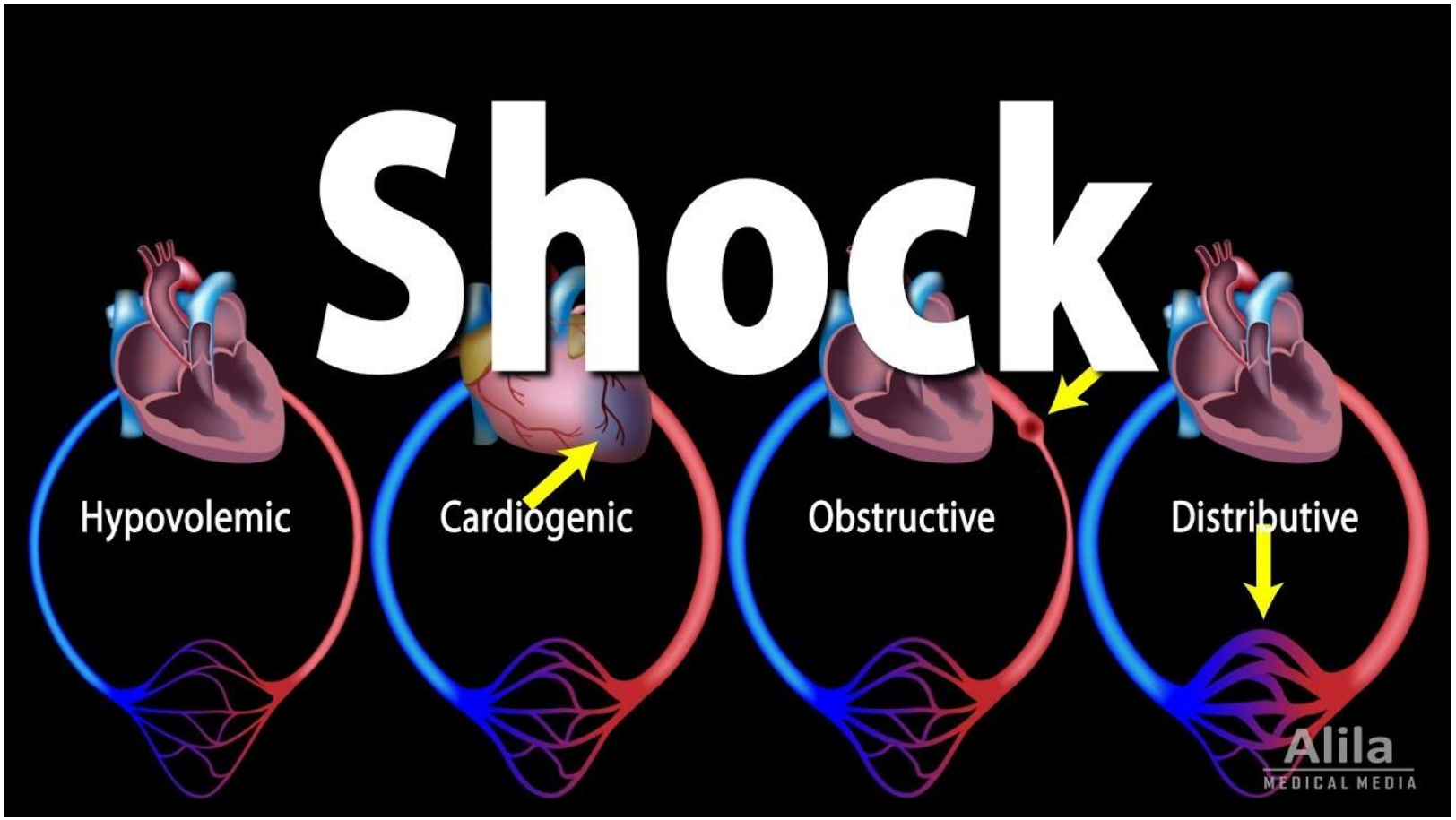


AFC

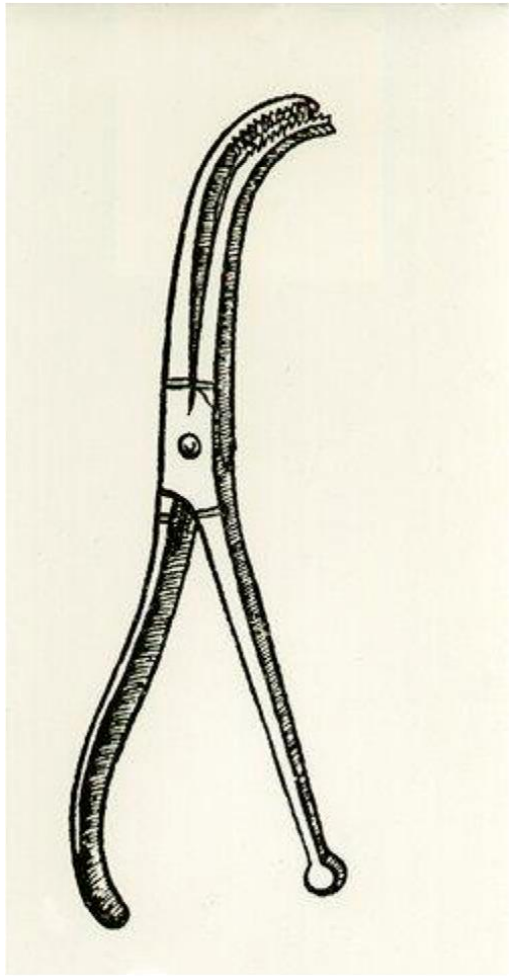
Ashraf Al-Faouri MD, MRCS, FACS

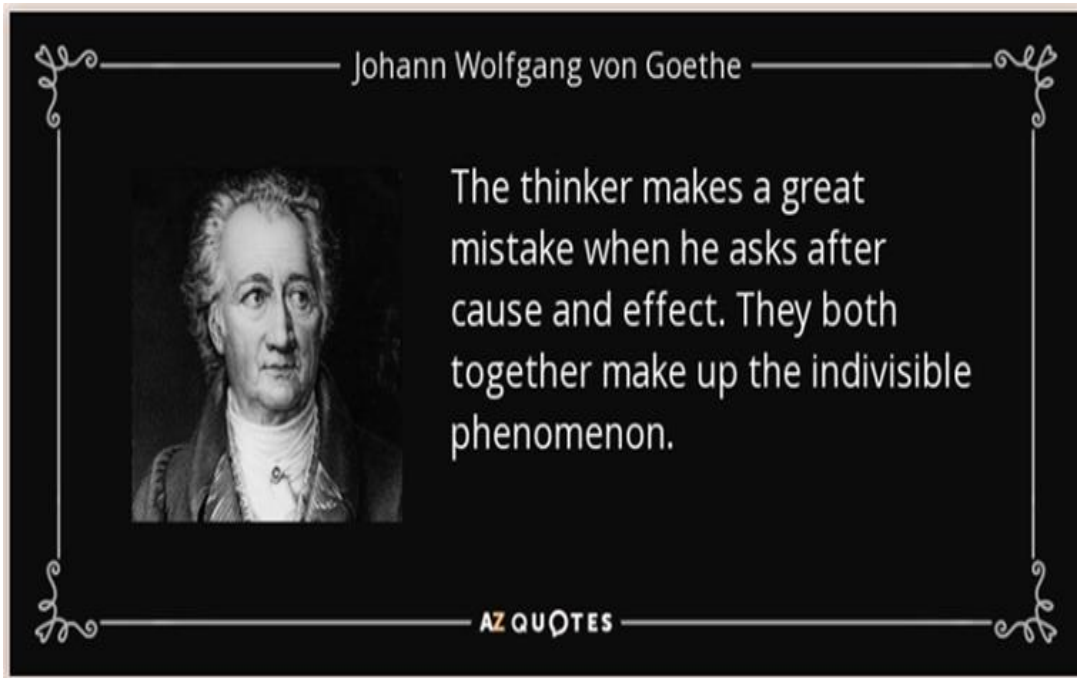
Consultant HBPS & Liver Transplantation

HISTORY

Ambroise Paré (1517-1590): Circulatory failure

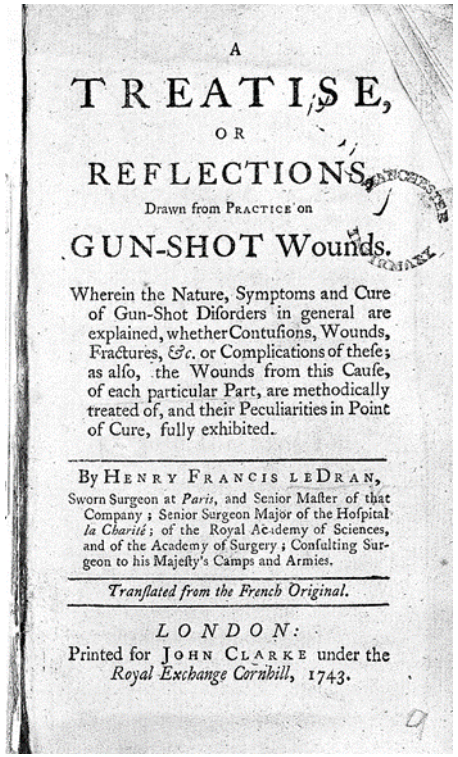
Je le pansai, Dieu le guérit ("I bandaged him and God healed him").





HISTORY

Henri François Le Dran (1685-1770):
Choc **is a bodily reaction to Missile**



A

TREATISE,

OR

REFLECTIONS,

Drawn from Practice on

GUN-SHOT Wounds.

Wherein the Nature, Symptoms and Cure of Gun-Shot Diſorders in general are explained, whether Contuſions, Wounds, Fractures, &c. or Complications of theſe; as alſo, the Wounds from this Cauſe, of each particular Part, are methodically treated of, and their Peculiarities in Point of Cure, fully exhibited.

By HENRY FRANCIS LEDRAN,

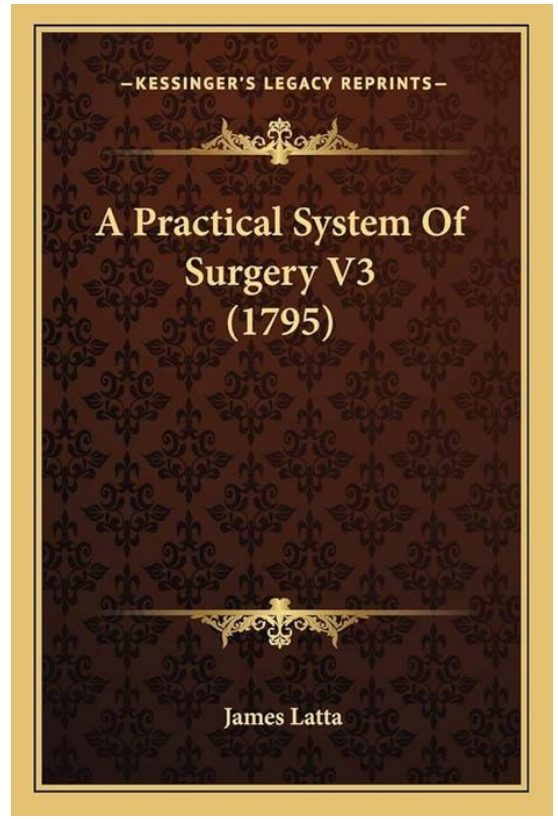
Sworn Surgeon at *Paris*, and Senior Maſter of that Company; Senior Surgeon Major of the Hoſpital *la Charité*; of the Royal Academy of Sciences, and of the Academy of Surgery; Conſulting Surgeon to his Majeſty's Camps and Armies.

Tranſlated from the French Original.

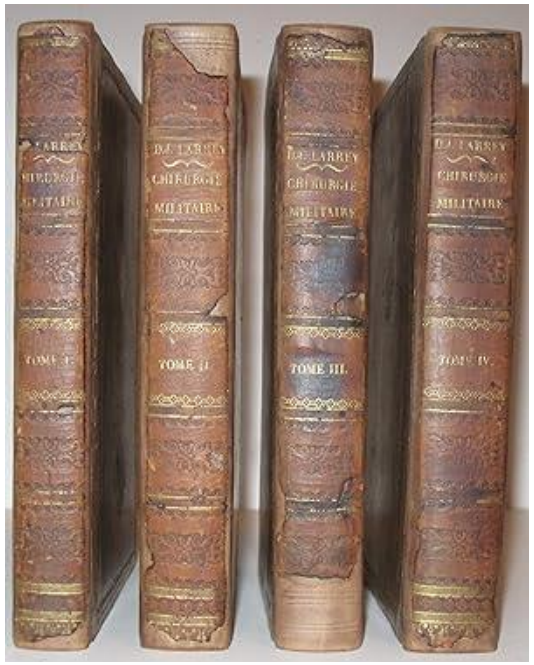
LONDON:

Printed for JOHN CLARKE under the *Royal Exchange Cornhill*, 1743.

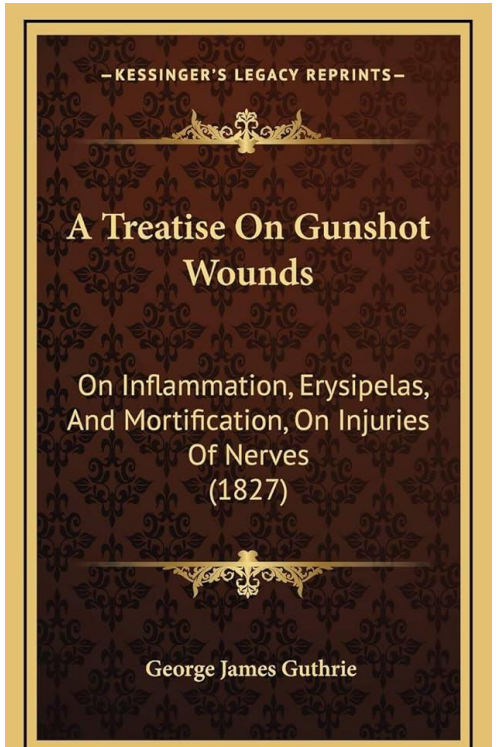
James Latta 1795 (*Shock* in English literature)



Dominique Jean Larrey(1766 –1842): Mémoires de chirurgie militaire

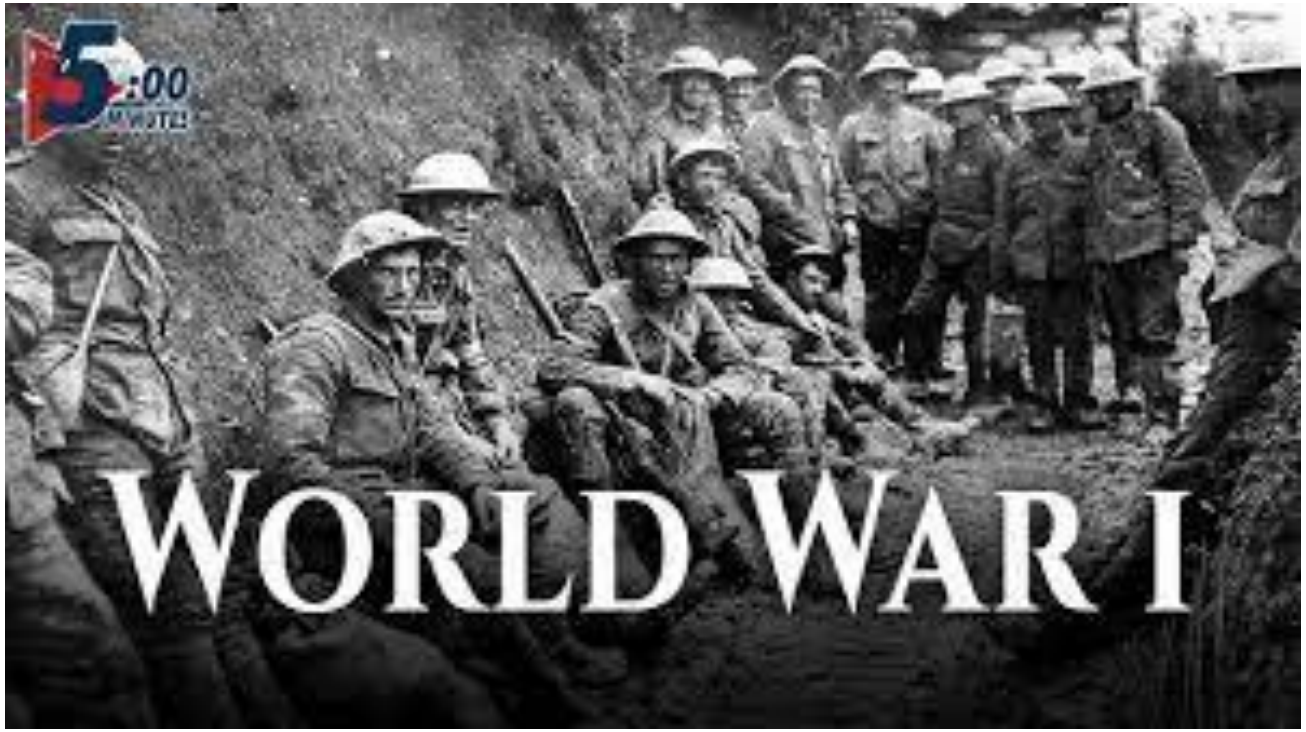


George James Guthrie (1785 - 1856)

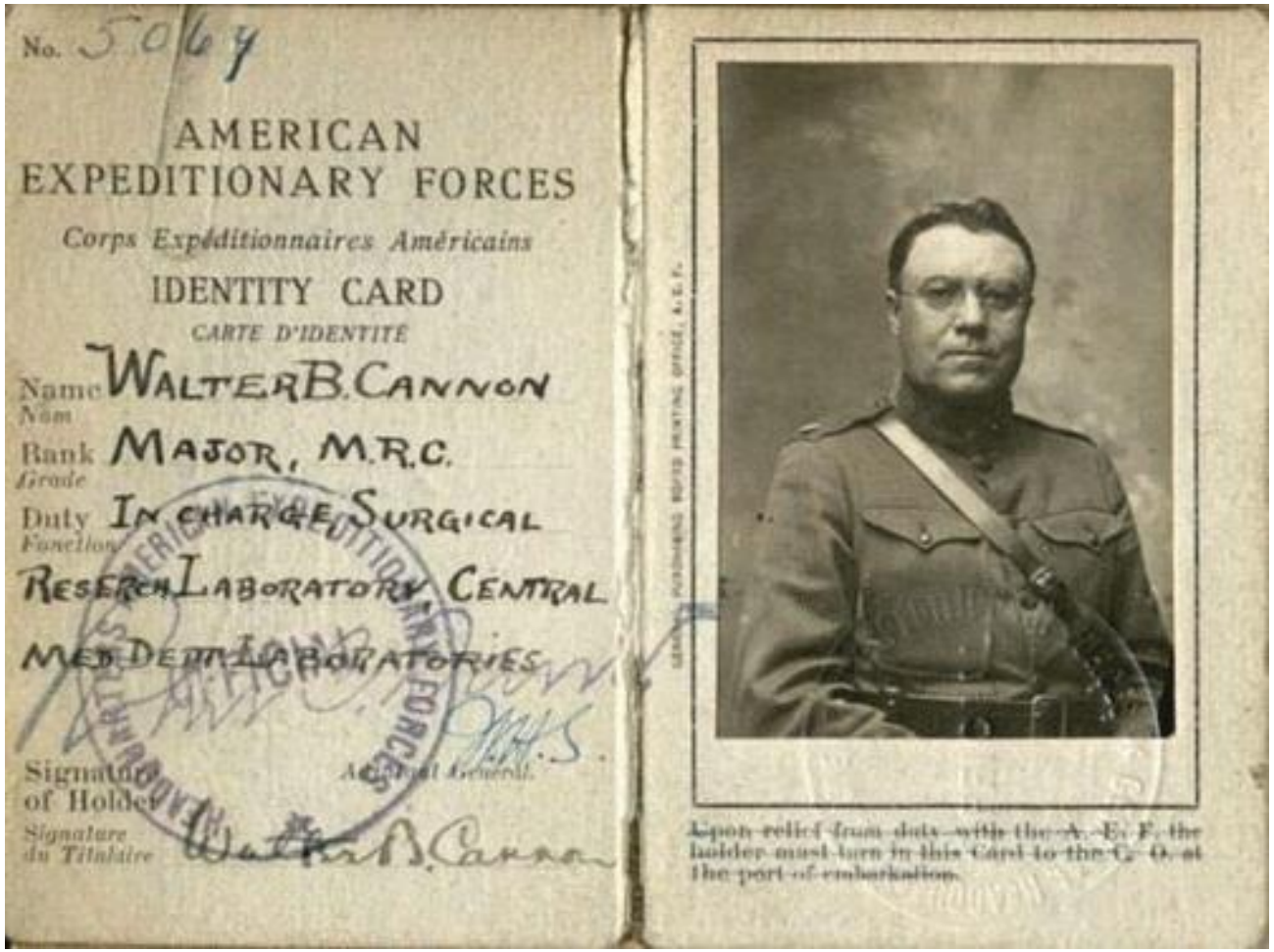


HISTORY

- George Crile 1899 (Vasomotor paralysis)
- Mapother 1879 (Vasoconstriction in shock)
- Malcom 1905 (Vasoconstrictor theory of shock)
- Bainbridge and Trevan (1917) noted the shock-producing properties of adrenaline in animals and recognized that depletion of blood volume was a basic mechanism in shock.
- Erlanger and Gasser (1919) suggested that an increased blood adrenaline level was a causative factor in shock



HISTORY



No. 5064

AMERICAN
EXPEDITIONARY FORCES

Corps Expéditionnaires Américains

IDENTITY CARD

CARTE D'IDENTITÉ

Name *Nom* WALTER B. CANNON

Rank *Grade* MAJOR, M.R.C.

Duty *Fonction* IN CHARGE SURGICAL RESEARCH LABORATORY, CENTRAL MED. DEPT. LABORATORIES

Signature of Holder *Signature du Titulaire* Walter B. Cannon

Adjutant General's

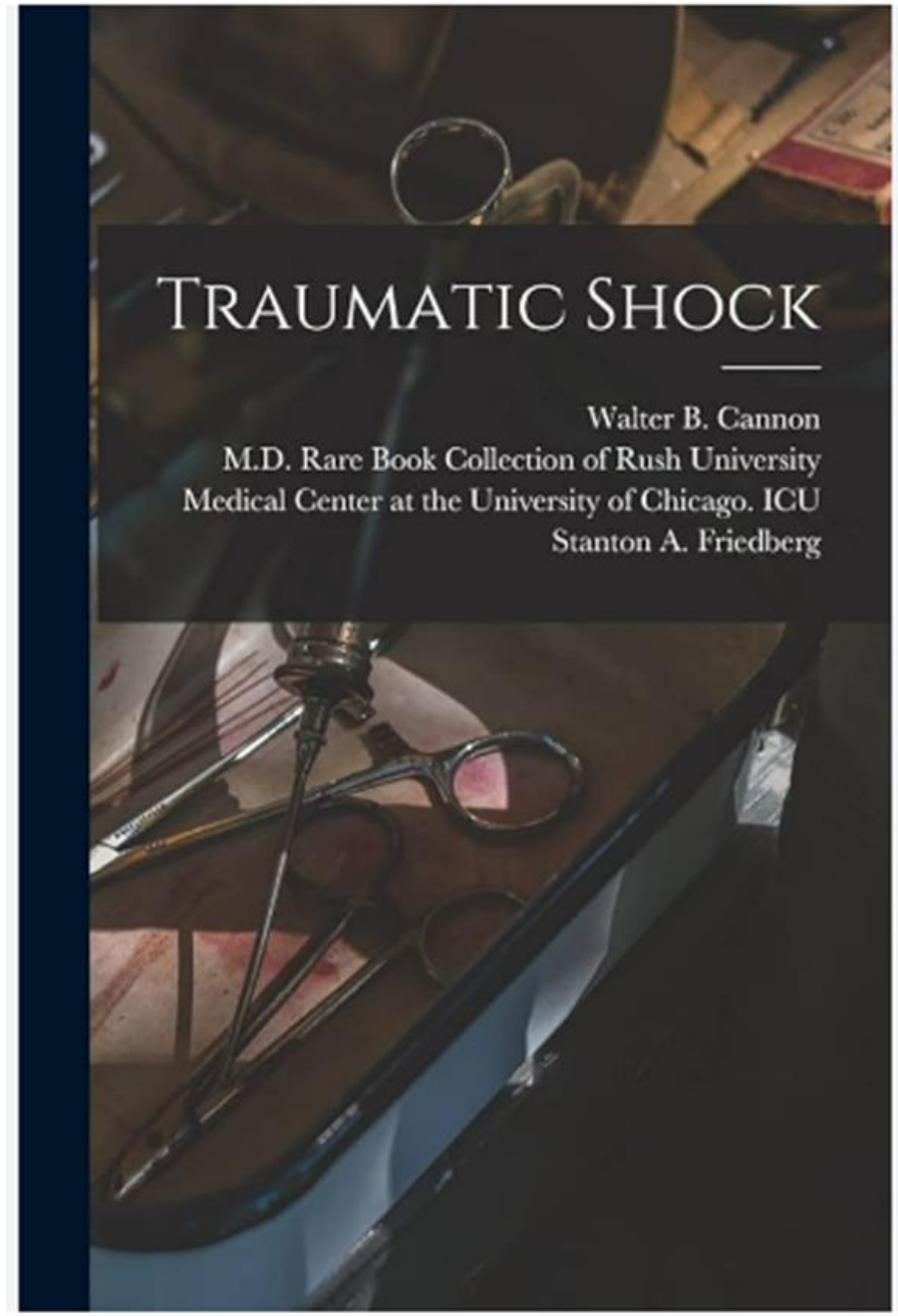
Upon relief from duty with the A. E. F. the holder must turn in this Card to the C. O. at the port of embarkation.

WALTER B. CANNON: PHYSIOLOGIC INVESTIGATOR

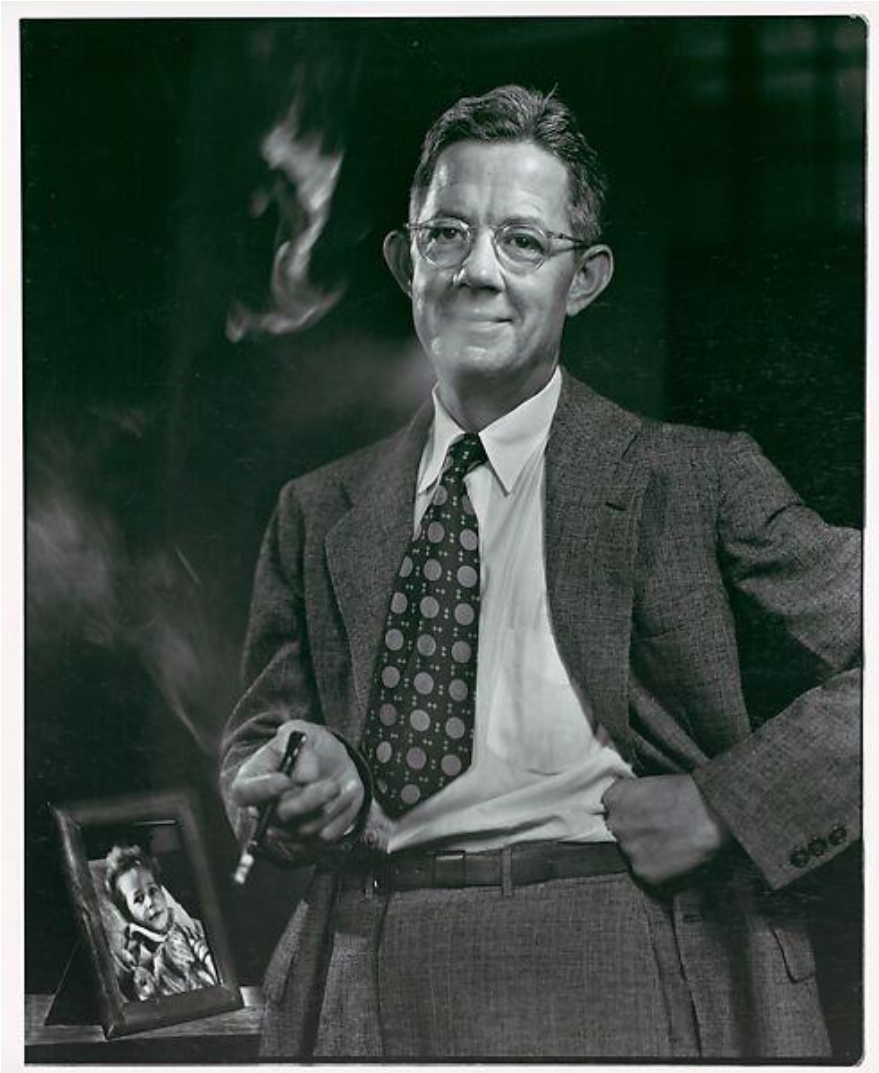
While a student at Harvard Medical School, Boston, in 1896, Walter B. Cannon (1871-1945), used newly discovered x-rays and opaque meals to study activities of digestive organs in animals. Professor Cannon's lifetime of research on physiologic processes contributed much new knowledge to medicine.

