Fundamentals of Critical Care:

Hemodynamic Monitoring

&

Optimal Antibiotic Use

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Definitions and Principles

- The measurement and interpretation of biological systems that describe performance of the cardiovascular system
- Monitoring is NOT therapy
- Clinicians must know how to interpret the data
- Very few randomized controlled trials

Oxygen Delivery is the Goal

Oxygen Delivery

DO_2 (mL O_2/min) = CO (L/min) x CaO_2 (mL O_2/dL) x 10

CO (L/min) = HR (beats/min) x SV (L/beat)

CaO_2 (mL O_2/dL) = [1.34 x (Hb)(g/dL) x SaO_2] + [.003 x PaO_2 mm Hg]

Oxygen Consumption

CVO_2 (mL O_2/dL) = [1.34 x (Hb)(g/dL) x SVO_2] + [.003 x PVO_2 mm Hg]

$\dot{V}O_2$ (mL O_2/min) = CO x 3(CaO_2 – CVO_2) x 10

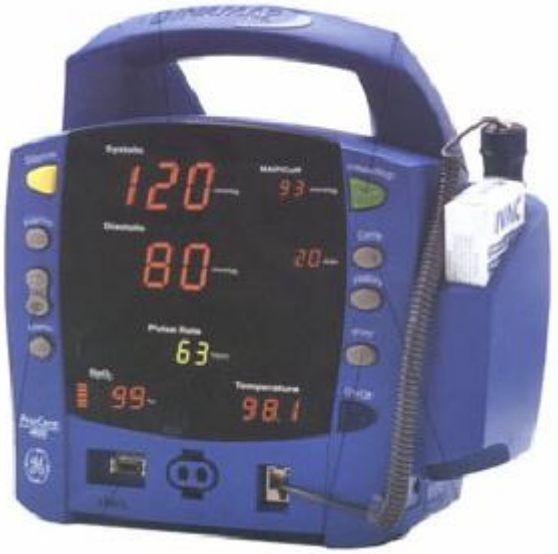
Determinants of Cardiac Performance

- Preload
  - Estimated by end-diastolic volume (pressure)
  - CVP for RVEDV, PAOP (wedge) for LVEDV
- Afterload
  - SVR = [MAP-CVP]/CO x 80
- Contractility

Methods of Hemodynamic Monitoring

- Arterial Blood Pressure
  - Non-invasive
  - Direct arterial pressure measurement
- Central Venous Pressure
- The Pulmonary Artery Catheter
- Cardiac Output Measurement
- Tissue Oxygenation

