Sepsis
Two-thousand sixteen

Tom Ahrens PhD RN FAAN

&

Michael Ackerman DNS RN FCCM

Rory's Regulation

NYS Regulation

Prevention

- VAP, what do we know. The bundle works, use it. There was a recent Cochrane that showed that NNT with an aggressive oral care product with CHG was 15.
- CAUTI, everyone is struggling. There is a bundle that works. Compliance is difficult. The new definitions should help as we were counting things that were not truly infections.
- CLABSI, insertion and maintenance bundles do work with rigorous oversight and “staying on it”.

CHG Bathing

- Well we thought we had the answer to this and that it worked.....

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Daily Chlorhexidine Bathing on Hospital-Acquired Infection

Michael W. Climo, M.D., Deborah S. Yokoe, M.D., M.P.H., David K. Warren, M.D., Trish M. Perl, M.D., Maureen Bolon, M.D., Loreen A. Herwaldt, M.D., Robert A. Weinstein, M.D., Kent A. Sepkowitz, M.D., John A. Jernigan, M.D., Kakotan Sanogo, M.S., and Edward S. Wong, M.D.

n engl j med 368;6 nejm.org february 7, 2013

And then this came out....

JAMA. 2015 Jan 27;313(4):369-78. doi: 10.1001/jama.2014.18400.
Chlorhexidine bathing and health care-associated infections: a randomized clinical trial.
Noto MJ1, Domenico HJ2, Byrne DW2, Talbot T1, Rice TW1, Bernard GR1, Wheeler AP1.

OBJECTIVE:
To determine if daily bathing of critically ill patients with chlorhexidine decreases the incidence of health care-associated infections.

RESULTS:
During the chlorhexidine bathing period, 55 infections occurred: 4 CLABSI, 21 CAUTI, 17 VAP, and 13 C difficile. During the control bathing period, 60 infections occurred: 4 CLABSI, 32 CAUTI, 8 VAP, and 16 C difficile. The primary outcome rate was 2.86 per 1000 patient-days during the chlorhexidine and 2.90 per 1000 patient-days during the control bathing periods (rate difference, -0.04; 95% CI, -1.10 to 1.01; P = .95). After adjusting for baseline variables, no difference between groups in the rate of the primary outcome was detected. Chlorhexidine bathing did not change rates of infection-related secondary outcomes including hospital-acquired bloodstream infections, blood culture contamination, or clinical cultures yielding multidrug-resistant organisms. In a prespecified subgroup analysis, no difference in the primary outcome was detected in any individual intensive care unit.

CONCLUSION AND RELEVANCE:
In this pragmatic trial, daily bathing with chlorhexidine did not reduce the incidence of health care-associated infections including CLABSIs, CAUTIs, VAP, or C difficile. These findings do not support daily bathing of critically ill patients with chlorhexidine.


SAFE
DISEASE
SANITATION
OCTOBER 15
NAILS
PERSONAL
BEFORE EATING FOOD
PREVENTION
HANDLING
CHEMICAL
WIPES
GELS
CLEANER
FINGERS
SICK
RUB
ALCOHOL
AFTER TOILET
SOAP
NaOH
PERSONAL
DRY
HANDS
BASIN
TOILET
SNEEZE
GERMS
HEALTH
ILLNESS
BACTERIUM
INFECTIONS
EFFECTIVE
LEARN
DISEASE
WASH
HANDS
SICK
DANGER
IMPORTANT
KILL
DISINFECT
VIRUS
WASHING
RUB
WC
FOAM
SANITIZER
FAUCET
CLEAN
WATER
ANTIBACTERIAL
HYGIENE
SODIUM HYDROXIDE
AGENTS
LEARN
DIRT
GERMS
BATHROOM
ILLNESS
LIQUID SOAP
BASIN
SOAP
CONTROL
HEALTH
PETS
TOUCHING
FREQUENT
PUBLIC
STAY HEALTHY!
ANTIOXIDANT
FOAM
PALM
RUB
PREVENT
PRESERVATION
SANITIZERS
MICROBES
DESTROY
INGREDIENTS
GARBAGE
LATHER
WASTE
HYGIENE
SAVE
DRY
GELS
CLEANING
DIRTY
BACTERIA
TOWEL
FAUCET
INFECTION
HANDWASHING
CHEMICAL
HYGIENE
AIR DRY
VIRUSES
SEPTIC
PUBLIC HEALTH
RUNNING WATER
PROTECTION PROCEDURE
HANDWASHING
WARNING
LATHER
ALCOHOL BASED
FOAM
DANGER
PEOPLE
MICROBES
ANTISEPTIC
CARE
DISPENSER
HANDSOAP
METHODS
RINSE

Use of a Patient Hand Hygiene Protocol to Reduce Hospital-Acquired Infections and Improve Nurses' Hand Washing

By Cherie Fox, RN, MSN, CCRN-CSC, Teresa Wavra, RN, MSN, CNS, CCRN, Diane Ash Drake, RN, PhD, Debbie Mulligan, RN, MSN, PHN, CIC, Yvonne Pacheco Bennett, RN, BSN, JD, CCRN, Carla Nelson, BSN, CIC, Peggy Kirkwood, RN, MSN, ACNPC, CHFN, AACC, Louise Jones, RN, MSN, CCRN, and Mary Kay Bader RN, MSN, CCNS

AMERICAN JOURNAL OF CRITICAL CARE, May 2015, Volume 24, No. 3

So what are we talking about?

Sepsis can be subtle until it is so obvious you can’t miss it

Pathophysiology of Sepsis

What do we need to know

Sepsis

- *Sepsis is a genus of flies. See Sepsidae.*
- **Sepsis From Wikipedia, the free encyclopedia**
- **Sepsis/Septicaemia**
  Classification & external resources **ICD-10**A40. - A41.0**ICD-9**038 **Sepsis** (in Greek *Σήψις*, putrefaction) is a serious medical condition, resulting from the immune response to a severe infection. **Septicaemia** is sepsis of the bloodstream caused by bacteremia, which is the presence of bacteria in the bloodstream. The term *septicaemia* is also used to refer to sepsis in general.
- http://www.youtube.com/watch?v=hNoBF6bsNUU

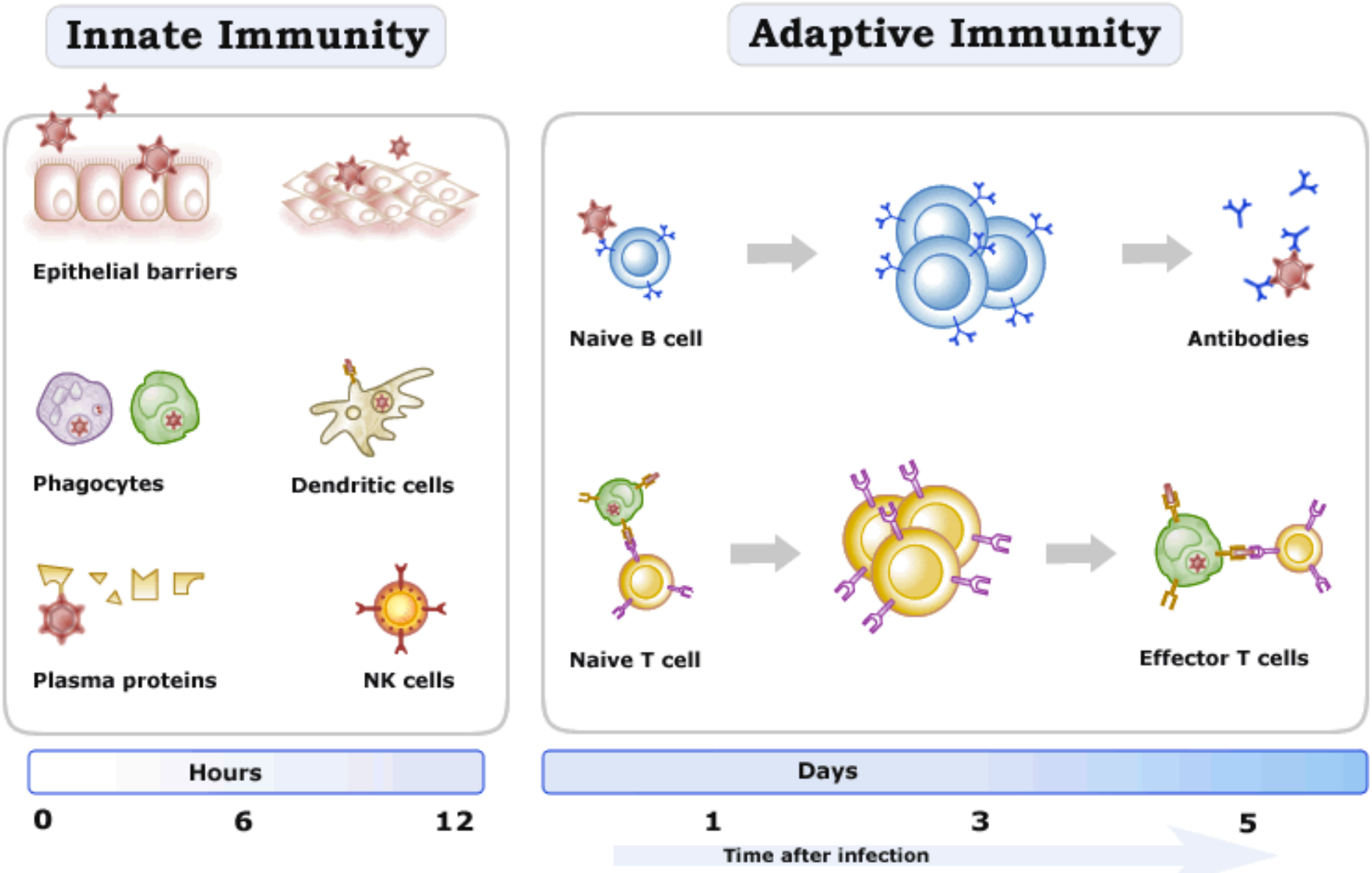
“Except on few occasions, the patient appears to die from the body's response to infection rather than from it.”

Sir William Osler – 1904

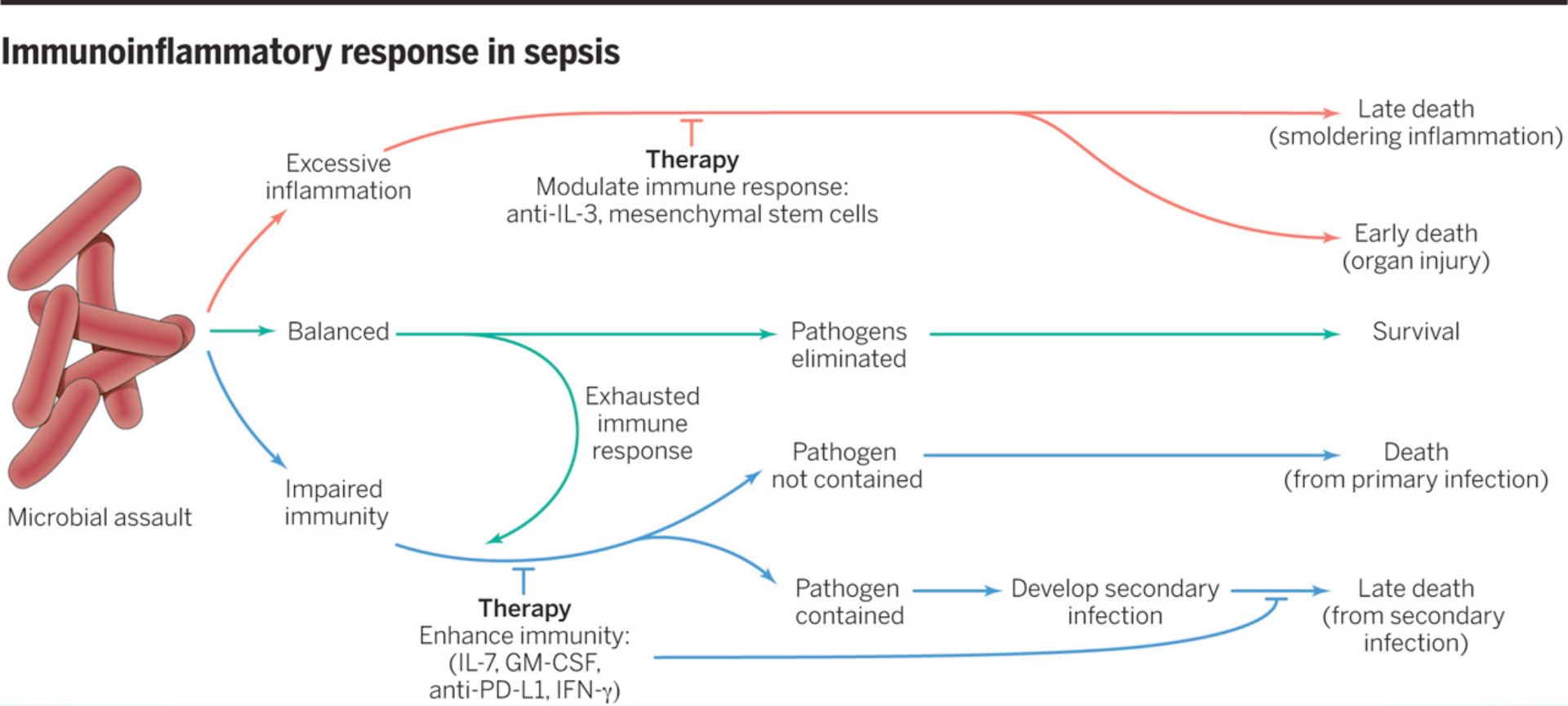
The Evolution of Modern Medicine

Immune Response

- Initial Response (Innate)
  - Neutrophils
  - Monocytes
  - Survival depends on success of neutrophils
- Secondary response (Adaptive)
  - Antibody production
  - Takes 4-7 days for initial exposure
    - 1-2 days for subsequent exposures