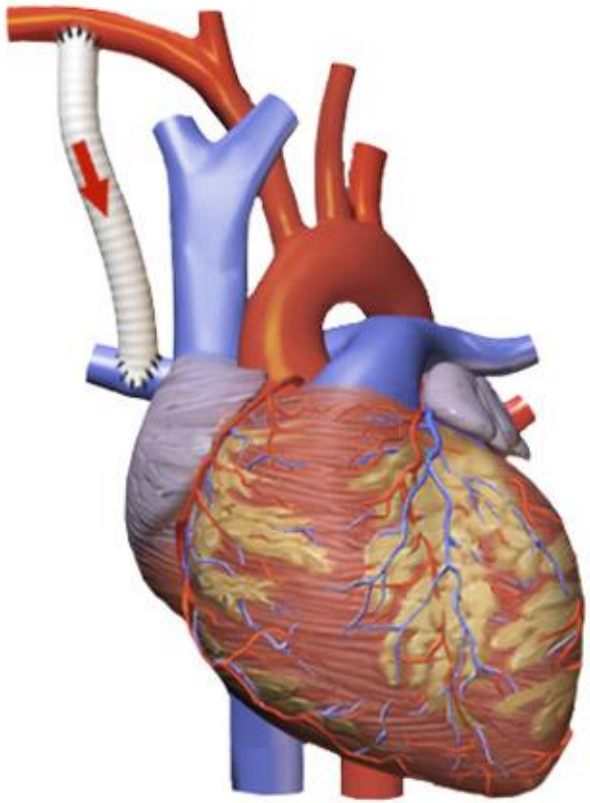
One of a series: *A History of Medicine In Pictures* presented by Parke, Davis & Company

Painted by Robert A. Thom



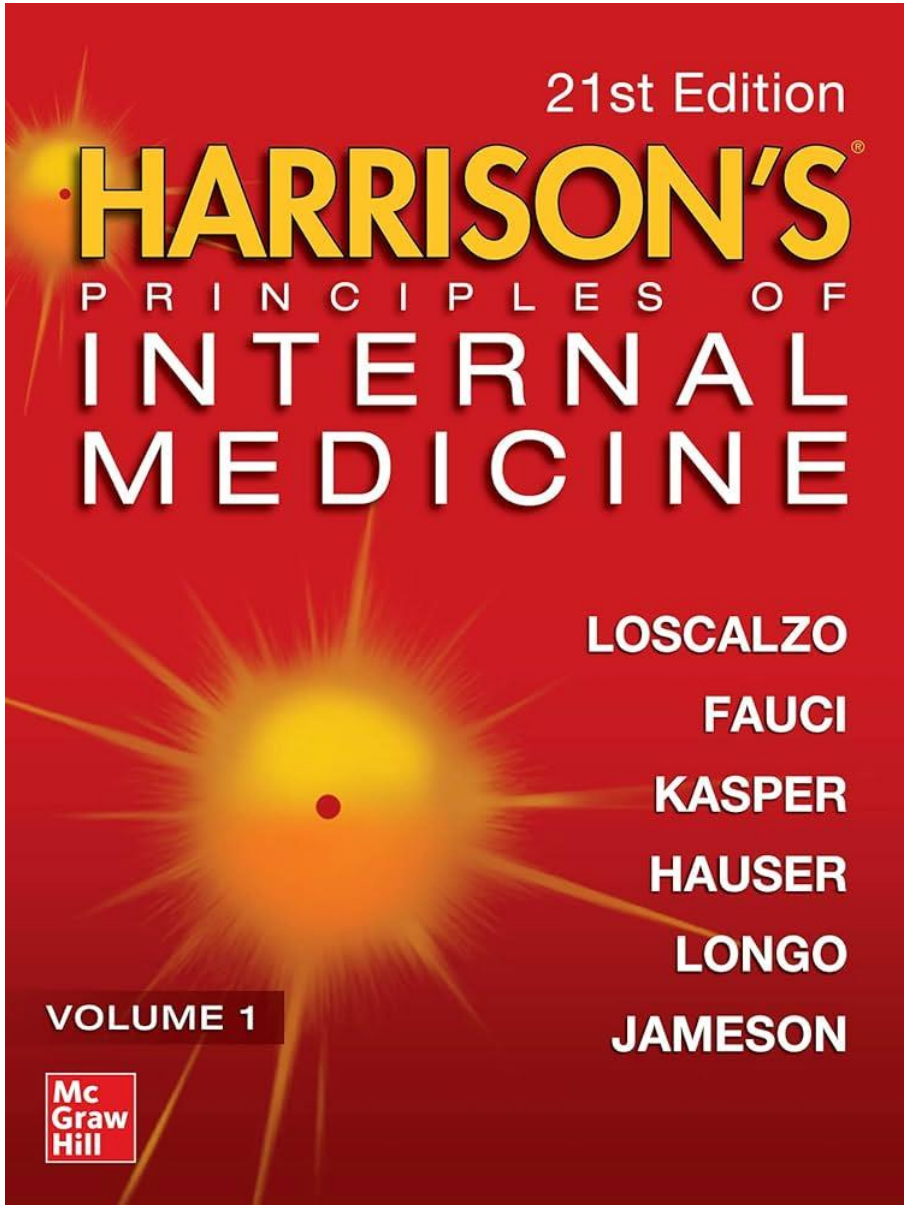
ALFRED BLALOCK





Blalock–Thomas–Taussig shunt

TINSLEY HARRISON



ELLIOT CUTLER

- President of ASA
- “ Old & New views of Traumatic shock” June 1934
- In May Cannon Wrote he intended to discuss “commonly acknowledged facts” avoiding “Theories” but recognizing the “stress laid on toxic shock”
- Cannon is said to have taken a balanced approach in his talk. Blalock did not. He discussed his published work and more recent studies, systematically dispatching toxins, vasoconstrictors, and other popular concepts. The cause of shock, argued Blalock, was simple fluid loss. Blalock's arguments were persuasive: during the discussion period, surgeons of the day (including Owen Wangensteen, whose remarks were transcribed) were vehement in their support of Blalock's position.
- Did not communicate for next 6years

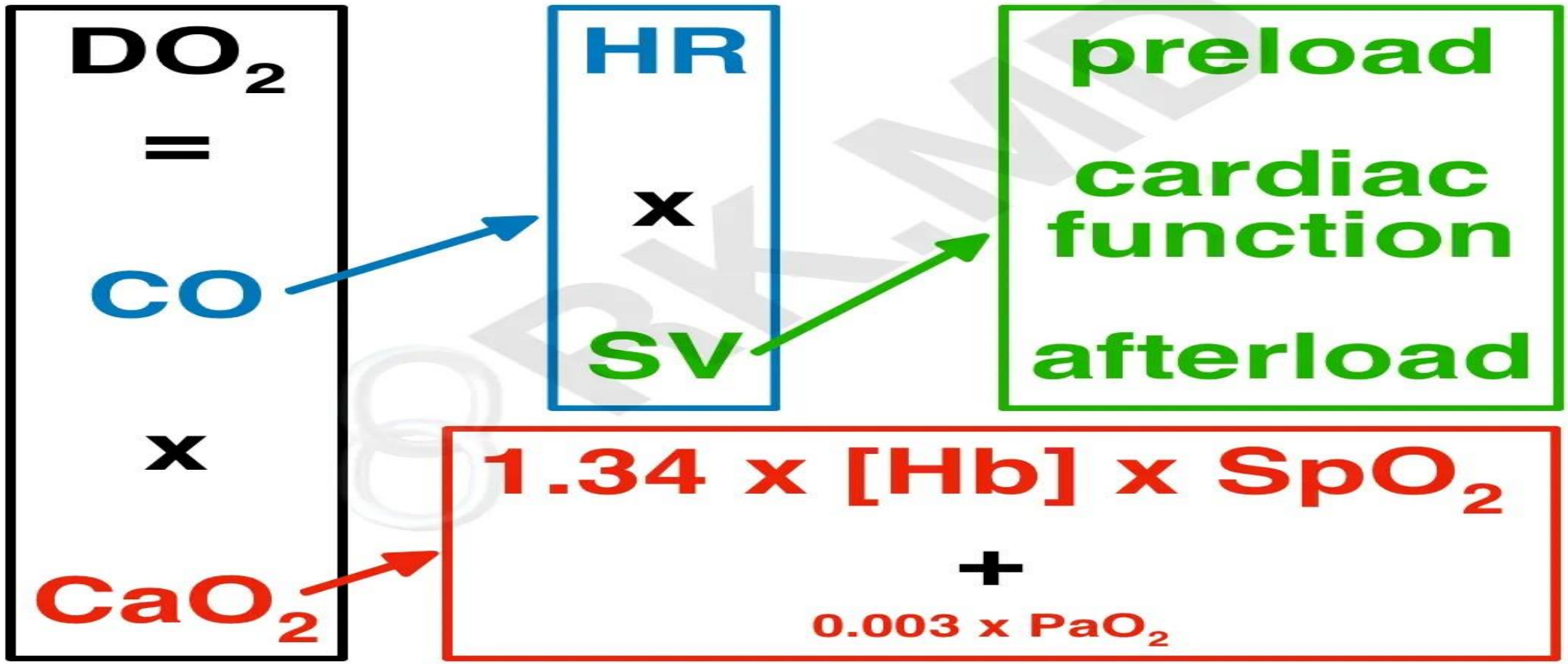
Vietnam War (1955-1975)

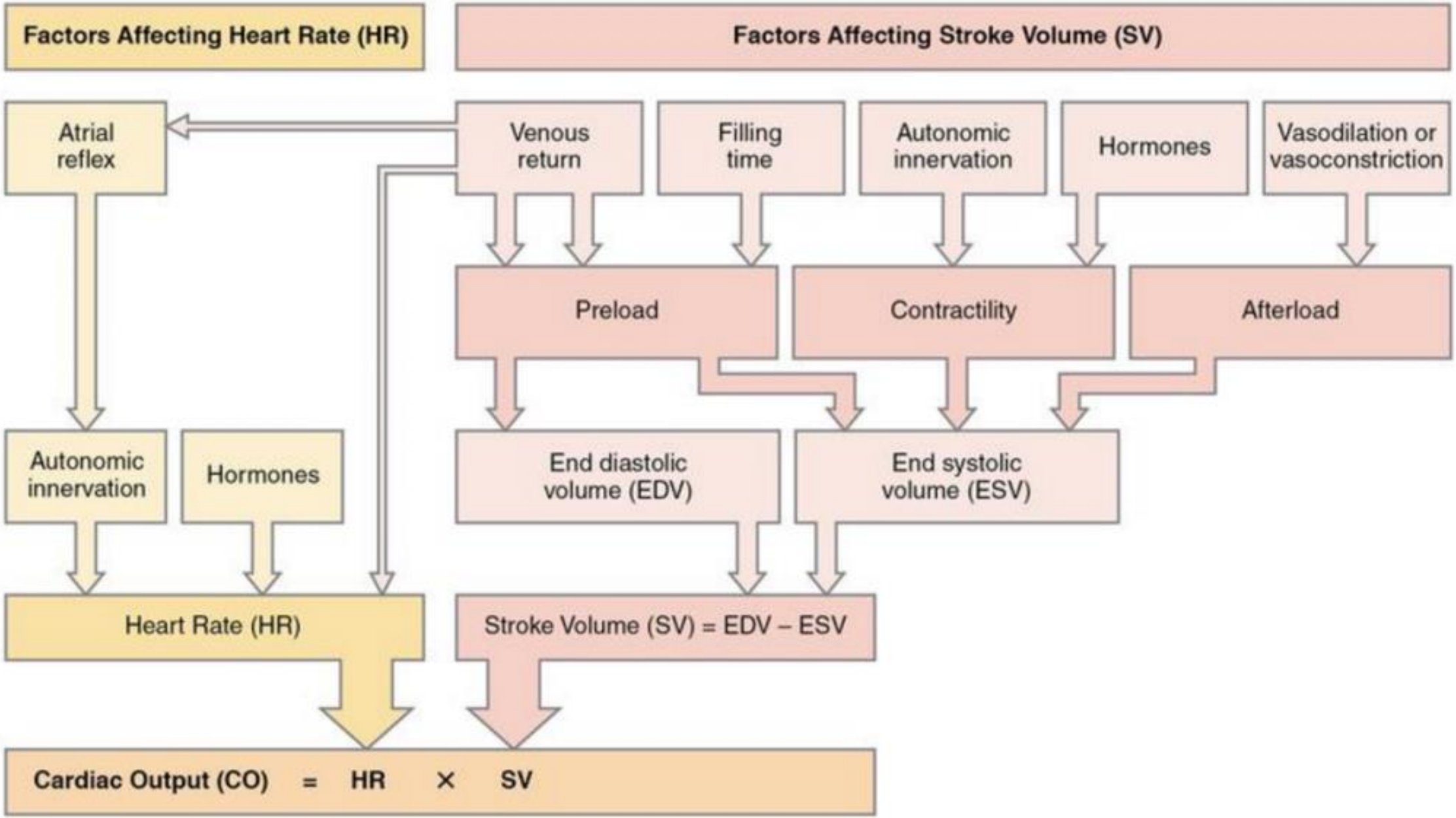
- Trauma doctors involved in treating victims of war had long been familiar with this syndrome, which came to be known as "wet lung", "shock lung" or "Da-nang lung".
- This problem had been identified during World War II but with the advent of advanced trauma (M.A.S.H. units during the Vietnam war) the prevalence of this form of respiratory failure was truly recognized.
- Over the past 30 or so years, this syndrome has come to be one of the central problems of intensive care: lung injury arising from a variety of different etiologies, each characterized by bilateral diffuse infiltrates on x-ray, hypoxemia, and non-cardiogenic pulmonary edema.

DEFINITION

- Inadequate tissue perfusion marked by decreased delivery of required metabolic substrates and inadequate removal of cellular waste products.
- This involves failure of oxidative metabolism that can involve defects of oxygen (O2) delivery, transport, and/or utilization.
- Current investigations focus on determining the cellular events that often occur in parallel to result in organ dysfunction, shock irreversibility, and death.

ARTERIAL OXYGEN DELIVERY (DO_2)




Factors Affecting Heart Rate (HR)
Factors Affecting Stroke Volume (SV)
Atrial reflex
Venous return
Filling time
Autonomic innervation
Hormones
Vasodilation or vasoconstriction
Preload
Contractility
Afterload
Autonomic innervation
Hormones
End diastolic volume (EDV)
End systolic volume (ESV)
Heart Rate (HR)
Stroke Volume (SV) = EDV – ESV
Cardiac Output (CO) = HR × SV

TYPES

1. Hypovolumeic/ Hemorrhagic shock
2. Septic shock (Vasogenic/ Vasodilatory/ Distributive)
3. Neurogenic (A form of Vasogenic shock)
4. Cardiogenic Shock
5. Traumatic Shock
6. Obstructive shock

Systemic response to injury (SRI)

A. Neuroendocrine response.

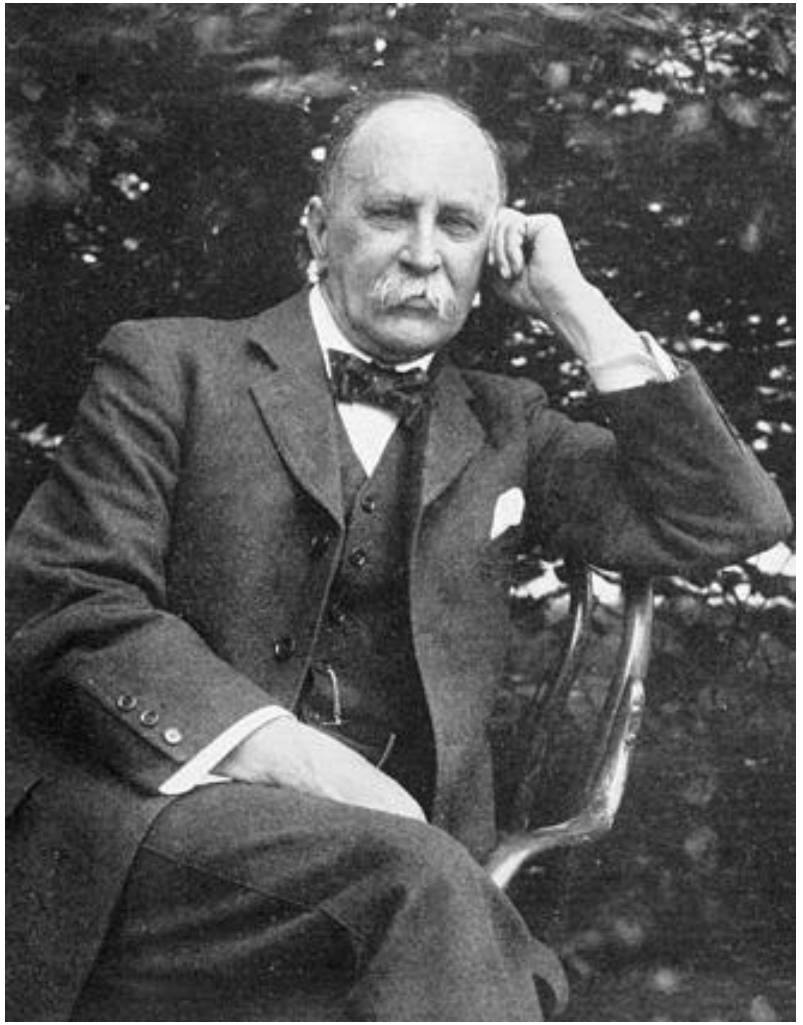
B. Inflammatory/ Immune response (SIR).

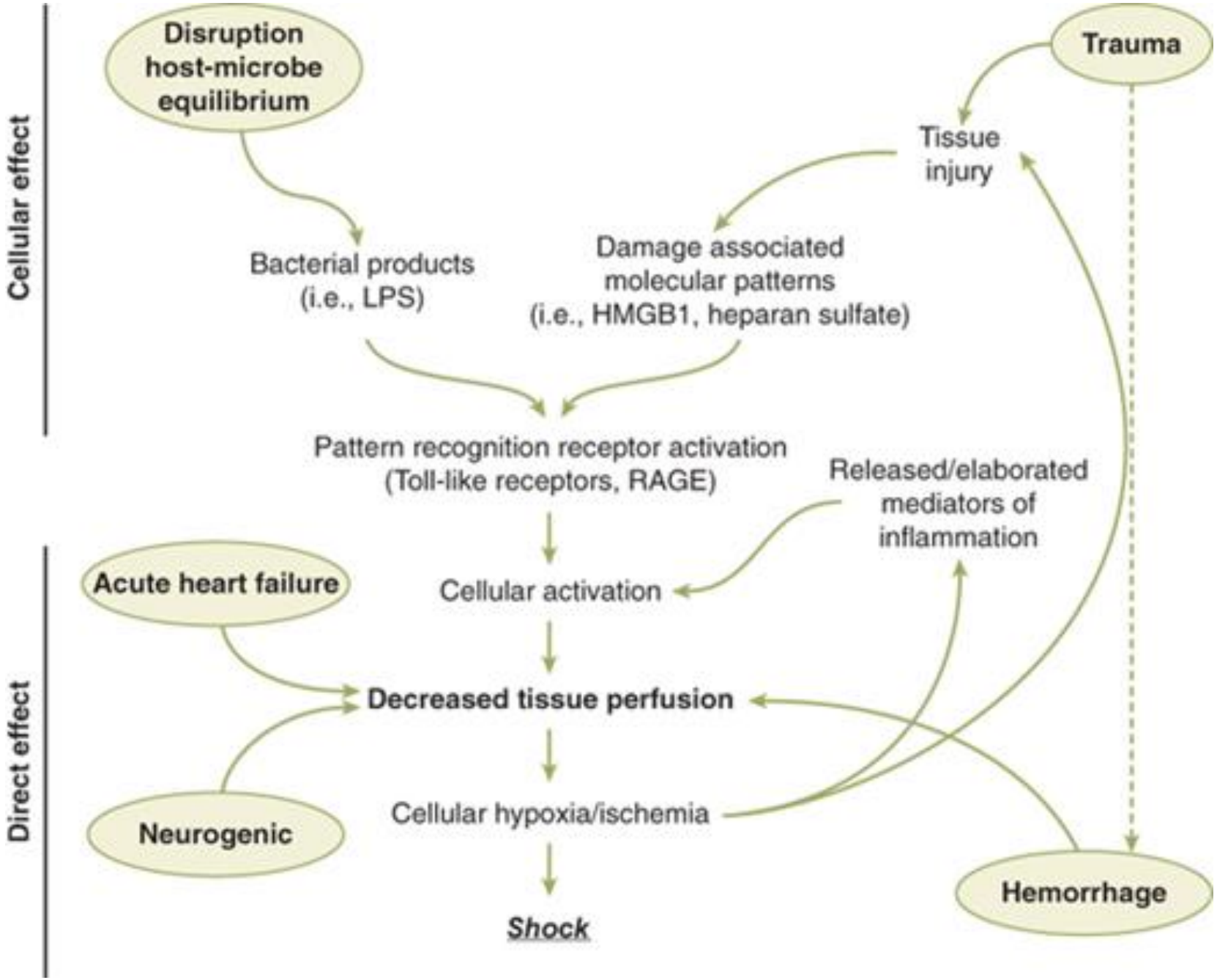
C. Cellular response.

Homeostasis

William Osler (1849 –1919)

- He stated that *"Except on few occasions, the patient appears to die from the body's response to infection rather than from it."*
- The discovery of cytokines began to allow insight into the human organism's response to infection, and led to an explosion in our understanding of the host inflammatory response.
- The design of new therapies targeted at modifying the inflammatory response to infection, which seems to cause much of the organ dysfunction and failure.

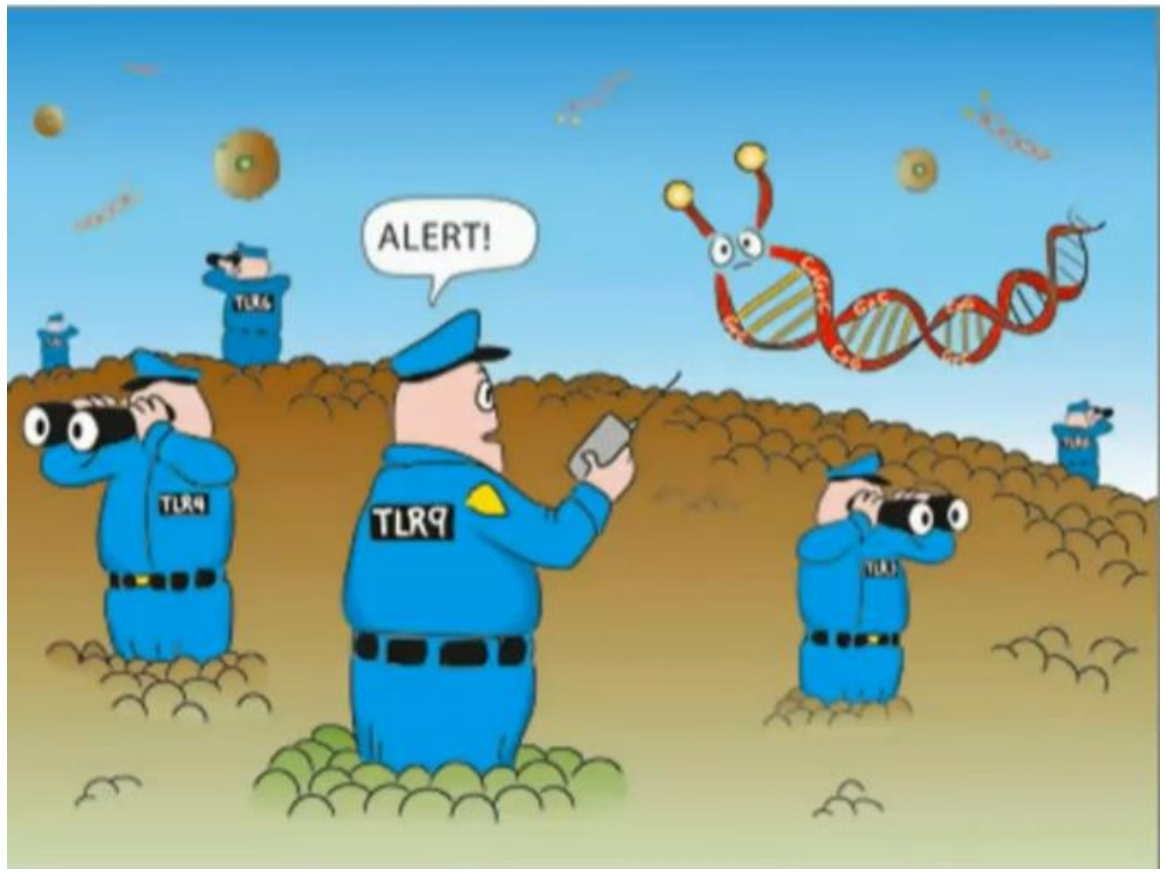


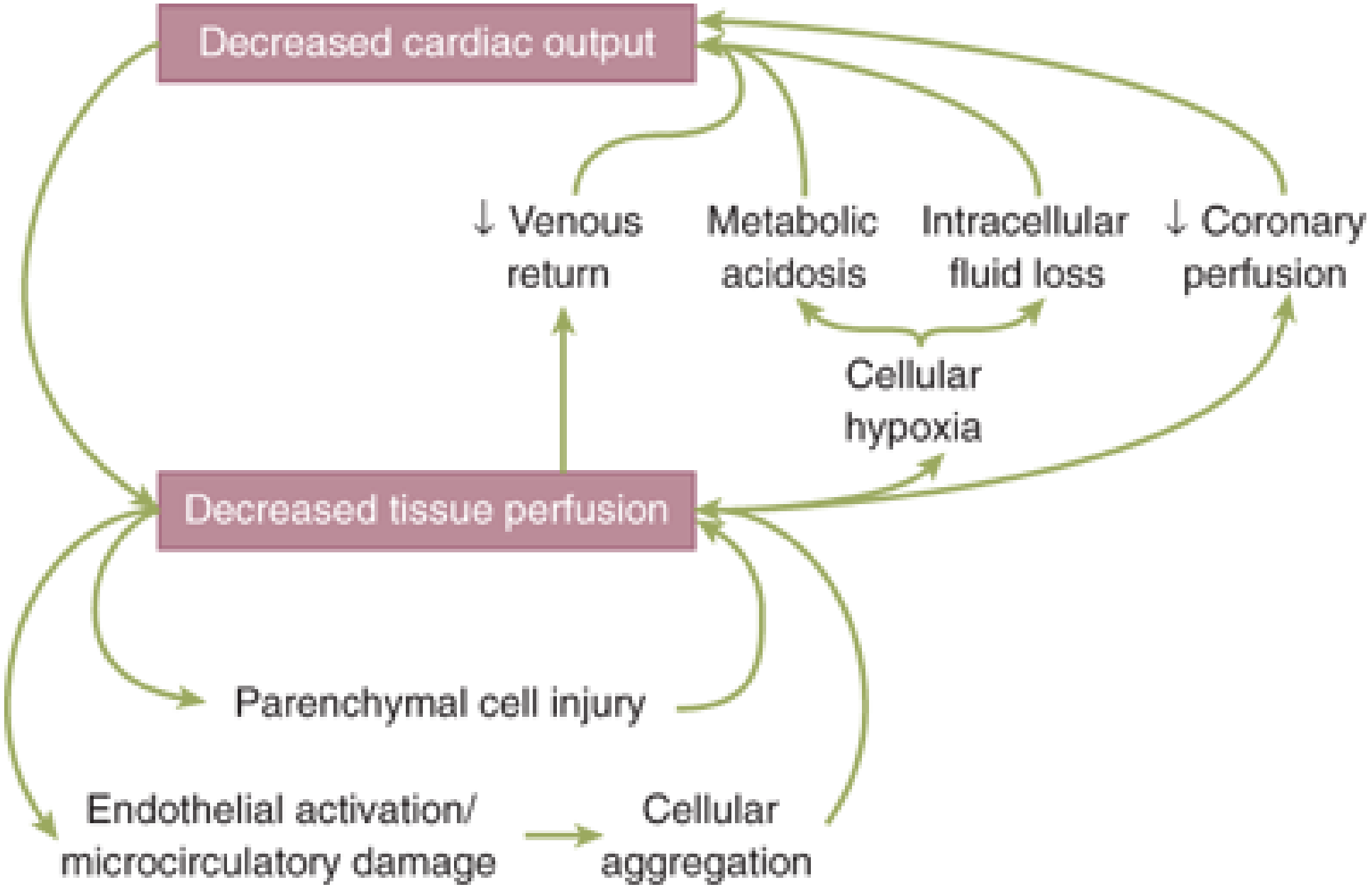

Cellular effect
Direct effect
Disruption host-microbe equilibrium
Trauma
Tissue injury
Bacterial products (i.e., LPS)
Damage associated molecular patterns (i.e., HMGB1, heparan sulfate)
Pattern recognition receptor activation (Toll-like receptors, RAGE)
Released/elaborated mediators of inflammation
Acute heart failure
Cellular activation
Decreased tissue perfusion
Neurogenic
Cellular hypoxia/ischemia
Hemorrhage
Shock

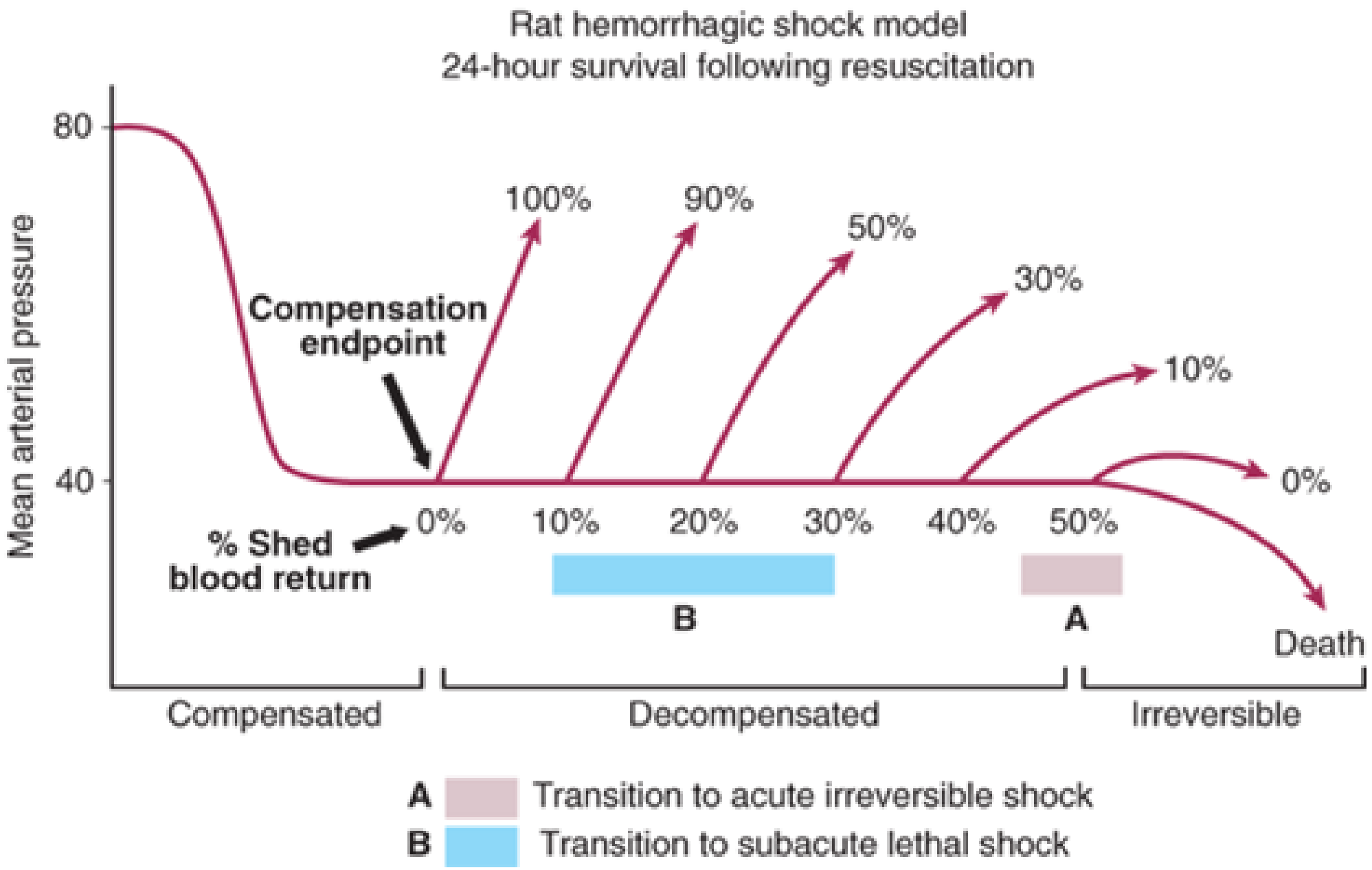
DETECTION OF CELLULAR INJURY

DAMAGE-ASSOCIATED MOLECULAR PATTERN FAMILY (DAMPS OR ALARMINS)
PATHOGEN-ASSOCIATED MOLECULAR PATTERN FAMILY (PAMPS)

