alternative for patients >90 days out from transplant with adequate renal function
 - Patients on AC for arrhythmia but who are currently in NSR do not need bridging
- INR management
 - Tube feeds (hold 1 hr pre/post admin)
 - Medication interactions (see table)
 - APPs manage inpatient; AC pharmacists manage outpatient (Courtney Wong/Louise de Souza Miller)
 - Diet education for new warfarin start (place nutrition consult for warfarin education)
 - Reversal w/ vitamin K for biopsies/invasive procedures; the higher dose given; the longer it will take for INR to become therapeutic again. Start low. *if reversing d/t high INR/bleeding, can be more aggressive*

Medications that interfere with the effect of warfarin

y increase INR	
loetaminophen	
depurind	
miodarone	
undrogens Methylkestesterone Coundrolone Testosterone	
utbiotics Cephalosponns Dorsyndine Plaorogunolones Ceptfloxacin Levofloxacin Monfloxacin Monfloxacin Matrolides Azthromycin Clarthnomycin Enythnomycin Enythnomycin	

the INC Amountille

Azole antihungais*

Fluconagole

Capecitabine

decrease the INR)

 Fenofibrate · Fluvastatin

Gemlibrozii

 Lovistatio Rosuvastatin Simvastatin

Methylprednisolone

Prednisone

Cimetidine Glucocorticoids

 Fluorouracil (S-FU) Insatisti Tamoxifen

Cholesterol-lowering agents (exception: cholestyramine ma

 Miconazole (oral) Vonconazole Cancer therapies

 Amoxicilin-davukanate Trimethoprim-sulfamethoxazoli

tay decrease INR	
Antibiotics Dictionacilin Griseofutivin Nafolin Rifampin	
Azathioprine	
Cholestyramine	
Enzyme inducing antiepileptic drugs Cartiamaziepine Phenobarbital Phenobarbital Phenytoin (mixed effects described)	
Ritonavie	
Saint John's wort	
Sucralitate	
Vitamin K	

Via uptodate – warfarin dosing

Guideline recommendations for management of warfarin-associated bleeding and/or high INR

Clinical setting	2018 ASH guideline	2012 ACCP guideline	
 Serious or life- threatening bleeding Any INR 	 4-factor PCC Vitamin K (intravenous) Hold warfarin 	 4-factor PCC* Vitamin K (intravenous) Hold warfarin 	
No bleedingINR >10	(No recommendations given)	Vitamin K (oral)Hold warfarin	
No bleedingINR 4.5 to 10	 Hold warfarin No vitamin K 	 Hold warfarin Vitamin K (low dose, oral) is optional 	

Clinical judgment is required to assess the severity of bleeding, urgency of warfarin reversal, and need for other interventions. Refer to UpToDate for details.

Omeprazole (case reports with other proton pump inhibitors,	
Serotonin reuptake inhibitors • Dukoxetine • Flucixetine • Flucixetine • Sertraline • Venlafazine	
Sitaxentan (not available in United States)	
Tranadol	

Transfusion Parameters

- PRBC if Hgb <7
 - May have higher threshold of 8 for active bleeding or early post-op
- Platelets
 - <100 if OR imminent
 - \circ < 50 invasive procedure, active bleeding
 - < 10 Stable, nonbleeding
 </p>
- \circ FFP
 - INR reversal if INR >3.5 in the presence of active bleeding or if vitamin K is inadequate prior to planned procedure
 - After receiving 3 units PRBC in a short time frame
- Cryo
 - Transfuse if fibrinogen <100

Microangiopathic Hemolytic Anemia (MAHA)

- Non-immune hemolysis resulting from intravascular red blood cell fragmentation that produces schistocytes on the peripheral blood smear
- Offending agents:
 - Prograf, Cyclosporine, Rapamune, Dapsone
- Presentation:
 - Thrombocytopenia, bleeding, clotting

- Diagnostics:
 - CBC with diff
 - Can no longer order peripheral smear....
 Will be automatically added if concerning
 - LDH, haptoglobin
- Treatment:
 - Stop offending agent
 - PLEX
 - Transfusion as needed