Non-invasive Blood Pressure Monitoring



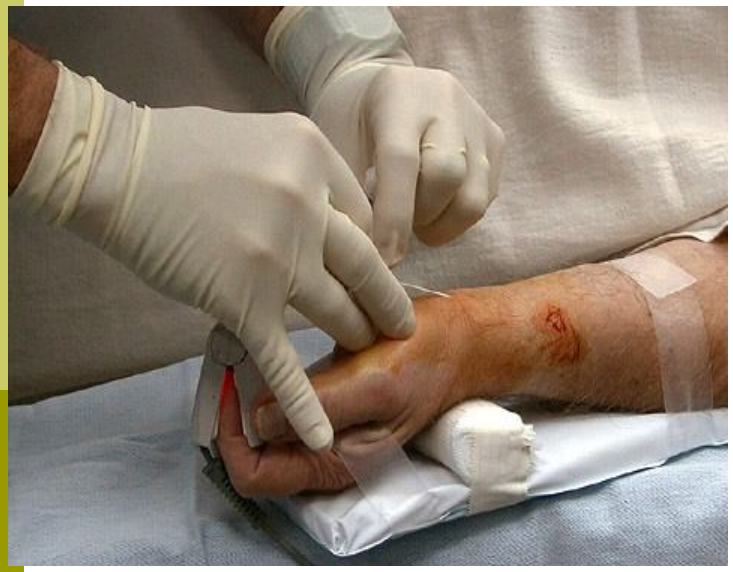
Non-invasive Blood Pressure Measurement

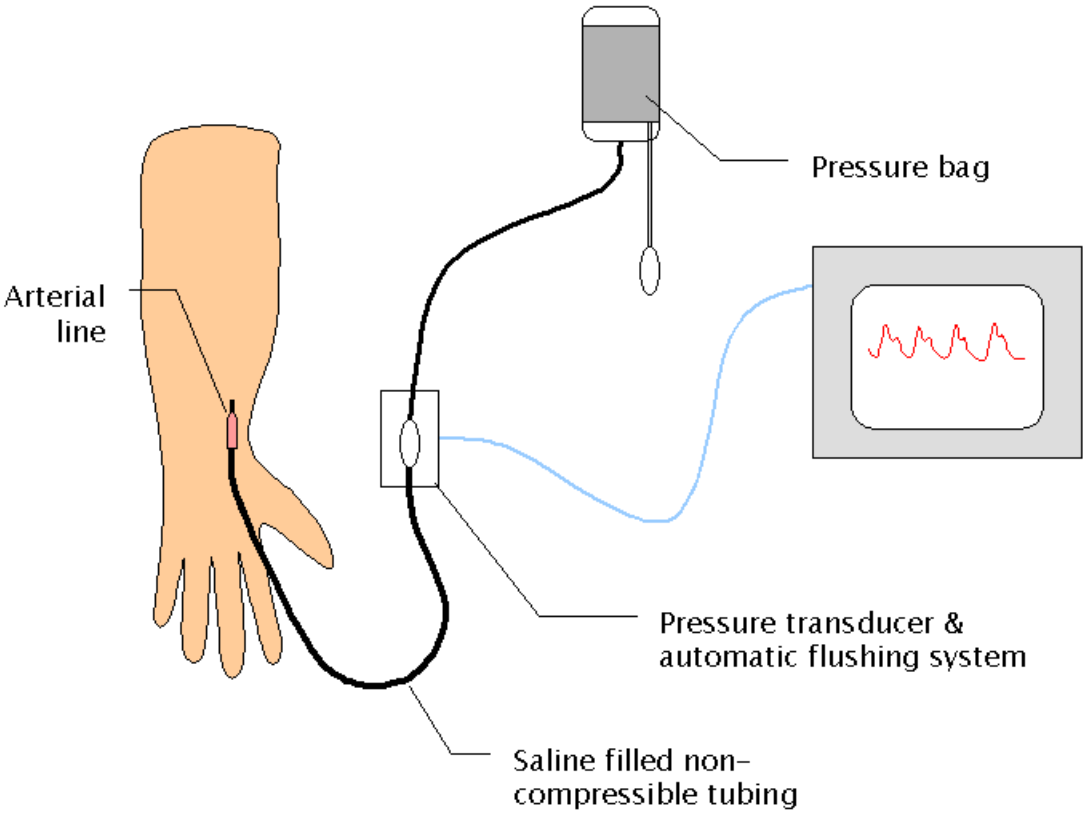
- Manual or automated devices
- Method of measurement
  - Oscillometric (most common)
    - MAP most accurate, DP least accurate
  - Auscultatory (Korotkoff sounds)
    - MAP is calculated
  - Combination

Limitations of Non-invasive Blood Pressure Monitoring

- Cuff must be placed correctly and must be appropriately sized
- Auscultatory method is very inaccurate
  - Korotkoff sounds difficult to hear
  - Significant underestimation in low-flow (i.e. shock) states
- Oscillometric measurements also commonly inaccurate (> 5 mm Hg off directly recorded pressures)

Direct Arterial Blood Pressure Measurement





Indications for Arterial Catheterization

- Need for continuous blood pressure measurement
  - Hemodynamic instability
  - Vasopressor requirement
- Respiratory failure
  - Frequent arterial blood gas assessments
- Most common locations: radial, femoral, axillary, and dorsalis pedis

Complications of Arterial Catheterization

- Hemorrhage
- Hematoma
- Thrombosis
- Proximal or distal embolization
- Pseudoaneurysm
- Infection