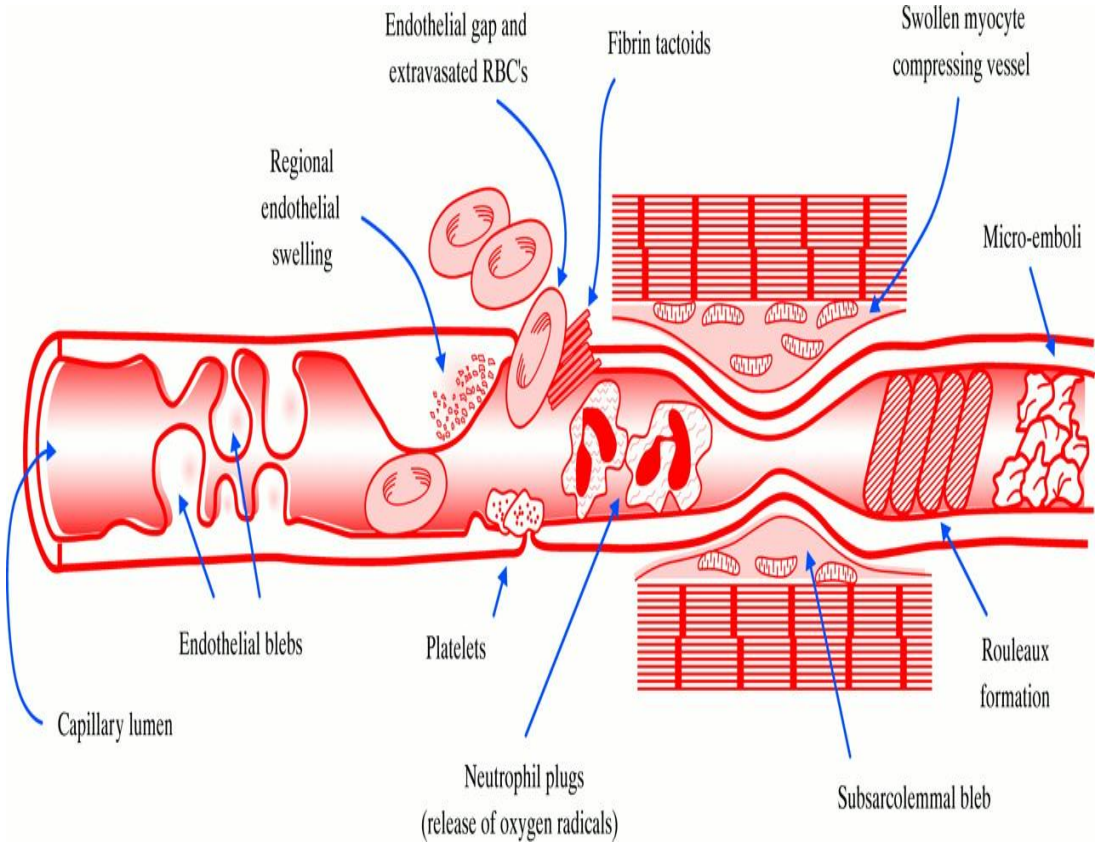
DAMP molecule	Putative receptors (PRRs)
High-mobility group protein B1 (HMGB-1)	TLRs (2,4,9), RAGE (Receptor of advanced glycosylation end products), CD24
Heat shock proteins (HSPs)	TLR (2,4), CD40, CD14, Singlecs
S100 protein	TLR 4, RAGE
Mitochondrial DNA	TLR 9
Hyaluran	TLR (2,4), CD44
Biglycan	TLR (2,4)
Mitochondrial Formyl peptides	Formyl peptides Receptor 1
IL-1α	IL-1 Receptors

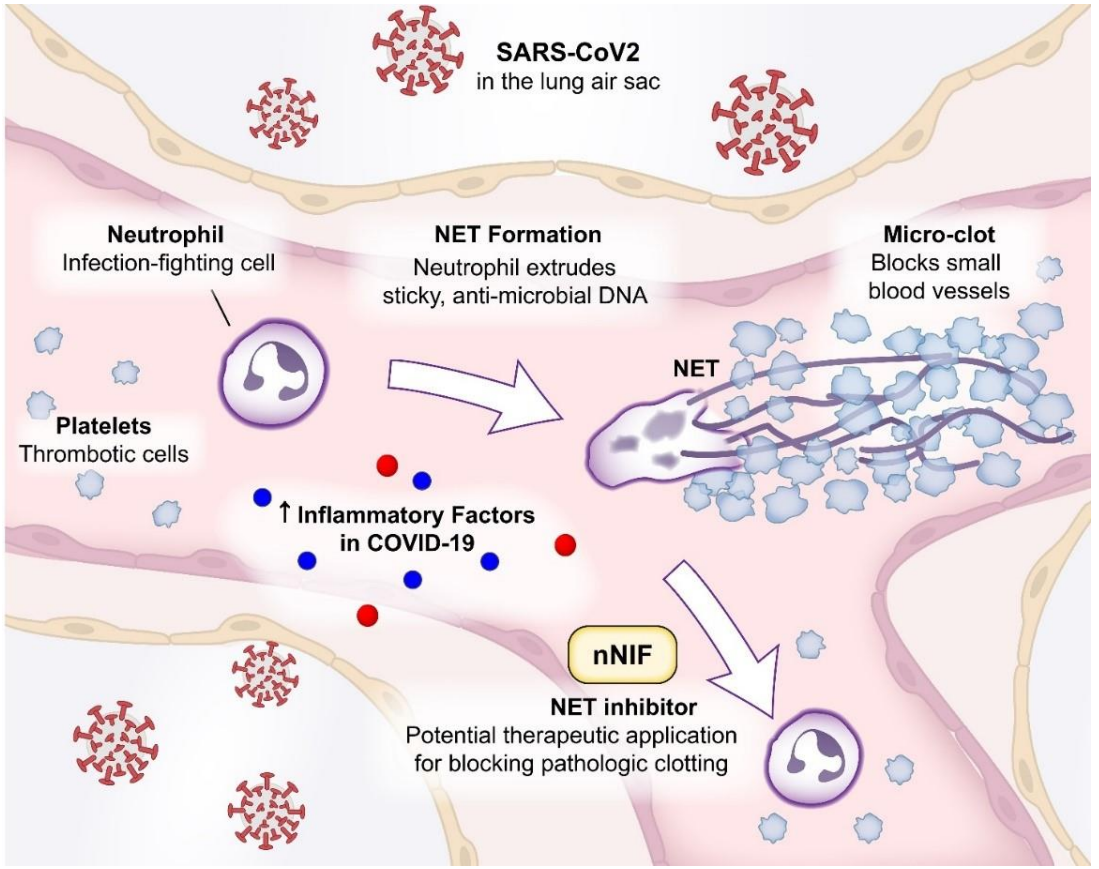



Decreased cardiac output
↓ Venous return
Metabolic acidosis
Intracellular fluid loss
↓ Coronary perfusion
Cellular hypoxia
Decreased tissue perfusion
Parenchymal cell injury
Endothelial activation/ microcirculatory damage
Cellular aggregation


Rat hemorrhagic shock model
24-hour survival following resuscitation
Mean arterial pressure
80
40
Compensation endpoint
100%
90%
50%
30%
10%
0%
% Shed blood return
0%
10%
20%
30%
40%
50%
B
A
Death
Compensated
Decompensated
Irreversible
A Transition to acute irreversible shock
B Transition to subacute lethal shock

CAPILLARY DYSFUNCTION





PATHOPHYSIOLOGY
NEUROENDOCRINE RESPONSE

- Stimuli:

1. *Loss of circulating blood pain*
2. Hypoxia
3. hypercapnia
4. Acidosis
5. Infection
6. Change in body temperature
7. Emotional arousal
8. hypoglycemia

NEUROENDOCRINE RESPONSE- AFFERENT SIGNALS BARORECEPTORS

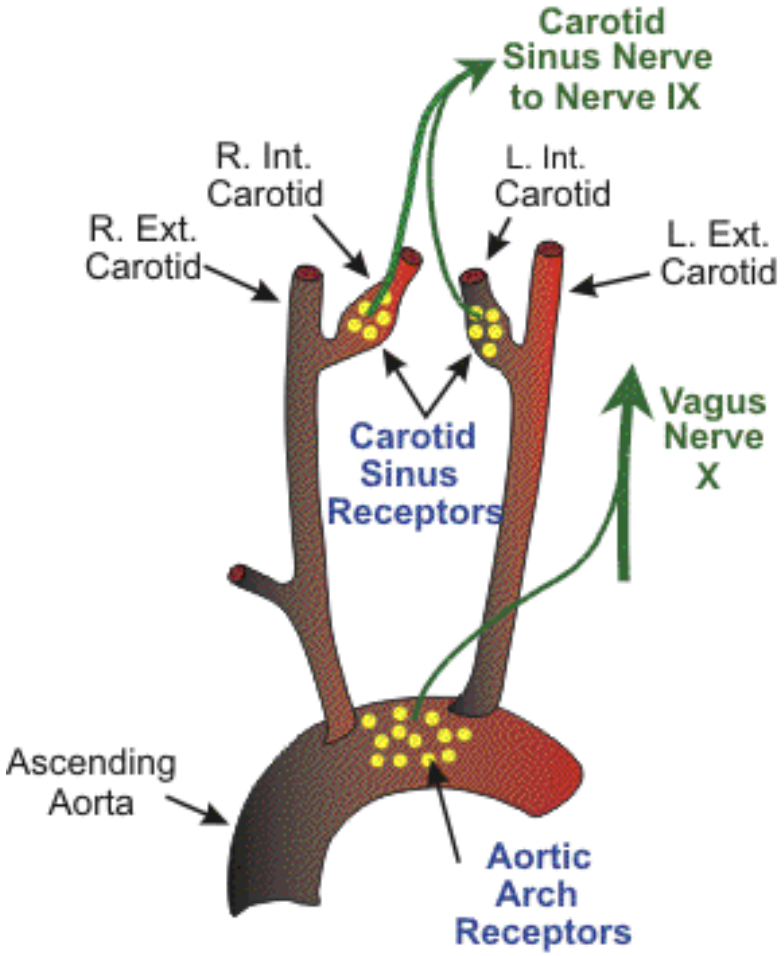
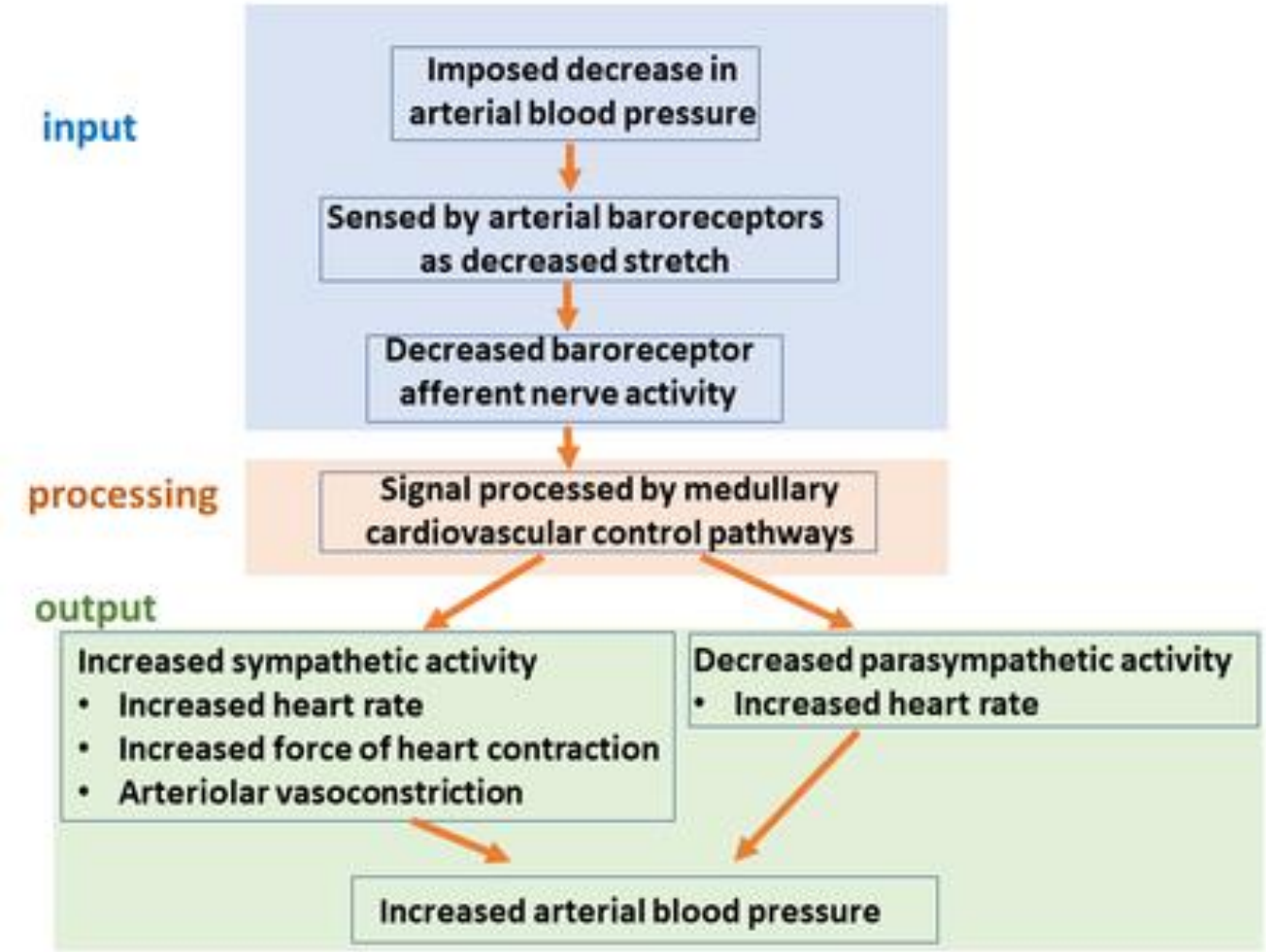
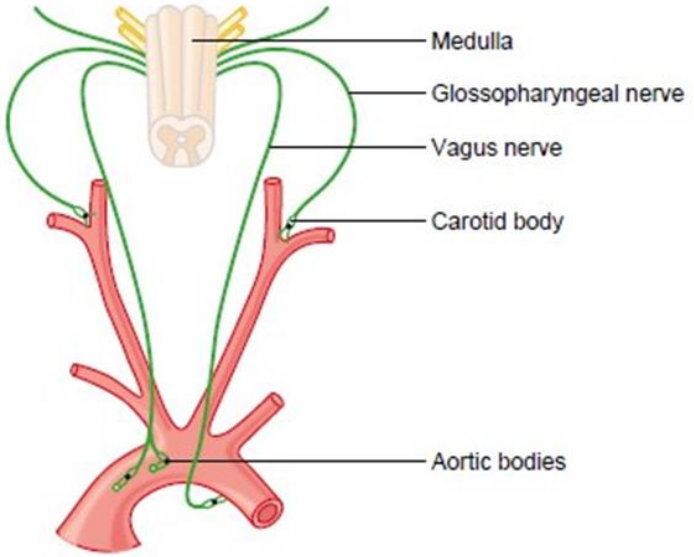
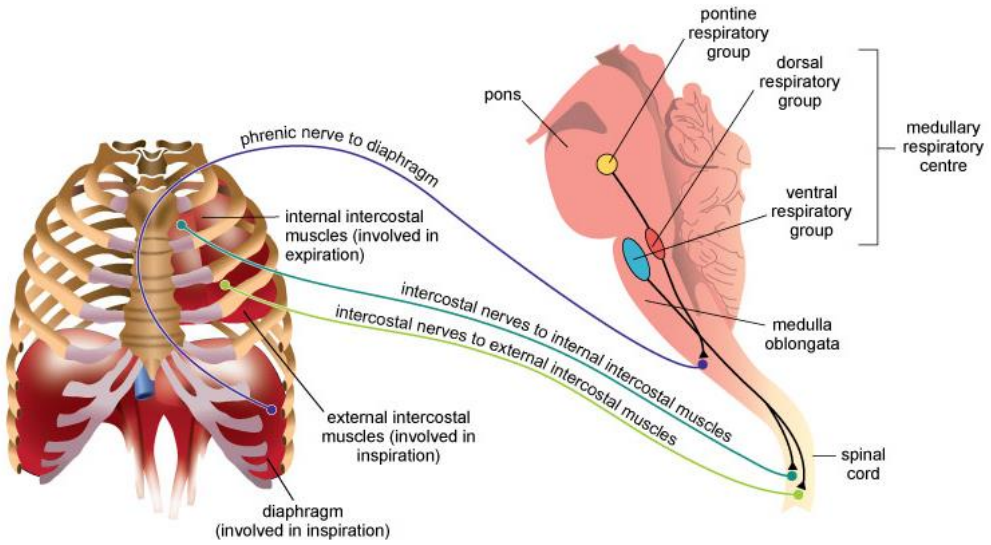


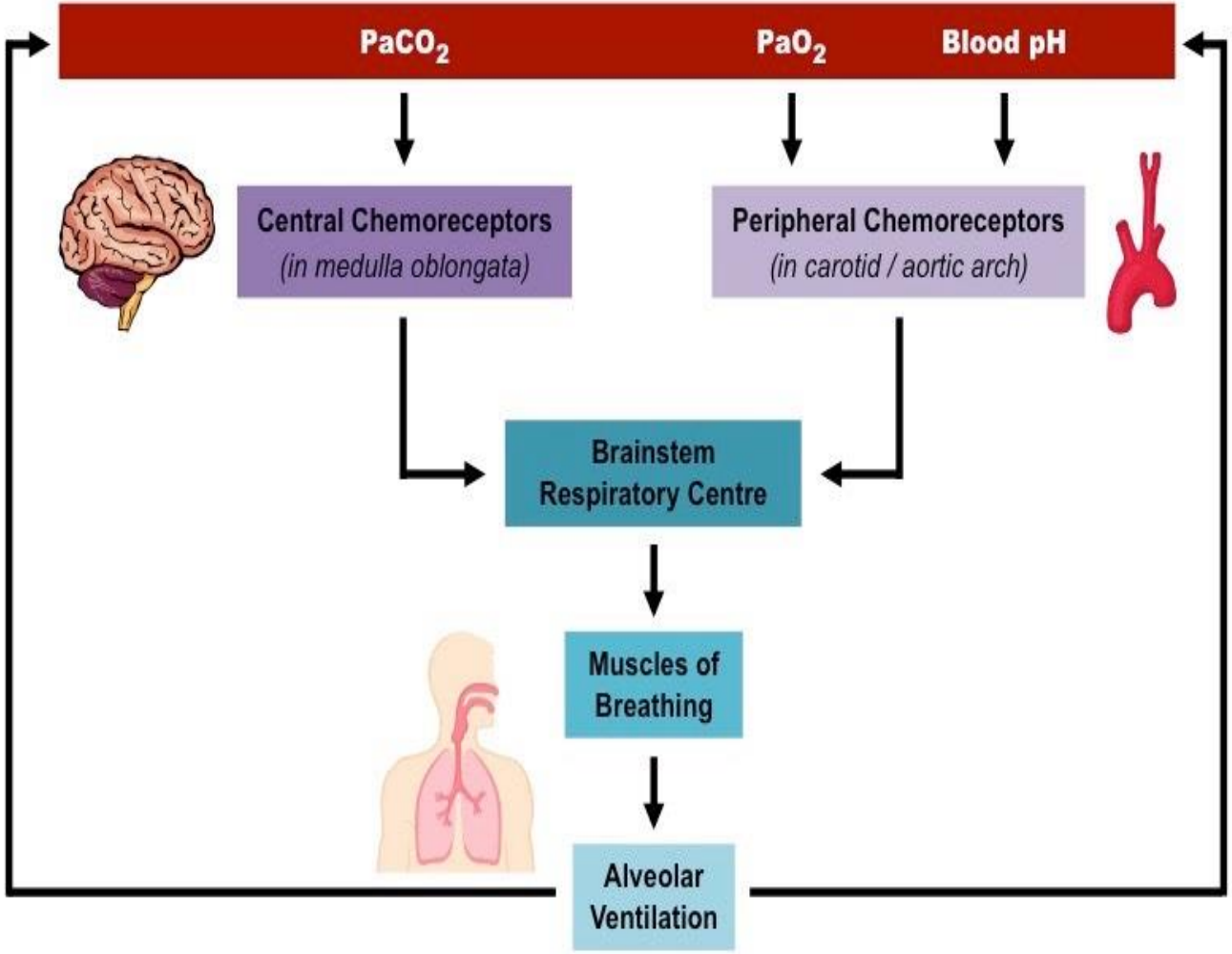
Figure 1. Location and innervation of arterial baroreceptors.



NEUROENDOCRINE RESPONSE- AFFERENT SIGNALS CHEMORECEPTORS

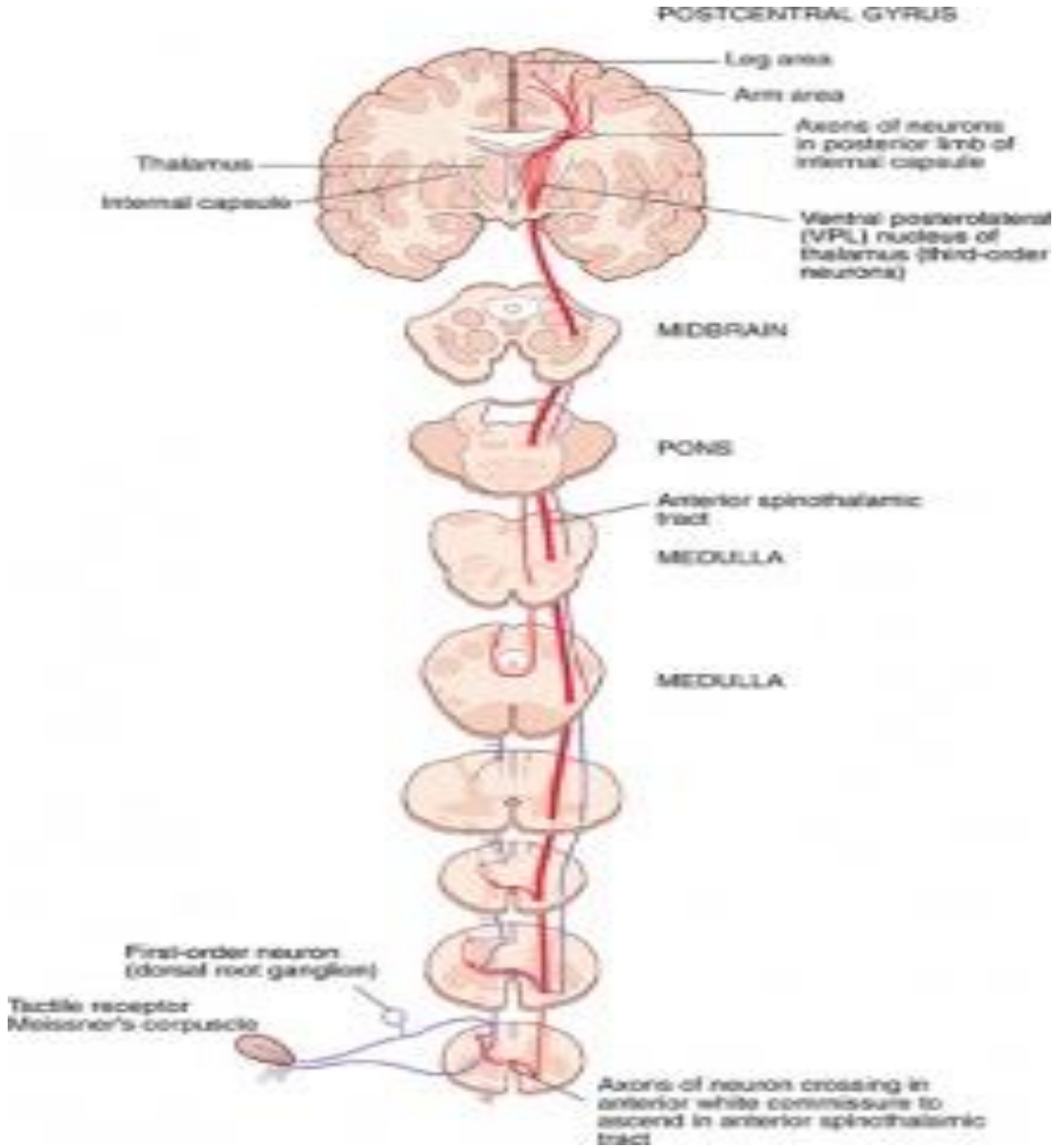






NEUROENDOCRINE RESPONSE- AFFERENT SIGNALS SPINOTHALAMIC PATHWAY

- Pain & Change of body temperature are transmitted by STP →→→ Activation of HPA axis→ Sympathetic NS & Adrenal medulla activation→→→→ Catecholamines



NEUROENDOCRINE RESPONSE- EFFERENT SIGNALS

Cardiovascular response

- β1 Receptors: ↑↑ HR & Contractility→ ↑↑ Myocardial O2 Consumption
- α1 Receptors:
  - ✓ Arteriolar Vasoconstriction→ ↑ SVR & BP
  - ✓ Venous Vasoconstriction→ ↑ Venous return
  - ✓ Exception: Heart & Brain

Hormonal Response- Adrenal medulla

- Adrenaline & Noradrenaline
- Hepatic gluconeogenesis & Glycogenolysis
- Skeletal muscle Glycogenolysis
- Suppression of Insulin Release
- ↑ Glucagon release

NEUROENDOCRINE RESPONSE- EFFERENT SIGNALS

Hormonal Response

- CRH→ACTH → Cortisol
  - ✓ Insulin resistance & Gluconeogenesis
  - ✓ Lipolysis & Muscle protein breakdown
  - ✓ Sodium & water retention
- ADH (Arginine Vasopressin)
- ↓ water & Na losses
- Mesenteric vasoconstriction
- ↑Hepatic gluconeogenesis & Glycolysis

Renin-Angiotensin-Aldosterone system

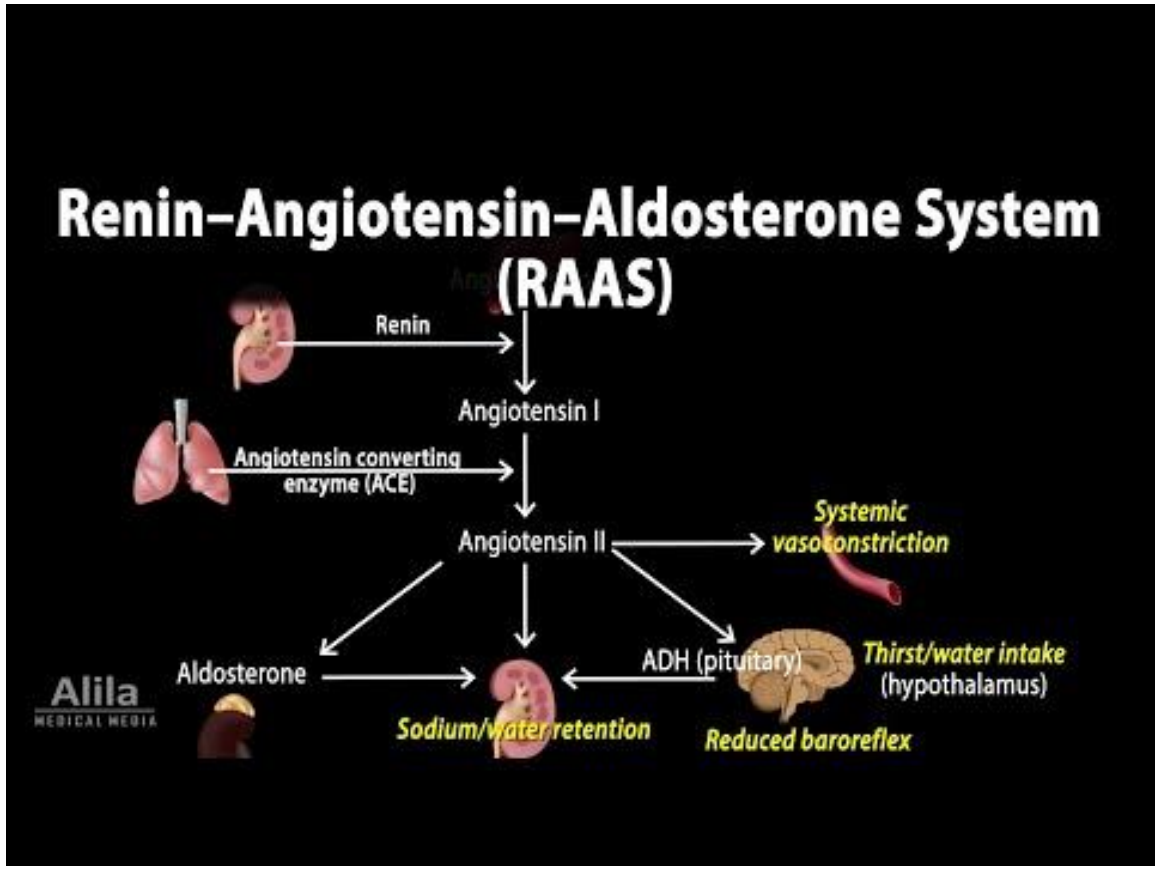


Table 5-2 Hemodynamic responses to different types of shock

TYPE OF SHOCK	CARDIAC INDEX	SVR	VENOUS CAPACITANCE	CVP/PCWP	SVO2	CELLULAR/METABOLIC EFFECTS
Hypovolemic	↓	↑	↓	↓	↓	Effect
Septic	↑↑	↓	↑	↑↓	↑↓	Cause
Cardiogenic	↓↓	↑↑	→	↑	↓	Effect
Neurogenic	↑	↓	→	↓	↓	Effect

PATHOPHYSIOLOGY- METABOLIC EFFECTS

- With cellular dysoxia, cells shifts from aerobic metabolism and oxidative phosphorylation (38 ATPs/ Glc) to anaerobic metabolism and glycolysis (2 ATPs/ Glc) with production of pyruvate → Lactate→ Intracellular acidosis.