Disseminated Intravascular Coagulation (DIC)

- Systemic process with the potential for causing thrombosis and hemorrhage
- Can lead to organ dysfunction: AKI, liver injury, CVA, SAH/SDH, active lung injury, pulmonary hemorrhage, PE
- Etiology:
 - Sepsis, malignancy, trauma, obstetric complications, intrav ascular hemolysis, ABO incompatibility blood transfusion
- Presentation:
 - Bleeding, petechiae, ecchymosis, hematoma formation, thromboembolism
 - Abnormal labs: Thrombocytopenia, low fibrinogen, prolonged PT/PTT, elev ated ddimer
- Diagnostics:
 - CBC, PT/PTT, INR, fibrinogen, ddimer, peripheral blood smear
- Treatment:
 - Treat underlying cause
 - Supportive measure
 - Blood, FFP and platelet transfusion as indicated
 - Avoid TXA, TPA and other antifibrinolytics
 - Not necessary to anticoagulate

Heparin Induced Thrombocytopenia (HIT)

- Typically will have recent heparin exposure and a positive lab testing for heparin – PF4 antibodies (HIT antibodies)
- Presentation:
 - Thrombocytopenia with a drop in platelet count >50%, thrombosis, necrotic skin lesions at heparin injection site, bleeding, systemic symptoms (fever, chills, tachycardia, dyspnea)
 - Acute anaphylactic reaction or cardiac arrest can occur
- Diagnostics:
 - HIT panel, CBC, Rotem, Coags
 - 4T scoring system
- Treatment:
 - STOP HEPARIN list as allergy
 - Start Argatroban or Bivalirudin
 - Warfarin can be started once patient is stably anticoagulated and platelet count has recovered

Active Bleeding

- Presentation: Acute pain, dropping H/H, bruising
- Diagnostics:
 - CBC
 - Coags
 - Type and screen
 - Dedicated CT
- Treatment:
 - Stop any anticoagulation
 - Mark any bruising present
 - Transfuse as needed
 - May require surgical/IR intervention
 - If AC necessary, re-introduce gradually

- Massive Transfusion Protocol
 - Familiarize yourself with the Belmont
 - Usually try to replace what the patient is losing
 - Give 1 FFP for every 4 units PRBC
 - Consider platelets if platelet count <100 as patient may have to return to OR
 - Give CaCL (10/20ml for every 500 ml blood loss)

Oncology

- Post-transplant lymphoproliferative disorder (PTLD)
 - $\,\circ\,$ Majority are associated with EBV
 - Proliferative B-cell disorder
 - Presentation
 - Malaise, fatigue, fever, night sweats, weight loss, lymphadenopathy, tumor site specific symptoms, asymptomatic
 - Diagnosis
 - EBV PCR
 - CT
 - PET
 - Biopsy
 - Treatment
 - Consult Oncology to direct care
 - Rituxan, R-CHOP, radiation
 - Minimize immunosuppression

- Other common malignancies
 - Non-melanoma skin cancers
 - Imuran and Voriconazole higher risk of skin cancer than alternatives
 - Prevention and screening are important!
 - Lung cancer
 - Most cases arise in native lung following single lung transplantation
 - Incidental finding on explant also common
 - Colorectal cancer