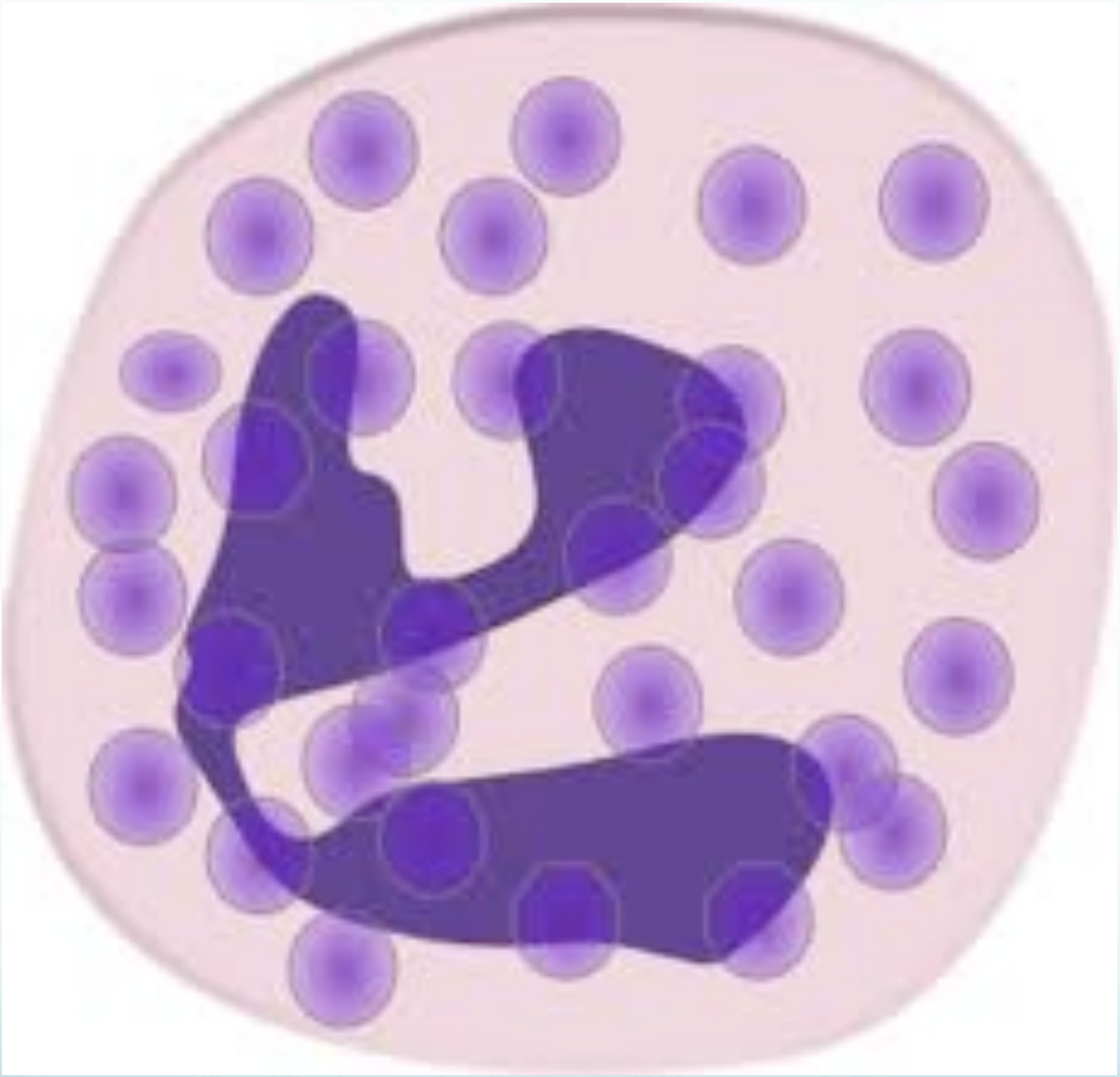


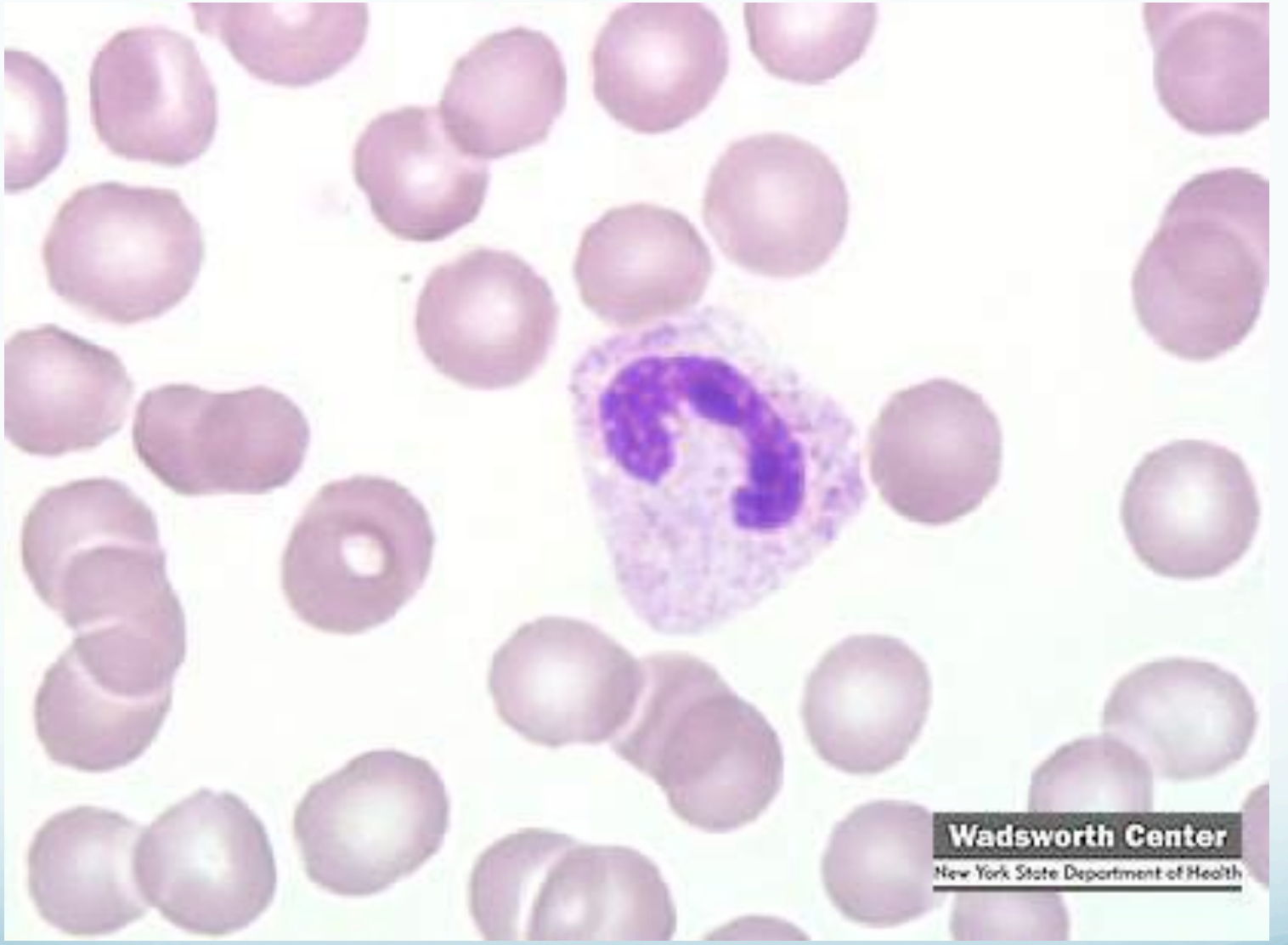
http://missinglink.ucsf.edu/lm/immunology_module/prologue/objectives/obj02.html Module created by Patrick Fisher MS2

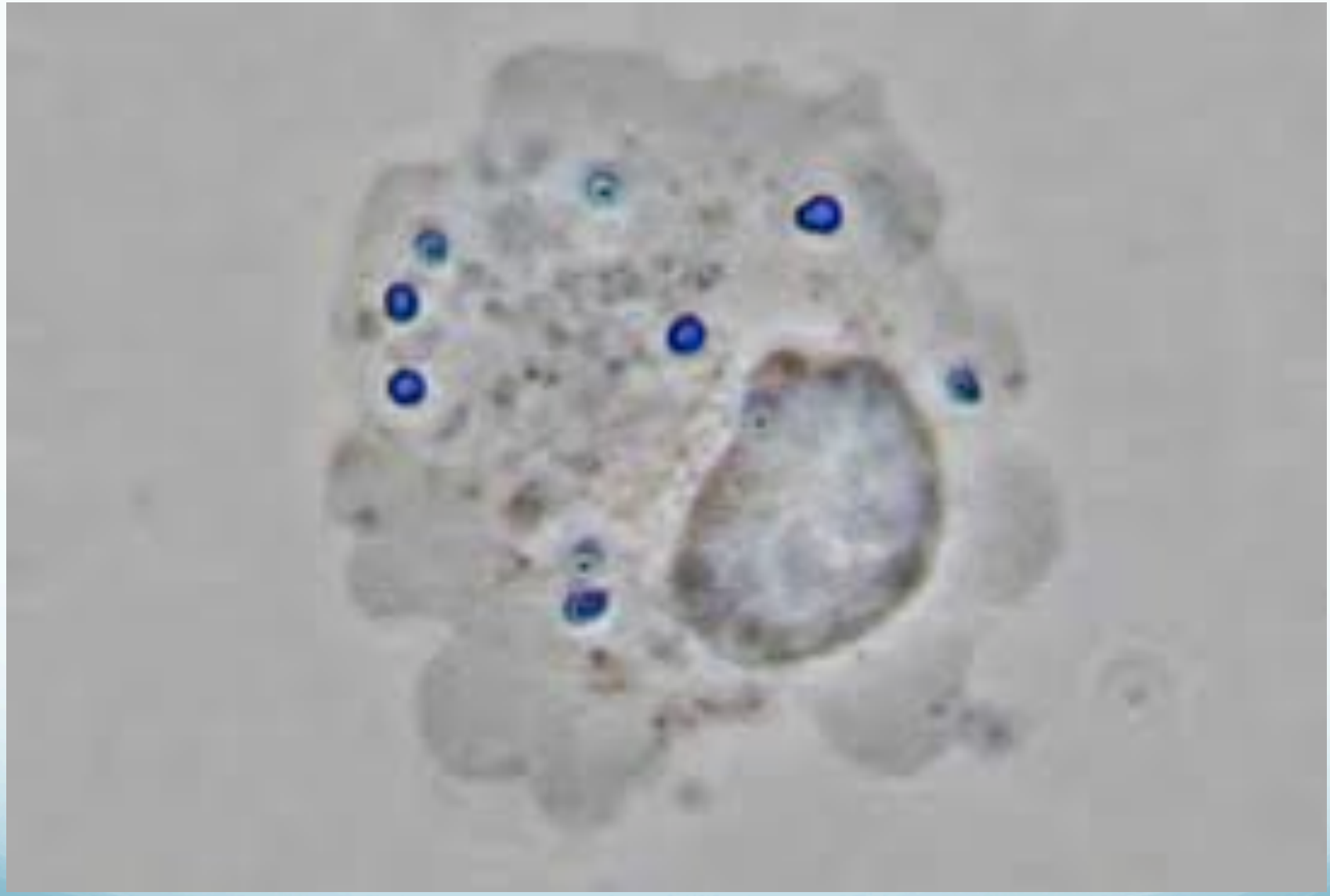


Inflammatory response to sepsis.

Potential immune therapies can modulate immune responses that provoke excessive inflammation or enhance immunity if there is an impaired immune response to microbial infection. IFN-γ, interferon-γ. "ILLUSTRATION: ADAPTED BY P. HUEY/SCIENCE"




Wadsworth Center
New York State Department of Health



Immune Response

- Initial Response (Innate)
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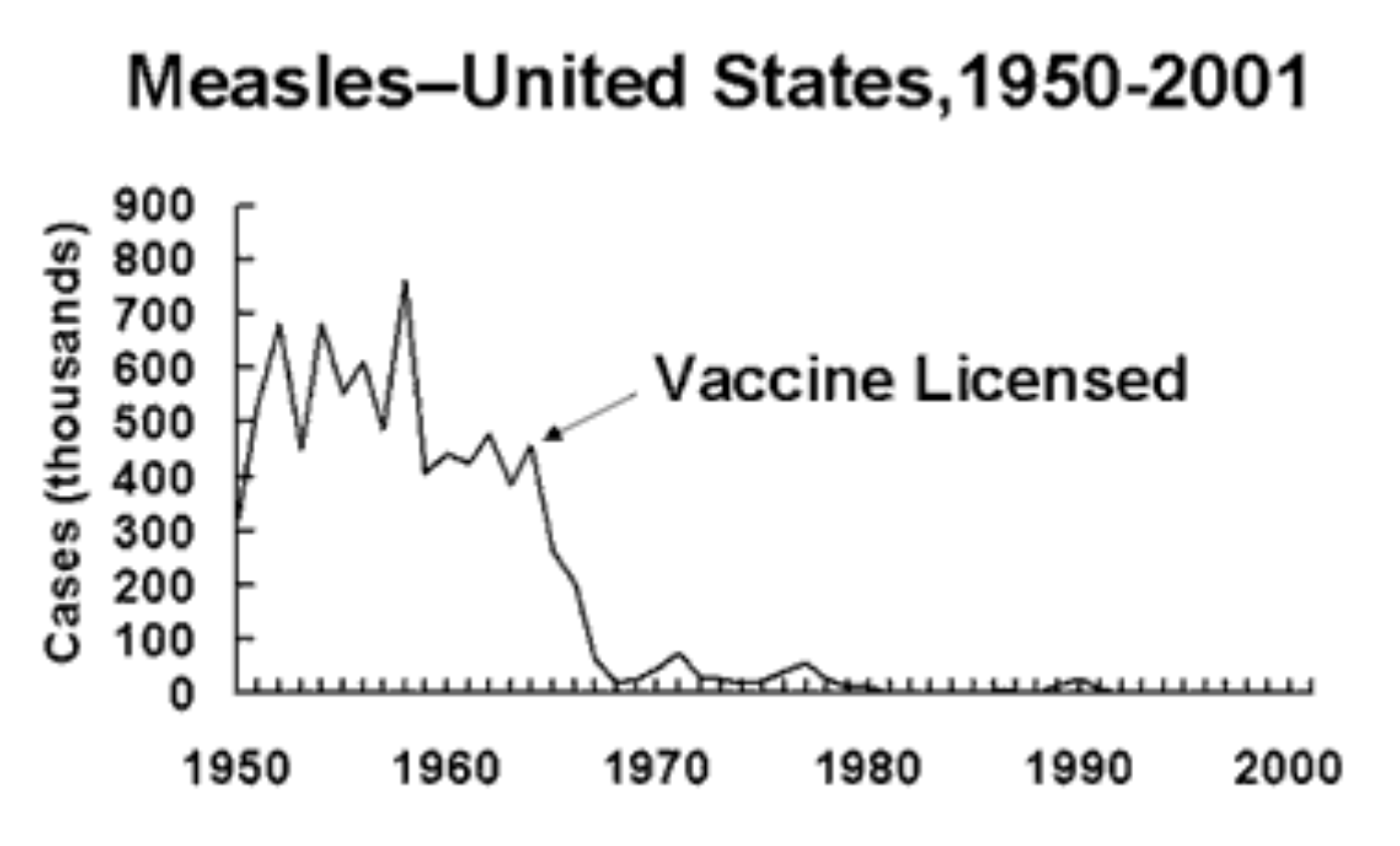
    - 1-2 days for subsequent exposures

5 second rule

Impact of Vaccines
Measles Example



But few bacteria are dangerous

- Only a small amount of bacteria and viruses are dangerous
- Those are not likely to be on the floor
- But they can be on your hands or in the air
- Protecting yourself