Pseudoaneurysm

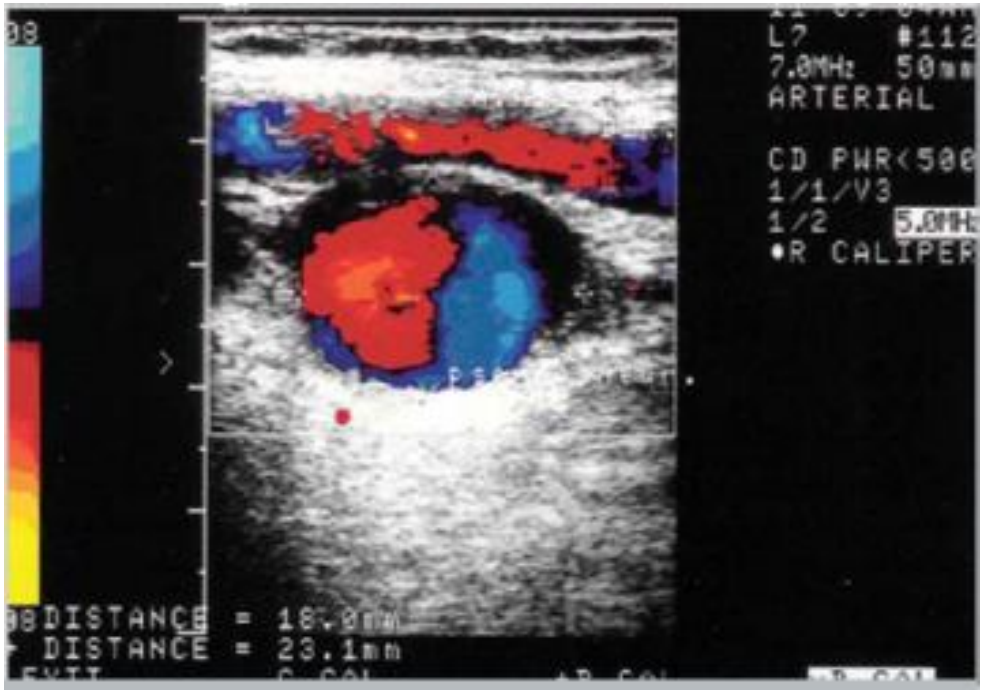
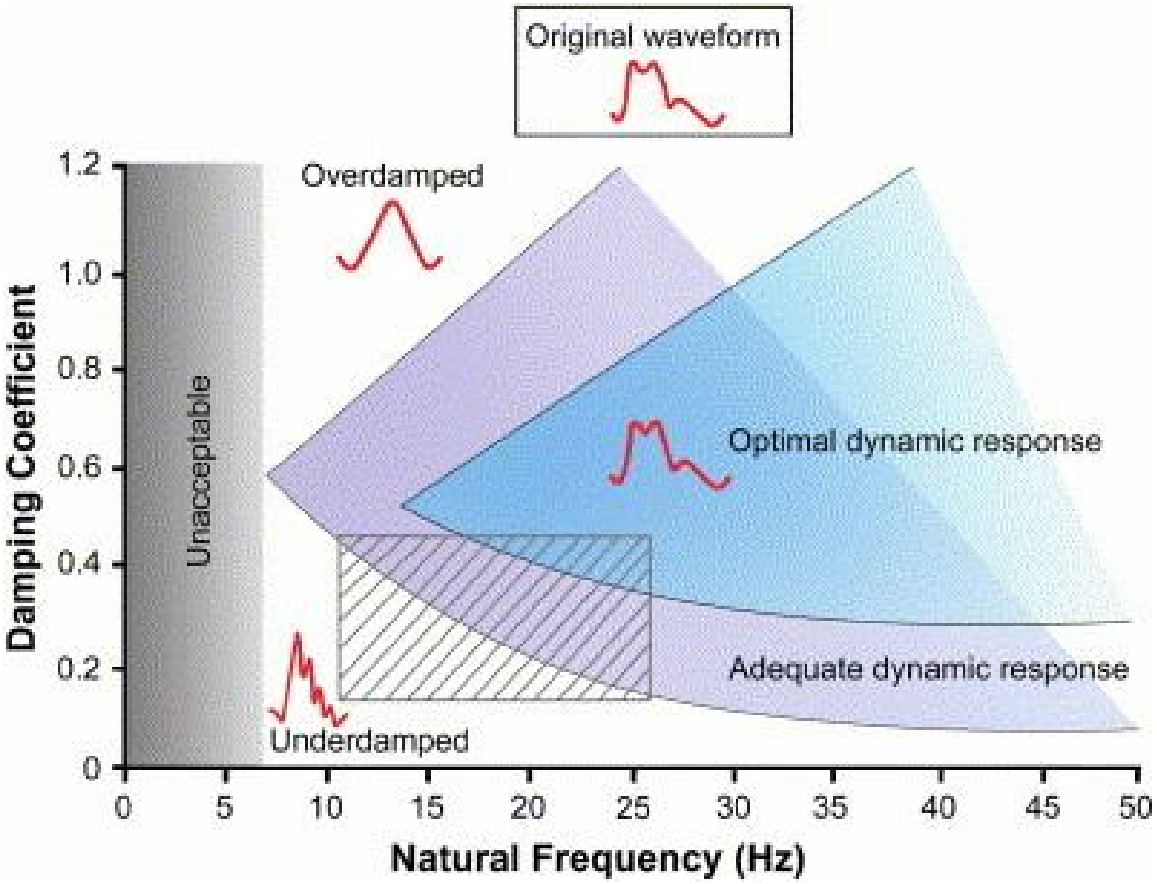


Fig. 1 – Photography of colour Doppler result showing right axillary artery pseudoaneurysm

Limitations of Arterial Catheterization

- Pressure does not accurately reflect flow when vascular impedance is abnormal
- Systolic pressure amplification
  - Mean pressure is more accurate
- Recording artifacts
  - Underdamping
  - Overdamping