Lung Transplant Specific

NEURO

AMS: Common Causes

Preso	ription medications (eg. opioids, sedative-hypnotics, antipsychotics, lithium, skeletal muscle relaxers, polyp
Nonp	rescription medications (ep. antihistamines)
Drug	s of abuse (eg. ethanol, heroin, hallucinogens, nonmedicinal use of prescription medications)
with	frawal states (eg. ethanol, benzodiazepines)
Medic	ation side effects (eg. hyperammonemia from valproic acid, confusion from quinolones, serotonin syndrome
Poise	na:
A	vpical alcohols (ethylene glycol, methanol)
1r	haled toxins (carbon monoxide, cyanide, hydrogen sulfide)
Ph	nt-derived (eq. Jimson weed, Salvia)
Infecti	ons
Seps	8
Syste	mic infections; fever-related delirium
Metab	olic derangements
Elect	olyte disturbance (elevated or depressed): sodium, calcium, magnesium, phosphate
Endo	crine disturbance (depressed or increased): thyroid, parathyroid, pancreas, pituitary, adrenal
Hype	rcarbia
Hype	rglycemia and hypoglycemia
Hype	rosmolar and hypossmolar states
Hypo	semia
Inbor	n errors of metabolism: porphyna, Wilson disease, etc
Nutrit	ional: Wemicke encephalopathy, vitamin B12 deficiency, possibly folate and niacin deficiencies
Brain o	lisorders
CNS	nfections: encephalitis, meningitis, brain or epidural abscess
Epile	otic seizures, especially nonconvulsive status epilepticus*
Head	injury"
Hype	densive encephalopathy
Psyd	iatric disorders*
System	nic organ failure
Card	ac falure
Hem	tologic: thrombocytosis, hypereosinophila, leukemic blast cell crisis, polycythemia
Liver	failure: acute, chronic
Pulm	onary disease, including hypercarbia and hypoxemia
Rena	Ifailure: acute, chronic
Physic	al disorders
Burn	
Elect	poution
Hype	themia
Hand	thermia
	and with the state of the state

other aspects.

Common causes of delirium and confusional states



Altered mental status

• History

- Recent falls?
- Change in medications?
- Recent infection?
- Respiratory status/oxygen needs/BiPAP compliance
- Duration of symptoms?
- Associated symptoms?
- Differentials: see previous slide
 - Common to Lung Transplant:
 - Medications
 - Infection!
 - Hypercapnia!
 - Renal failure
 - Electrolyte imbalance
 - Post-op delirium/delirium (long complicated course)
 - MAHA (rare but seen)

- Diagnostics:
 - Labs (CMP, CBC, ammonia, lactate, drug levels, etc)
 - CT Head (or MRI brain depending on pt)
 - ABG
 - Infection workup-Pan-cultures
 - Urine drug screen
 - Lumbar puncture (get imaging BEFORE LP)
 - SLP consult for cognitive assessment
 - Consult Neuropsych
- Treatment:
 - Treat underlying cause
 - Minimize sedating medications
 - Continue home anti-depressant regimen
 - Delirium precautions
 - Frequent reorientation
 - Sitter if needed
 - Seroquel qhs
 - Can use Precedex in ICU after extubation

Stroke

- Acute episode of focal neurological dysfunction that persists for more than 24 hours
- Hemorrhagic
 - Blood vessel rupture
 - Types
 - Intracerebral hemorrhage
 - Subarachnoid hemorrhage
- Ischemic
 - Blockage of a bleed vessel resulting in restricted blood flow
- Presentation
 - Always assess "Last known well"!
 - N/V, headache, seizures, neck pain, photophobia, AMS, LOC, ataxia, vertigo
 - Neurological deficits on exam
 - Hemiparesis, dysarthria, facial droop
 - If concerned, call RRT who will initiate code stroke



- Diagnosis
 - Non contrasted CT head*
 - MRI brain
 - CTA or MRA if infarct noted to guide potential thrombectomy
 - LP if CT negative but high clinical suspicion
 - Serial imaging in setting of hemorrhage to assess expansion
 - Carotid US
 - Echocardiogram
 - Coags
- Treatment
 - Ensure adequate airway, utilize supplemental oxygen if hypoxic
 - Manage BP (goal < 180/105), fever and glucose derangements
 - Hemorrhagic
 - Reverse anticoagulation
 - Surgical intervention for hematoma evacuation or aneurysm coiling/clipping
 - Ischemic:
 - IV alteplase 0.9 mg/kg with initial 10% given in bolus over first minute within 3-4.5 hours of symptom onset
 - Watch for hemorrhagic transformation
 - Mechanical thrombectomy
 - Anti-platelet therapy after 24-48 hours

Posterior Reversible Encephalopathy Syndrome (PRES)

- Etiology:
 - Prograf, Cyclosporine
- Presentation:
 - Headache, AMS, visual disturbances, seizures
 - May be preceded by hypertension
- Diagnostics:
 - MRI brain
- Treatment:
 - Stop offending agent
 - Control blood pressure
 - Seizure management if present