The Power of Our Immune System

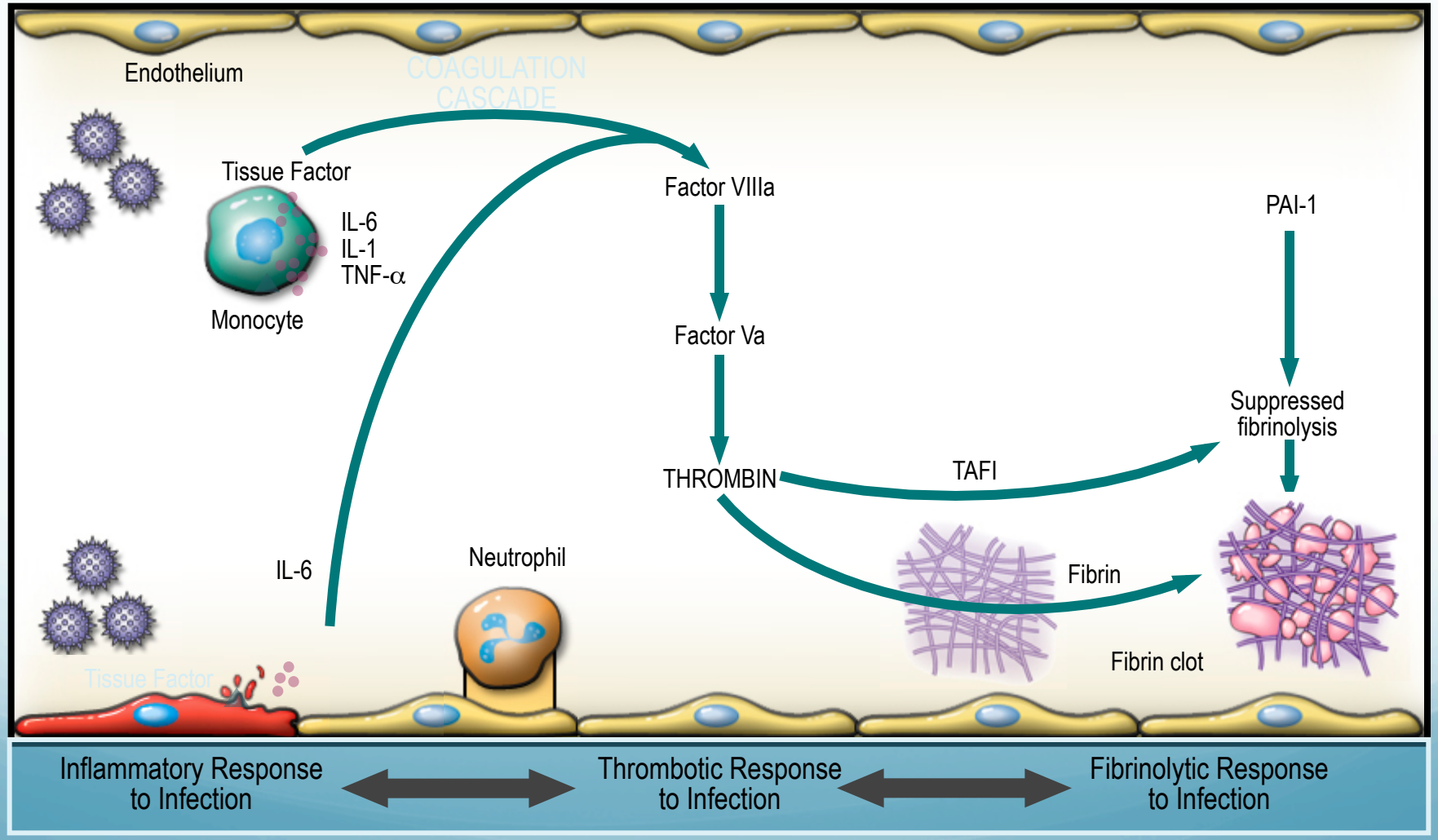
"Our arsenals for fighting off bacteria are so powerful, and involve so many different defense mechanisms, that we are more in danger from them than from the invaders.

"We live in the midst of explosive devices; we are mined!"

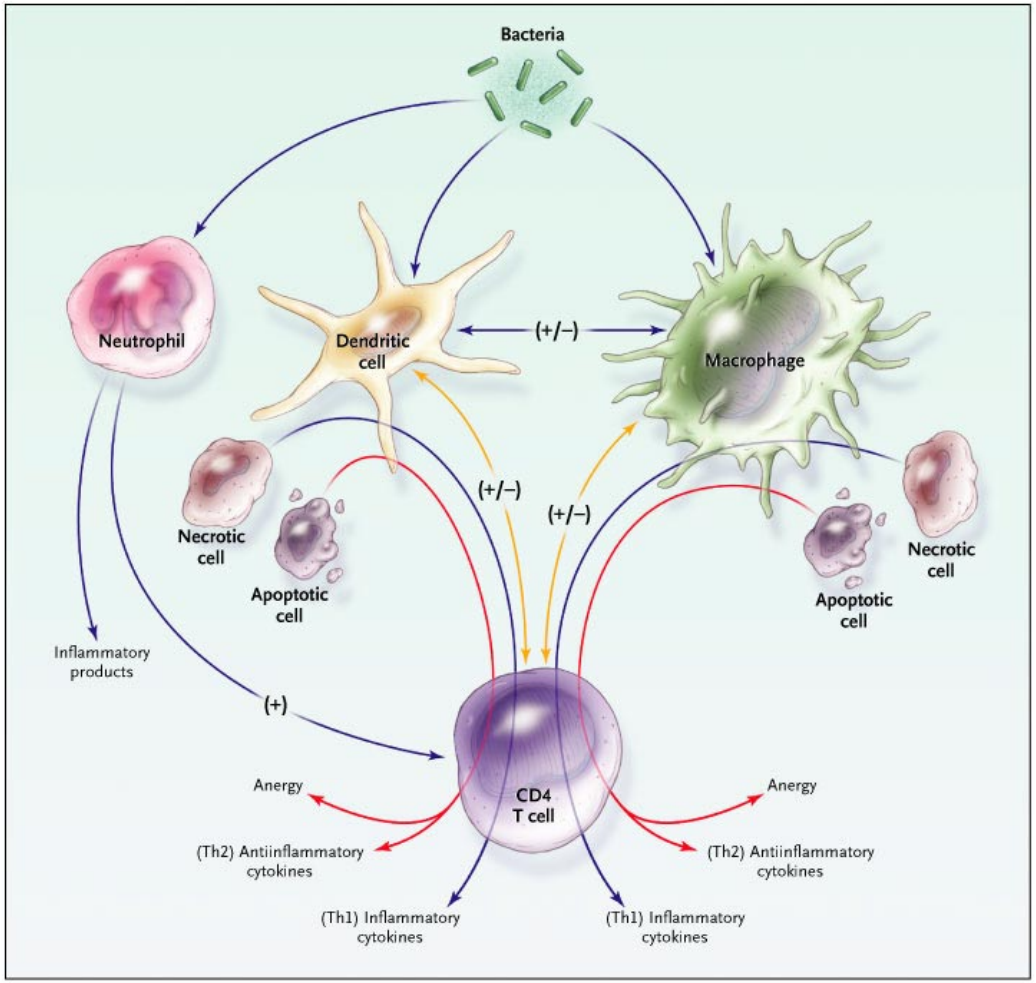
Lewis Thomas - 1972

Germs, *New England Journal Of Medicine*

Coagulation and Impaired Fibrinolysis In Severe Sepsis



The Response to Pathogens, Involving "Cross-Talk" among Many Immune Cells, Including Macrophages, Dendritic Cells, and CD4 T Cells



Hotchkiss, R. S. et al. N Engl J Med 2003;348:138-150

“Sepsis” referring to the “decomposition of animal or vegetable organic matter in the presence of bacteria” 1 first appeared over 2700 years ago in the poems of Homer

The burden of sepsis-associated mortality in the United States from 1999 to 2005: an analysis of multiple-cause-of-death data

Alexander Melamed[1] and Frank J Sorvillo[2]

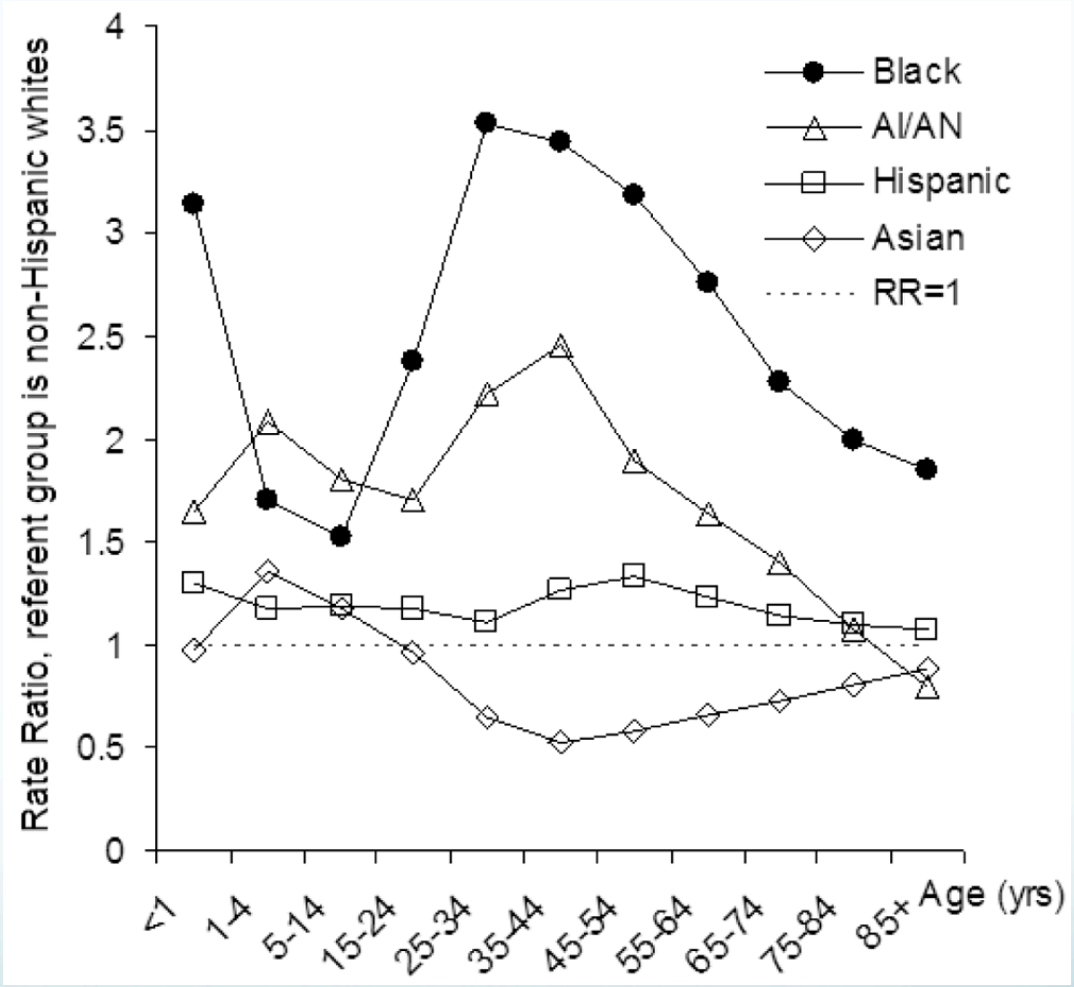
[1]Keck School of Medicine of the University of Southern California, 1975 Zonal Avenue, Keith Administrative Building, Room 100-B, Los Angeles, CA 90089, USA
[2]Department of Epidemiology, School of Public Health, University of California, Los Angeles, CA 90095, USA

Corresponding author: Alexander Melamed, melameda@usc.edu

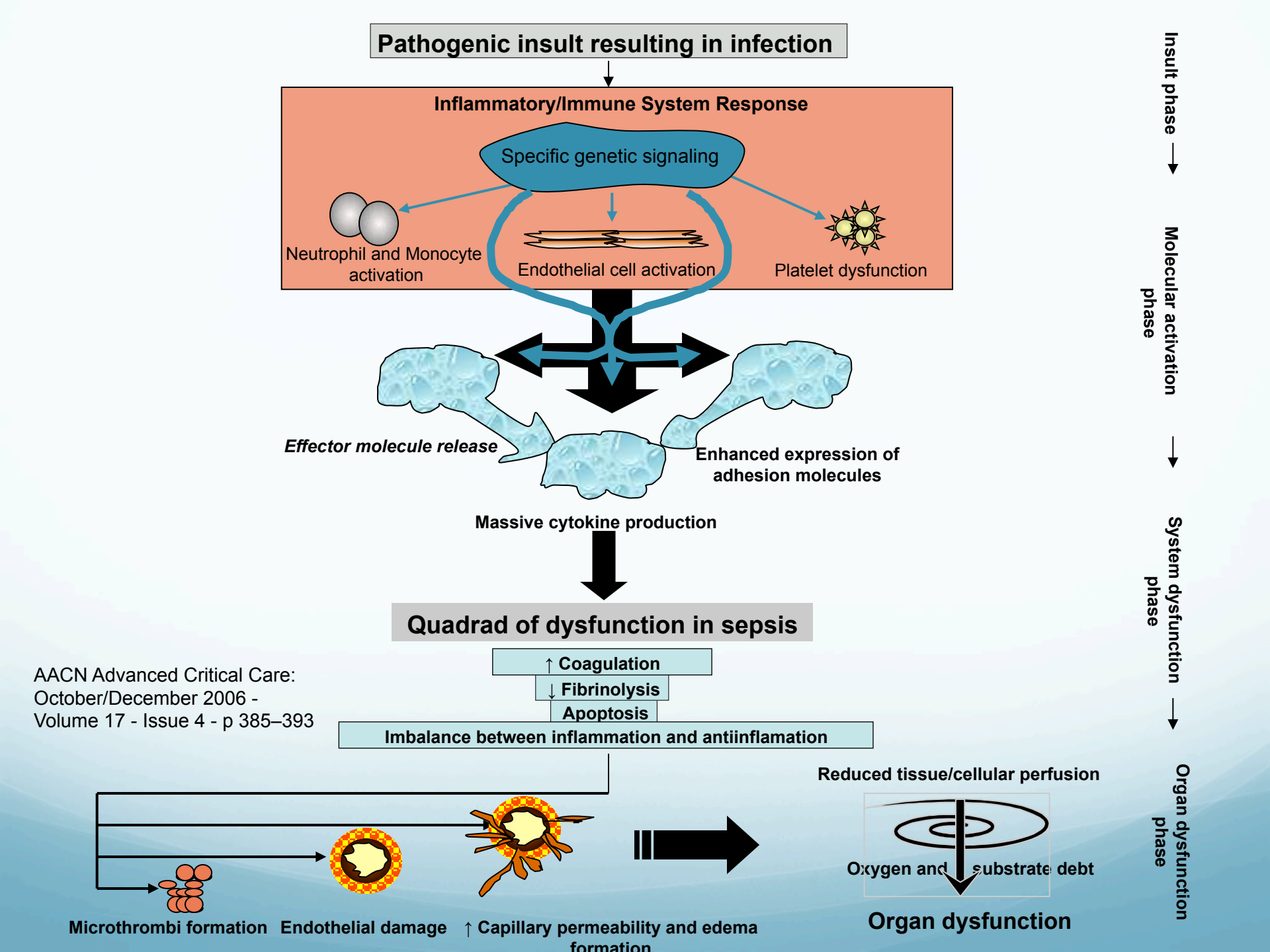
Received: 25 Nov 2008 Revisions requested: 27 Jan 2009 Revisions received: 6 Feb 2009 Accepted: 27 Feb 2009 Published: 27 Feb 2009

Critical Care 2009, **13**:R28 (doi:10.1186/cc7733)