- ↓↓ *ATP & pH:*
  - ✓Maintenance of cell membrane potential
  - ✓Synthesis of enzymes & proteins
  - ✓Cell signaling
  - ✓DNA repair
  - ✓Impaired calcium signaling & metabolism
  - ✓Cell death

PATHOPHYSIOLOGY- METABOLIC EFFECTS

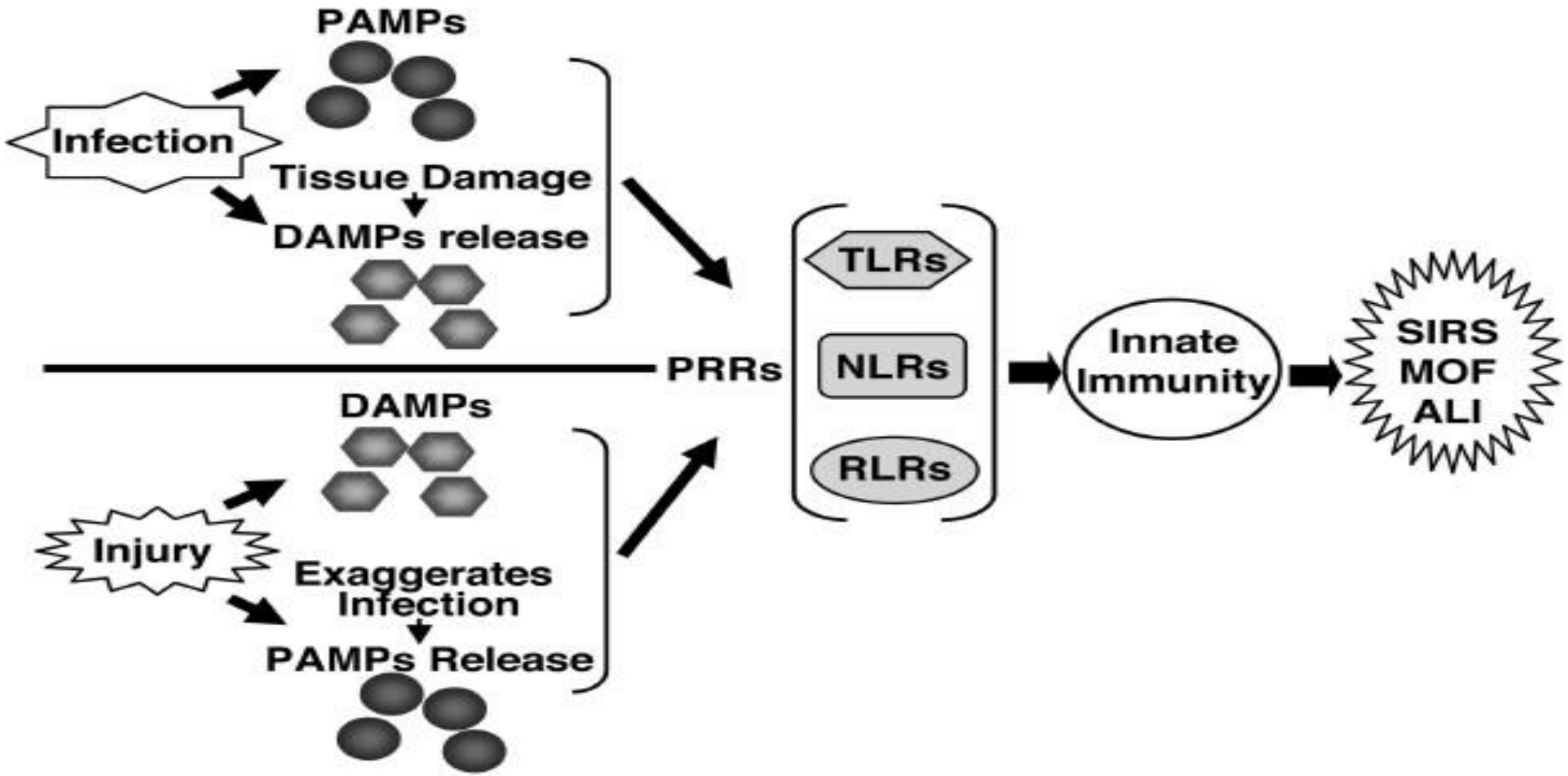
- Mediated by Epinephrine, Norepinephrine, Cortisol, Glucagon, ADH & Insulin resistance:
  a) Hepatic gluconeogenesis & Glycogenolysis
  b) Skeletal muscle Glycogenolysis & protein breakdown
  c) Ketogenesis
  d) Lipolysis
  e) Negative nitrogen balance
  f) Hyperglycemia (Heart & Brain)

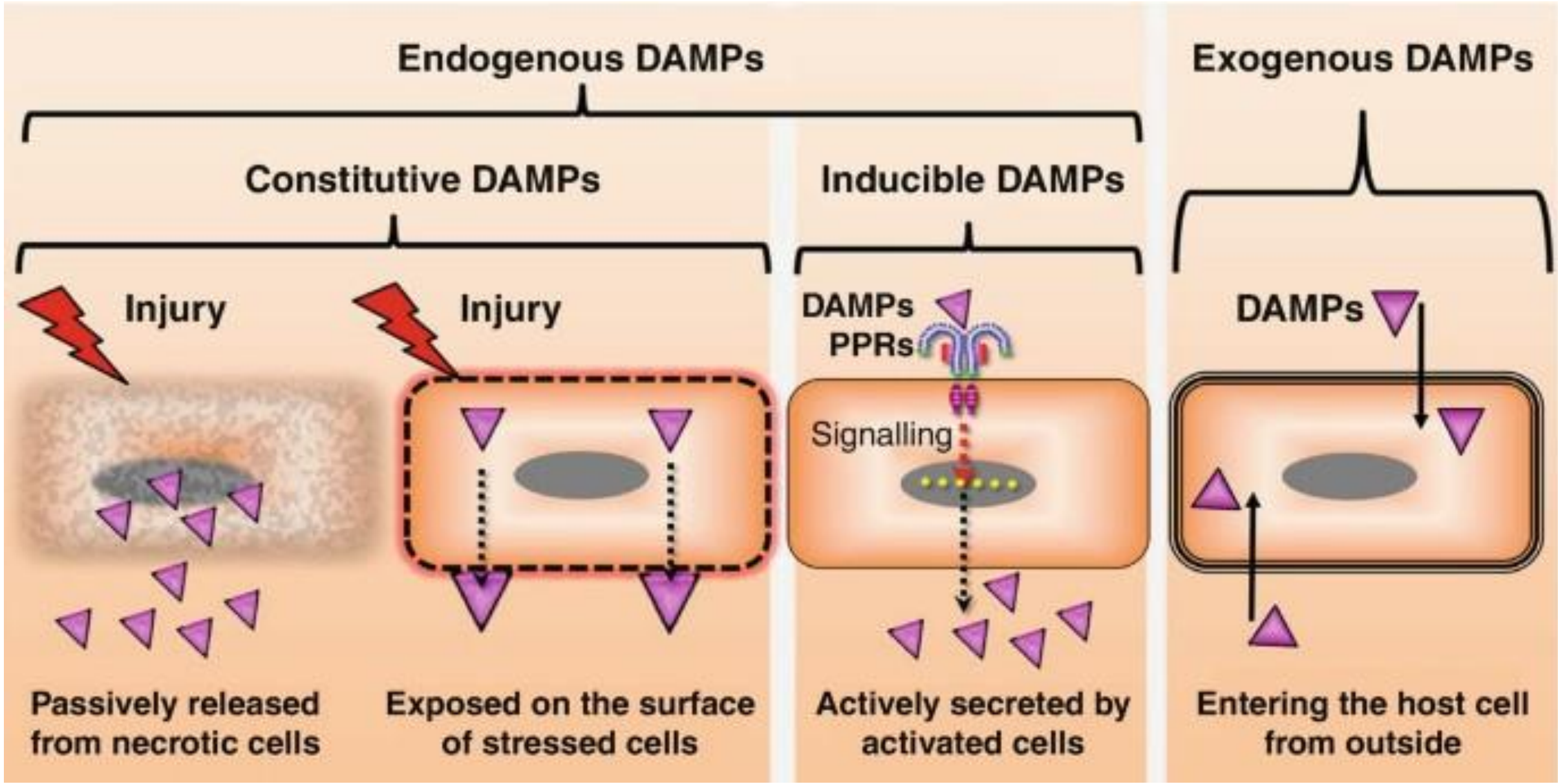
- Changes in gene expression:

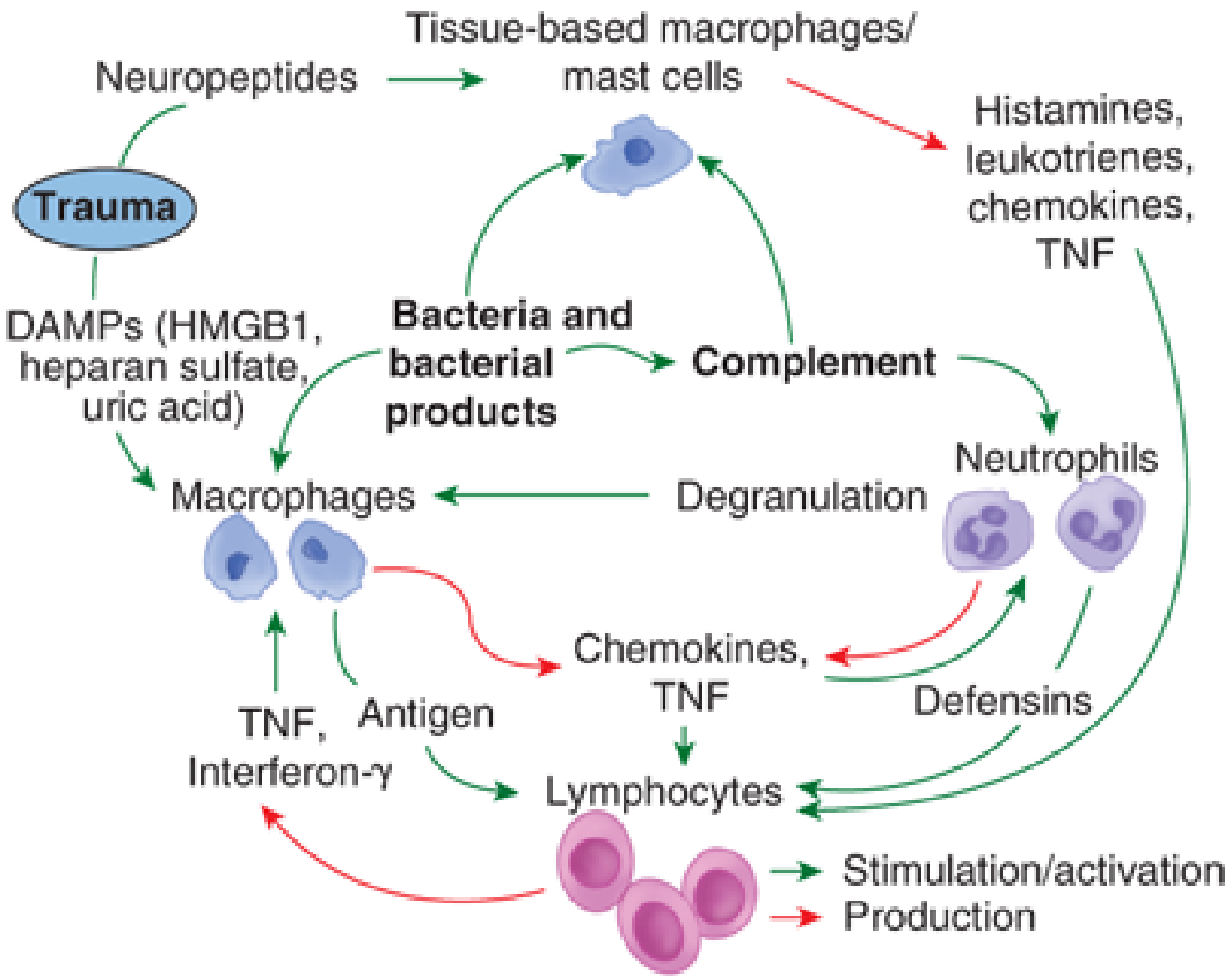
a) HSPs
b) VEGF
c) iNO synthase
d) Heme-oxygenase 1
e) Cytokines

PATHOPHYSIOLOGY

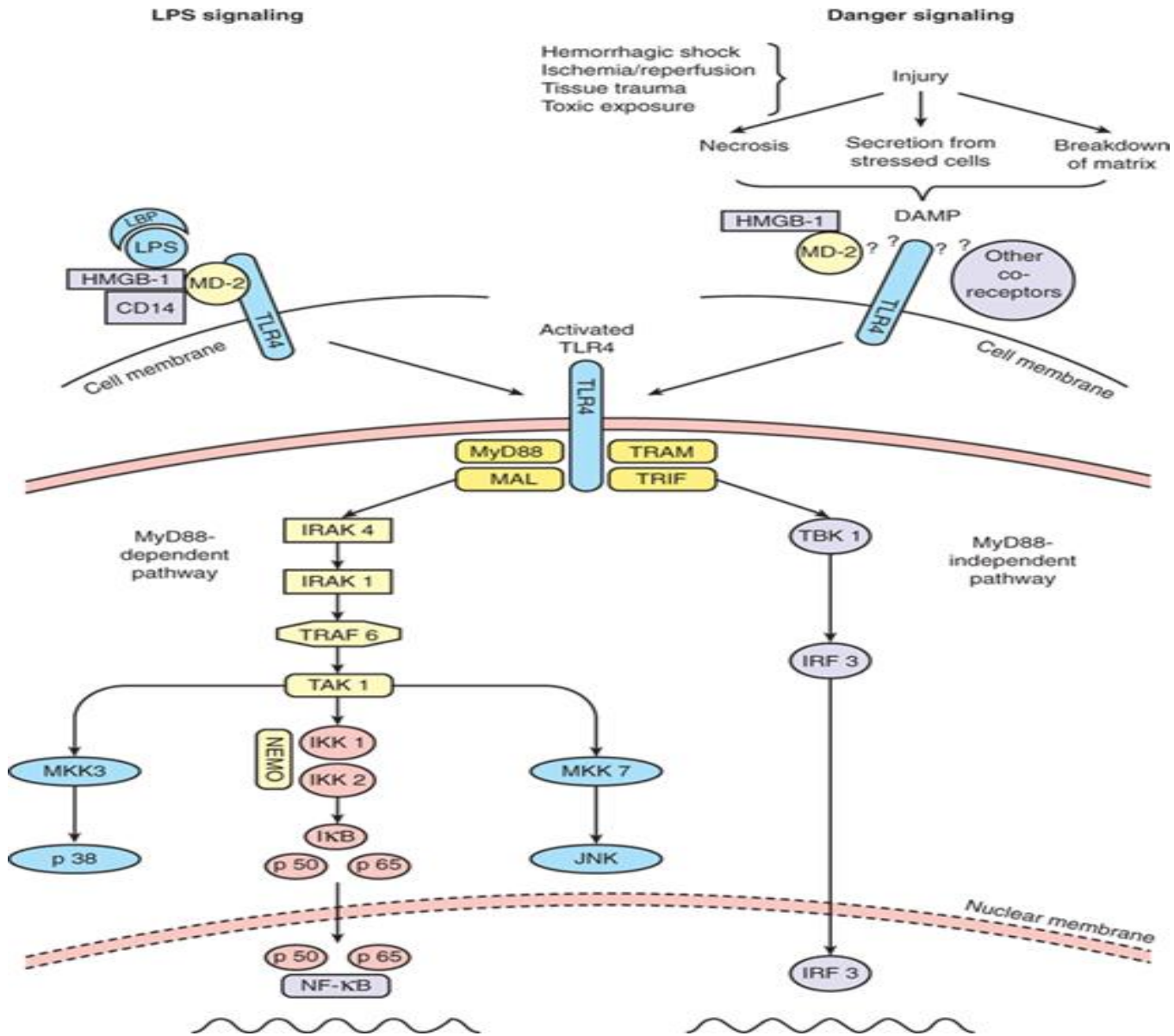
IMMUNE & INFLAMMATORY RESPONSES




Endogenous DAMPs
Exogenous DAMPs
Constitutive DAMPs
Inducible DAMPs
Injury
Injury
DAMPs
PPRs
Signalling
DAMPs
Passively released from necrotic cells
Exposed on the surface of stressed cells
Actively secreted by activated cells
Entering the host cell from outside


Tissue-based macrophages/
mast cells
Neuropeptides
Histamines,
leukotrienes,
chemokines,
TNF
Trauma
DAMPs (HMGB1,
heparan sulfate,
uric acid)
Bacteria and
bacterial
products
Complement
Neutrophils
Macrophages
Degranulation
Chemokines,
TNF
Defensins
TNF,
Interferon-γ
Antigen
Lymphocytes
Stimulation/activation
Production

SIR


LPS signaling
Danger signaling
Hemorrhagic shock
Ischemia/reperfusion
Tissue trauma
Toxic exposure
Injury
Necrosis
Secretion from stressed cells
Breakdown of matrix
HMGB-1
DAMP
MD-2
Other co-receptors
LBP
LPS
HMGB-1
MD-2
CD14
TLR4
Cell membrane
Activated TLR4
TLR4
Cell membrane
MyD88
MAL
TRAM
TRIF
MyD88-dependent pathway
IRAK 4
IRAK 1
TRAF 6
TAK 1
TBK 1
MyD88-independent pathway
IRF 3
NEMO
IKK 1
IKK 2
MKK3
MKK 7
p 38
IKB
p 50
p 65
JNK
Nuclear membrane
p 50
p 65
NF-KB
IRF 3

CYTOKINES/CHEMOKINES

PROINFLAMMATORY	ANTI-INFLAMMATORY
Interleukin-1α/β	Interleukin-4
Interleukin-2	Interleukin-10
Interleukin-6	Interleukin-13
Interleukin-8	Prostaglandin E2
Interferon	TGFβ
TNF	
PAF	

TNF-α

- One of the first cytokines to be described and is one of the earliest cytokines released in response to injurious stimuli.
- Monocytes, macrophages, and T cells release this potent proinflammatory cytokine.
- Peaks within 90 minutes of stimulation & return frequently to baseline levels within 4 hours.
- Release of TNF-α may be induced by bacteria or endotoxin and leads to the development of shock and hypoperfusion, most commonly observed in septic shock.
- In contrast, the increase in serum TNF-α levels reported in trauma patients is far less than that seen in septic patients.
- Production of TNF-α also may be induced following other insults, such as hemorrhage and ischemia.

- TNF-α levels correlate with mortality in animal models of hemorrhage.
- TNF-α Actions:
  - ✓Produces Peripheral vasodilation.
  - ✓Activates the release of other cytokines.
  - ✓Induces procoagulant activity.
  - ✓Stimulates a wide array of cellular metabolic changes.
  - ✓Contributes to the muscle protein breakdown and cachexia.

Interleukin-1 (IL-1)

- has actions similar to those of TNF-α.
- IL-1 has a very short half-life (6 min) and primarily acts in a paracrine fashion to modulate local cellular responses.
- Systemically, IL-1 produces a febrile response to injury by activating prostaglandins in the posterior hypothalamus, and causes anorexia by activating the satiety center.
- This cytokine also augments the secretion of ACTH, glucocorticoids, and β-endorphins.
- In conjunction with TNF-α, IL-1 can stimulate the release of other cytokines such as IL-2, IL-4, IL-6, IL-8, granulocyte-macrophage colony-stimulating factor, and interferon-γ.

Interleukin-2 (IL-2)

- IL-2 is produced by activated T cells in response to a variety of stimuli and activates other lymphocyte subpopulations and natural killer cells.
- Some investigators have postulated that increased IL-2 secretion promotes shock-induced tissue injury and the development of shock.
- Others have demonstrated that depressed IL-2 production is associated with, and perhaps contributes to, the depression in immune function after hemorrhage that may increase the susceptibility of patients who develop shock to suffer infections.
- Emphasizing the importance of temporal changes in the production of mediators, both the initial excessive production of IL-2 and later depressed IL-2 production are probably important in the progression of shock.

Interleukin-6 (IL-6)

- IL-6 is elevated in response to hemorrhagic shock, major operative procedures, or trauma.
- Elevated IL-6 levels correlate with mortality in shock states.
- IL-6 contributes to *lung, liver, and gut* injury after hemorrhagic shock.
- IL-6 and IL-1 are mediators of the hepatic acute phase response to injury; enhance the expression and activity of complement, C-reactive protein, fibrinogen, haptoglobin, amyloid A, and α1-antitrypsin; and promote neutrophil activation.

Interleukin-10 (IL-10)

- IL-10 is considered *an anti-inflammatory* cytokine that may have immunosuppressive properties.
- Its production is increased after shock and trauma, and it has been associated with depressed immune function clinically, as well as an increased susceptibility to infection.
- IL-10 is secreted by T cells, monocytes, and macrophages, and inhibits proinflammatory cytokine secretion, O2 radical production by phagocytes, adhesion molecule expression, and lymphocyte activation.
- Administration of IL-10 depresses cytokine production and improves some aspects of immune function in experimental models of shock and sepsis

COMPLEMENT

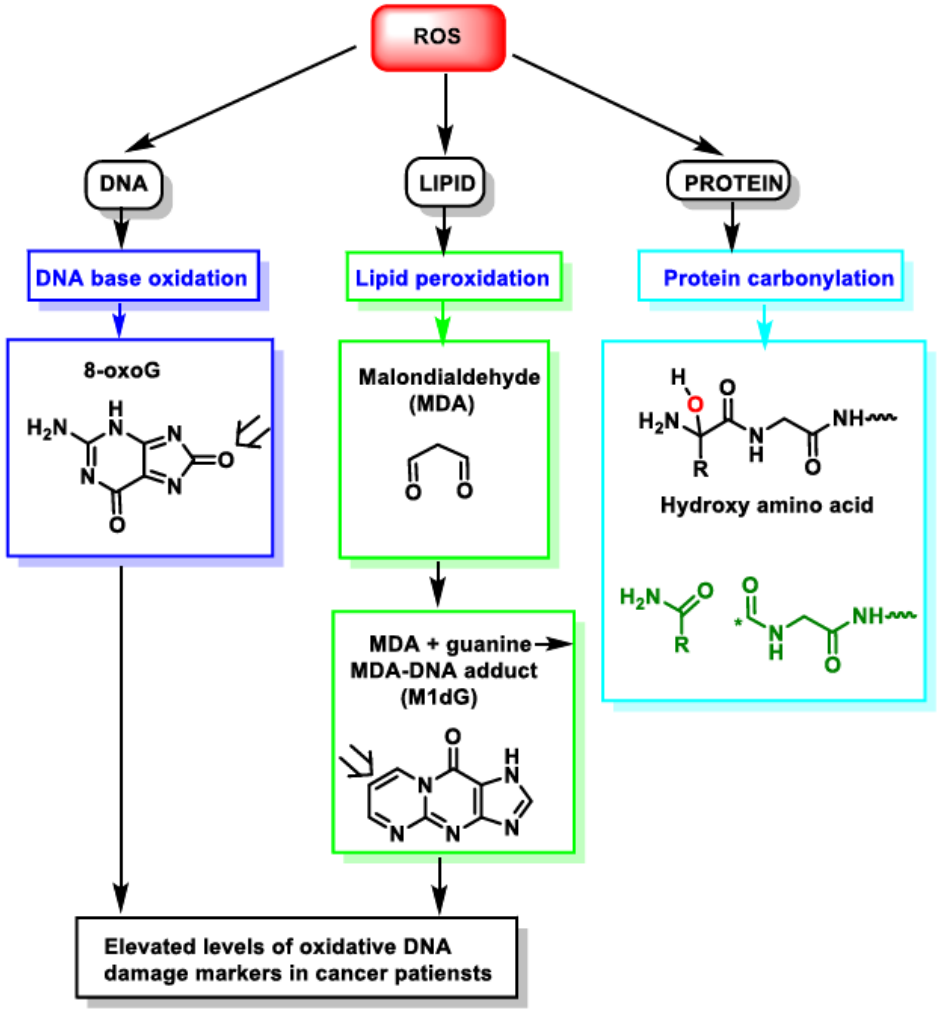
- The complement cascade can be activated by injury, shock, and severe infection, and contributes to host defense and proinflammatory activation.
- Significant complement consumption occurs after hemorrhagic shock.
- In trauma patients, the degree of complement activation is proportional to the magnitude of injury and may serve as a marker for severity of injury.
- Patients in septic shock also demonstrate activation of the complement pathway, with elevations of the activated complement proteins C3a and C5a.

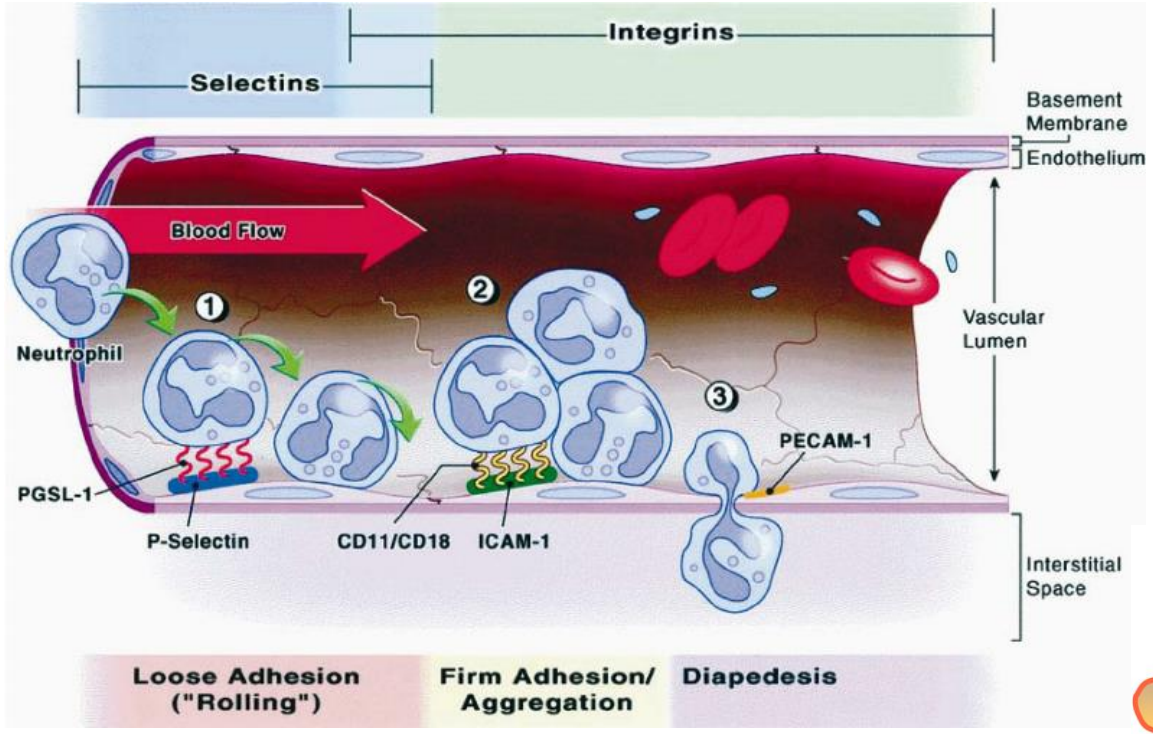
COMPLEMENT

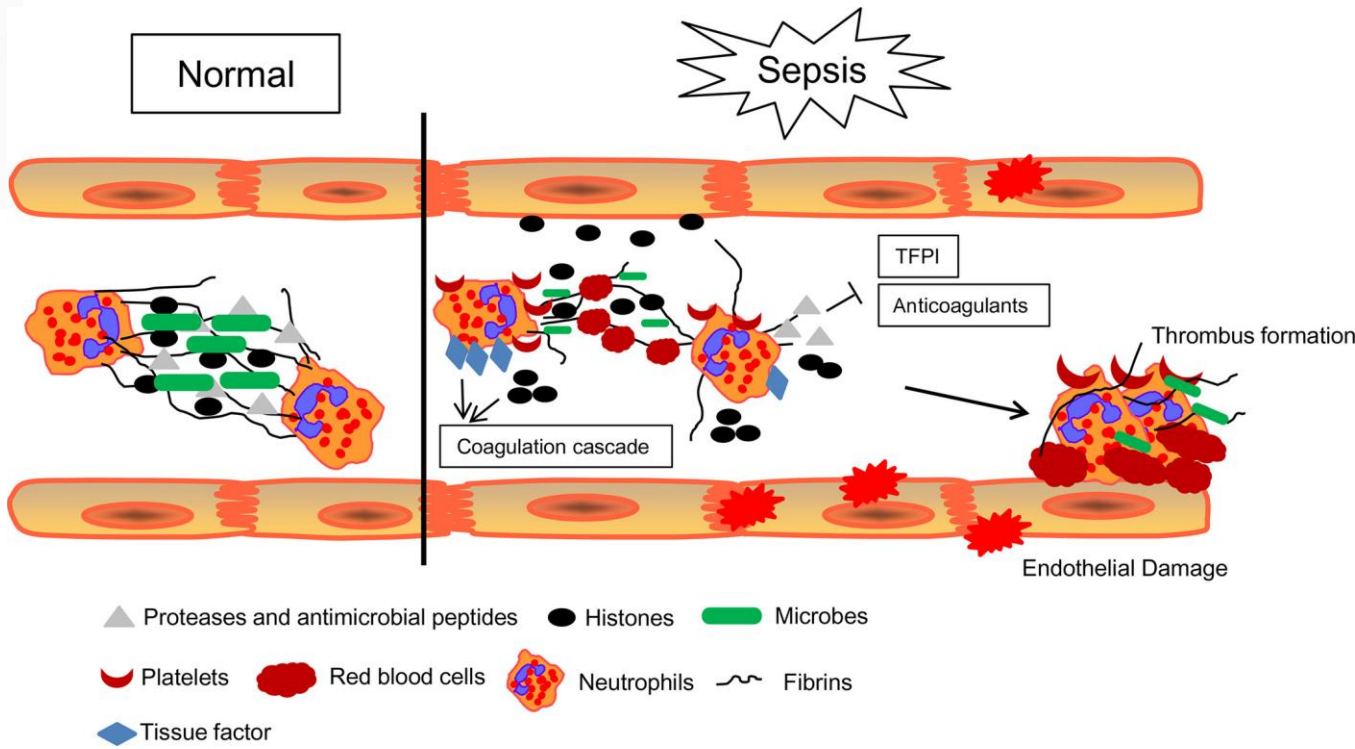
- Activation of the complement cascade can contribute to the development of organ dysfunction & ARDS and MODS in trauma patients correlates with the intensity of complement activation. The development of Complement and neutrophil activation may correlate with mortality in multiply injured patients.
- Activated complement factors C3a, C4a, and C5a are potent mediators of increased vascular permeability, smooth muscle cell contraction, histamine and arachidonic acid by-product release, and adherence of neutrophils to vascular endothelium.
- Activated complement acts synergistically with endotoxin to induce the release of TNF-α and IL-1.