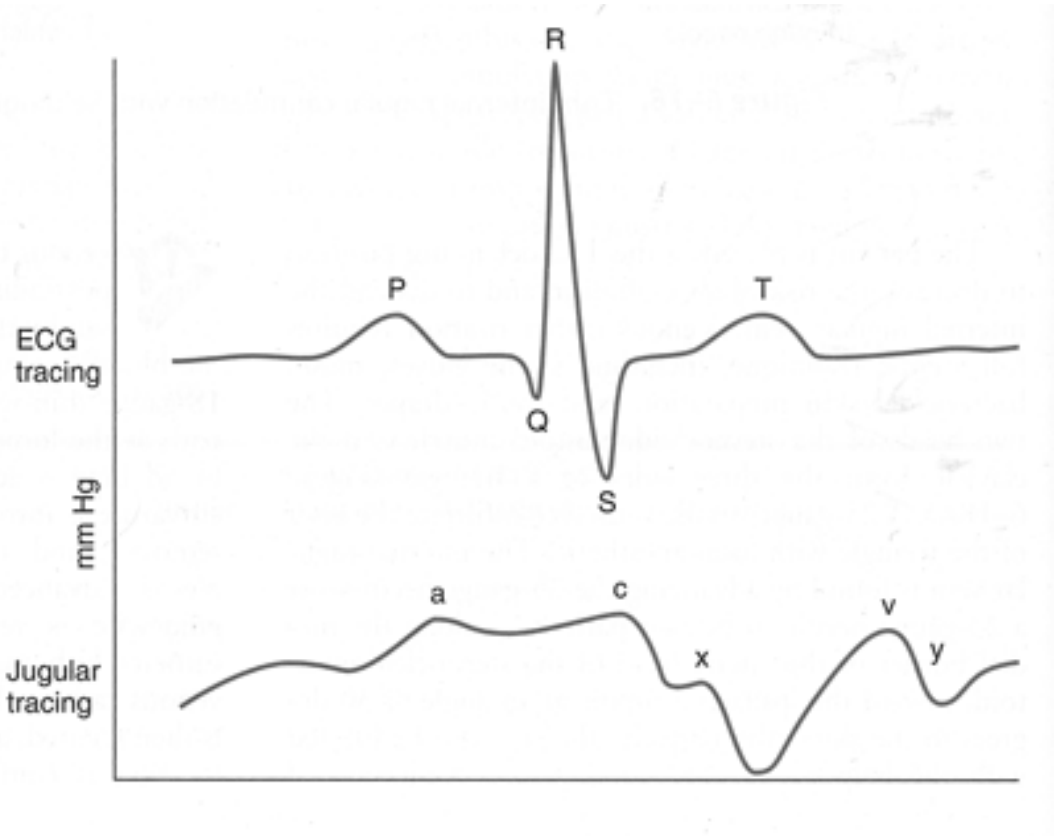
Waveform Distortion



Central Venous Catheterization

- Central venous pressure
  - Right atrial (superior vena cava) pressure
  - Limited by respiratory variation and PEEP
- Central venous oxygen saturation
  - $SCVO_2$
  - Correlates with $SMVO_2$ assuming stable cardiac function
  - Goal-directed resuscitation in severe sepsis and septic shock (Rivers, et al)

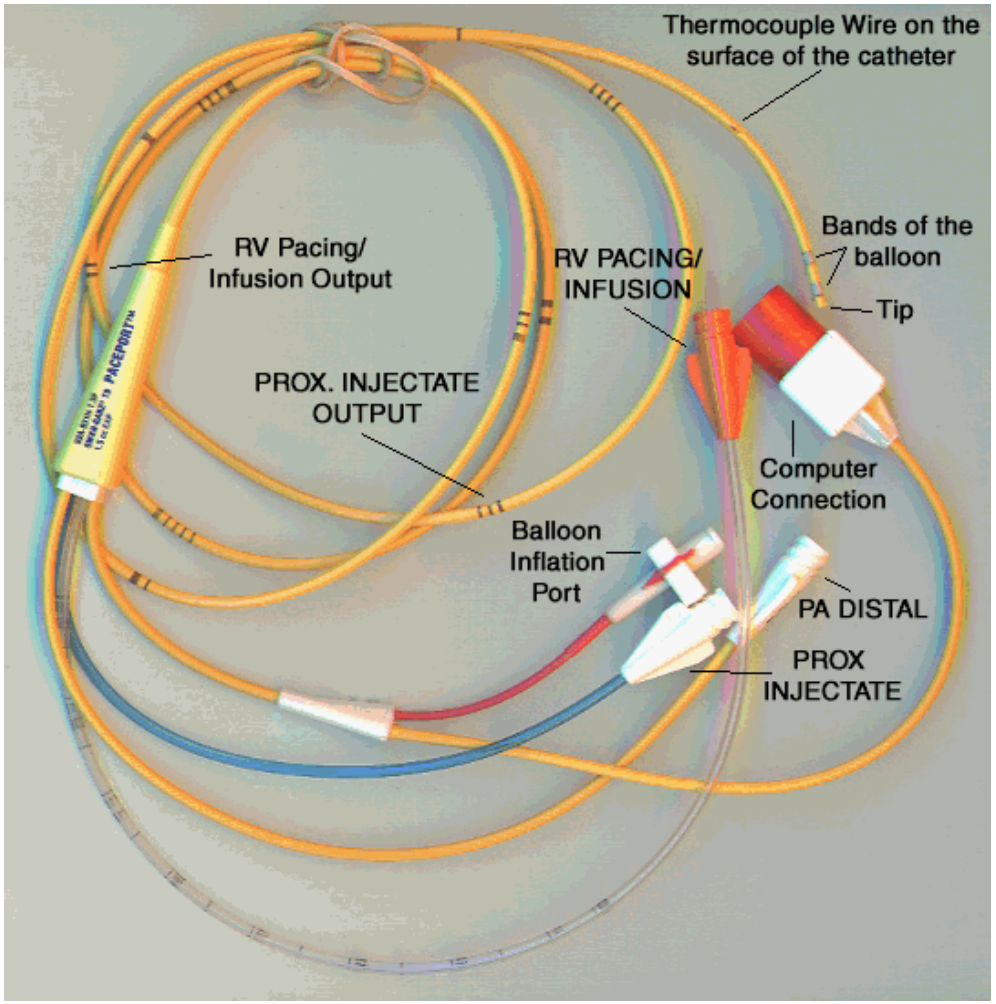
Central Venous Pressure Waveform



The Pulmonary Artery Catheter

- HJC Swan and sailboats
- Widespread use in critically ill patients
- Remains controversial
  - Lack of prospective, randomized trials
  - PAC data are only as good as the clinicians' interpretation and application
- Measures CVP, PAP, PAOP, Cardiac Index and SvO_2