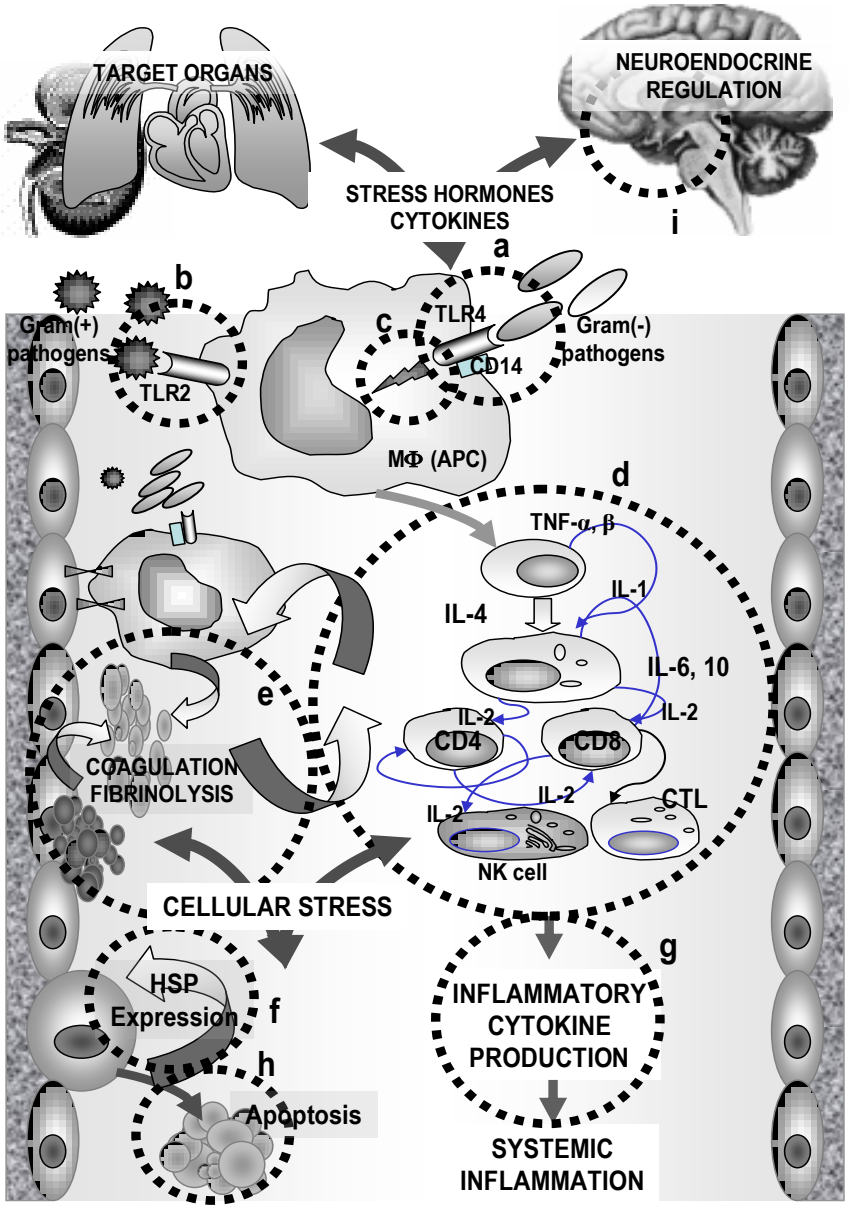
Figure 1



Age-specific rate-ratios for sepsis-associated death by race/ethnicity category in the United States, 1999 to 2005. Non-Hispanic whites were used as the referent group. AI/AN = American Indian/Alaska Native.



AACN Advanced Critical Care: October/December 2006 - Volume 17 - Issue 4 - p 385–393



AACN Advanced Critical Care:
October/December 2006 -
Volume 17 - Issue 4


THE PRECISION MEDICINE INITIATIVE

WHAT IS IT?

Precision medicine is an emerging approach for disease prevention and treatment that takes into account people's individual variations in genes, environment, and lifestyle.

The Precision Medicine Initiative will generate the scientific evidence needed to **move the concept of precision medicine into clinical practice.**

WHY NOW?

The **time is right** because of:

Sequencing of the human genome

Improved technologies for biomedical analysis

New tools for using large datasets

NEAR TERM GOALS

Intensify efforts to apply precision medicine to **cancer.**

Innovative **clinical trials** of targeted drugs for adult, pediatric cancers

Use of **combination therapies**

Knowledge to overcome **drug resistance**

LONGER TERM GOALS

Create a research cohort of **> 1 million American volunteers** who will share genetic data, biological samples, and diet/lifestyle information, all linked to their electronic health records if they choose.

Pioneer **a new model for doing science** that emphasizes **engaged participants, responsible data sharing, and privacy protection.**


Google™ X

So how do we treat this patient?

86 year old Caucasian female admitted from the nursing home with urosepsis.
Causative organism: e-coli

Treatment

- Fluids
- Antibiotics
- Pressors
- Lactate
- Organ support

So how do we treat this patient?

86 year old Caucasian female admitted from the nursing home with urosepsis. Causative organism: e-coli

28 year old Asian male with abdominal Sepsis s/p surgery related to GSW. Causative organism: enterobacter

Treatment

- Fluids
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So how do we treat this patient?

86 year old Caucasian female admitted from the nursing home with urosepsis. Causative organism: e-coli

28 year old Asian male with abdominal sepsis s/p surgery related to GSW. Causative organism: enterobacter

55 year old African American male with sepsis from CAUTI s/p CABG. Causative organism: MRSA

Treatment

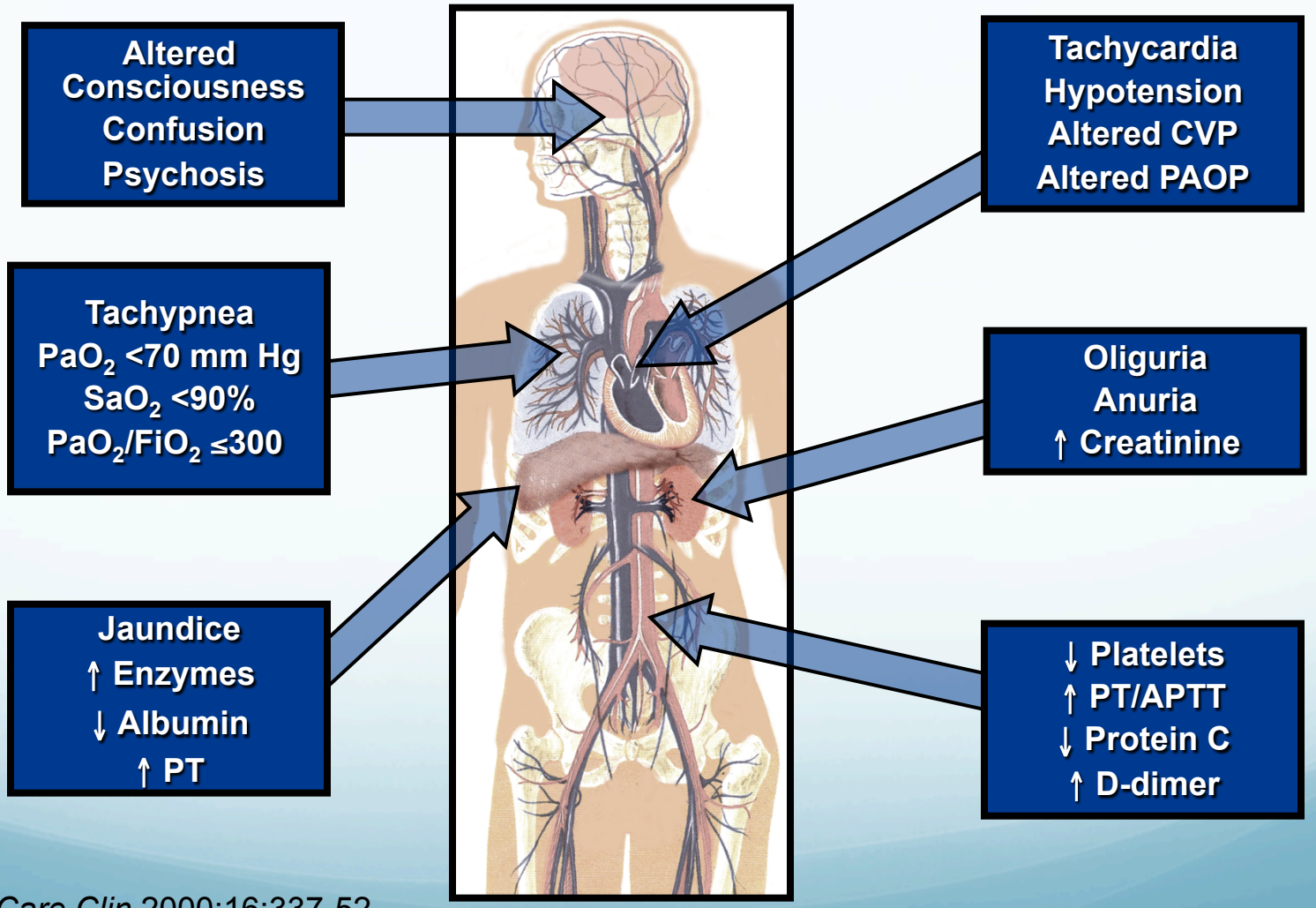
- Fluids
- Antibiotics
- Pressors
- Lactate
- Organ support

Impact of Sepsis Acute Organ System Dysfunction

Group Question

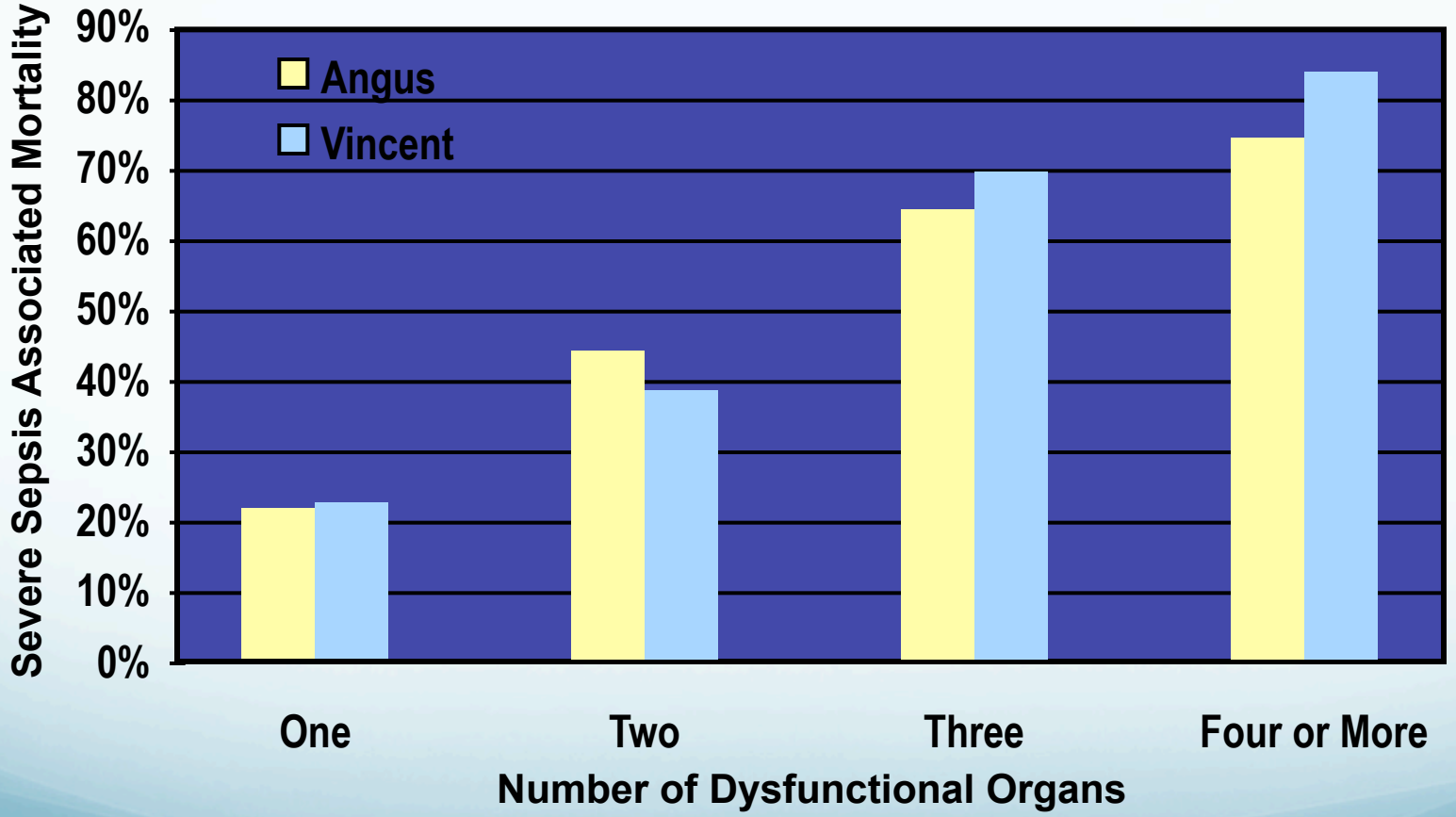
- What does the typical sepsis patient look like?

Identifying Acute Organ Dysfunction as a Marker of Severe Sepsis



Balk RA. *Crit Care Clin* 2000;16:337-52.

Severe Sepsis-Associated Mortality Increases With the Number of Dysfunctional Organs



Vincent JL, et al. *Crit Care Med* 1998;21:1793-800; Angus DC et al. *Crit Care Med* 2001;29:1303-10.

Now playing LIVE in New Orleans

A Chaotic look at Sepsis

The Actors

- 2 people named Gene (Jean)
- Gram negative bacteria (Black shirts)
- Antibiotic (Pink shirt) (Ann)
- TNF (1)
- Macrophage/monocyte (Yellow)
- Platelet (Lt blue shirts)
- Neutrophil (Neon green) (Phil)

2016 Guidelines

Hot off the presses.....
(kind of)

The New Surviving Sepsis Campaign Bundles – April 2015

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION*:

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L

Remains the Same

* *"Time of presentation" is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review.*

TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg
6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings according to Table 1.
7. Re-measure lactate if initial lactate elevated.

Screening

- Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy (grade 1C).
- Hospital based performance improvement efforts in severe sepsis

Initially

- Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ ?4 mmol/L). Goals during the first 6 hrs of resuscitation:
  - a) Central venous pressure 8–12 mm Hg
  - b) Mean arterial pressure (MAP) ≥ ?65 mm Hg c) Urine output ≥ ?0.5 mL/kg/hr d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).
- In patients with elevated lactate levels targeting resuscitation to normalize lactate

Antibiotics

- Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.
- Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).
- 2b. Antimicrobial regimen should be reassessed daily for potential deescalation (grade 1B).
- 3. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection

Antibiotics (cont.)

- Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known (grade 2B).
- Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with S. aureus; some fungal and viral infections or immunologic deficiencies, includingneutropenia (grade 2C).
- Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin (grade 2C).
- Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause

Source control

- A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible (grade 1C).
- When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (grade 2B).
- When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess) (UG).
- 4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established

Resuscitation

- Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
- Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B).
- Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
- Initial fluid challenge in patients with sepsis induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
- Fluid challenge technique be applied where in fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables

Vasopressors

- Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg .
- Norepinephrine as the first choice vasopressor (grade 1B).
- Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (grade 2B).
- Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).
- Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents) .
- Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia)

Vasopressors (cont.)

- Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low or (c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target.
- Low-dose dopamine should not be used for renal protection (grade 1A).
- All patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available

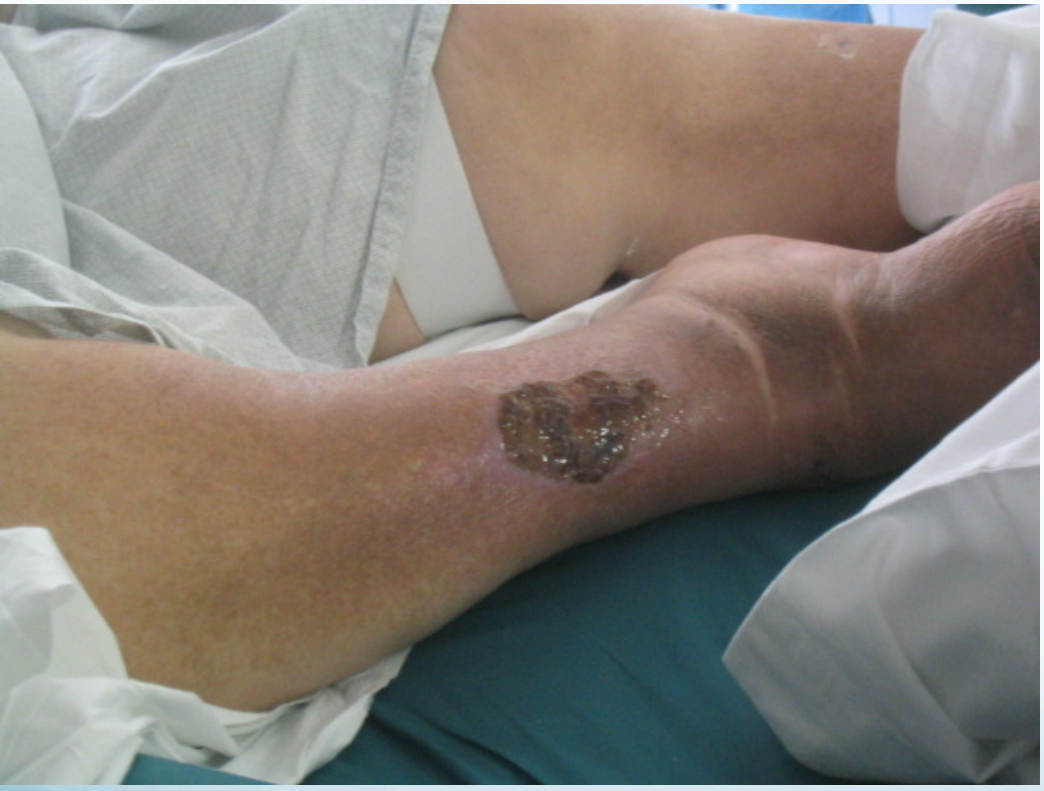
Inotropic therapy

- A trial of dobutamine infusion up to 20 micrograms/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP (grade 1C).
- Not using a strategy to increase cardiac index to predetermined supranormal levels

Corticosteroids

- Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day (grade 2C).
- Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone (grade 2B).
- In treated patients hydrocortisone tapered when vasopressors are no longer required
- Corticosteroids not be administered for the treatment of sepsis in the absence of shock.
- When hydrocortisone is given, use continuous flow

Rapid Identification



- Nursing's role in identifying and helping in the treatment of sepsis is more important than ever before

How do We Identify Sepsis Now?

In absence of biomarkers, must rely on crude physical indicators

New Volume and Tissue Perfusion Elements

TABLE 1

DOCUMENT REASSESSMENT OF VOLUME STATUS AND TISSUE PERFUSION WITH:

EITHER

- Repeat focused exam (after initial fluid resuscitation) by licensed independent practitioner including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings.

OR TWO OF THE FOLLOWING:

- Measure CVP
- Measure $ScvO_2$
- Bedside cardiovascular ultrasound
- Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge

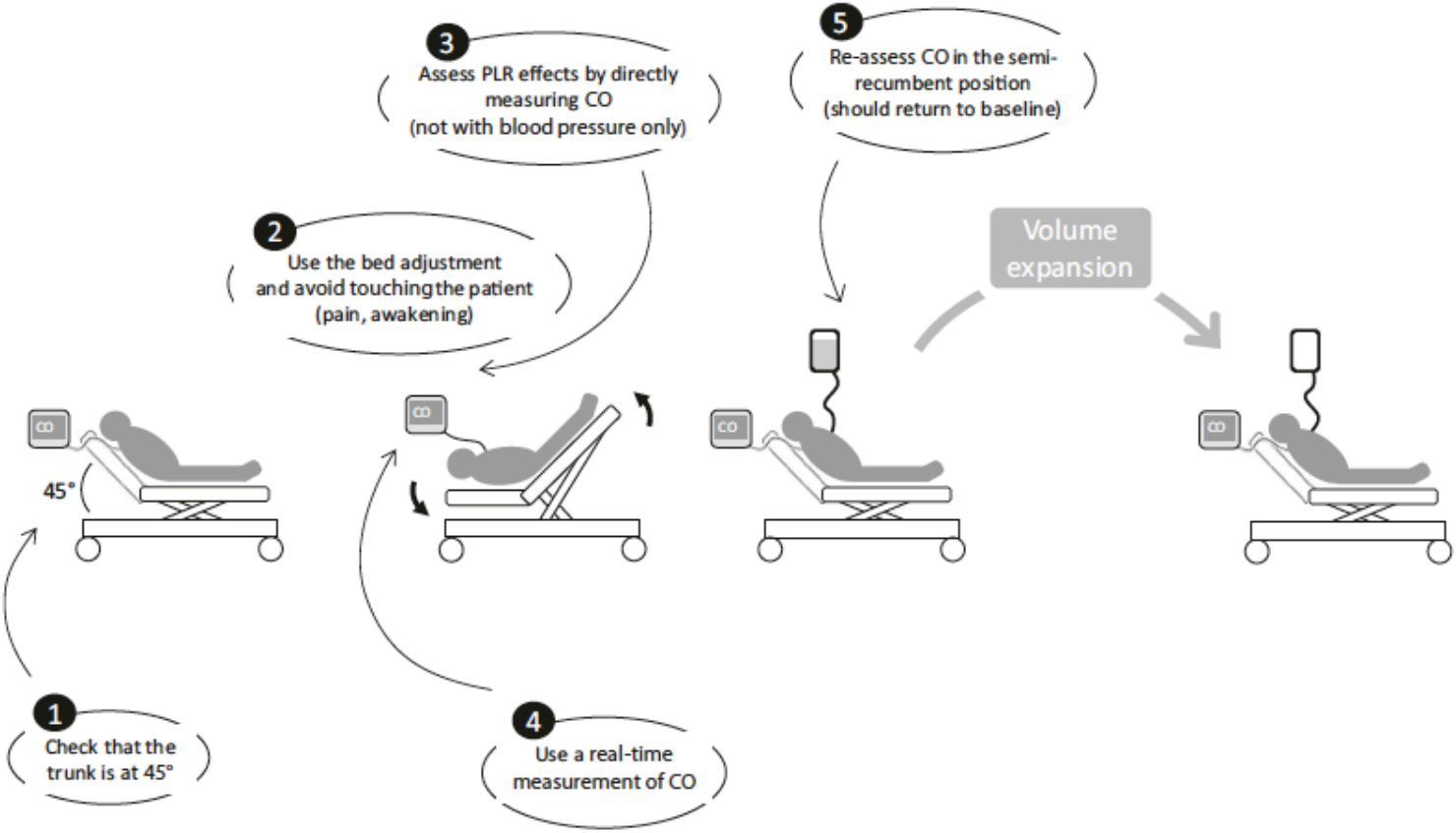


Figure 1 The best method for passive leg raising, indicating the five rules to be followed. CO, cardiac output; PLR, passive leg raising.

Equipment to Evaluate Patient

- Procalcitonin
- Don't take vital signs, take a lactate
  - Point of care
- Evaluation of ventilation
  - Capnography
  - Blood Gases
    - Point of care
- Hemodynamic Assessment
  - Stroke Volume

Evolutionary Basis

- Has bactericidal properties
- Present in all mammals tested
- Probably was an early host defense against infection
- Replaced by more robust defenses such as antibody system and enhanced leukocyte defenses
- Most important, perhaps, in defending the body against invasion of bacteria during feeding.

64

Procalcitonin (PCT) algorithm for stewardship of antibiotic therapy in patients with LRTI

< 0.1 µg/l	0.1 - 0.25 µg/l	>0.25 – 0.5 µg/l	>0.5 µg/l
Bacterial etiology very unlikely	Bacterial etiology unlikely	Bacterial etiology likely	Bacterial etiology very likely
NO antibiotics !	No antibiotics	Antibiotics yes	Antibiotics YES !

Control PCT after 6-24 hours

Initial antibiotics can be considered in case of:

- Respiratory or hemodynamic instability
- Life-threatening comorbidity
- Need for ICU admission
- PCT < 0.1 µg/l: CAP with PSI V or CURB65 >3, COPD with GOLD IV
- PCT < 0.25 µg/l: CAP with PSI ≥IV or CURB65 >2, COPD with GOLD > III
- Localised infection (abscess, empyema), L.pneumophilia
- Compromised host defense (e.g. immuno-suppression other than corticosteroids)
- Concomitant infection in need of antibiotics

Consider the course of PCT

If antibiotics are initiated:

- Repeated measurement of PCT on days 3, 5, 7
- Stop antibiotics using the same cut offs above
- If initial PCT levels are >5-10 µg/l, then stop when 80-90% decrease of peak PCT
- If initial PCT remains high, consider treatment failure (e.g. resistant strain, empyema, ARDS)
- Outpatients: duration of antibiotics according to the last PCT result:
  - >0.25-0.5 µg/l: 3 days
  - >0.5 - 1.0 µg/l: 5 days
  - >1.0 µg/l: 7 days

PCT: procalcitonin, CAP: community-acquired pneumonia, PSI: pneumonia severity index, COPD: chronic obstructive pulmonary disease, GOLD: global initiative for obstructive lung disease

Case 1

- 68 y/o male with h/o CHF, COPD, CAD previously hospitlaized two months ago for exacerbation of COPD. Presents with difficulty breathing, SOB. No chest pain, but has cough with clear to yellow sputum. ABG in ED 7.11/76/91 BNP 1301 Trop < .03 WBC 18,000, 0 Bands.

Case 1

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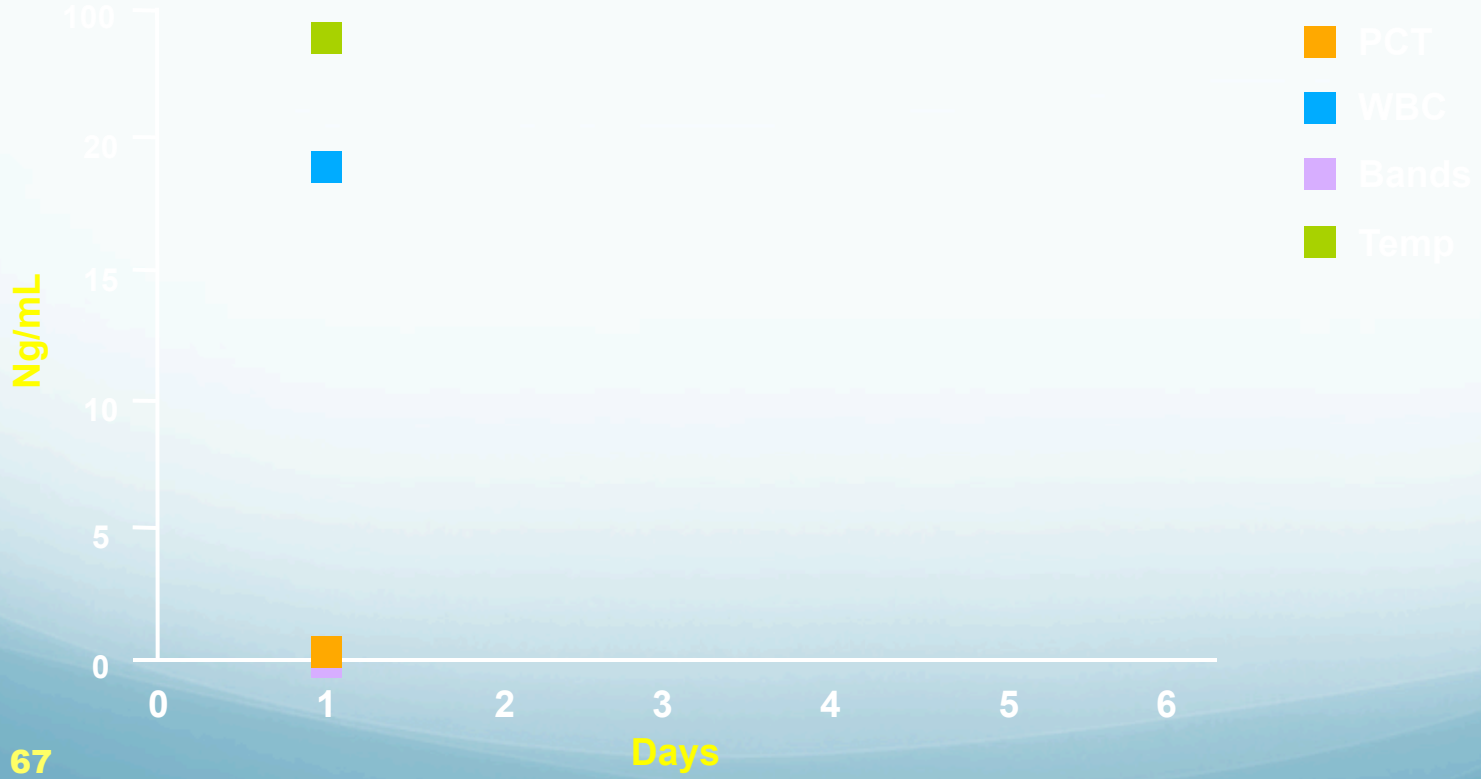