NEUTROPHILS (PMNS)

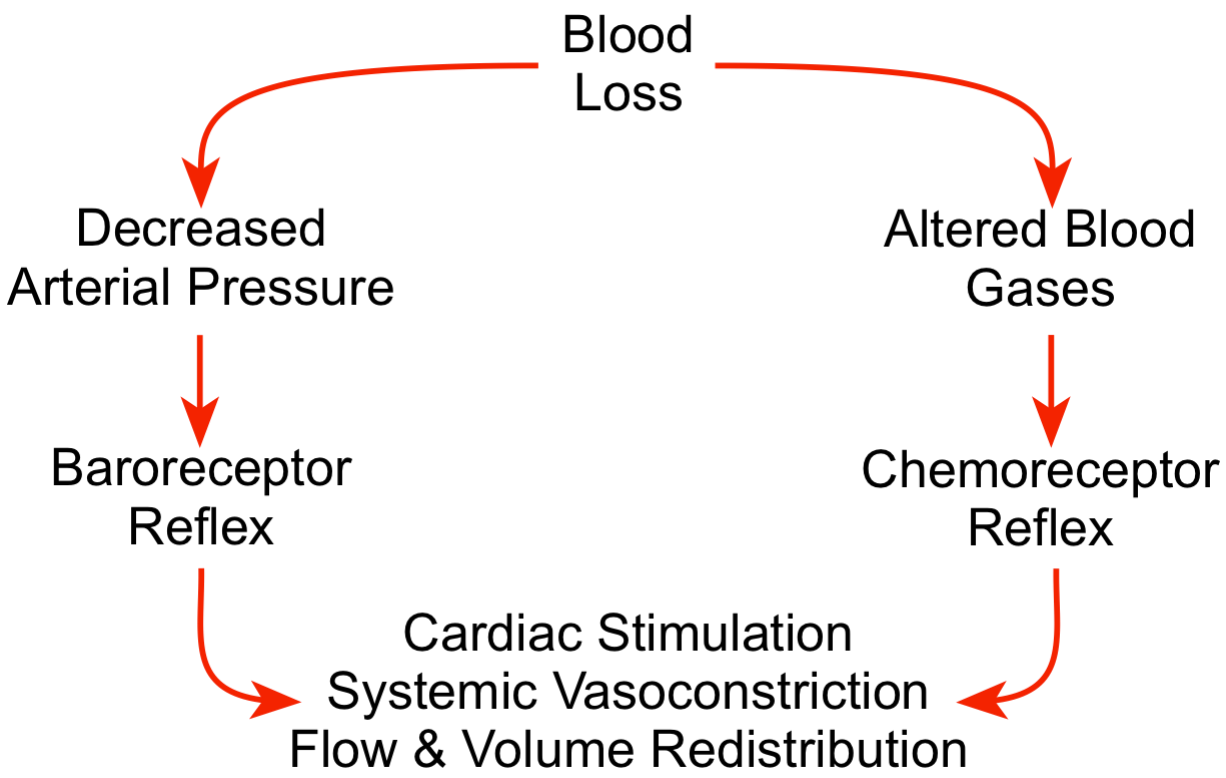
- Produce:
  - ✓ROS (hydrogen peroxide (H_2O_2), superoxide ($O_2^{\cdot -}$),hydroxyl radical ($OH^{\bullet}$)
  - ✓Lipid-peroxidation products
  - ✓Elastase
  - ✓Cathepsin G
  - ✓VA mediators (Leukotrienes, eicosanoids, PAF)

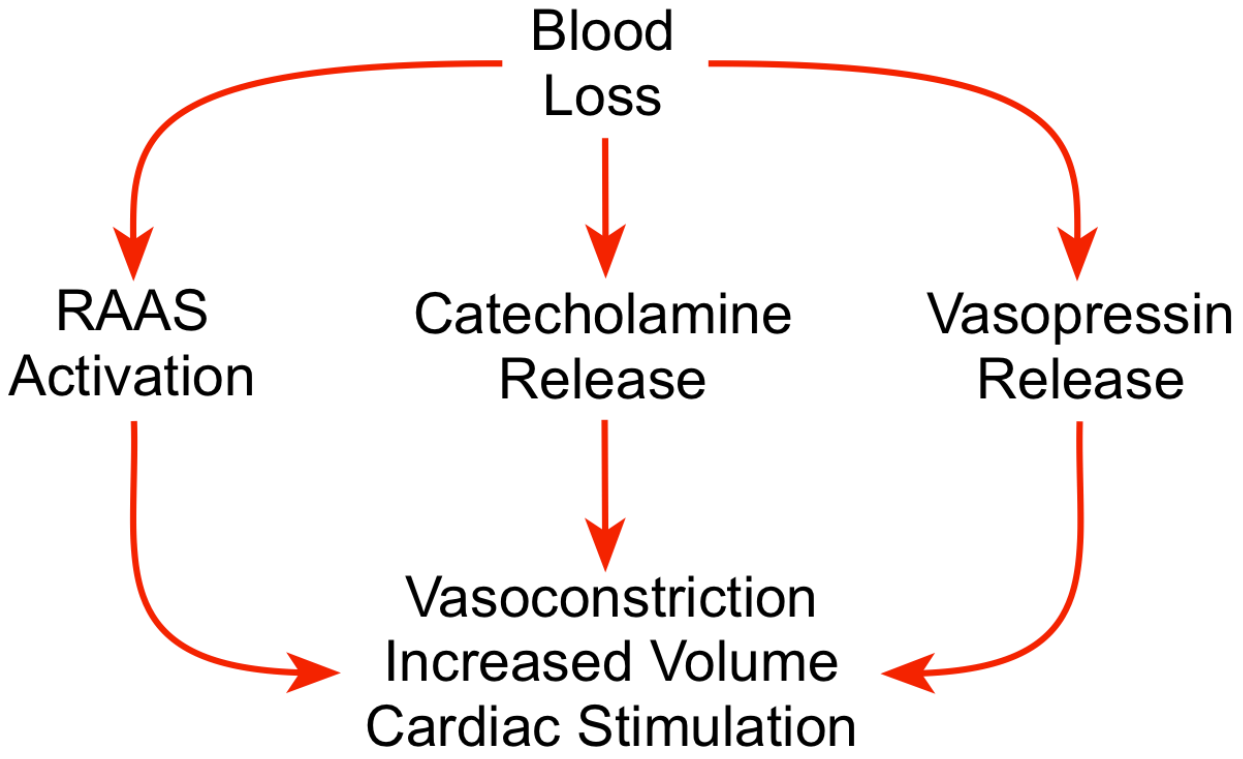



Integrins
Selectins
Basement Membrane
Endothelium
Blood Flow
Neutrophil
1
2
3
Vascular Lumen
PECAM-1
PGSL-1
P-Selectin
CD11/CD18
ICAM-1
Interstitial Space
Loose Adhesion ("Rolling")
Firm Adhesion/ Aggregation
Diapedesis


Normal
Sepsis
TFPI
Anticoagulants
Thrombus formation
Coagulation cascade
Endothelial Damage
Proteases and antimicrobial peptides
Histones
Microbes
Platelets
Red blood cells
Neutrophils
Fibrins
Tissue factor

Forms of Shock- Hypovolumeic/ Hemorrhagic





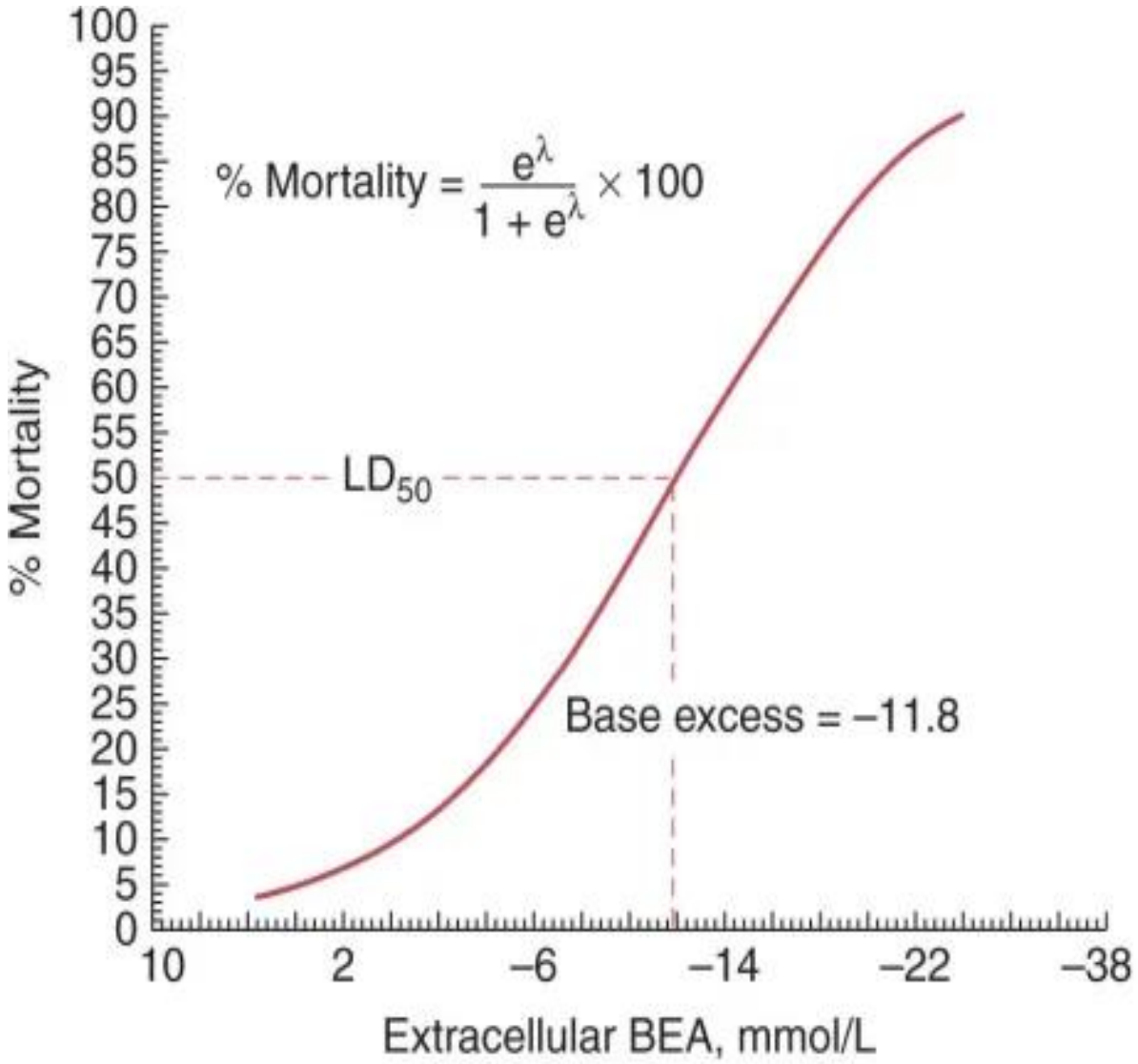
Hypovolumeic/ Hemorrhagic - Diagnosis

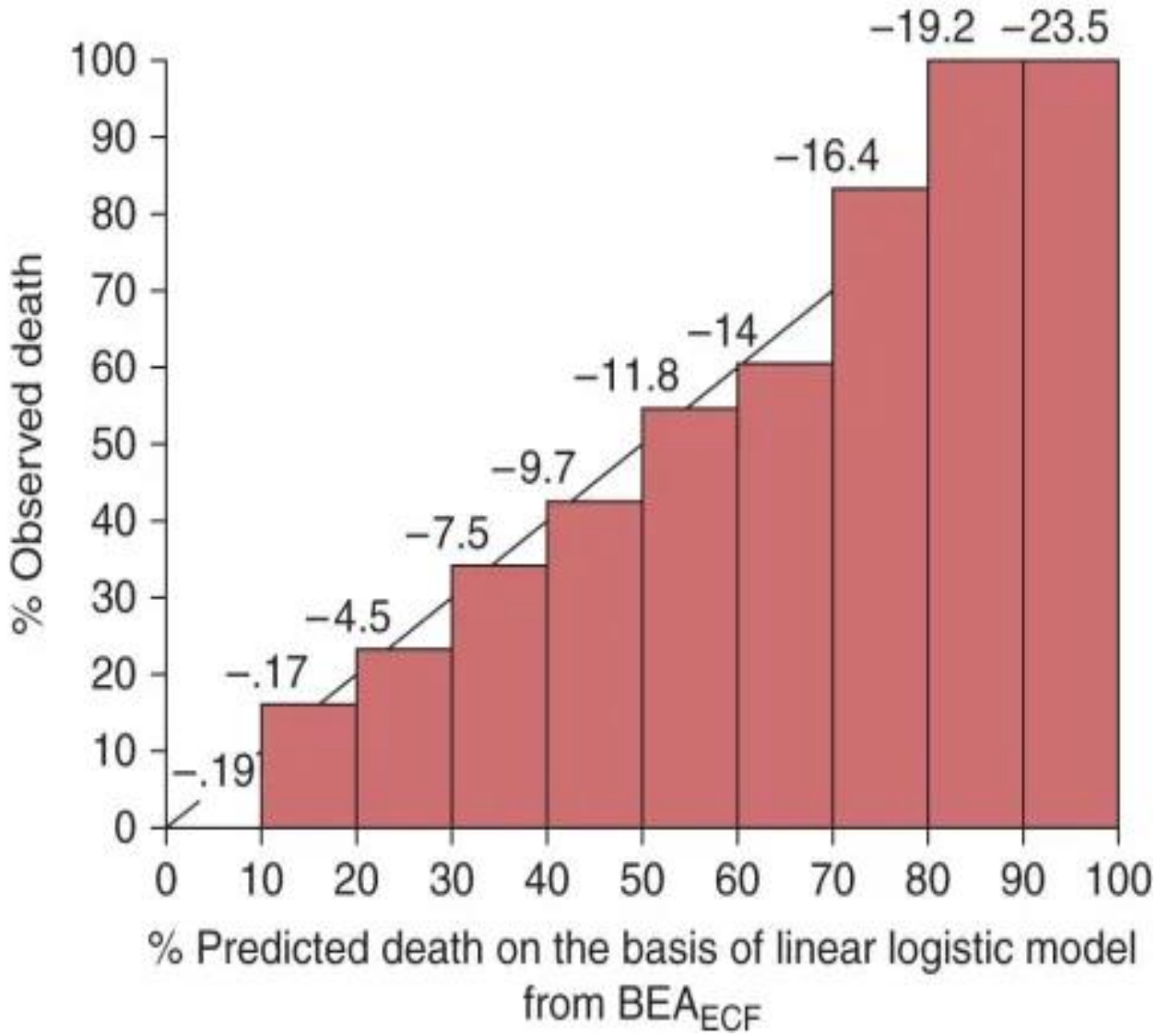
Sx & Sg

- ✓Agitation & Anxiety→→→ LOC
- ✓Thirst
- ✓Tachycardia & Hypotension
- ✓Cold clammy extremities
- ✓Weak or absent peripheral pulses
- ✓Decrease in urine output
- ✓Tachypnea

Lab

- Serum lactate
- Base deficit
- Hct


% Mortality = $\frac{e^{\lambda}}{1 + e^{\lambda}} \times 100$
LD50
Base excess = −11.8
% Mortality
Extracellular BEA, mmol/L
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
10
2
−6
−14
−22
−38


−19.2
−23.5
−16.4
−14
−11.8
−9.7
−7.5
−4.5
−.17
−.19
% Observed death
% Predicted death on the basis of linear logistic model from BEA_{ECF}
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
80
90
100

HEMORRHAGE CLASSIFICATION - MANAGEMENT

CLASS	BLOOD LOSS	HR	BP	PULSE PRESSURE	RR	URINARY OUTPUT	GCS	BASE DEFICIT	TRANSFUSE
I	<15%	↔	↔	↔	↔	↔	↔	0 to (-2)	Monitor
II (MILD)	15 – 30%	↔/↑	↔	↓	↔	↔	↔	(-2) to (-6)	Possible
III (MODERATE)	31 – 40%	↑	↔/↓	↓	↔/↑	↓	↓	(-6) to (-10)	Yes
IV (SEVERE)	>40%	↑/↑↑	↓	↓	↑	↓↓	↓	(-10) or less	Massive Transfusion

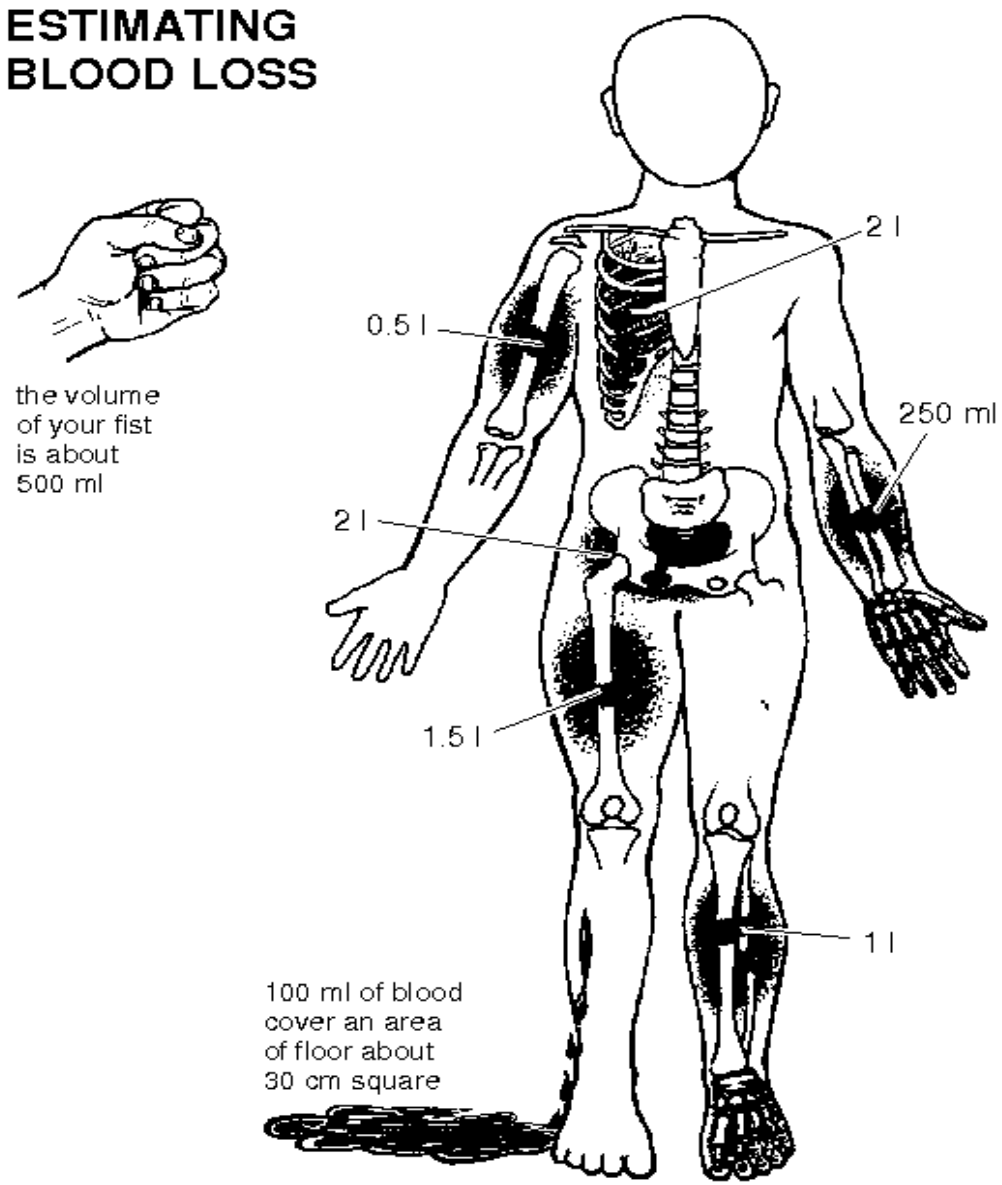
Management

	Rapid response	Transient response	Minimal or no response
Vital signs	Return to normal	Transient improvement, recurrence of decreased blood pressure and increased heart rate	Remain abnormal
Estimated blood loss	Minimal (10% to 20%)	Moderate and ongoing (20% to 40%)	Severe (>40%)
Need for more crystalloid	Low	Low to moderate	Moderate as bridge to transfusion
Need for blood	Low	Moderate to high	Immediate
Blood preparation	Type and crossmatch	Type-specific	Emergency blood release
Need for operative intervention	Possibly	Likely	Highly likely
Early presence of surgeon	Yes	Yes	Yes

Table reprinted with permission from the American College of Surgeons [57]. *Isotonic crystalloid solution, 2,000 ml in adults; 20 ml/kg in children.

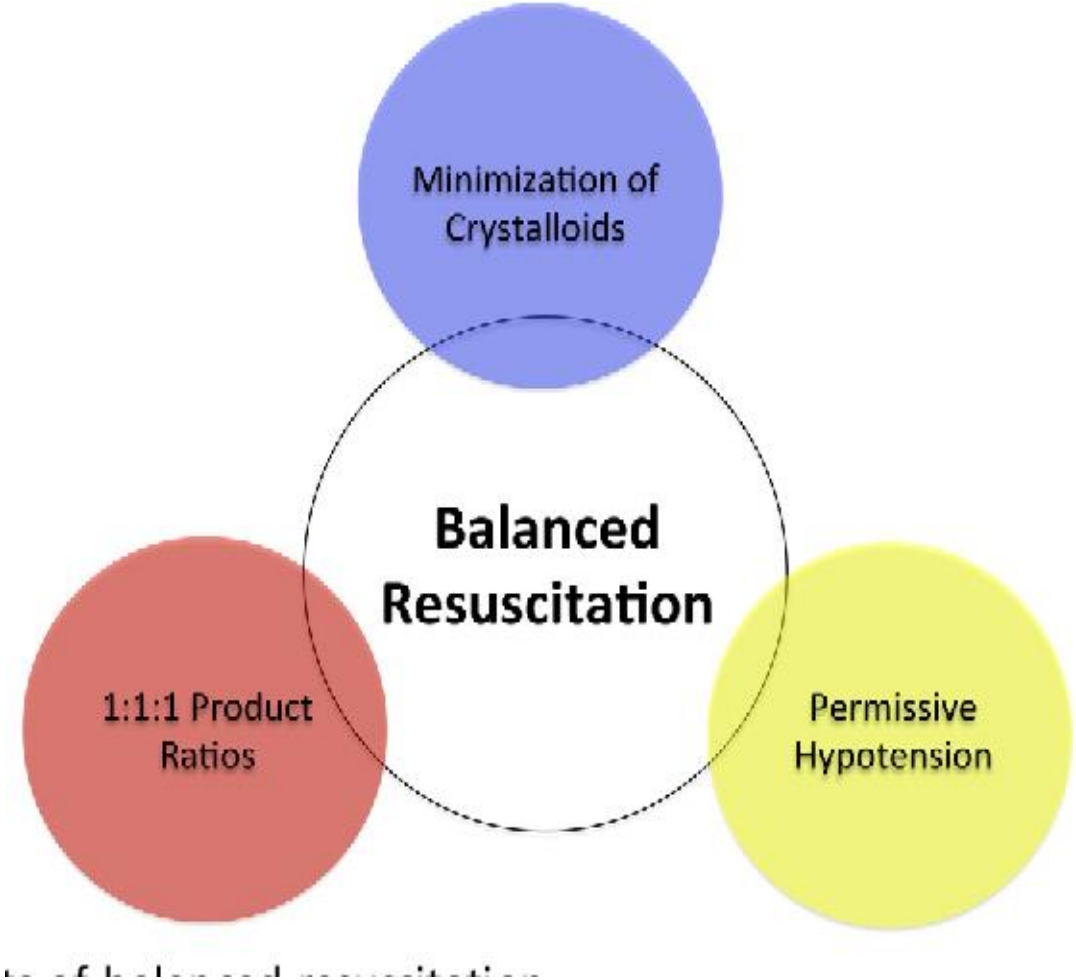
Identification of Source of bleeding

- External
- Intrathoracic
- Intraperitoneal
- Retroperitoneal
- Long bone fractures
- GI hemorrhage



Hypotensive resuscitation (Damage control resuscitation)

- Any delay in surgery for control of hemorrhage increases mortality (1%/ each 3 minutes)
- With uncontrolled hemorrhage, attempting to achieve normal BP increases mortality
- A Goal of SBP of 80-90mmHg is reasonable in patients with penetrating trauma (Exc: Brain injury)
- Profound hemodilution should be avoided by early blood transfusion



Fluid resuscitation

- Crystalloids better than colloids
- Hypertonic Saline has immunomodulatory effects:
  - ✓↓ ROS & reperfusion injury
  - ✓Less impairment of immune function
  - ✓Less brain swelling in multi-trauma patients
  - ✓Decrease incidence of ARDS

- Blood products:
  - ✓Should be used early in severely hypotensive patients
  - ✓Ratio Plasma-Platelets-RBCs= 1:1:1
  - ✓Adjuncts:
    - Fibrinogen concentrates
    - Prothrombin complex concentrates
    - Early use of Tranexamic acid (TXA)
  - ✓Maintenance of Normothermia

Tranexamic acid- Crash -2 Trial

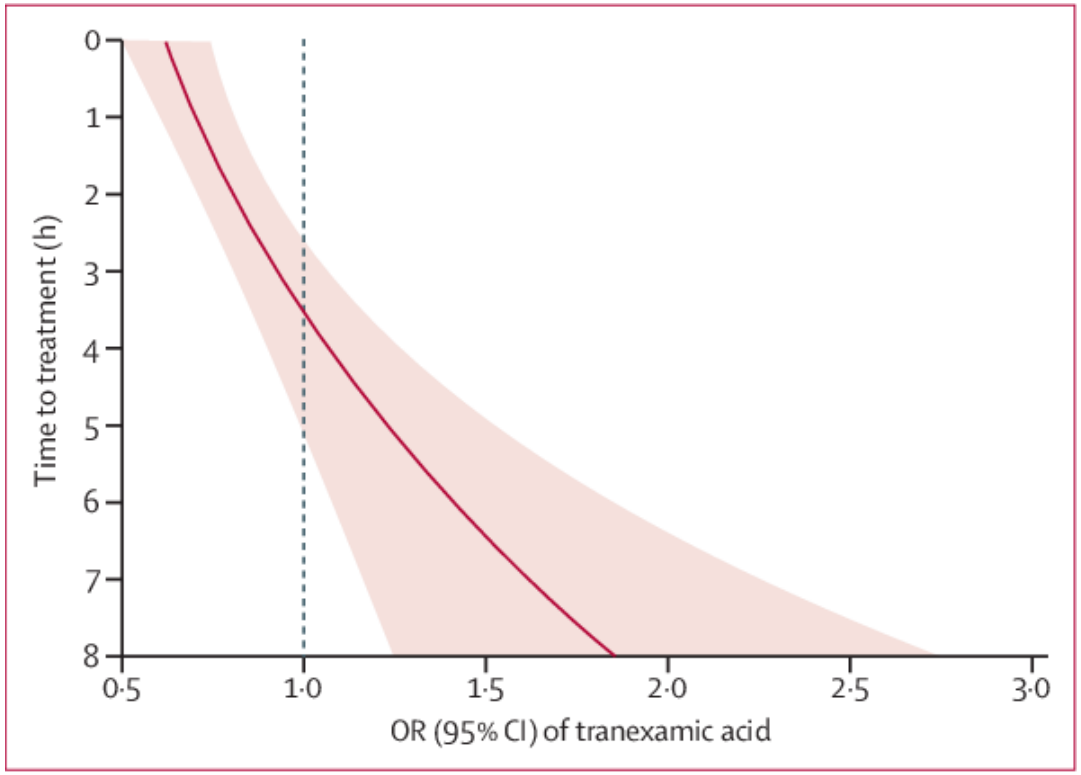


Figure 2: **Effect of tranexamic acid on death due to bleeding by time to treatment**

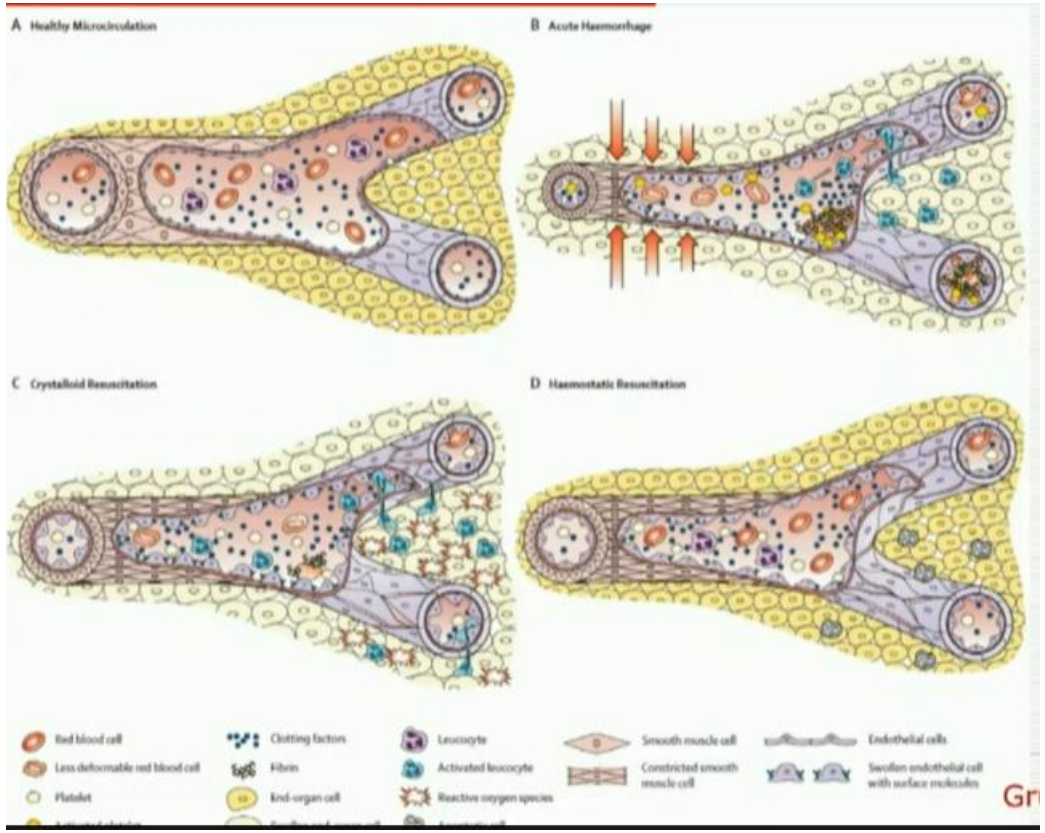
Shaded area shows 95% CI. OR=odds ratio.

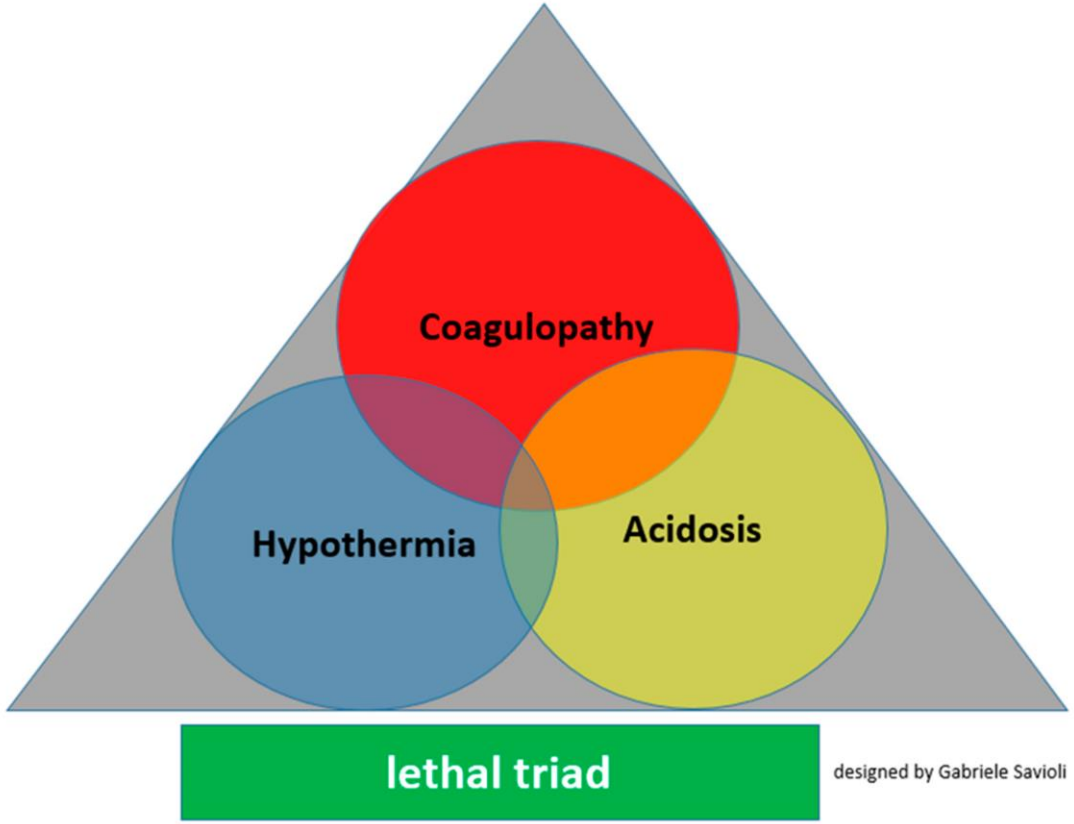
Homeostatic resucitation

Basic Requirement for Clotting

- Membranes
- Clotting factors (enzymes!)
- Energy (High energy phosphate bound ~ ATP)
- Optimal physical, chemical environment
  - Temperature, pH, Calcium ...
- Cells

Homeostatic resucitation



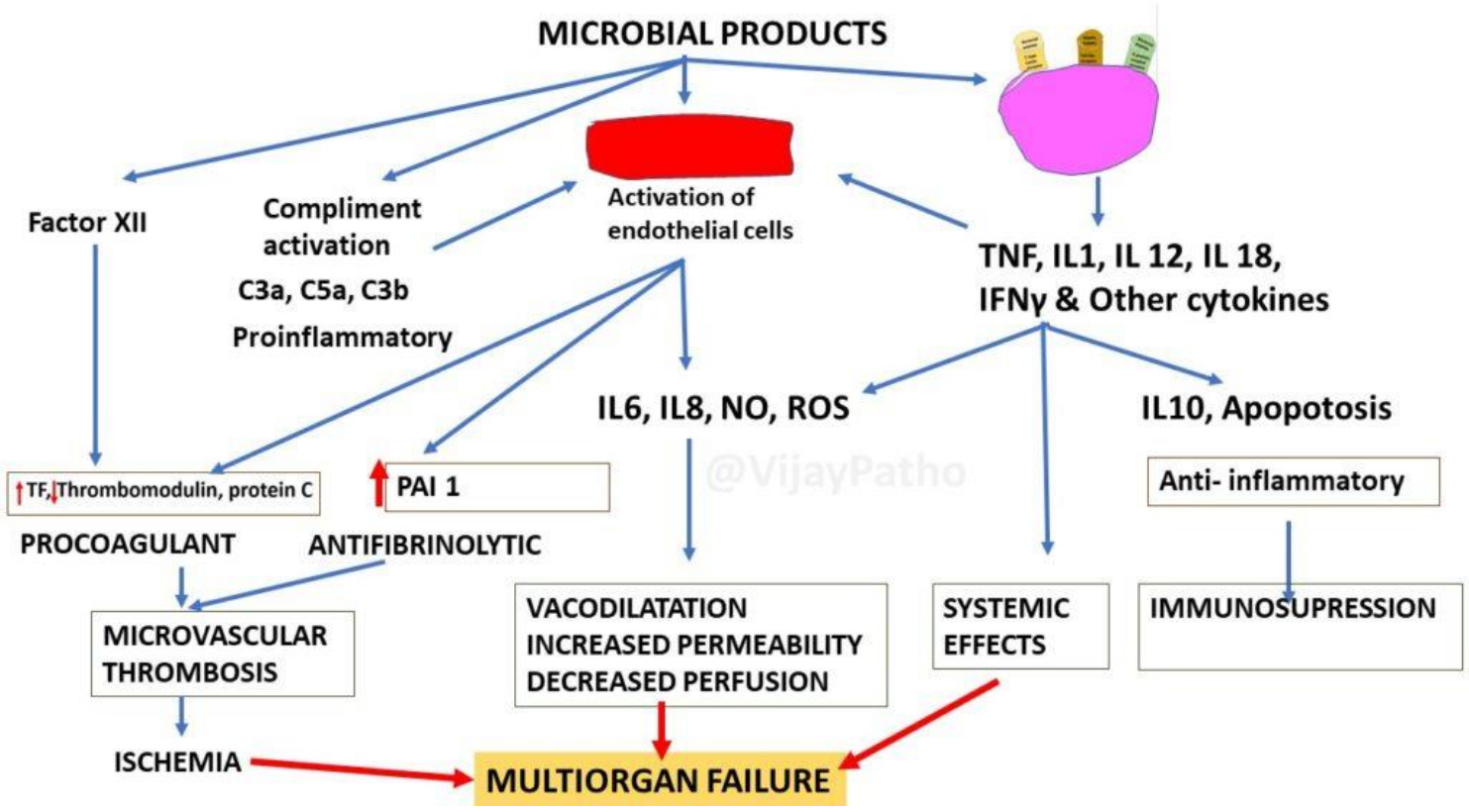


ACOT

Forms of Shock- Traumatic Shock

- Traumatic shock= Hemorrhagic shock + Severe tissue injury
- The usual response to Hemorrhagic shock is compounded by SIR to DAMPs.
- Lethal with significantly less blood loss & More likely to be complicated by MOFS
- Management:
  - Prompt control of Hemorrhage
  - Adequate volume resuscitation
  - Debridement of nonviable tissue
  - Stabilization of fractured bone
  - Appropriate treatment of Soft tissue / Internal organ injuries

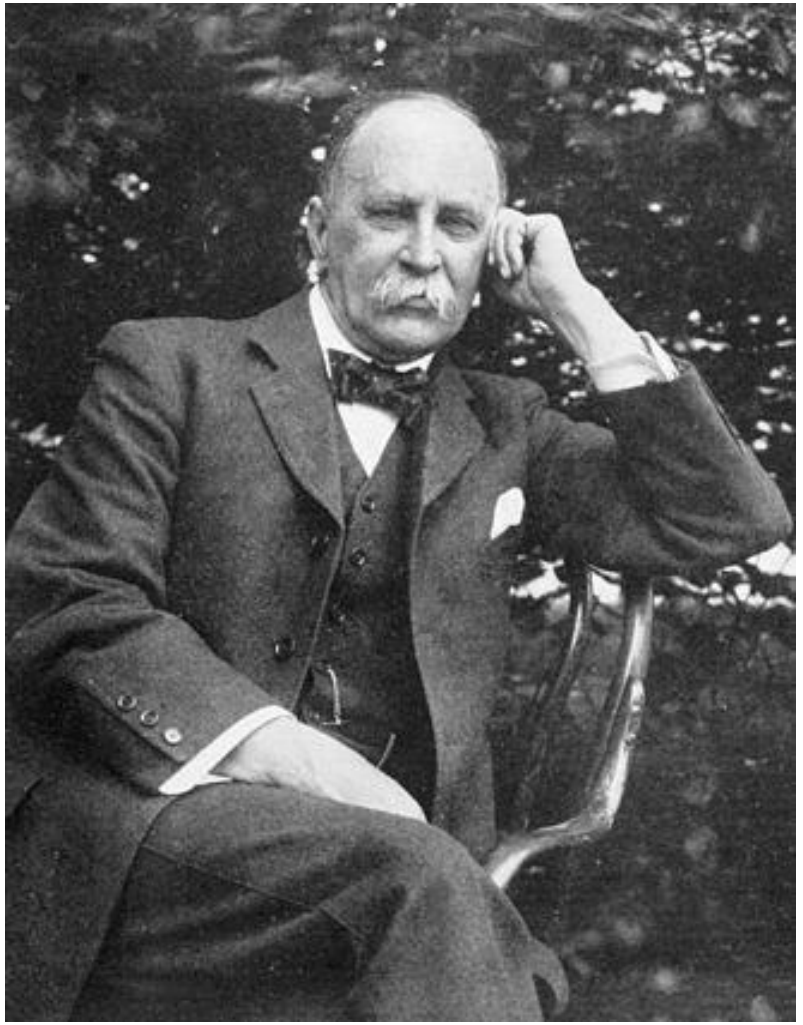
Forms of Shock- Septic Shock



- Sepsis
- Pancreatitis
- Burns
- Anaphylaxis
- Acute adrenal insufficiency
- Prolonged severe shock (HS, CS, CPB)
- Hypoxic lactic acidosis
- CO poisoning

William Osler (1849 –1919)

- He stated that *"Except on few occasions, the patient appears to die from the body's response to infection rather than from it."*
- The discovery of cytokines began to allow insight into the human organism's response to infection, and led to an explosion in our understanding of the host inflammatory response.
- The design of new therapies targeted at modifying the inflammatory response to infection, which seems to cause much of the organ dysfunction and failure.