Pulmonary Artery Catheter



Indications for Pulmonary Artery Catheterization

- Identification of the type of shock
  - Cardiogenic (acute MI)
  - Hypovolemic (hemorrhagic)
  - Obstructive (PE, cardiac tamponade)
  - Distributive (septic)
  - Many critically ill patients exhibit elements of more than 1 shock classification
- Monitoring the effectiveness of therapy

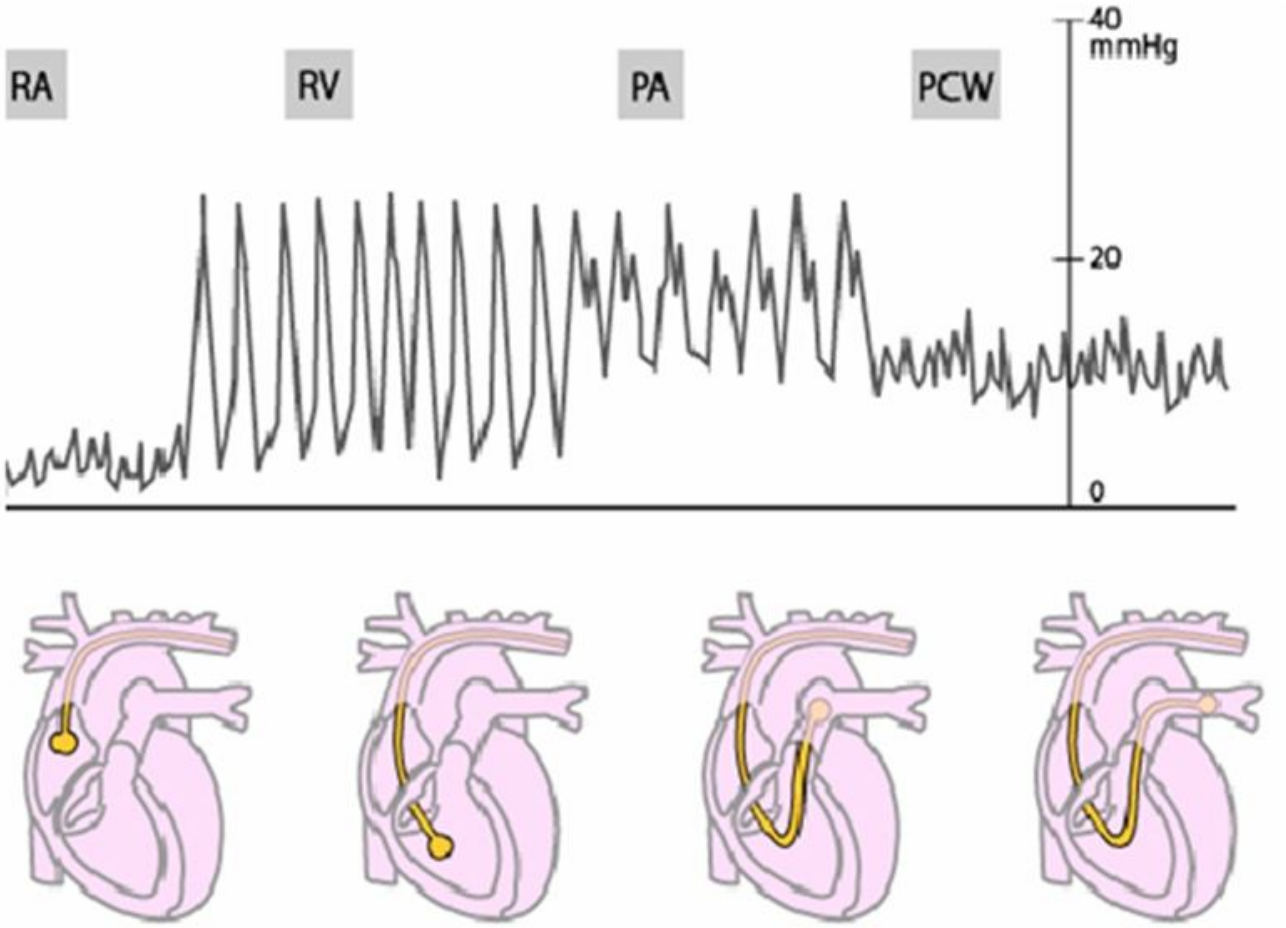
Normal Hemodynamic Values

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 $L/min/M^2$
MAP	60-100 mm Hg
CVP	2-6 mm Hg
PAP systolic	20-30 mm Hg
PAP diastolic	5-15 mm Hg
PAOP (wedge)	8-12 mm Hg
SVR	900-1300 $dynes \cdot sec \cdot cm^{-5}$

Hemodynamic Profiles in Shock

Class of Shock	CVP	PAOP	CO / CI	SVR
Cardiogenic	↑	↑	↓	↑
Hypovolemic	↓	↓	↓	↑
Hyperdynamic septic	↕	↔	↑	↓
Hypodynamic septic	↕	↓	↓	↓

Pulmonary Artery Catheter Placement



Complications of Pulmonary Artery Catheterization

- General central line complications
  - Pneumothorax
  - Arterial injury
  - Infection
  - Embolization
- Inability to place PAC into PA
- Arrhythmias (heart block)
- Pulmonary artery rupture