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Case 1

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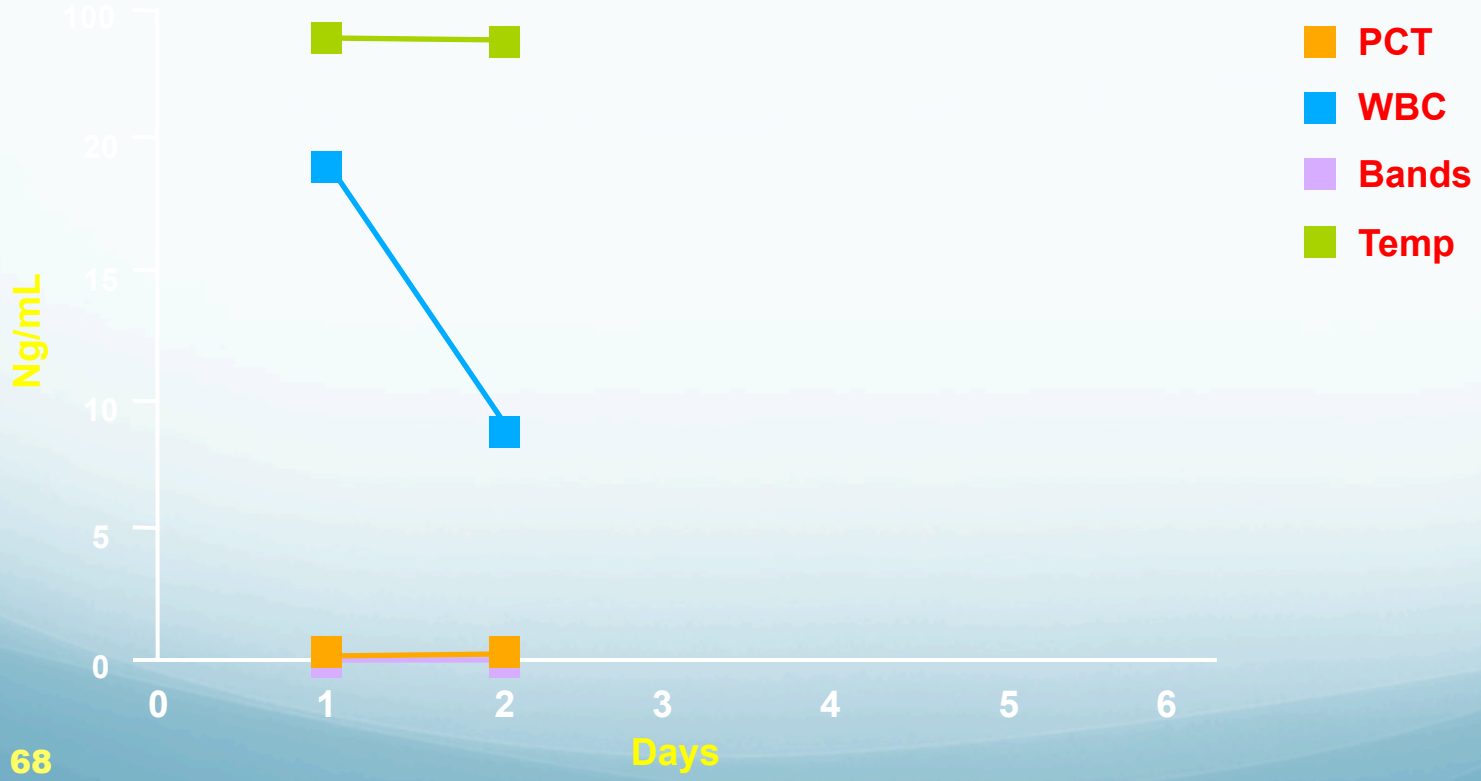

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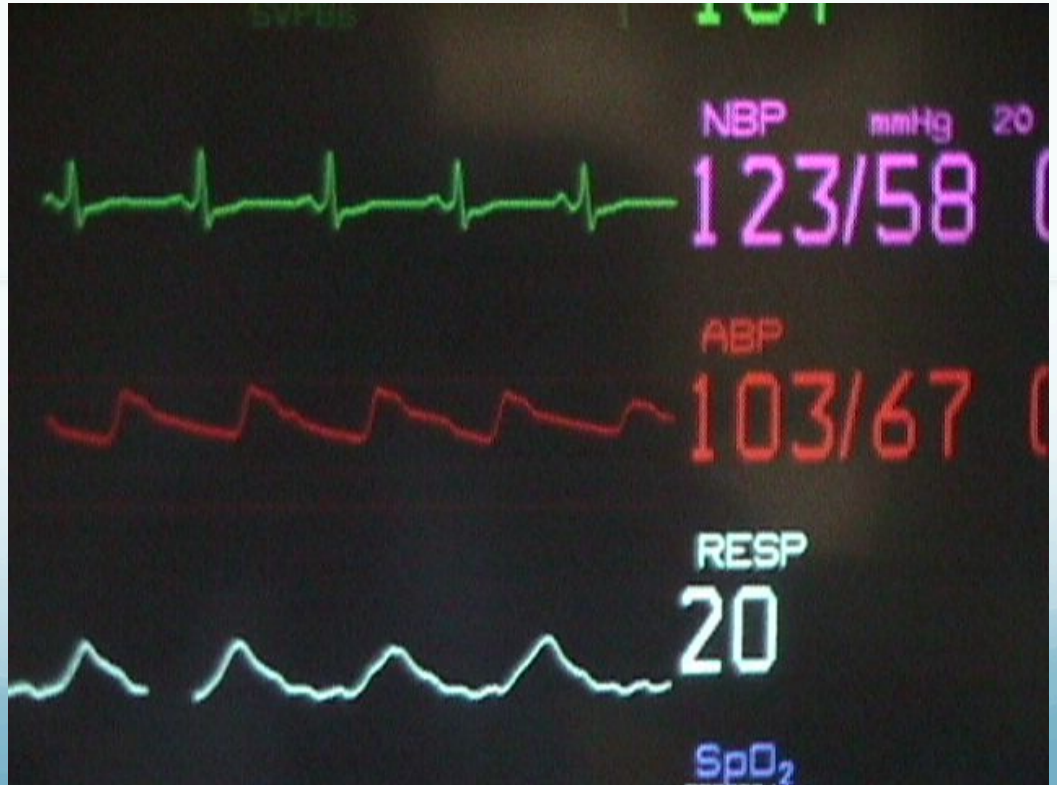
Blood Pressure and Blood Flow

Do they equal each other?



What Type of Hemodynamic Monitoring?

- CVP and PAOP should never be used in isolation
  - Inconsistent in revealing information about volume and flow
  - *Marik et al. Based on the results of our systematic review, we believe that CVP should no longer be routinely measured in the ICU, operating room, or emergency department.*

Marik P, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A Systematic Review ofthe Literature and the Tale of Seven Mares. Chest 2008;134;172-178

Temporal order of events

(each event can take minutes to hours)

1. Stroke volume falls
   - Heart rate compensates to keep cardiac output normal
     - Many reasons for heart rate to increase
2. Cardiac output falls
   - Heart rate compensation fails
   - Vasoconstriction (increase in SVR), BP remains unchanged
3. Increased oxygen extraction of hemoglobin
   - Peripheral initially (StO_2)
   - Central later ($ScvO_2$)
4. Blood pressure, urine output change

Evidence (8 RCTs) of Using SV as Endpoint

- Chytra I, Pradl R, Bosman R, Pelnar P, Kasal, Zidkova A. Esophageal Doppler-guided fluid management decreases blood lactate levels in multiple-trauma patients: a randomized controlled trial. Critical Care 2007 Feb 22;11(1):1-9.

- Conway DH, Mayall R, Abdul-Latif MS, Gilligan S, Tackaberry C. Randomized controlled trial investigating the influence of intravenous fluid titration using esophageal Doppler monitoring during bowel surgery. Anesthesia 2002 Sept;57(9):845-849.

- Gan TJ, Soppitt A, Maroof M, El-Moalem H, Robertson K, Moretti E, Dwane P, Glass PS. Goal-directed intra-operative fluid administration reduces length of hospital stay after major surgery. Anesthesiology 2002;97:820-826.

- Mark JB, Steinbrook RA, Gugino LD, et al. Continuous noninvasive monitoring of cardiac output with esophageal Doppler during cardiac surgery. Anesth Anlg 1986;61:1013-1020. (NON RCT)

- McKendry M, McGloin H, Saberi D, Caudwell L, Brady AR, Singer M. Randomized controlled trial assessing the impact of a nurse delivered, flow monitored protocol for optimization of circulatory status after cardiac surgery. BMJ 2004;329(7460):258 (31 July), doi:10.1136/bmj.38156.767118.7C.

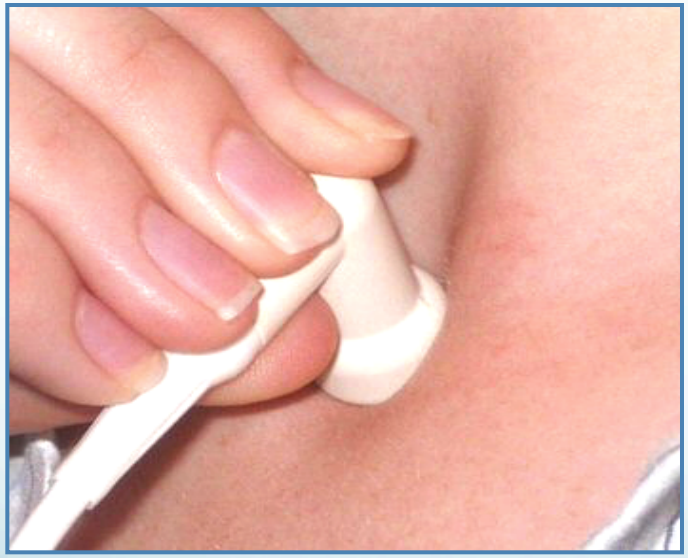
- Mythen MG, Webb AR. Peri-operative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. Archives of Surgery 1995;130:423-429.

Methods of Measuring SV

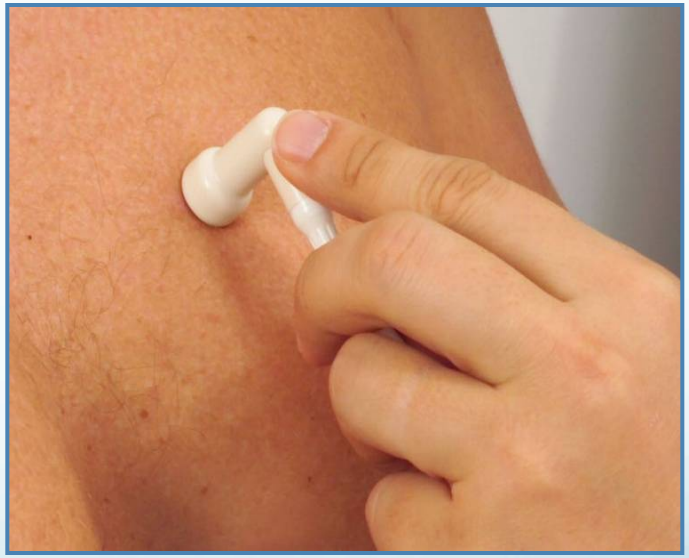
	Uses	Ease of use	Accuracy	Reimbursed
Doppler – USCOM	Anywhere	Good	Good	–
Doppler (EDM)	OR, ICU	Excellent	Excellent	$$$
ECON	OR, ICU	Good	Fair	–
Bioimpedance	Anywhere	Good	Fair	$
Pulse contour (FloTrac, LiddCo, PICCO)	OR, ICU	Difficult	Fair	–
NICO	OR, ICU	Difficult	Fair	–
PAC	OR, ICU	Difficult	Good	$$
Bioreactance	OR, ICU	Good	Good	–

Non Invasive Doppler Measurement of Blood Flow

Allows Both Left & Right Heart Measurement



AORTIC ACCESS

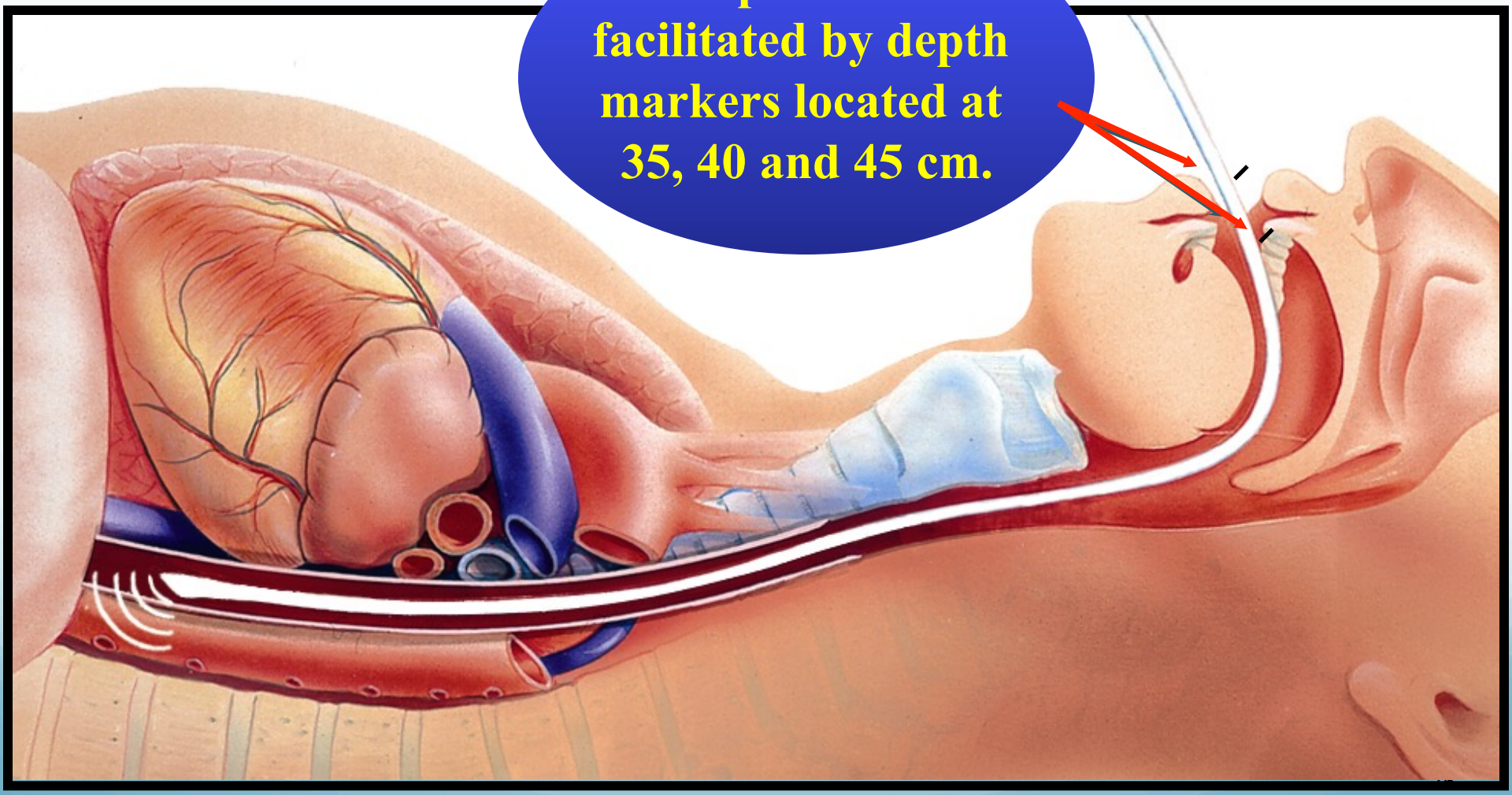


PULMONARY ACCESS

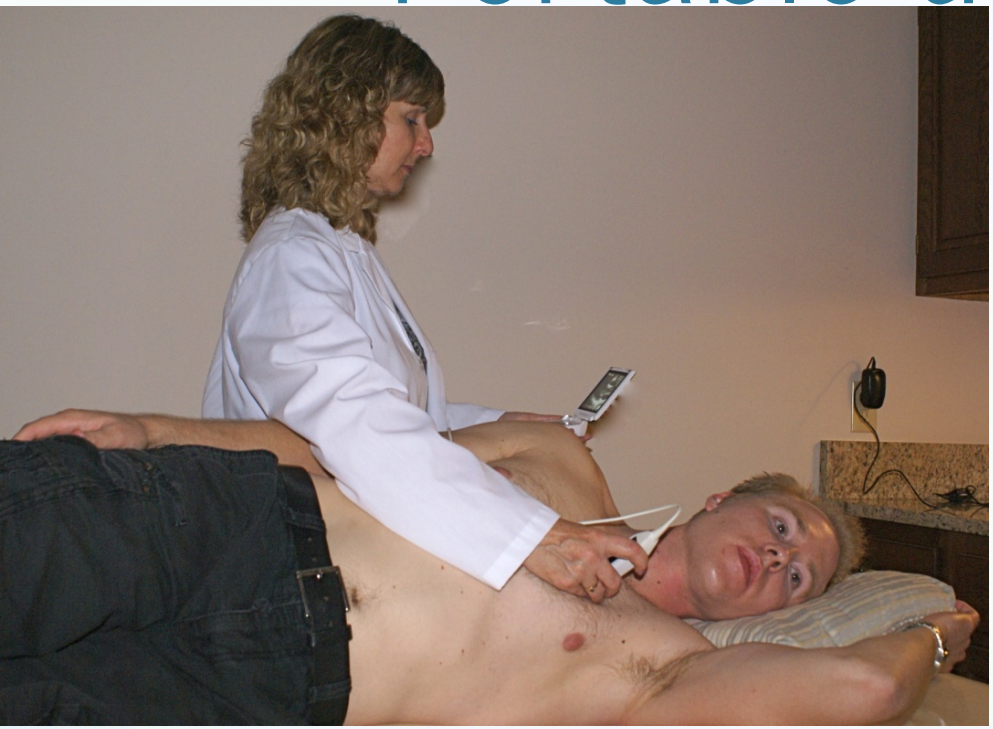
Why are we not measuring SV??