SOFA score and Definition of Sepsis & Septic shock

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

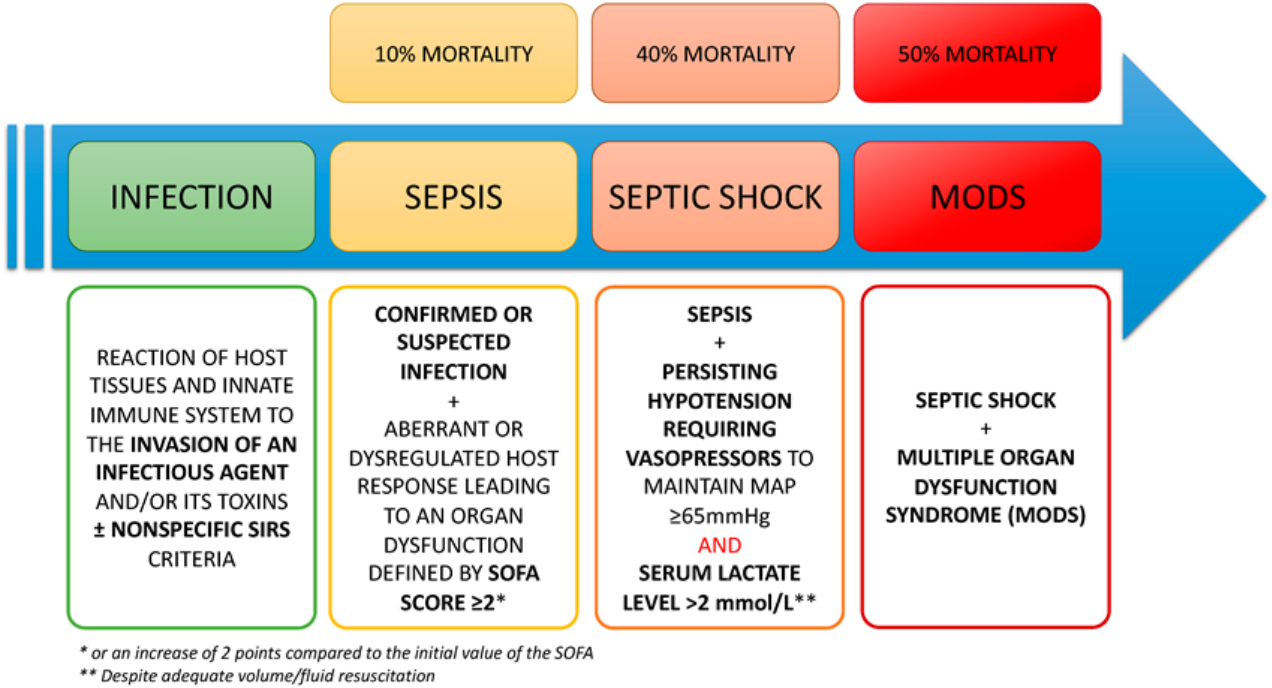
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

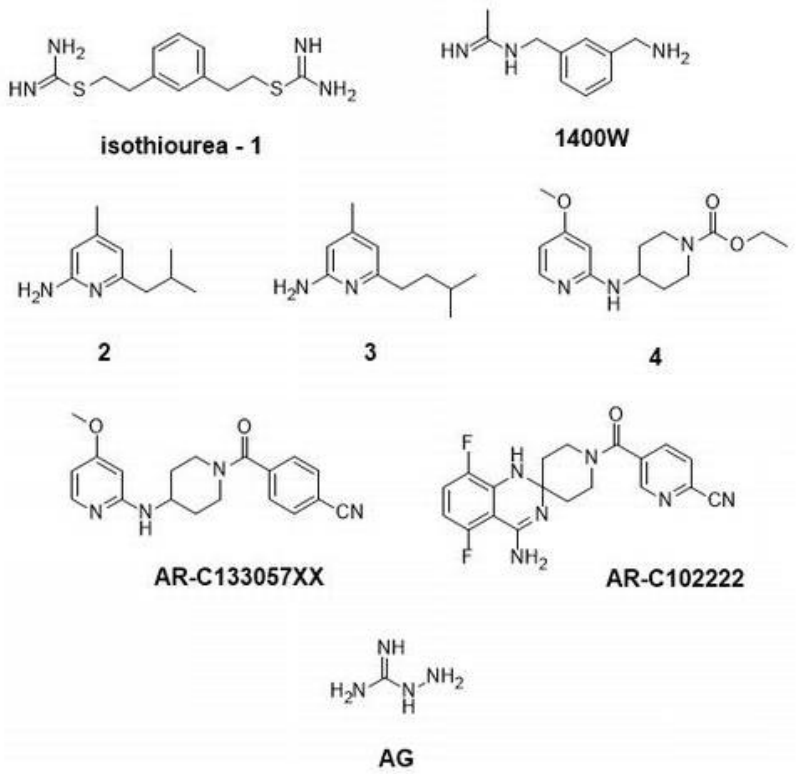
Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score

System	0	1	2	3	4
Respiration PaO2/FiO2, mmHg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation Platelets, x10³/uL	≥150	<150	<100	<50	<20
Liver Bilirubin, mg/dL (umol/L)	<1.2 (20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33 - 101)	6.0 - 11.9 (102 - 204)	>12.0 (204)
Cardiovascular	MAP ≥70mmHg	MAP <70mmHg	Dopamine <5 or Dobutamine (any dose)	Dopamine 5.1 - 15 or Epinephrine ≤0.1 or Norepinephrine ≤0.1	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1
CNS GCS Score	15	13 - 14	10 -12	6 - 9	<6
Renal Creatinine, mg/dL (umol/L) Urine Output, mL/d	<1.2 (110)	1.2 - 1.9 (110 - 170)	2.0 - 3.4 (171 - 299)	3.5 - 4.9 (300 - 440) <500	>5.0 (440) <200

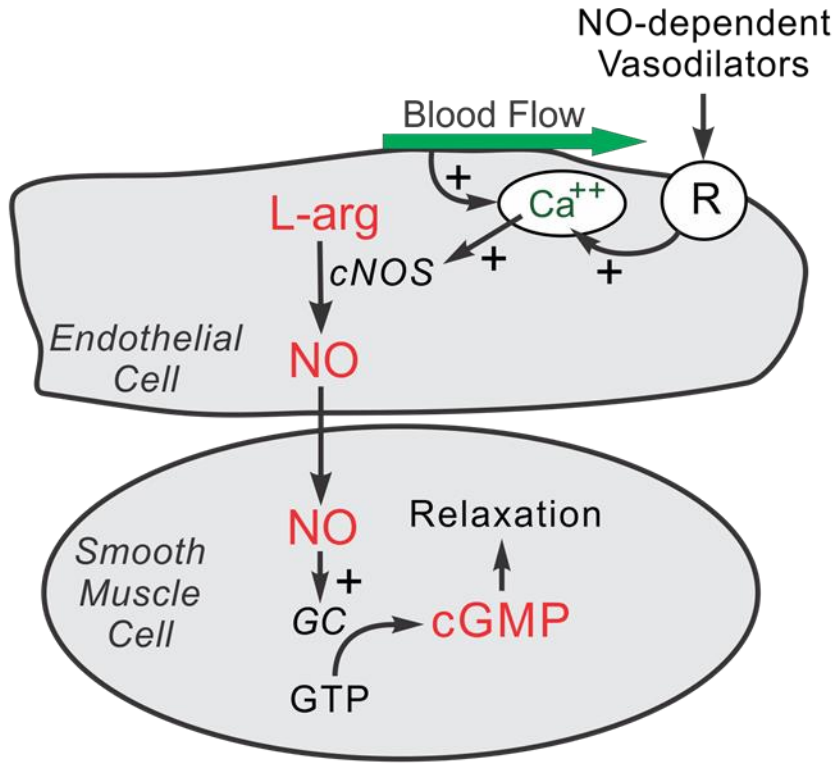
*Catecholamine Doses = ug/kg/min for at least 1hr



Inducible Nitric Oxide Synthase(iNOS)



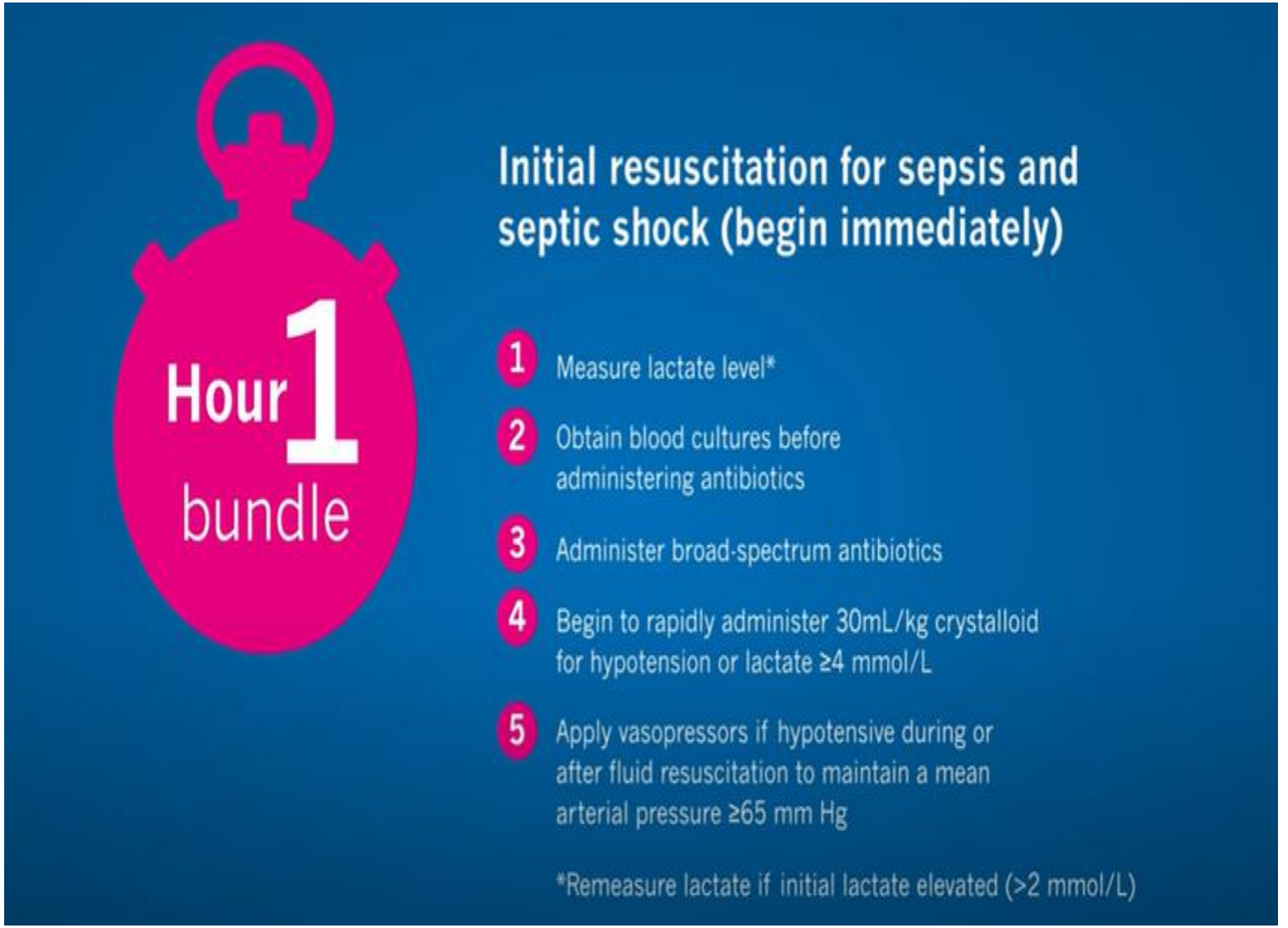
Inducible nitric oxide synthase (iNOS) inhibitors



R, receptor; *L-arg*, L-arginine; *cNOS*, constitutive nitric oxide synthase; *GC*, guanylyl cyclase; *GTP,* guanosine triphosphate; *cGMP,* cyclic guanosine monophosphate.

Diagnosis & Management

- Sx & Sg: Fever, ↑HR, ↓BP, Tachypnea, malaise , confusion, oliguria, warm extremities
- Examination to detect source of infection
- Blood culture
- Lactate level
- Imaging



Pulse index Contour Continuous Cardiac Output (PiCCO)

Stewart–Hamilton equation

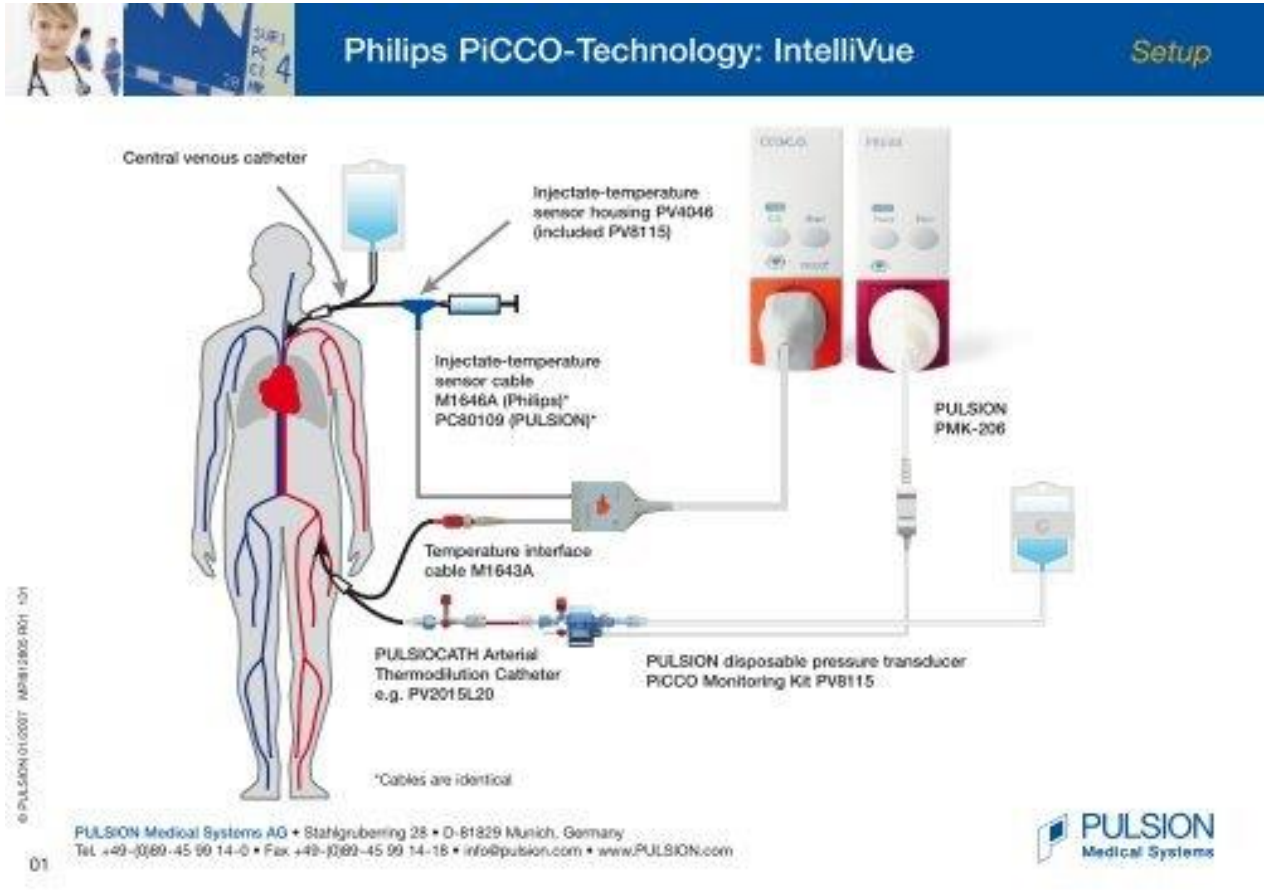
$$CO = \left(\frac{k \times (T_{blood} - T_{injectate}) \times V_{injectate}}{\int \Delta T_B \times dt} \right)$$

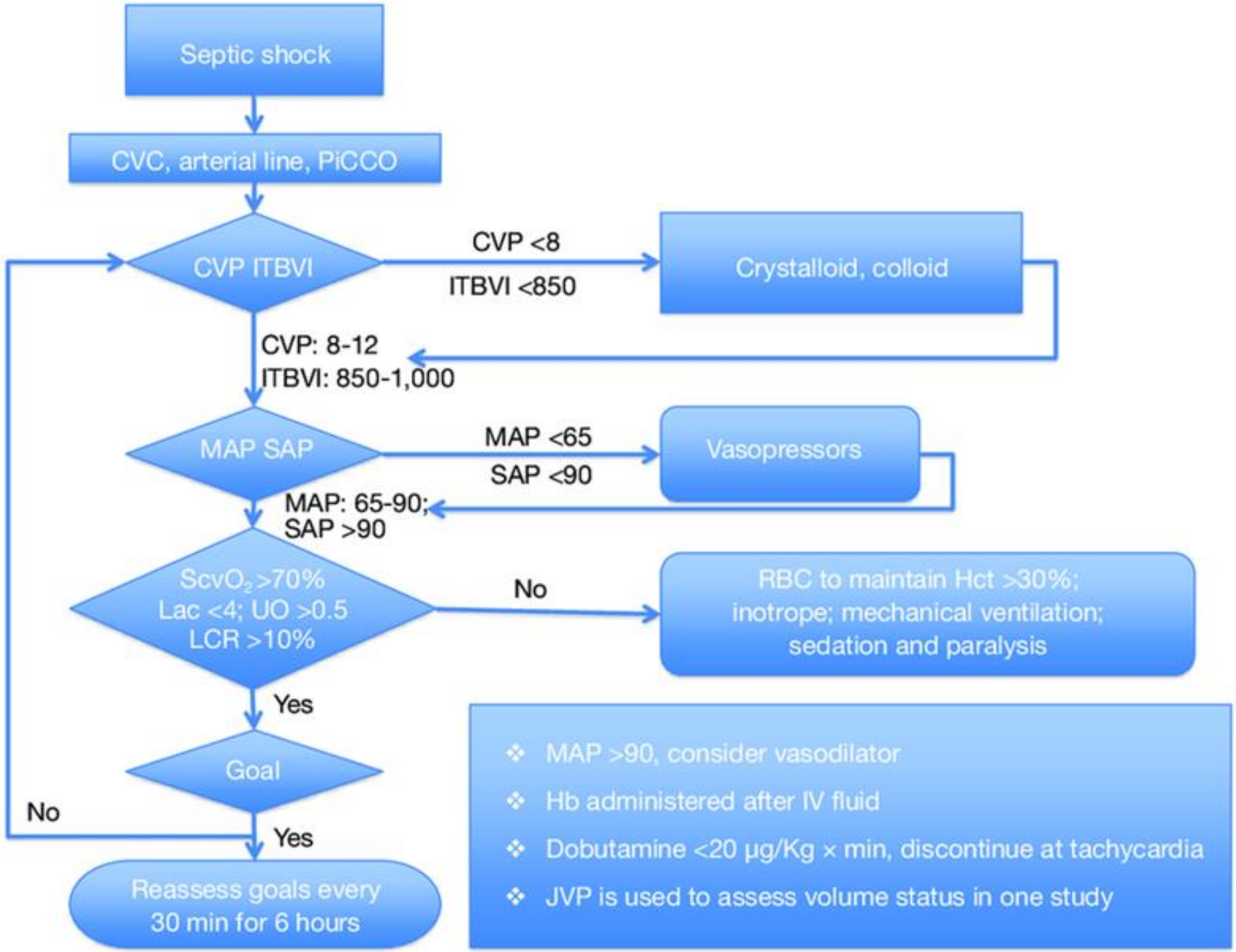
Or modified to suit dye-dilution techniques:

$$CO = \frac{\text{amount of injected indicator}}{\text{area under dilution curve}}$$

Definition of terms used

CO = cardiac output
$V_{injectate}$ = volume of injectate
k = correction factor
T_{blood} = temperature of blood
$T_{injectate}$ = temperature of injectate
$\int \Delta T_B \times dt$ = integral of area under temperature/time curve




Septic shock
CVC, arterial line, PiCCO
CVP ITBVI
CVP <8
ITBVI <850
Crystalloid, colloid
CVP: 8-12
ITBVI: 850-1,000
MAP SAP
MAP <65
SAP <90
Vasopressors
MAP: 65-90;
SAP >90
ScvO2 >70%
Lac <4; UO >0.5
LCR >10%
No
RBC to maintain Hct >30%;
inotrope; mechanical ventilation;
sedation and paralysis
Yes
Goal
No
Yes
Reassess goals every
30 min for 6 hours
MAP >90, consider vasodilator
Hb administered after IV fluid
Dobutamine <20 µg/Kg × min, discontinue at tachycardia
JVP is used to assess volume status in one study

Vasopressors

- Norepinephrine (1st line)
- Arginine Vasopressin (Arterial resistance to catecholamines)
- Dobutamine (Associated cardiac dysfunction)

Control of Hyperglycemia/ Insulin resistance

- Common in Septic even non diabetic patients
- Increases Mortality, duration of ABx therapy, prolonged ventilation support & Renal replacement therapy
- Insulin Therapy:
  - ✓Intensive Insulin Rx (BS 80-110) (MR 4.6%)
  - ✓Conventional therapy (BS>215) (MR 8.0%)

ARDS/ Ventilatory support

- Low Vt (6ml/Kg compared to 12)
- Higher level of PEEP
- Alveolar recruitment maneuvers
- Prone positioning

Corticosteroids

- Severe sepsis is associated with adrenal insufficiency
- Studies are contradictory
- SBP <90mmHg despite adequate fluid & Vasopressor therapy (200mg HC/day for 7 days)

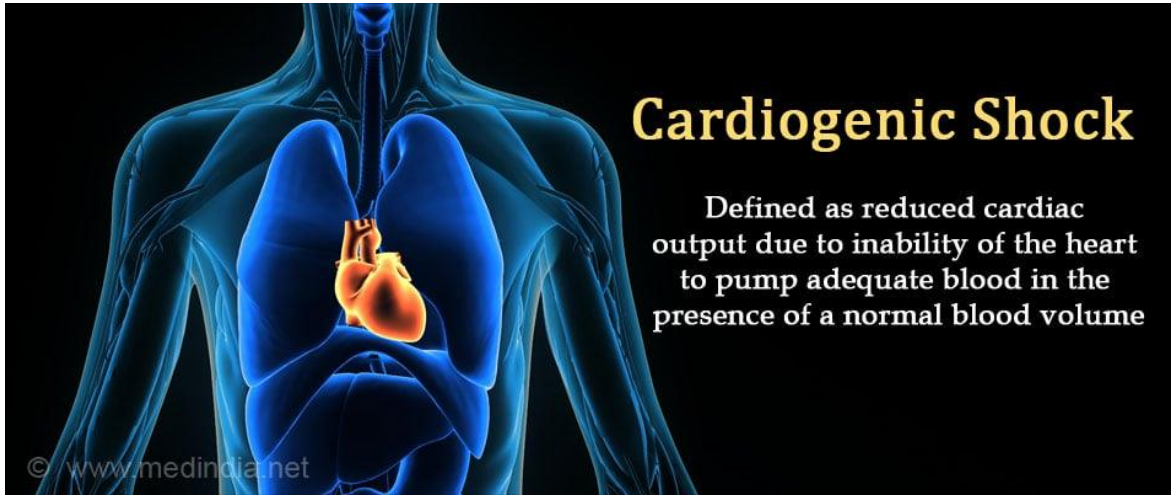
Adjunctive Immune therapy

- Anti-endotoxin Antibodies
- Anti-cytokine antibodies
- Cytokine – Receptors antagonists
- Immune enhancers
- Non-Isoform NOS- inhibitor
- O2-Radical scavengers

	Mechanism of action	Summary of evidence
IMMUNOSUPPRESSIVE COMPOUNDS		
anti-TNFα (various)	Blocks pro-inflammatory effects of TNFα	- Individual studies: no beneficial effects (94) - Meta-analysis: reduced 28-day mortality, OR = 0.91 [95% CI 0.83–0.99] (94)
IL-1RA (anakinra)	Blocks IL-1 receptor → inhibits downstream pro-inflammatory effects	- Study in unselected population of severe sepsis patients: no effect on mortality (21) - *Post-hoc* analysis in subgroup of hyperinflamed patients with macrophage activation syndrome: lower mortality (93)
IMMUNOSTIMULATORY COMPOUNDS		
GM-CSF	Enhances antigen presenting capacity and pro-inflammatory cytokine production	- Meta-analysis: no effect on 28-day mortality in sepsis patients (probably underpowered) (107) - Biomarker-guided study (based on mHLA-DR expression): restoration of monocytic immunocompetence, shorter duration of mechanical ventilation, and more swift improvement of disease severity scores as exploratory endpoints (95)
IFN-γ	Enhances antigen presenting capacity and pro-inflammatory cytokine production	- Human endotoxemia model (mimicking sepsis-induced immunoparalysis): increased mHLA-DR expression, restored TNFα production and further attenuated IL-10 production (43) - Case series in patients suffering from opportunistic infections not responding to regular treatment: increased mHLA-DR expression and cytokine production by *ex vivo*-stimulated leukocytes (97)
Recombinant human IL-7	Reduces apoptosis and enhances lymphocyte function	- Phase 2 trial in septic shock patients with severe lymphopenia: safe, well-tolerated and reversal of lymphopenia (111)
anti-PD-(L)1	Inhibits PD-1-PD-L1 interaction → reduces apoptosis and promotes T-cell responses	- Preclinical data in sepsis models: promising results (e.g., prevention of sepsis-induced depletion of lymphocytes, increased TNF-α and IL-6 production, decreased IL-10 production, enhanced bacterial clearance, improved survival (102) - Clinical data in the oncology field: effective, especially in advanced melanoma and non-small cell lung cancer. - No clinical trials in sepsis patients yet.

TNFα, tumor necrosis factor alpha; IL1RA, Interleukin-1 receptor antagonist; IL-1, interleukin-1; GM-CSF, granulocyte-macrophage colony stimulating factor; IFNγ, interferon gamma; IL-7, interleukin-7; anti-PD-L1, programmed death-1 ligand antagonist; OR, odds ratio.