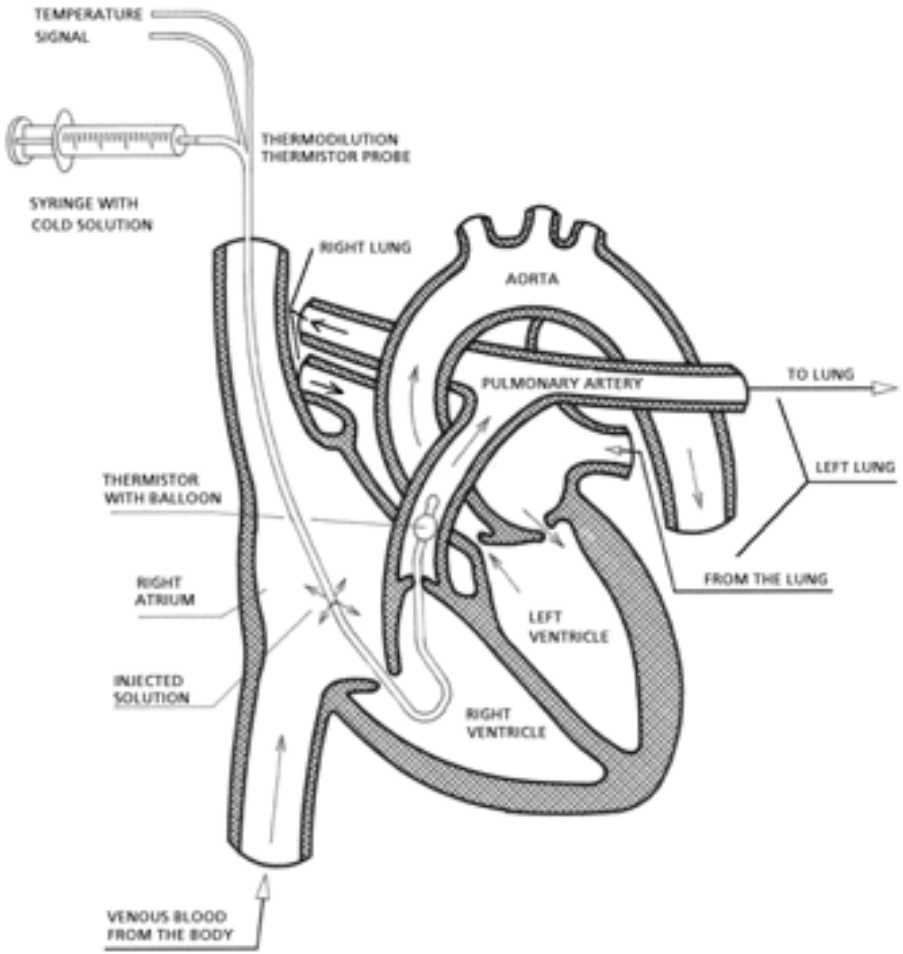
The Pulmonary Artery Catheter Controversy

- Accuracy of data affected by many conditions common in critically ill patients
- Lack of prospective randomized data supporting better outcomes with PAC
- Limited by the ability of the clinician to accurately interpret PAC data

Cardiac Output Measurement

- Multiple techniques
  - Thermodilution – most common
  - Transpulmonary
  - Pulse contour analysis
  - Esophageal Doppler
- Newer pulmonary artery catheters offer continuous cardiac output measurement

Thermodilution Method of Cardiac Output Measurement



Tissue Oxygenation

- Despite advances, our ability to monitor the microcirculation and tissue perfusion is limited
- Laboratory tests for metabolic acidosis are global and insensitive
- Newer technology on the horizon
  - Gastric tonometry
  - Sublingual capnometry

Conclusions

- Multiple different methods of hemodynamic monitoring
- Keys to success
  1) Know when to use which method
  2) Technical skills for device placement
  3) Know how to interpret the data
- Remember the limitations of the technology

Segue……

Q: Why is hemodynamic monitoring really important?

A: To ensure that the antibiotics get to the tissues……

Optimal Antibiotic Use

- Antimicrobial prophylaxis for surgery
- Empiric antimicrobial therapy
- Challenges of therapeutic antibiotics
  - Correct antibiotic(s)
  - Correct dosing
  - Length of therapy
- Ventilator-associated pneumonia
- Antimicrobial resistance
  - Strategies against resistance
- Bad bugs

Antimicrobial Prophylaxis for Surgery: NSIPP

- Bratzler DW, Houck PM, et al. *American Journal of Surgery.* 2005 Apr;189(4):395-404
- First dose of antibiotics within 60 minutes of surgical incision
- Prophylactic antibiotics should be discontinued within 24 hours of surgery
- Specific antibiotic should be chosen based on activity against bacteria likely to be encountered and having smallest possible impact on normal flora

Principles of Empiric Antimicrobial Therapy

- Vigilance and high index of suspicion
  - Local and systemic signs
  - Laboratory and radiographic findings
- **Prompt initiation of therapy**
- Appropriate choice of empiric coverage
  - Suspected site of infection
  - Most likely microbial etiologies
  - Likelihood of antimicrobial resistance – institution specific
  - Patient-specific toxicity and allergic concerns
- Modification of empiric coverage after 48-72 hours