Diabetic Ketoacidosis

- Hyperglycemia, acidosis and ketonemia often triggered by new onset diabetes, infection or noncompliance
- Presentation
 - Polyphagia, polyuria, polydipsia, N/V, headache, confusion
 - Low urine output, dry mouth, decreased sweating present once volume-depleted
 - Infectious symptoms if underlying infection present
 - Tachycardia, tachypnea, hypotension, fruity breath may be present on physical exam

- Diagnosis
 - Blood glucose > 250 mg/dl
 - ∘ pH < 7.3
 - Serum bicarb <15 mEq/l
 - Ketonemia or ketonuria
 - Increased anion gap
 - Electrolyte derangements; falsely low sodium may be present
 - 3-beta-hydroxybutyrate level
- Treatment
 - Hydration with NS
 - Insulin infusion
 - Electrolyte replacement with close monitoring



Pre-Discharge Thinking

- What would be a barrier for this patient to go home?
 - Medication costs/co-pays pre-send scripts to pharmacy to assess (usually immunosuppressants, -Azoles, Ribavirin, Valcyte, any liquid meds, etc)
 - When in doubt, just send and note "price check/PA" in pharmacy note
 - IV Medication set-up (care coordination; make sure orders are in)
 - Tube feed set-up (care coordination; place orders, make sure to include tube feed pump, pole, tubing, plus specific orders for TF)
 - Home health care/PT/OT/SLT (look at PT/OT/SLT recs and place orders accordingly. If patient has PICC or other line/port, will need "skilled HH" for dressing changes/line care)
 - Wound care for any wounds requiring dressing changes
 - BiPAP/CPAP needs (care coordination; place order w/ specifics)
 - Durable Medical Equipment needs (PT note; then place orders for care coordination)
 - Oxygen: will need walking oximetry within 48 hours prior to discharge
 - Anticoagulation: will need INR clinic follow up. Send discharge summary to Courtney Wong and Abraham Jolly, the coumadin pharmacists. Outpt coordinator will place referral

Discharge Tips & Tricks

 Readmissions: Most home health companies will require "Continue previously arranged " order

 Care Coordination: The sooner you can get the orders in the computer; the sooner they can work on them. Make sure to discuss any questions/concerns/additional needs daily in the AM with them


Accessing Policies

<u>http://clinicalportal.swmed.edu/</u>



Clinical portal →university hospital policies
(quick links on left side) → sign in → solid organ
transplant program and clinic folder
→transplant guidelines → lung policies are on
3rd page

Other Resources

- UT Southwestern library
- Grand rounds: Grand Rounds Internal Medicine (utsouthwestern.net)
- Grand rounds video archive: <u>Grand Rounds Archive Internal Medicine</u> <u>(utsouthwestern.net)</u>
- Transplant Seminar slide: G drive -> Share -> Transplant -> lung transplant seminar
- ISHT: ISHLT: The International Society for Heart & Lung Transplantation Home
- MD Calc: <u>www.mdcalc.com</u>
- $\circ\,$ Up to Date



Helpful Numbers

- Get a "badge buddy" from the HUC: has list of most commonly used extensions
- RNs: Number/assigned RN on "storyboard" in Epic or Vocera 5-7229
- APP room: 3-6030, 3-2530, 3-6032
- Floor Pharmacist: 3-8162
- Front Desk: 3-1000
- Bronch Scheduler: 3-4210
- Bronchoscopy suite: 3-4203
- Long Distance code: 8028400 (on badge buddy)
- HLA Lab: 214-648-0900
- Retail pharmacy: 3-4122
- Translator 3-4070



References

- Hospital Policies: <u>http://clinicalportal.swmed.edu/</u>
- Pilewski, J. (2018, November 12). Chronic lung transplant rejection: Bronchiolitis obliterans. Retrieved January 28, 2020, from https://www.uptodate.com/contents/chronic-lung-transplant-rejection-bronchiolitis-obliterans
- UptoDate: <u>www.uptodate.com</u>