Forms of Shock- Cardiogenic shock



CAUSES OF CARDIOGENIC SHOCK

Myocardial Infarction
(Can be a primary reason, a cause or be a consequence of many of the pathologies listed below)

Mechanical defect
- Acute mitral regurgitation - papillary muscle rupture
- Ventricular wall rupture - septal or free wall
- Tamponade
- Left ventricular outflow obstruction - HOCM, AS
- Left ventricular inflow obstruction – MS, atrial myxoma

Contractility defect
- Arrhythmias
- Cardiomyopathy
- Direct cardiac trauma
- Drugs
- Sepsis
- Myocarditis
- Pancreatitis
- Endocrine causes
- Pulmonary embolus
- Right ventricular infarction with hypovolaemia

1. SBP<90mmHg for at least 30 minutes
2. Reduced cardiac Index <2.2L/min per m^2
3. Elevated PAWP >15mmHg

Cardiogenic shock

- Mortality ≈50-80%
- MI is the most common cause (7–24Hrs after onset of MI)
- Early recognition is of paramount importance to prevent progression

Neuroendocrine response

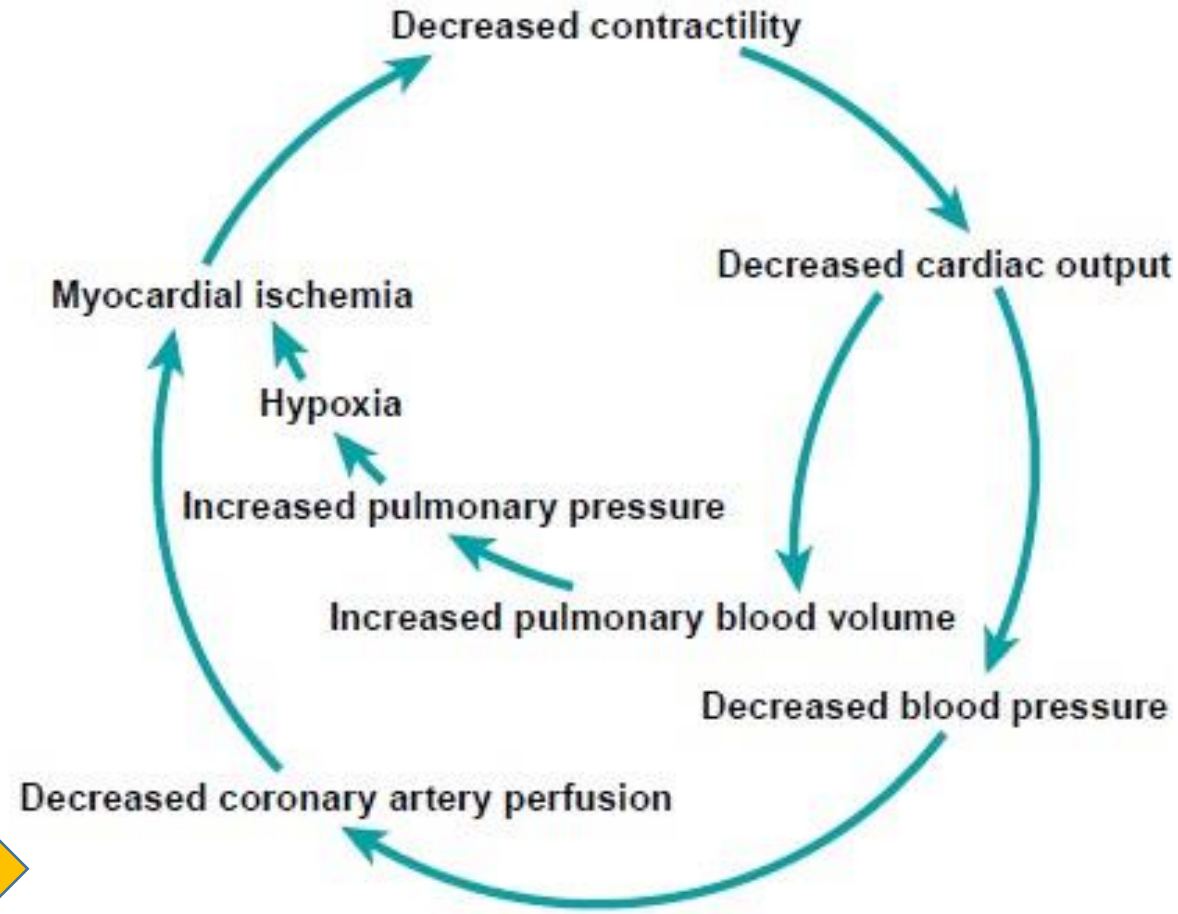
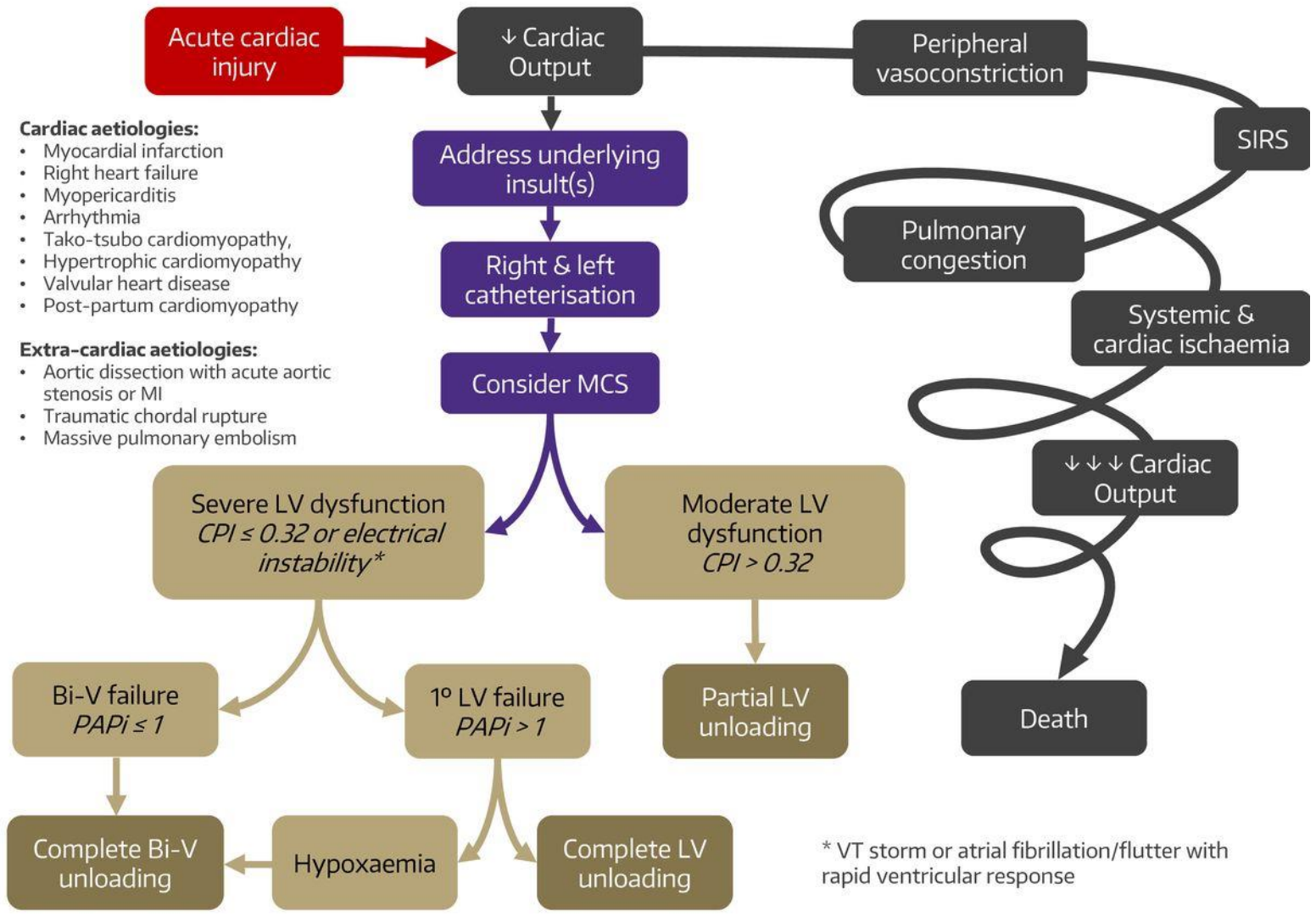


FIGURE 30-3 Pathophysiology of cardiogenic shock.

Diagnosis

- ECG
- ECHO
- CXR
- CBC
- ABGs
- Electrolytes (K, Mg, Ca)
- Cardiac Enzymes
- Coronary angio

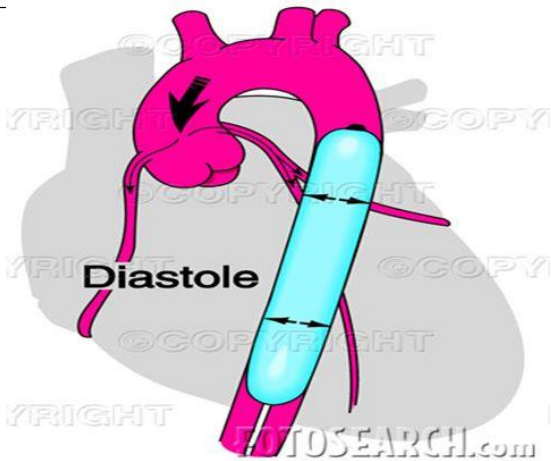


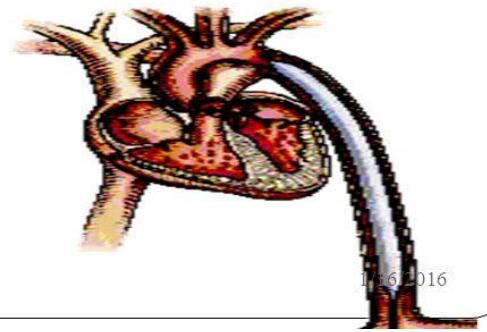
Management

- Airway & Breathing
- R/O Hypovolemia
- O2
- Judicious fluid administration
- Pain control
- Electrolyte (K, Ca, Mg)
- Arrhythmias
- Inotropes (Dobutamine, Dopamine, Adrenaline, Phosphodiesterase inhibitors Amrinone & Milrinone)
- Anticoagulation
- B-Blockers
- ACE-inhibitors
- Intra-aortic Balloon Pump
- Coronary Revascularization
  - PTCA
  - CABG

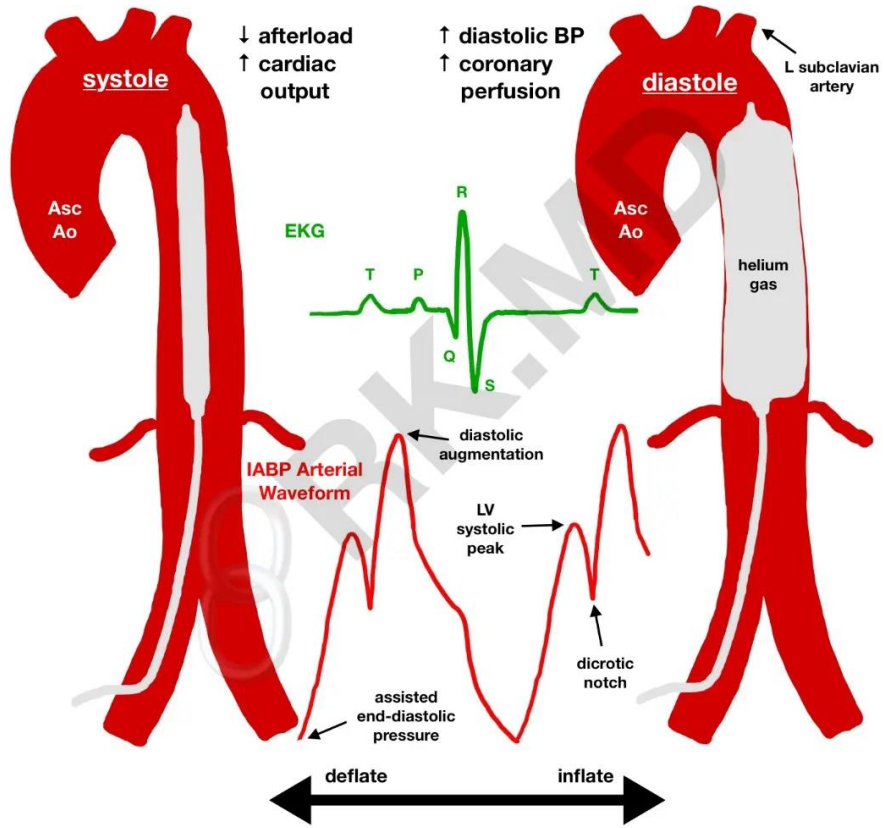
Inflation

- It inflates immediately following aortic valve closure to to augment diastolic coronary perfusion pressure.



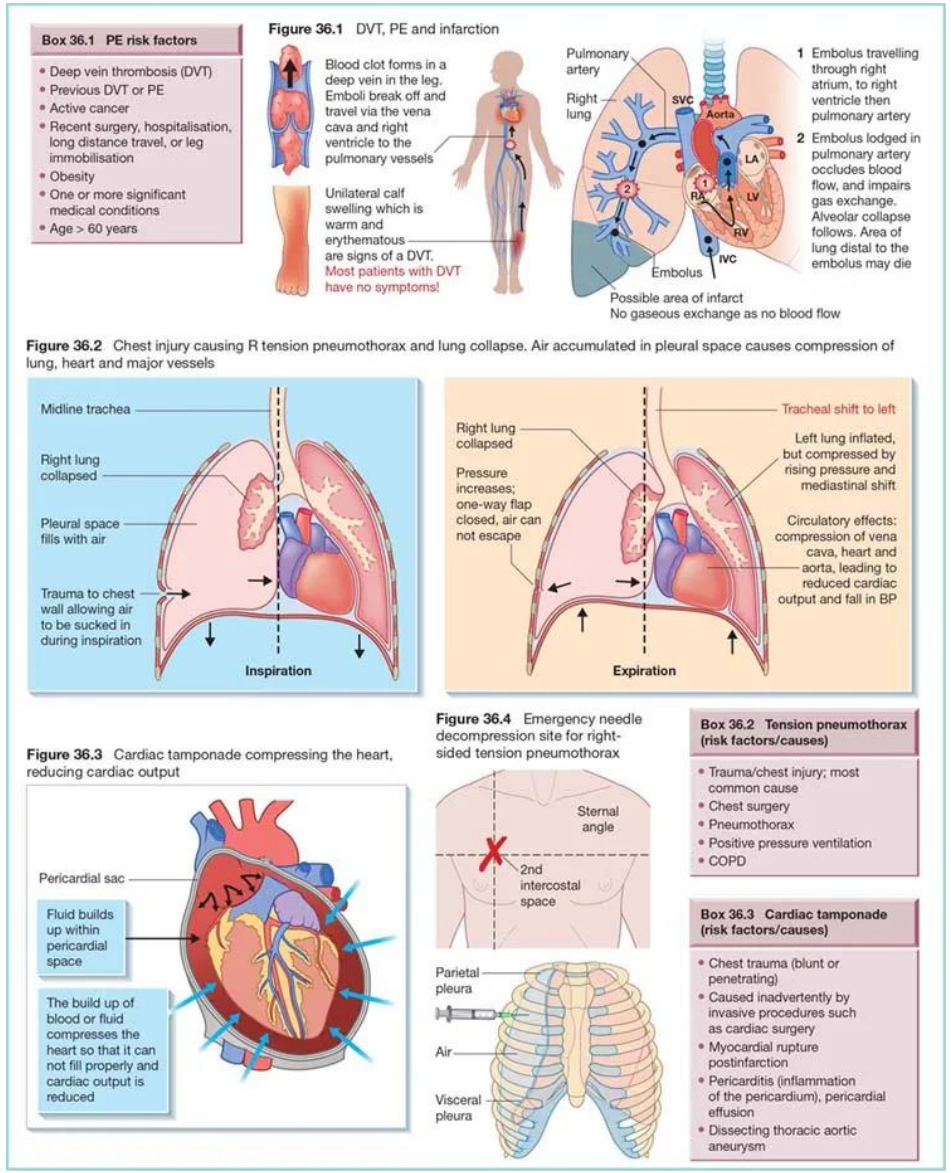


INTRA-AORTIC BALLOON PUMP (IABP)

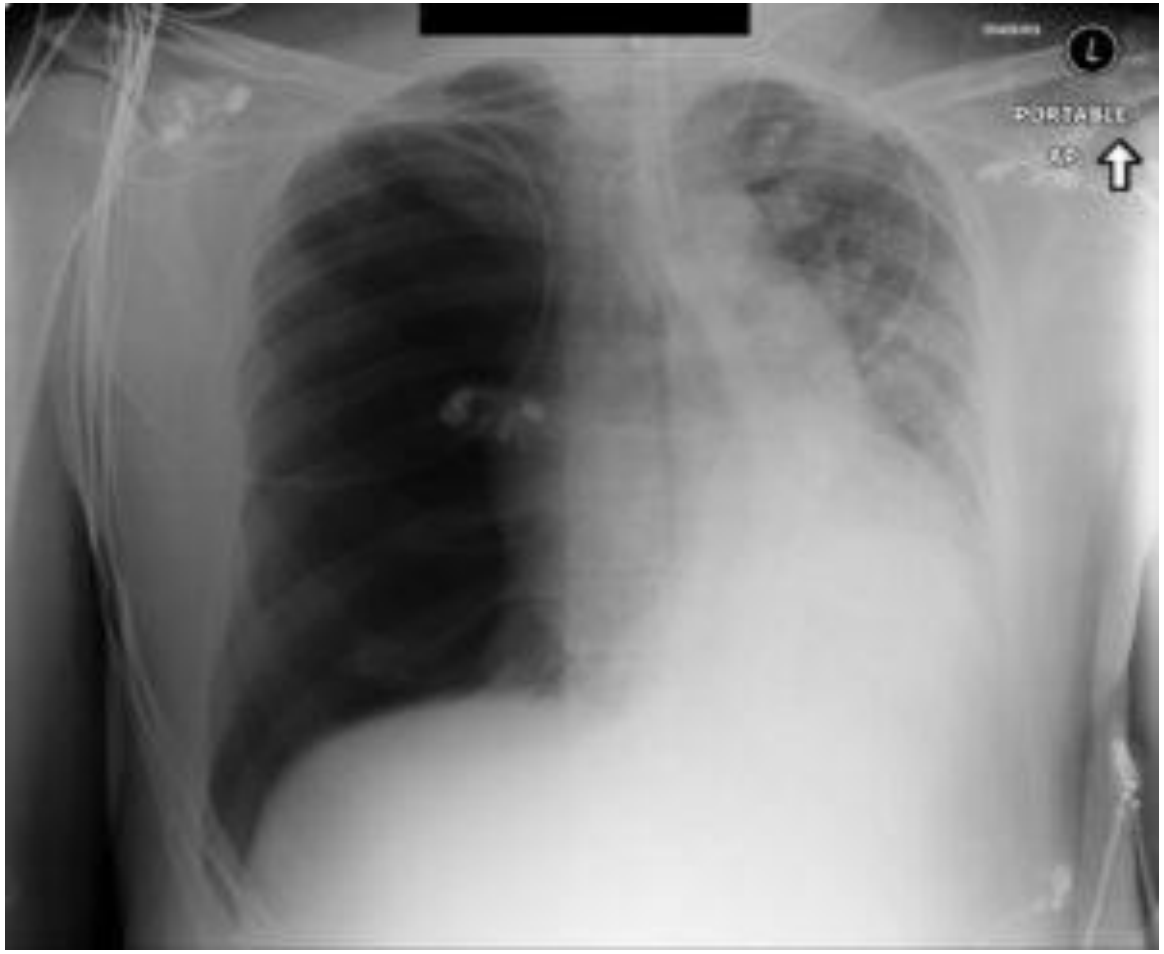


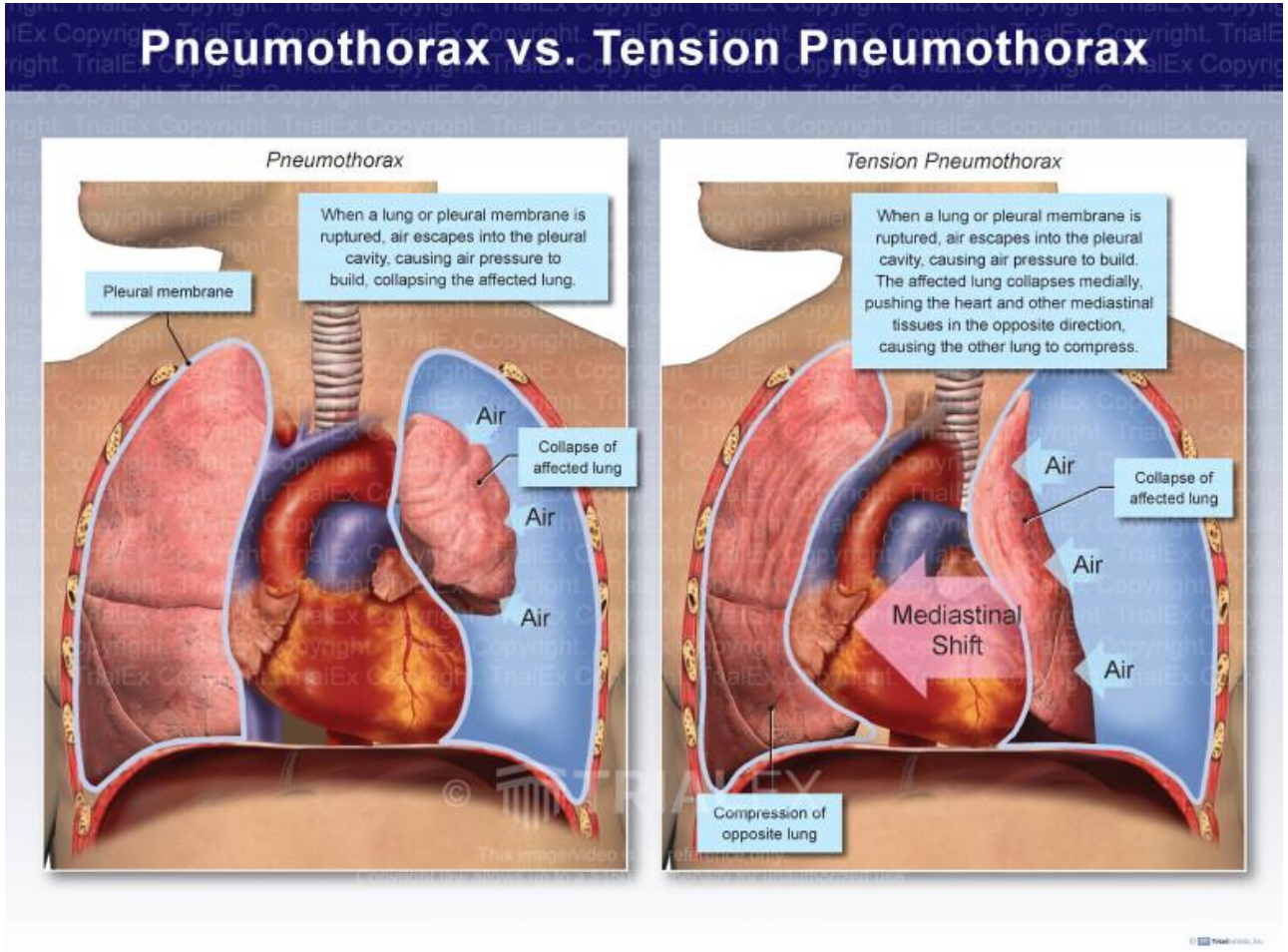
Forms of Shock- Obstructive Shock

- Causes:
  - Tension Pneumothorax
  - Cardiac tamponade
  - Massive PE
  - Caval Obstruction
  - Increased Intrathoracic pressure
  - Aortic dissection
  - Severe AS
  - CHDs



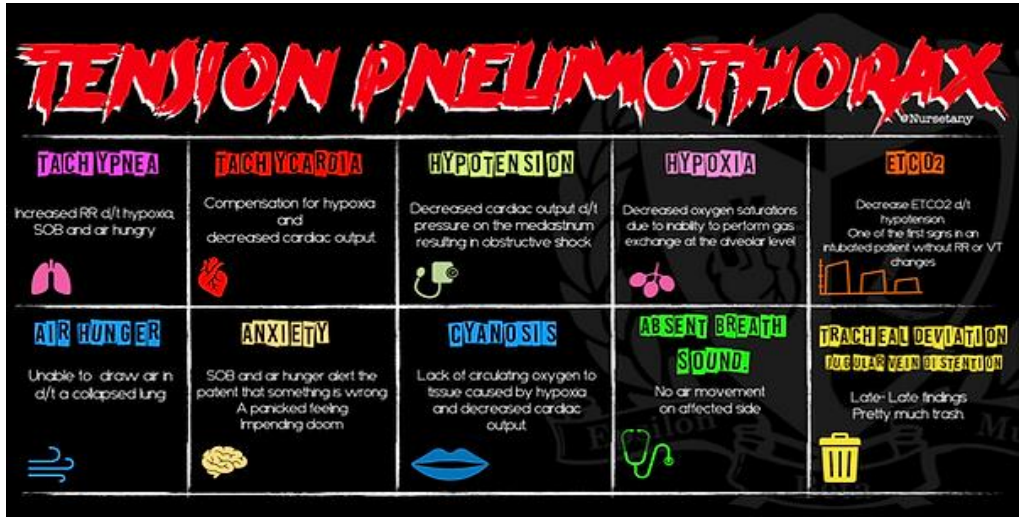
Tension Pneumothorax

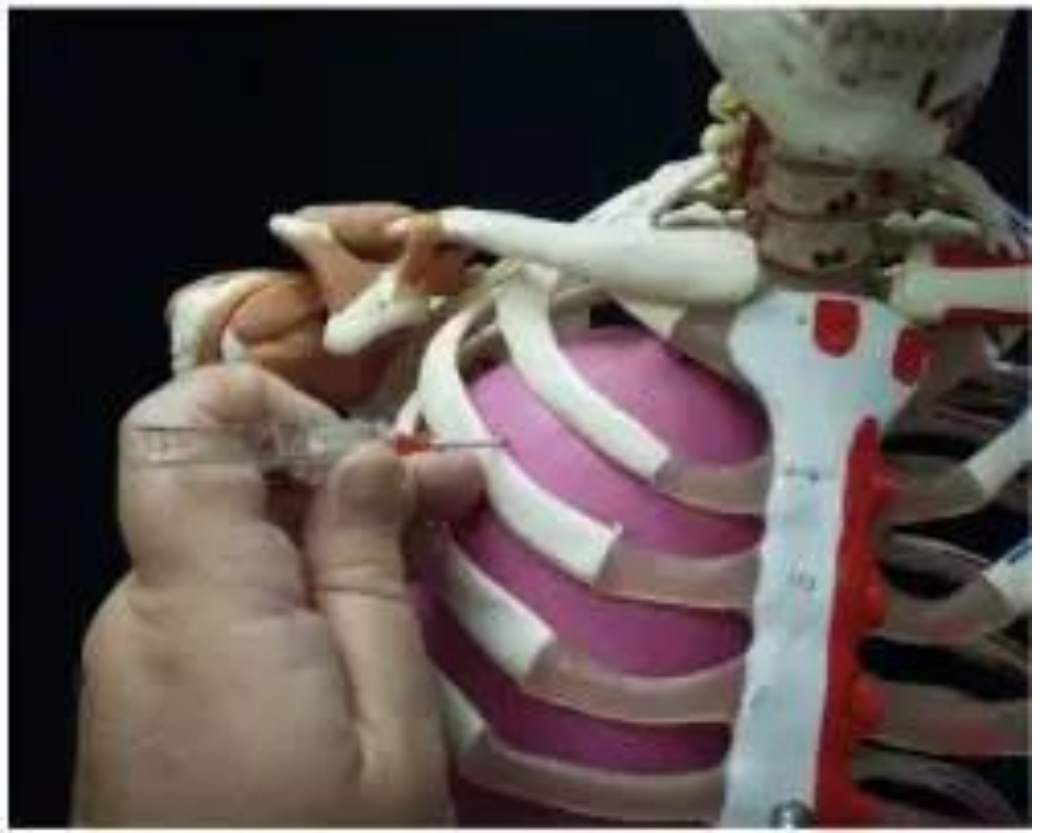




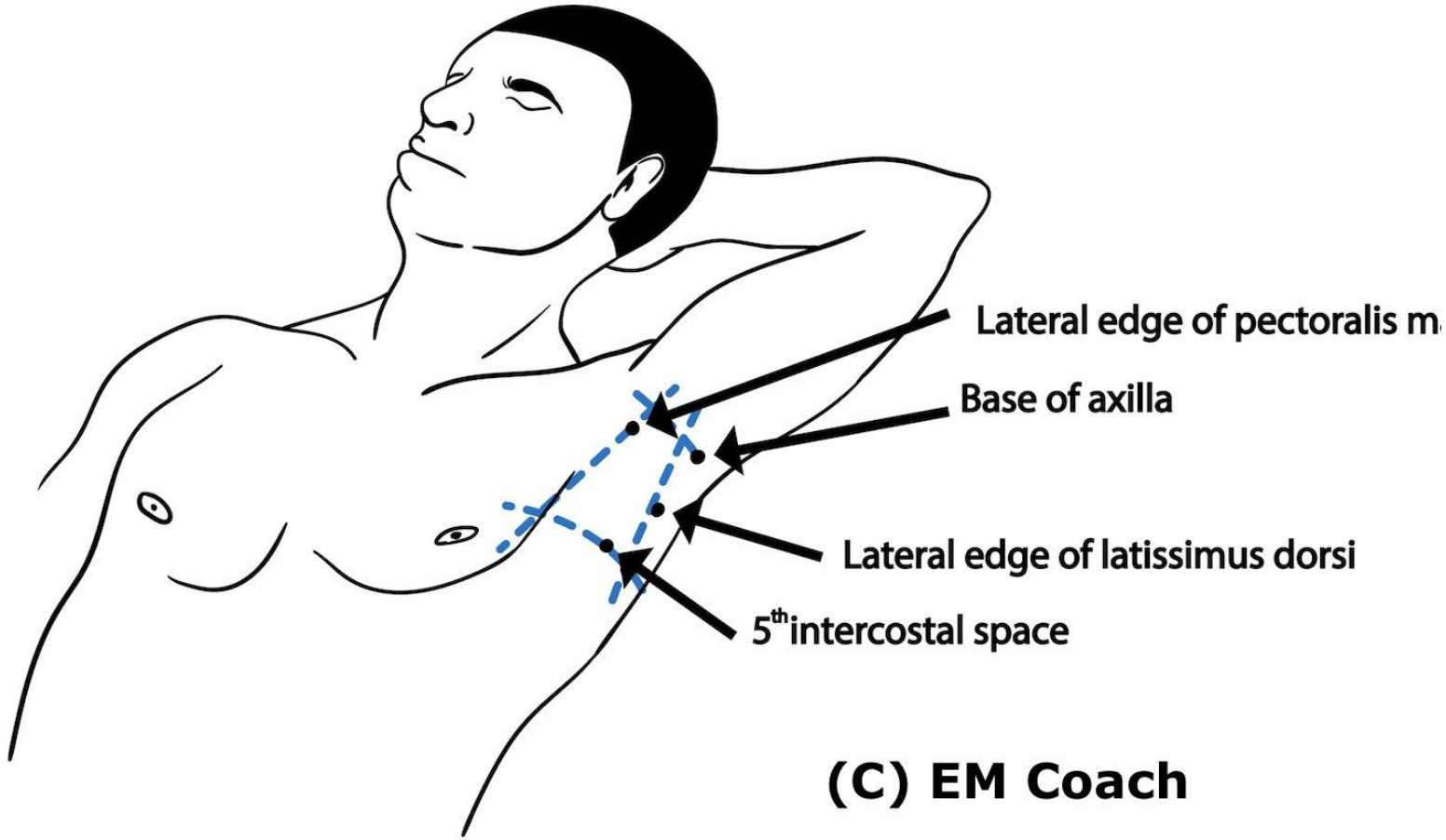
Tension Penumothorax Sx & Sg

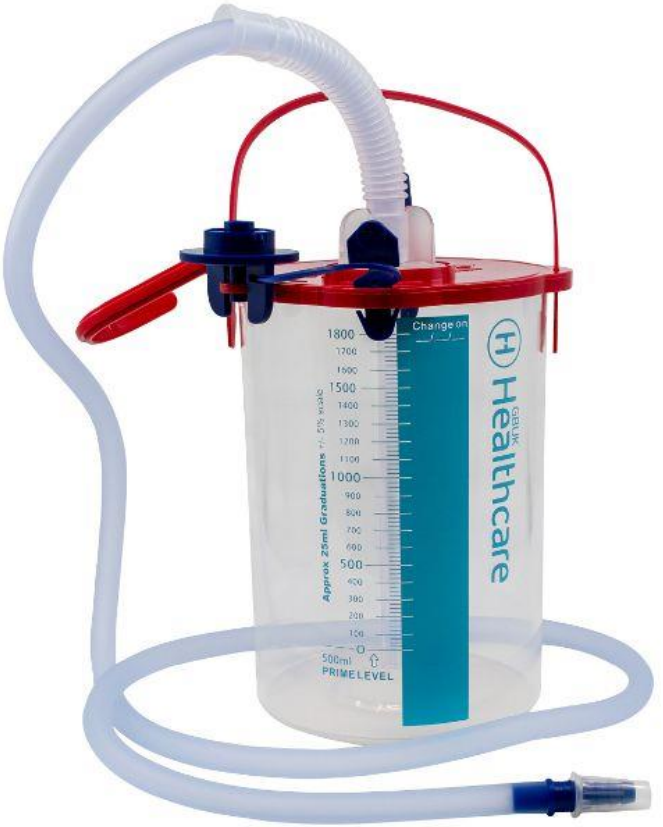
- Respiratory distress
- Chest pain
- Ipsilateral reduced breath sounds
- Ipsilateral hyperinflation of the hemithorax with hyper-resonance on percussion
- Tachycardia
- Low blood pressure.
- Cyanosis
- Jugular vein distention
- Tracheal deviation