The Risks of Inadequate Empiric Antimicrobial Treatment

- Prospective cohort study of 2000 ICU patients
  - Hospital mortality rate greater (52% vs. 12%) in patients who received inadequate antimicrobial treatment
  - Most important independent determinant of hospital mortality by logistic regression
- 655 patients infected
  - 169 (25.8%) received inadequate antimicrobial treatment
    - Risk factors: prior antibiotic use, presence of bloodstream infection, higher APACHE II scores, decreasing age
  - Infection-related mortality rate 42% vs. 17.7%

Kollef MH, et al. *Chest.* 1999; 155; 462-474

The Risks of Inadequate Empiric Antimicrobial Treatment: Bloodstream Infections

- Prospective cohort study of 492 patients with documented bloodstream infections
- 147 (29.9%) received inadequate antimicrobial therapy
- Hospital mortality rate 61.9% vs 28.4%
- Risk factors for inadequate antimicrobials:
  - Candida bloodstream infection
  - Prior antibiotic use during same hospitalization
  - Decreasing serum albumin
  - Increasing central catheter duration

Ibrahim EH, et al. *Chest.* 2000; 118; 146-155

Modification of Empiric Coverage

- Based on clinical condition and culture results
- 48-72 hours after empiric antimicrobials initiated
- Interpret all results with caution
  - Negative cultures drawn after antibiotics initiated
  - Cultures with high incidence of false positives (tracheal aspirates)
  - Contaminants

Therapeutic Antimicrobials:
Choosing the Right Drug(s)

- Gram-positive infections
  - β-lactam antibiotics (penicillins, cephalosporins, carbapenems)
  - Fluoroquinolones
  - Vancomycin
  - Linezolid, Daptomycin
- Gram-negative infections
  - β-lactam antibiotics
  - Fluoroquinolones
  - Aminoglycosides

Therapeutic Antimicrobials:
Choosing the Right Drug(s)

- Anaerobic infections
  - Penicillins
  - Carbapenems
  - Second-generation cephalosporins
  - Metronidazole
- Fungal infections
  - Amphotericin
  - Triazoles
  - Echinocandins

Therapeutic Antimicrobials:
Bactericidal vs. Bacteriostatic

- Bactericidal
  - Penicillins*
  - Cephalosporins
  - Carbapenems
  - Monobactams
  - Vancomycin*
  - Quinolones
  - Aminoglycosides
  - Quinupristin-dalfopristin
  - Metronidazole
- Bacteriostatic
  - Trimethoprim-sulfamethoxasole
  - Clindamycin
  - Linezolid
  - Macrolides
  - Chloramphenicol
  - Tetracyclines

Therapeutic Antimicrobials:
Correct Dosing

- Important variables in critically ill patients:
  - Target organism
  - Site of infection
  - MIC
  - Host defenses
  - Volume of distribution
  - Hepatic and/or renal impairment
- Concentration-dependent vs. Time-dependent killing

Therapeutic Antimicrobials:
Duration of Therapy

- Very controversial
- Factors to consider:
  - Severity of infection
  - Presence of prosthetic material, abscess, necrotic tissue
  - Rapidity of clinical and microbiological response
  - Status of host defenses
- Balancing adequacy of therapy with prevention of resistance

Ventilator Associated Pneumonia

- Most frequent nosocomial infection in ICU
  - 80% of hospital-acquired pneumonia
  - 21-fold increased risk with artificial airway
  - Cumulative risk is 1% per day of mechanical ventilation
  - > $40,000 cost per patient (1999)
- Risk factors
  - Burns
  - Trauma
  - Male gender
  - Central nervous system disease
  - Aspiration

Diagnosis of Ventilator Associated Pneumonia

- Johanson criteria
  - Chest X-ray
    - Sensitive but not specific
  - Leukocytosis/leukopenia
  - Purulent secretions
- Clinical Pulmonary Infection Score
  - Adds fever, oxygenation, and culture results
  - Sensitivity and specificity are highly variable
- Bacteriologic data
  - Different methods of quantitative cultures seem equivalent