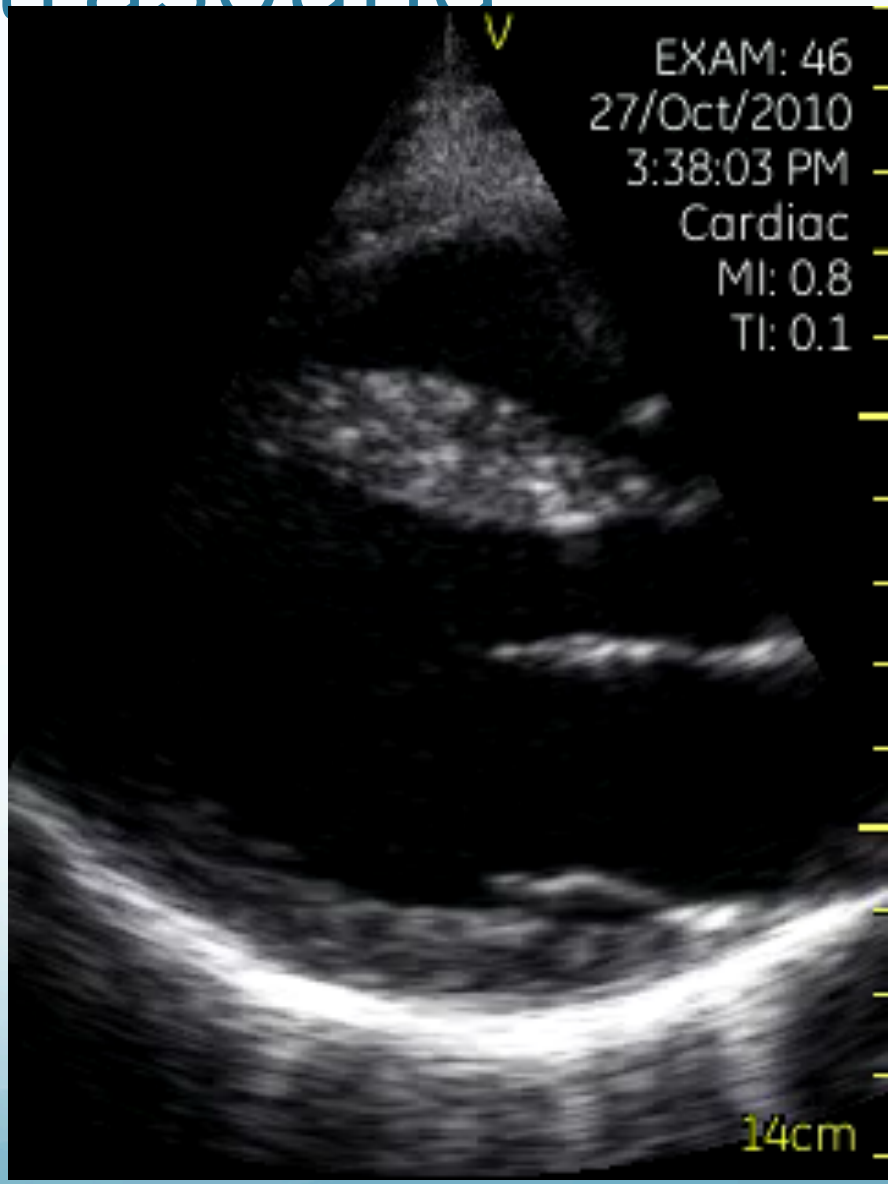
Probe Placement

Probe placement is facilitated by depth markers located at 35, 40 and 45 cm.

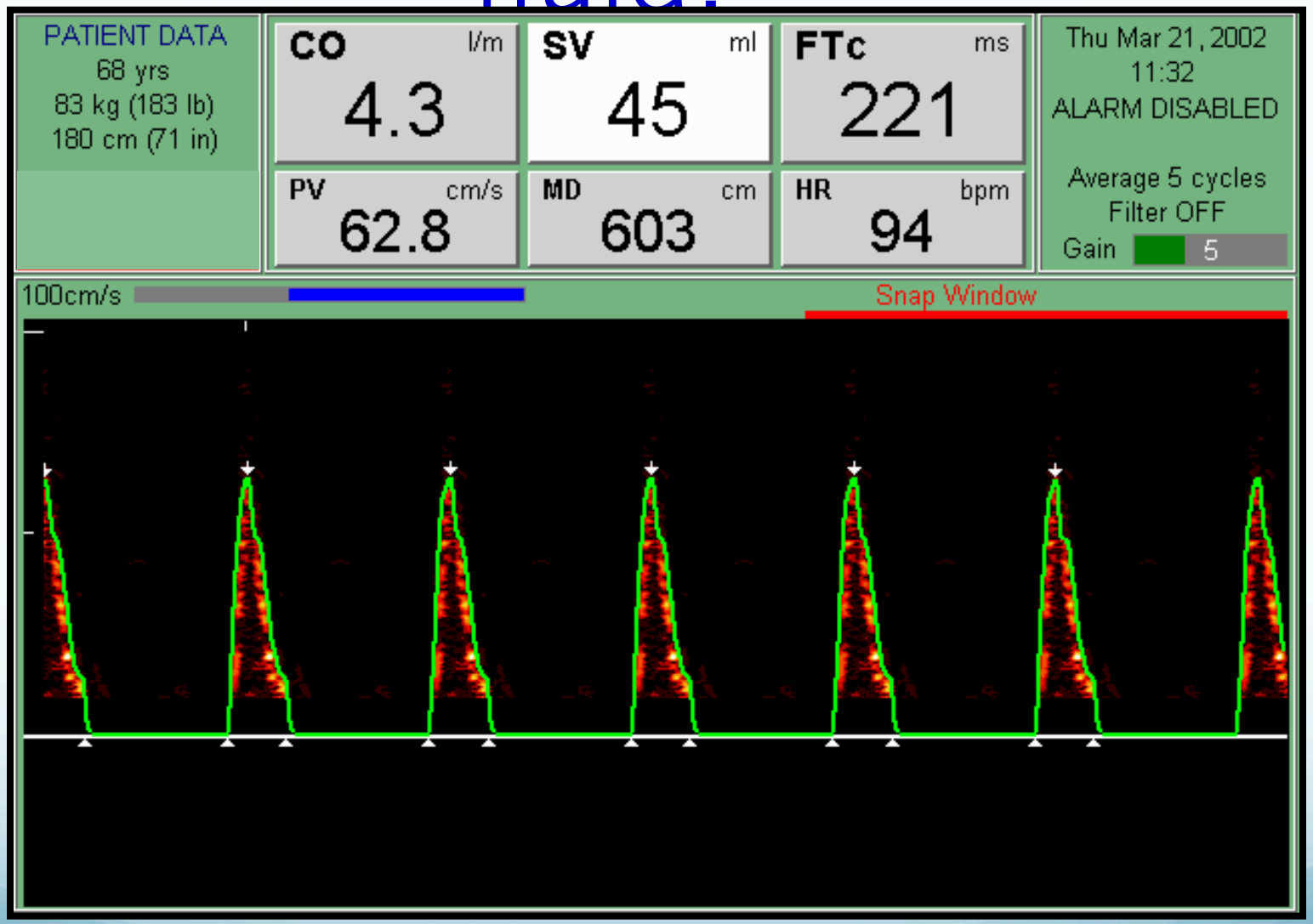


Portable ultrasound

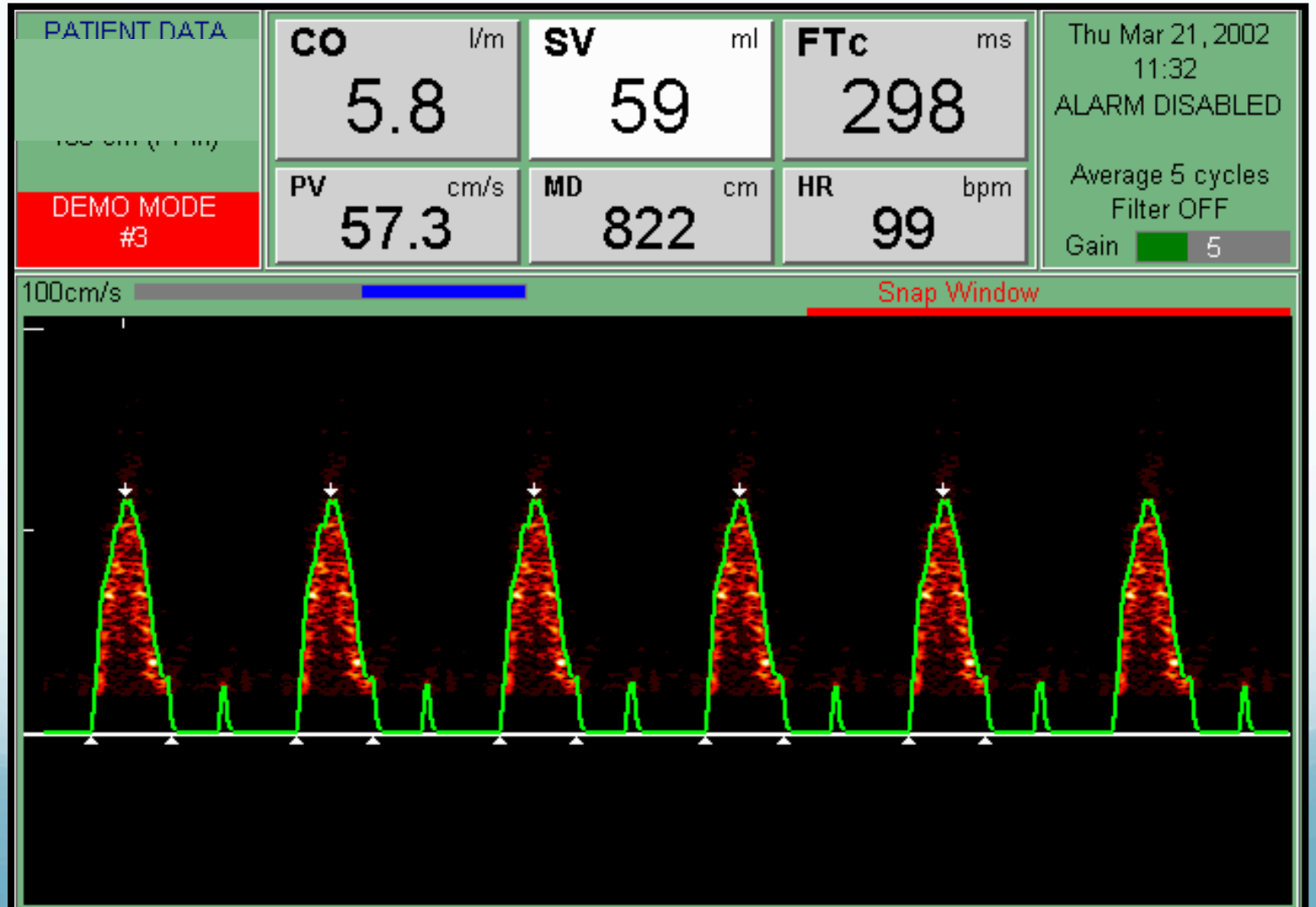




Does this patient need fluid?



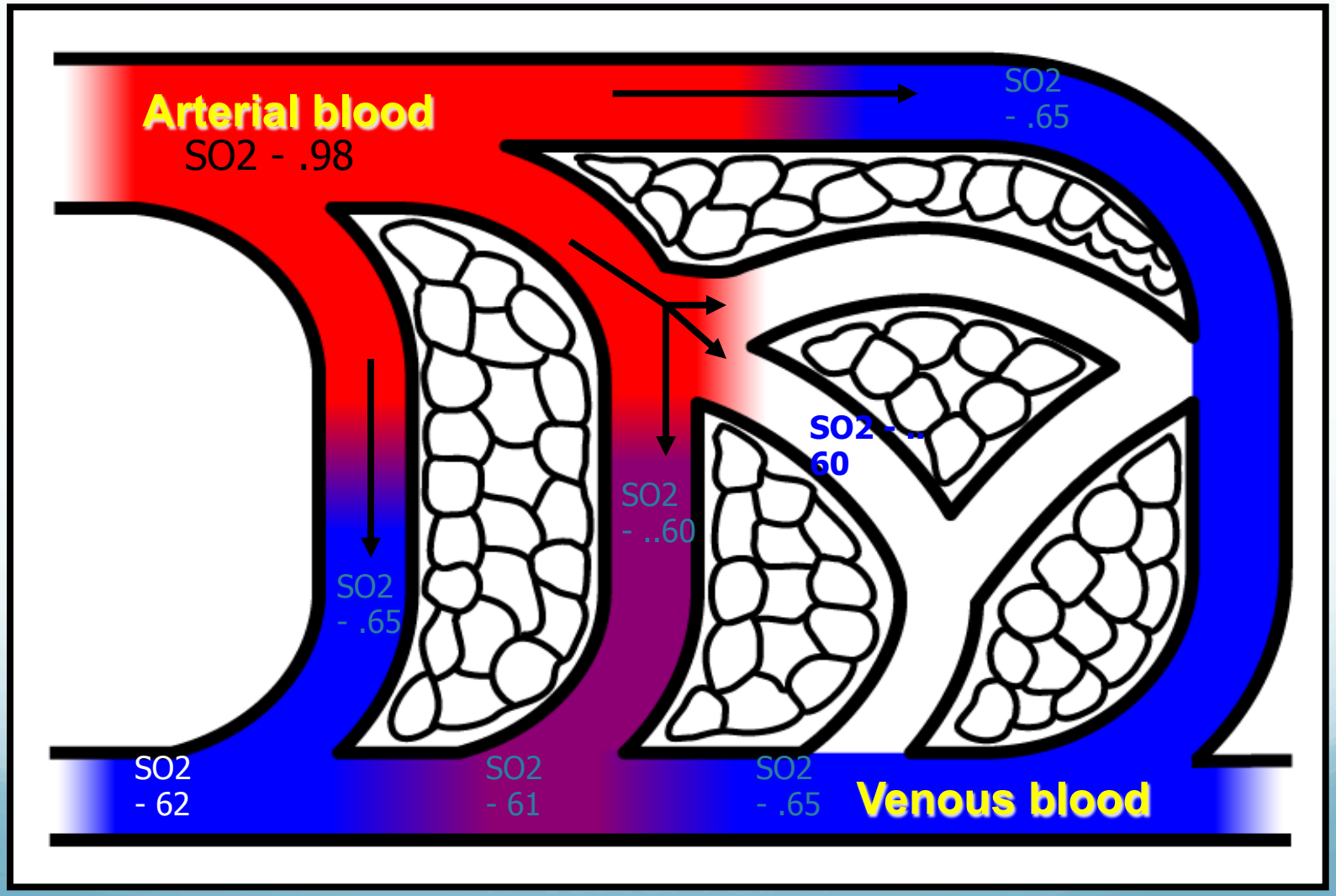
Response to fluid bolus – need more fluid or stop?