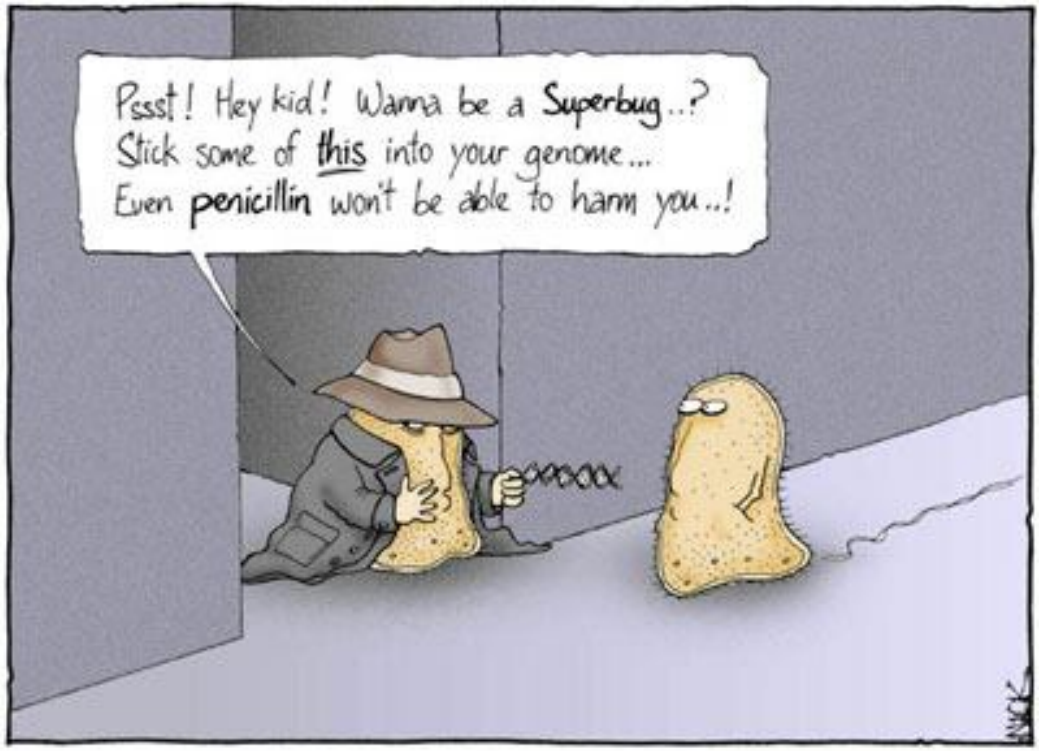
Strategies to Prevent Ventilator Associated Pneumonia

- Patient-oriented
  - Gown and glove use
  - Avoiding gastric distention
  - Head-of-bed elevation
  - Minimizing stress-ulcer prophylaxis
- Microorganism-oriented
  - **HAND WASHING**
  - Clorhexidine oral rinse
  - Selective gut decontamination
- Device-oriented
  - Subglottic drainage
  - Humidification

Management of Ventilator Associated Pneumonia

- Prompt initiation of adequate empiric therapy is the most important concept
- Considerations:
  - Prior antibiotic exposure
  - Comorbidities
  - Length of hospitalization
  - Local microbial epidemiology and susceptibilities
- Key questions:
  - Is the patient as risk of MRSA?
  - Is *A. baumannii* a problem at the institution?
  - Is the patient at risk of *P. aeruginosa*?

Antimicrobial Resistance



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Antimicrobial Resistance: CDC Programs

- National Nosocomial Infections Surveillance (NNIS) System
- Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology)
- Higher rates of resistance in the ICU correlate with more antibiotic use:
  - *Enterobacter* - 3rd-generation cephalosporins
  - Enterococci - vancomycin
  - *P. aeruginosa* - antipseudomonal penicillins and 3rd-generation cephalosporins
- Higher rates of resistance in the ICU that do not correlate with more antibiotic use:
  - MRSA and MR-CNS

Strategies to Minimize Antimicrobial Resistance: Individual Patient

- Use antimicrobials with highest potency
- Appropriate dose and dosing intervals
- Avoid known inducers of chromosomal resistance
- Chose agents with good penetration to site of infection
- Avoid antagonistic antimicrobial combinations
- Appropriate treatment duration
- Achieve therapeutic drainage and/or device removal

Strategies to Minimize Antimicrobial Resistance: ICU-based

- **HAND-WASHING**
- Appropriate glove and gown use
- Surveillance monitoring for resistant strains
  - MRSA
  - VRE
  - ESBL
- Appropriate patient isolation policies
- Antimicrobial cycling
- Computer-assisted antimicrobial prescription

Antimicrobial Resistance

Reasons for Antimicrobial Failure

- Undrained infected material
- Underlying host defenses
- Infected prosthetic material
- Poor tissue penetration
- Superinfection with (new) pathogen
- Evolved resistance
- Inadequate dosing
- Antagonistic antimicrobial combination

Bad Bugs

- Vancomycin-resistant Enterococci
- Methicillin-resistant *S. aureus*
- *Pseudomonas aeruginosa*
- ESBL strains
  - *Enterobacter*
  - *Klebsiella*
  - *Serratia*
- *Acinetobacter baumannii*

Vancomycin-resistant Enterococci

- Predominantly *E. faecium*
- Usually resistant to ampicillin
- Can be contaminant but bloodstream infections and purulent closed-space collections in symptomatic patients must be treated
- Linezolid
- Quinupristin/dalfopristin
- Daptomycin

Methicillin-resistant *S. aureus*

- Vancomycin remains useful, but be aware of limitations
  - Slow bactericidal activity
  - Poor lung and CNS penetration
  - Poor activity in biofilms
- Emergence of vancomycin-resistance
- Linezolid
- Quinupristin/dalfopristin
- Daptomycin

Pseudomonas aeruginosa

- Virulent: infection-associated mortality as high as 70% despite therapy
- Intrinsic and acquired resistance:
  - Chromosomal-mediated β-lactamase
  - Aminoglycoside modifying enzymes
  - Mutations of outer membrance porin channels
- Piperacillin-tazobactam
- Meropenem
- Aminoglycosides
- Colistin

ESBL strains

- Plasmid-mediated production of β-lactamases
- Resistance to aztreonam, piperacillin, and later generation cephalosporins
- ESBL strains commonly coexpress aminoglycoside and/or quinolone resistance
- Carbapenems are the most proven antimicrobial