Any Change in Blood Flow (CO) Should be Compared against an Oxygenation End Point

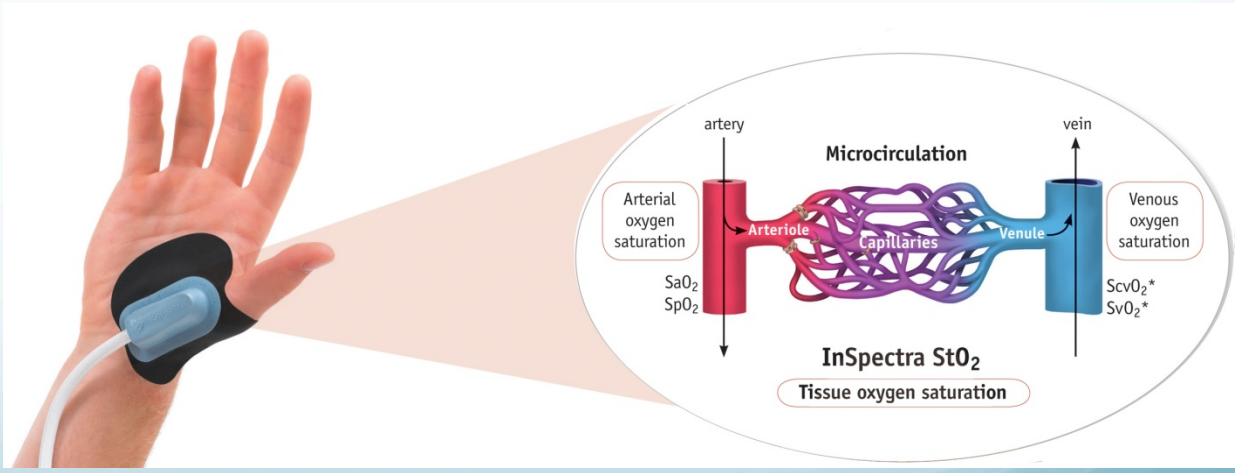
ScvO2 or StO2

Macrocirculation vs Regional Blood Flow

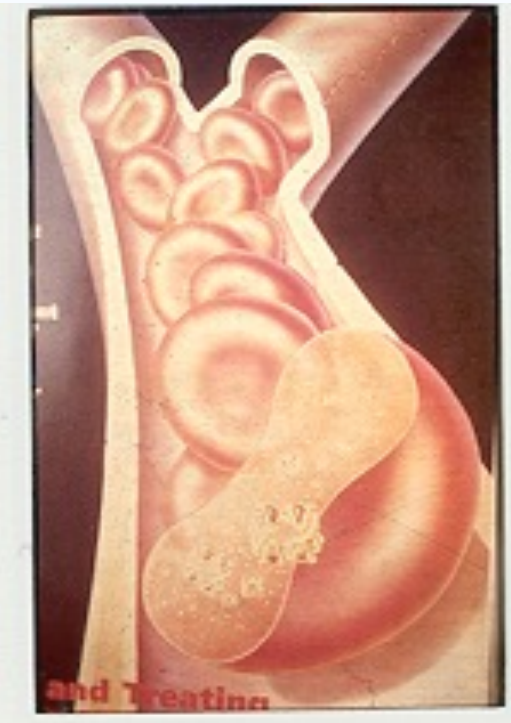


Tissue Oxygenation End Points

- ScvO2 – > 70%
- StO2 – > 75%
- Titration of drugs can occur against these values



Lactate as a easy, early marker for hypoxia



Needs to be repeated to evaluate condition or treatment

Don't take Vital Signs – Take a Lactate

Lactate Levels and Systolic Blood Pressure (SBP)

Lactate (N=530)	<2 (N=219)	2-4 (N=177)	>4 (N=104)
SBP >90	158/219 (72%)	116/177 (65%)	64/104 (62%)
SBP <90	61/219 (28%)	61/177 (34%)	40/104 (38%)

Sepsis: 1991 ACCP / SCCM Definitions

- Infection
  - Inflammatory response to microorganisms, or
  - Invasion of normally sterile tissues
- Systemic Inflammatory Response Syndrome (SIRS)
  - **Two or more of the following**:
    - Core temperature >38°C or <36°C (>100.4°F or <96.8°F)
    - Elevated heart rate (>90 beats/min)
    - Respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg or mechanical ventilation for acute respiratory process
    - WBC count >12,000/mm^3 or <4,000/mm^3 or >10% immature neutrophils

Bone RC, et al. *Chest* 1992;101:1644-55.

Sepsis: 1991 ACCP / SCCM Definitions (cont)

- Sepsis
  - Known or suspected infection, plus
  - ≥2 SIRS criteria
- **Severe Sepsis**
  - **Sepsis plus**
  - **≥1 organ dysfunction**
- Septic Shock
  - Sepsis with
  - Hypotension despite fluid resuscitation, and
  - Perfusion abnormalities

Bone RC, et al. *Chest* 1992;101:1644-55.

New Definitions

Sequential Organ Failure Assessment

SOFA Scores

Method of Predicting Outcomes in Critically Ill Patients

- An initial SOFA score of < 9 predicted a mortality of < 33%
- A SOFA > 11 predicted mortality of 95%

Respiratory

PaO2/FiO2 (mm Hg)	
<400	1
<300	2
<200 and on mechanical ventilation	3
< 100 and on mechanical ventilation	4

Nervous System

Glasgow Coma Scale	SOFA Score
13-14	1
10-12	2
6-9	3
<6	4

Cardiovascular System

Mean Arterial Pressure (MAP) OR Administration of Vasopressors Required	SOFA
MAP < 70 mm Hg	1
Dopamine <= 5 mcg/kg/min or Dobutamine mcg/kg/min (any dose)	2
Dopamine > 5 OR epi <= 0.1 OR Norepinephrine <= 0.1	3
Dopamine > 15 mcg/kg/min OR epi > 0.1 OR Norepinephrine > 0.1	4

Liver

Bilirubin (mg/dl)	SOFA
1.2-1.9	1
2-5.9	2
6 – 11.9	3
> 12	4

Coagulation

Platelets	SOFA
<150,000	1
<100,000	2
<50,000	3
<20,000	4

Renal

Creatinine	SOFA
1.2-1.9	1
2-3.4	2
3.5-4.9	3
>5	4

qSOFA

- RR > 22
- SBP < 100 mm Hg
- Change in LOC

New Sepsis Definition qSOFA

- An alteration in mental status (not the GCS)
- A decrease in SBP of less than 100 mm Hg
- A respiratory rate > 22 bpm

Key Differences in New Definition

- Sepsis as infection and 2 or more SIRS is now just an infection
- Severe sepsis is now sepsis
- Septic shock is
  - Blood lactate > 2 mmol/L despite volume resuscitation
  - Hypotension that persists after fluid resuscitation and requires vasopressors
- Sepsis definition now will carry a higher risk of death and increased ICU LOS

Rationale for New Definition

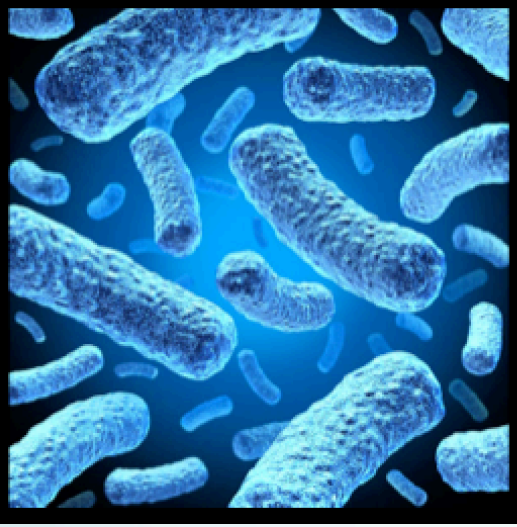
- Based on review of 2 million patients in sepsis studies
- SIRS based on expert opinion
- SIRS should still be used when evaluating sepsis

The resuscitation challenge

So what's all the hoopla?

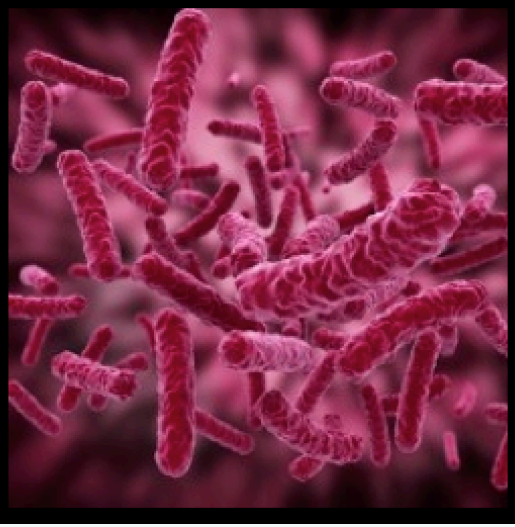
The Sepsis Trilogy

ProCESS



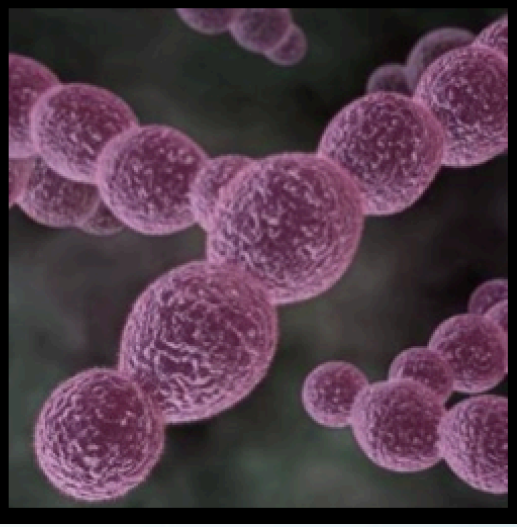
Protocolized Care for Early Septic Shock (ProCESS) – 31 ED's in US

ARISE



Australasian Resuscitation in Sepsis Evaluation (ARISE) – 51 ED's in Australia, New Zealand, Finland, Hong Kong, Ireland

ProMISe



The Protocolised Management in Sepsis (ProMISe) Trial – 56 ED's in the UK

Dr Salim Rezaie Clinical Assistant Professor of EM and IM at UTHSCSA

ProMise, ProCess and ARISE Trials

- Key points
  - Fluid administration similar in both control and experimental groups
  - Vasopressor use similar in both groups
  - Antibiotics administered similarly in both groups
  - Lactates obtained in both groups
  - Mortality rates (<20%) is not as common outside centers with well designed sepsis recognition/ management programs
- Problems– Antibiotics and fluids given in both control and experimental groups within 3 hours.
  - Hawthorne Effect Likely
    - Contamination of practice

Take away Points

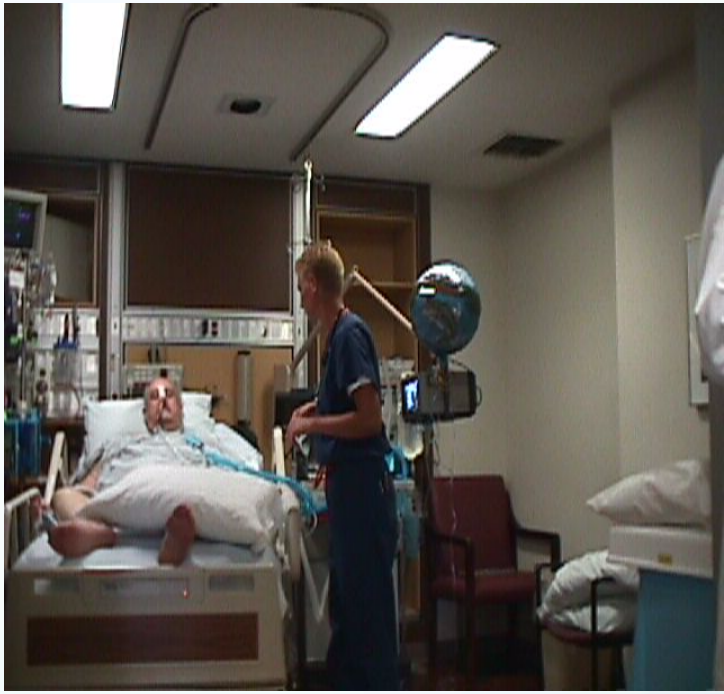
- If Patients are
  - identified early,
  - Receive antibiotics EARLY
  - receive IVF EARLY
- Then ScvO2 and CVP monitoring does not seem to add a benefit
- BUT EGDT with ScvO2 not really tested since resuscitation had already occurred

Types of Fluids

- Is normal saline normal?
- Lactated Ringers vs normal saline – are they comparable?

Setting Goals

- Discuss goals of care and prognosis with patients and families (grade 1B).
  - Sepsis has a high mortality rate. Families should understand and recognize that determining what the patient's wishes are may help dictate the aggressiveness of therapy



- Incorporate goals of care into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (grade 1B).
- Address goals of care as early as feasible, but no later than within 72 hours of ICU admission (grade 2C)

Implementing Sepsis Protocols

Benefits and Barriers

- Improved
  - Patient identification
    - Coding and reimbursement
    - SOI/ROM
  - Reduced mortality
  - Improved compliance with bundles
- Barriers
  - Multidisciplinary cooperation
  - Funding
  - Education

Where are we at from a National Public Health standpoint

- NYS: Rory's Regulation, you can look up the data dictionary to see what is being collected
- NQF: CMS – Public reporting, some time in 2016
- CDC – sepsis page: url: http://www.cdc.gov/sepsis/
- Staunton Foundation: url: http://rorystaunton.com/

JC Sepsis Designated Centers (late 2014)

Orange Park Medical Center	Orange Park	FL
Memorial Healthcare	Jacksonville	FL
Specialty Hospital Jacksonville	Jacksonville	FL
Grand Strand Medical Center	Myrtle Beach	SC
Colleton Medical Center	Walterboro	SC
Trident Medical Center	Charleston	SC
Mercy Health Youngstown	Youngstown	OH

Sepsis Funding by the NIH

	New Cases	Deaths	NIH $ (million) (yr)
Breast Ca	232620 (2010)	39,520 (2010)	$712 (2011)
Colorectal Ca	141210 (2010)	49,380 (2010)	$313 (2011)
Lung Ca	221130 (2010)	156,940 (2010)	$221 (2011)
Pancreatic Ca	44030 (2010)	37,600 (2010)	$113 (2011)
HIV/AIDS	~50000 (2011)	7,638 (2011)	$3,059 (2011)
Anthrax	0	0	$87 (2011)
Sepsis (Iwashyna, 2008)	1,000,000 (2008)	348,000 (2008)	$43 (2008)

Summary

- Recognize Sepsis Early
- Treatments quickly
  - Lactate
  - Cultures or remove source of infection
  - Antibiotics
  - Fluids
    - Pressors
    - Steroids
  - EOL discussion

Contact information

docacknp@gmail.com

@mhackerman

tsa2109@bjc.org