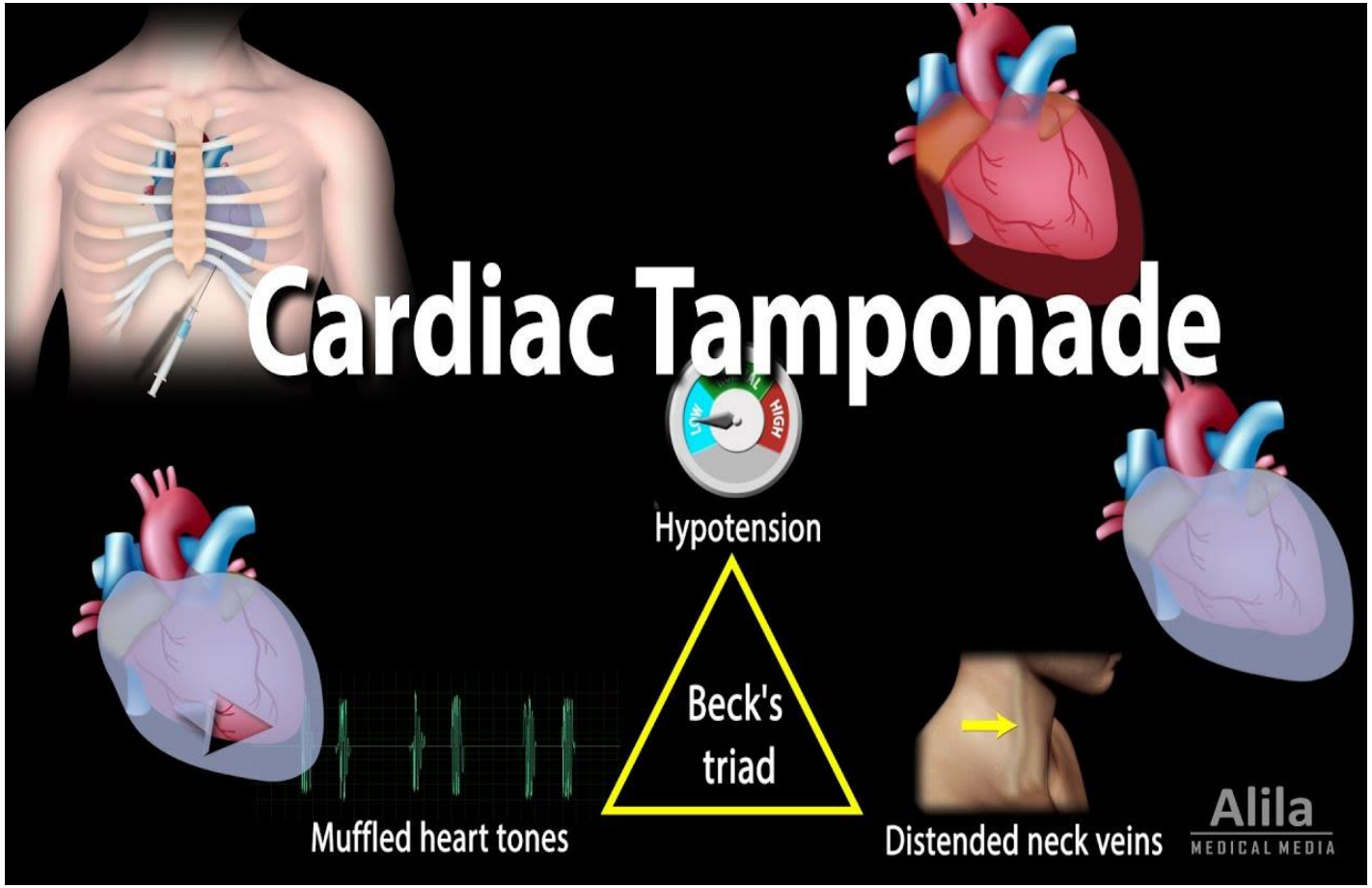


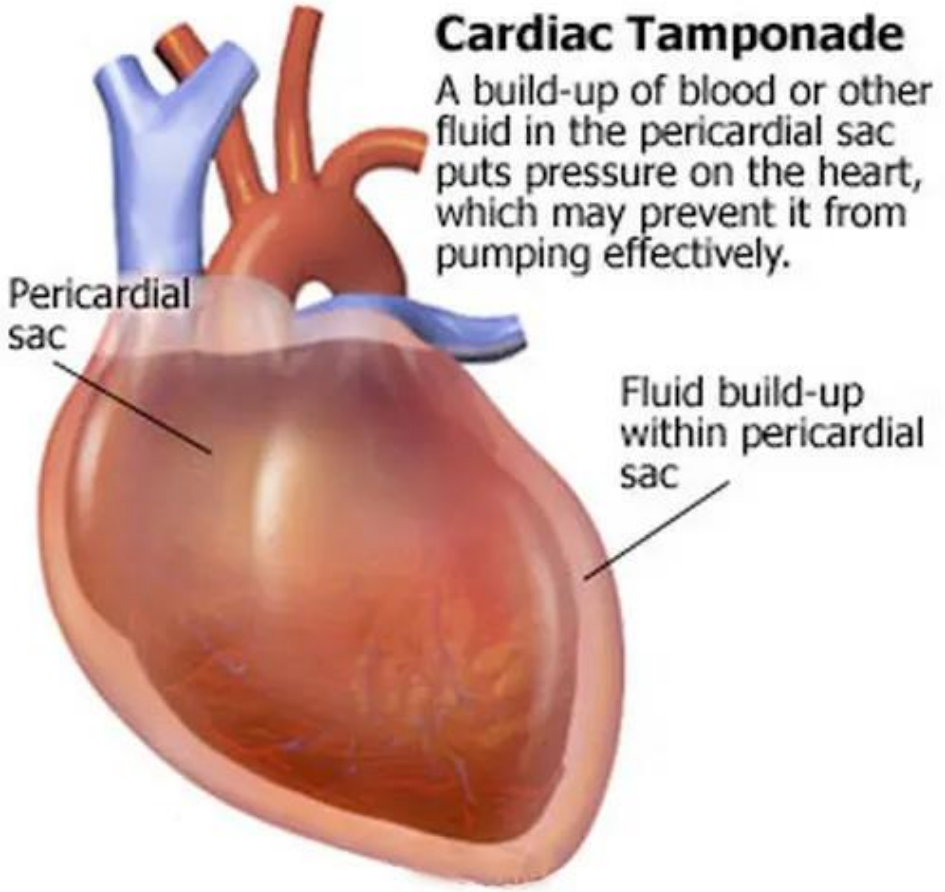
Tube thoracostomy





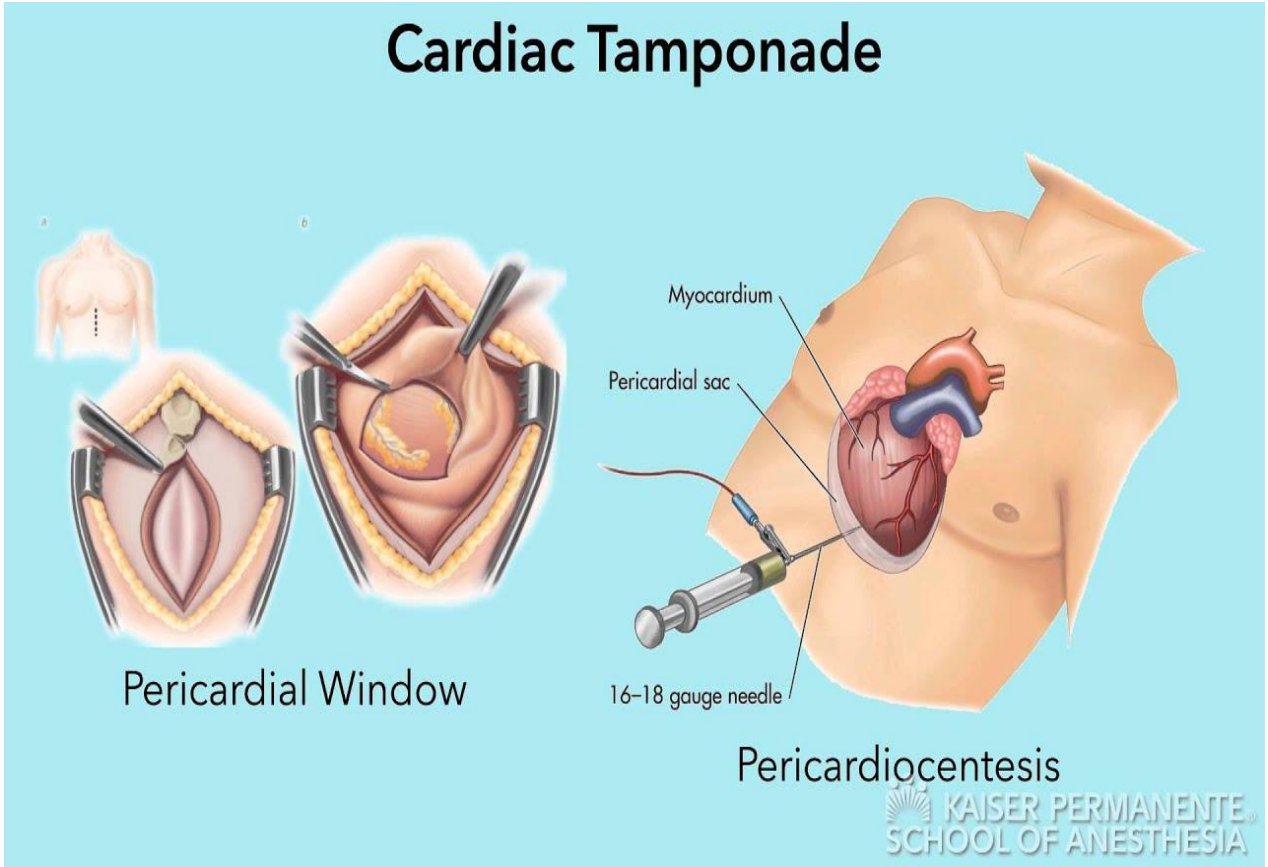
Cardiac tamponade



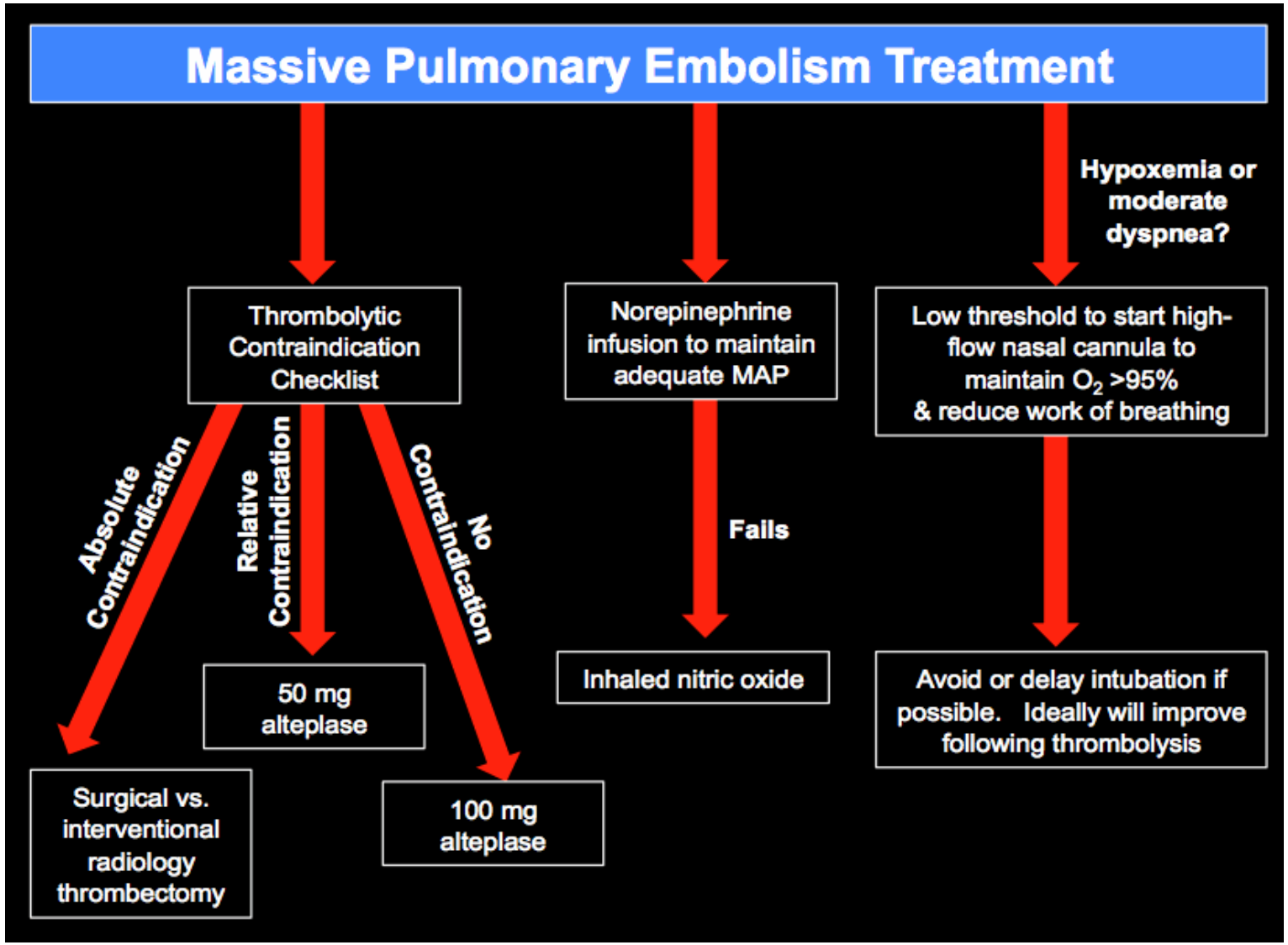


Diagnosis & Management

- Invasive monitoring (↑CVP, ↑RA & RV pressures, pulsus paradoxus)
- CXR
- Echocardiography
- FAST
- Pericardioentesis
- Pericardial window

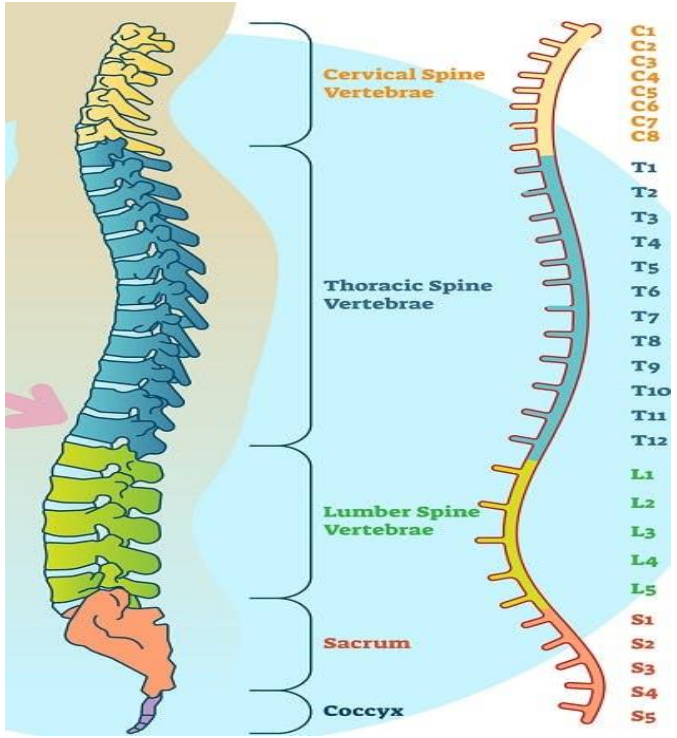


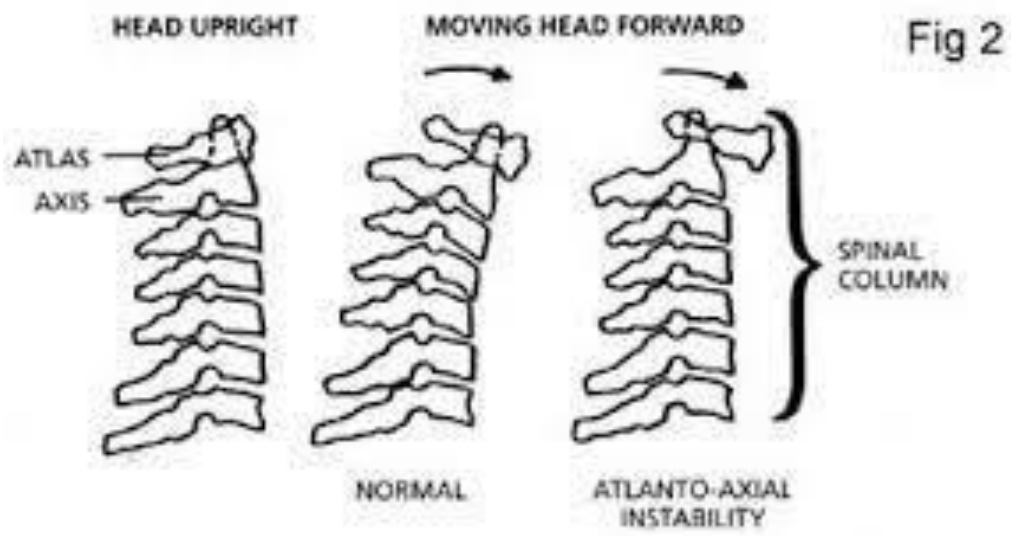
Massive PE

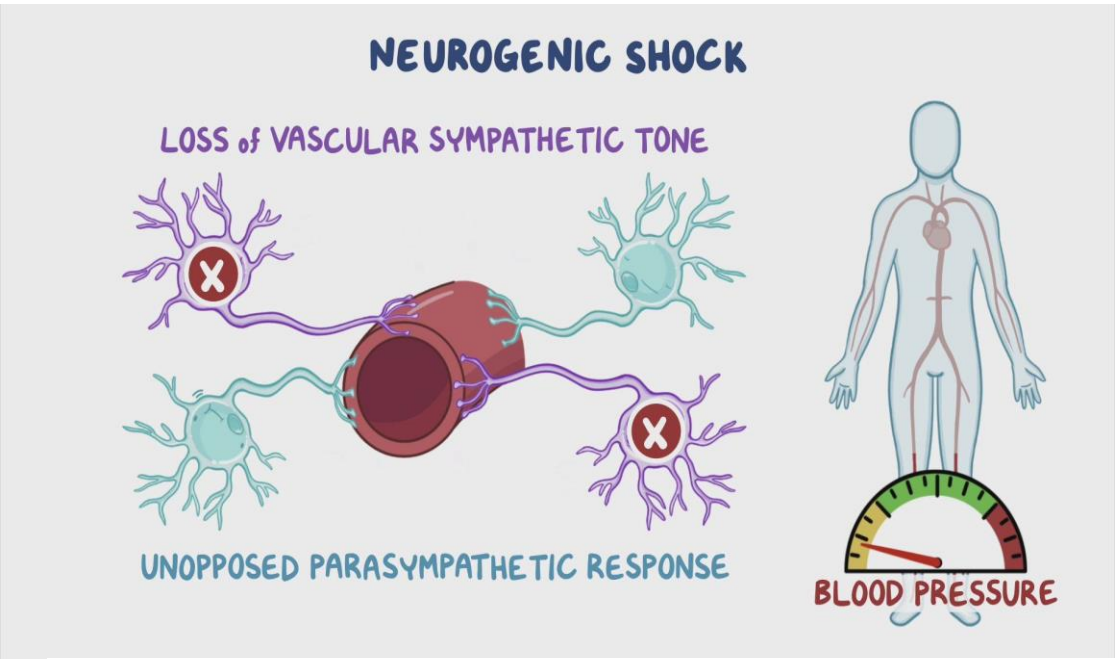

Massive Pulmonary Embolism Treatment
Thrombolytic Contraindication Checklist
Norepinephrine infusion to maintain adequate MAP
Hypoxemia or moderate dyspnea?
Low threshold to start high-flow nasal cannula to maintain O_2 >95% & reduce work of breathing
Absolute Contraindication
Relative Contraindication
No Contraindication
Falls
50 mg alteplase
Inhaled nitric oxide
Avoid or delay intubation if possible. Ideally will improve following thrombolysis
Surgical vs. interventional radiology thrombectomy
100 mg alteplase

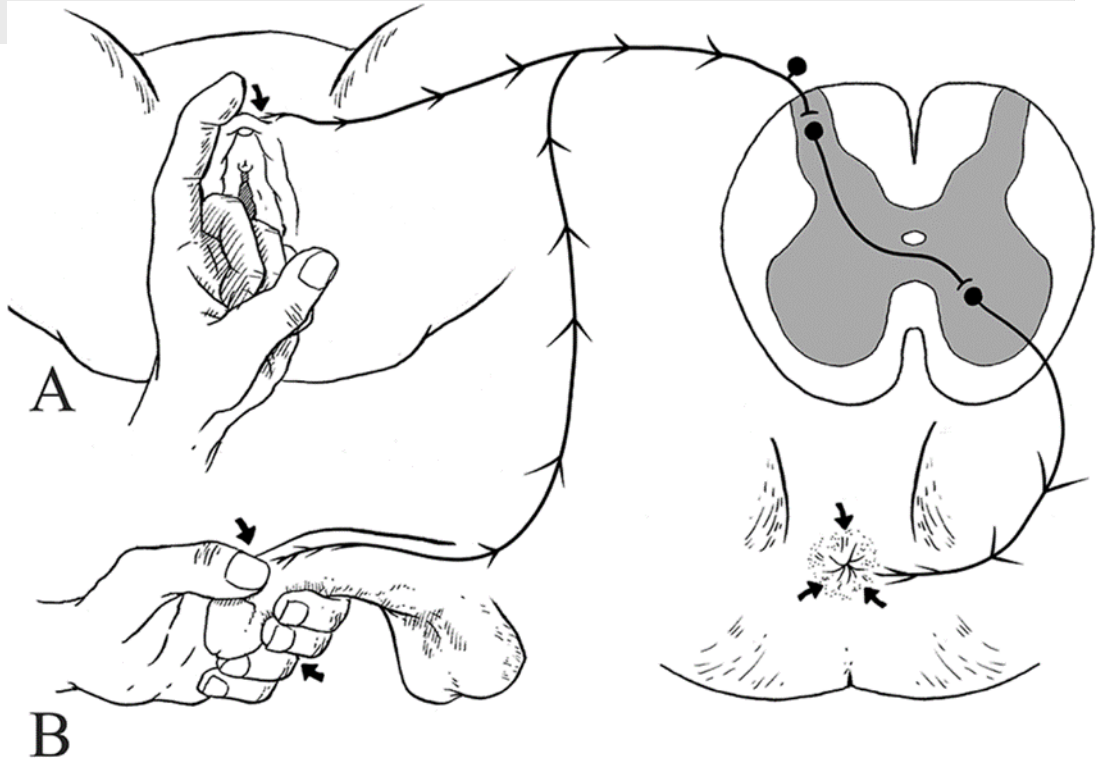
Forms of Shock- Neurogenic Shock

- Spinal cord trauma
- Spinal anesthesia
- Guillain-Barre Syndrome.
- ANS- toxins
- Transverse myelitis
- Trisomy 21 (atlanto-axial or atlanto-occipital instability)
- Skeletal dysplasia
- Other neuropathies









Spinal Shock vs Neurogenic Shock

Spinal Shock

- *Due to acute spinal cord injury
- *Absence all voluntary and reflex neurologic activity below level of injury
  - Decreased reflexes
  - Loss of sensation
  - Flaccid paralysis below injury
- Lasts days to months (Transient)
- *Spinal shock & neurogenic shock can in same patient-BUT not same disorder (some sources may group both together)

Neurogenic Shock*

- *Hemodynamic phenomenon-
  - * **Loss of vasomotor tone & Loss of sympathetic nervous system tone > inpaired cellular metabolism**
- *Critical features-
  - **Hypotension** (due to massive vasodilation
  - **Bradycardia**- due to unopposed paraynmpathetic stimulation
  - **Poikilothermia;** *Unable to regulate temperature-
- Occurs
  - Within 30 min cord injury level T 5 or above; last up to 6 weeks; also due to effect some drugs that effect vasomotor center of medulla as opioids, benzodiazedines
- Management (*Determine underlying cause)
  - **Airway support**
  - **Fluids as needed-** Typically 0.9 NS , rate depends upon need
  - **Atropine for bradycardia**
  - **Vasopressors as phenylelphrine** (Neo-synephrine) for BP support

Sx & Sg

- Hypotension
- Bradycardia
- Warm, dry extremities
- Peripheral vasodilation and venous pooling
- Poikilothermia
- Decreased cardiac output (with cervical or high thoracic injury)

- Secondary damage:
  1. Spinal cord ischemia
  2. Cellular response (Loss of membrane integrity & impaired energy metabolism)
  3. Neurotransmitter accumulation
  4. Release of free radicals
  5. DAMPs

Diagnosis & Management

- Clinical
- Imaging
- Neurogenic Shock is a diagnosis of exclusion. Consider it in your trauma patient with unexplained hypotension and bradycardia after ruling out hemorrhage or other internal injuries (Tension Pneumothorax, Pericardial Tamponade, etc.)

- IVF
- Vasopressors:
  - ✓Dopamine
  - ✓Norepinephrine
  - ✓Phenylephrine
- For Brady Cardia:
  - ✓Atropine
  - ✓Pacemaker
- Methylprednisolone
- Vertebral Stabilization

END POINTS IN RESUSCITATION

- Goal of Shock treatment is restoration of adequate organ perfusion & tissue oxygenation:
  - ✓Oxygen debt repaid
  - ✓Tissue acidosis corrected
  - ✓Aerobic metabolism restored
- *Persistent occcult hypoperfusion:*
  - ✓Increased lactate or Decreased Mixed venous O2 satuartion despite normalization of HR, BP & UOP 12 hours after admission
  - ✓Quite common (80-85% of trauma patients)
  - ✓Increase infection rate X3 (Infection increase Mortality X4)

END POINTS IN RESUSCITATION

Global/ Systemic

- Viatl signs
- Urine output
- Cardiac output
- PAWP
- Oxygen delivery & Consumption
- Lactate
- Base deficit
- *COMPENSATORY RESERVE INDEX*

Tissue Specific

- Gastric tenometry
- Tissue pH, O2 & CO2 levels
- Near infrared spectroscopy

Cellular parameters

- Membrane potential
- ATP

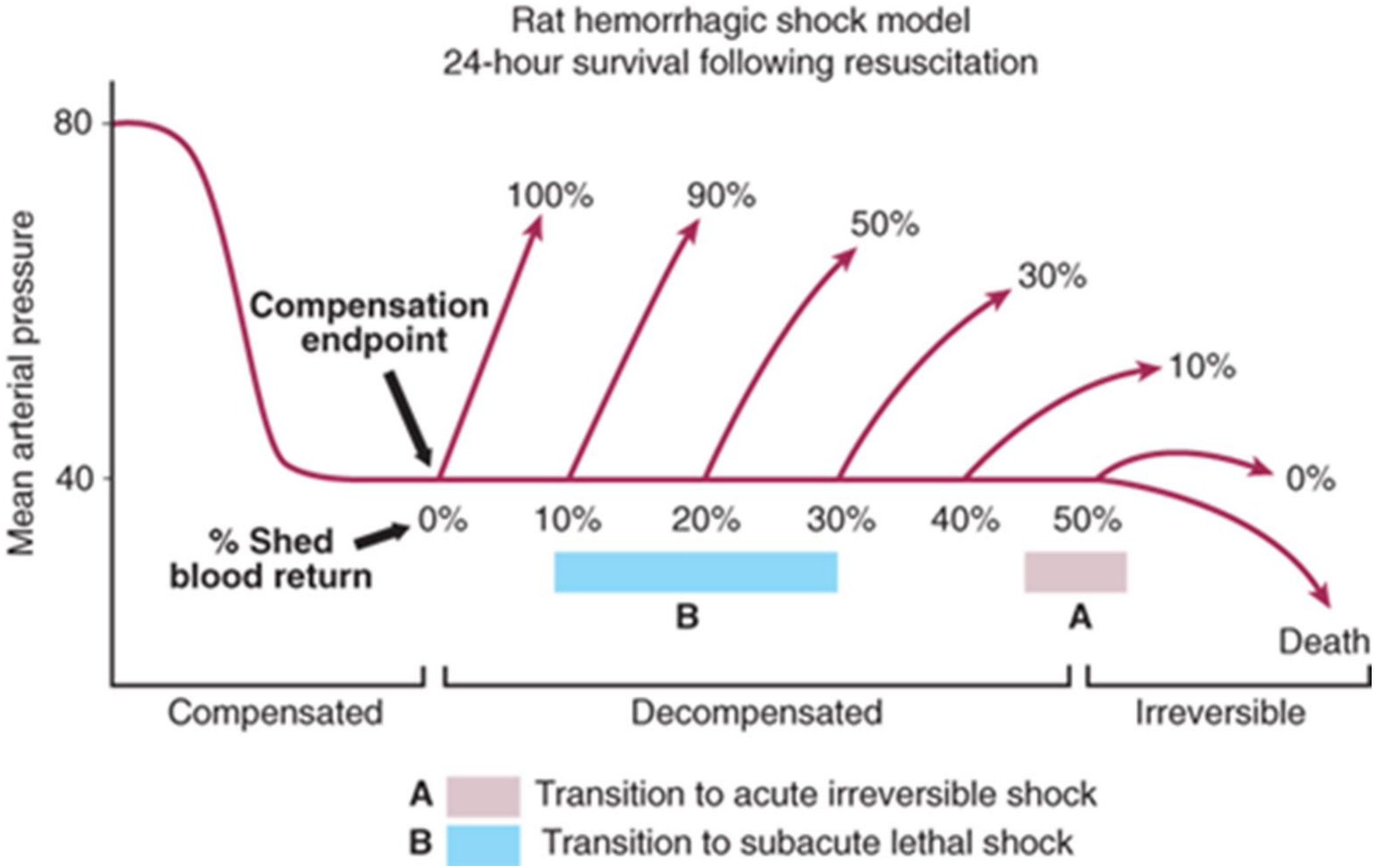
Ideal cardiac Output Monitor..?

ARE WE FAR FROM DEVELOPING A PERFECT MONITOR..??

- ***ACCURATE***
- ***CHEAP***
- ***EASY TO USE***
- ***NONINVASIVE***
- ***WITHOUT ANY COMPLICATIONS***
- ***CONTINUOUS***
- ***FAST RESPONSE TIME***
- ***OPERATOR INDEPENDENT***
- ***RELIABLE IN VARIOUS PHYSIOLOGICAL & PATHOLOGICAL CONDITIONS***

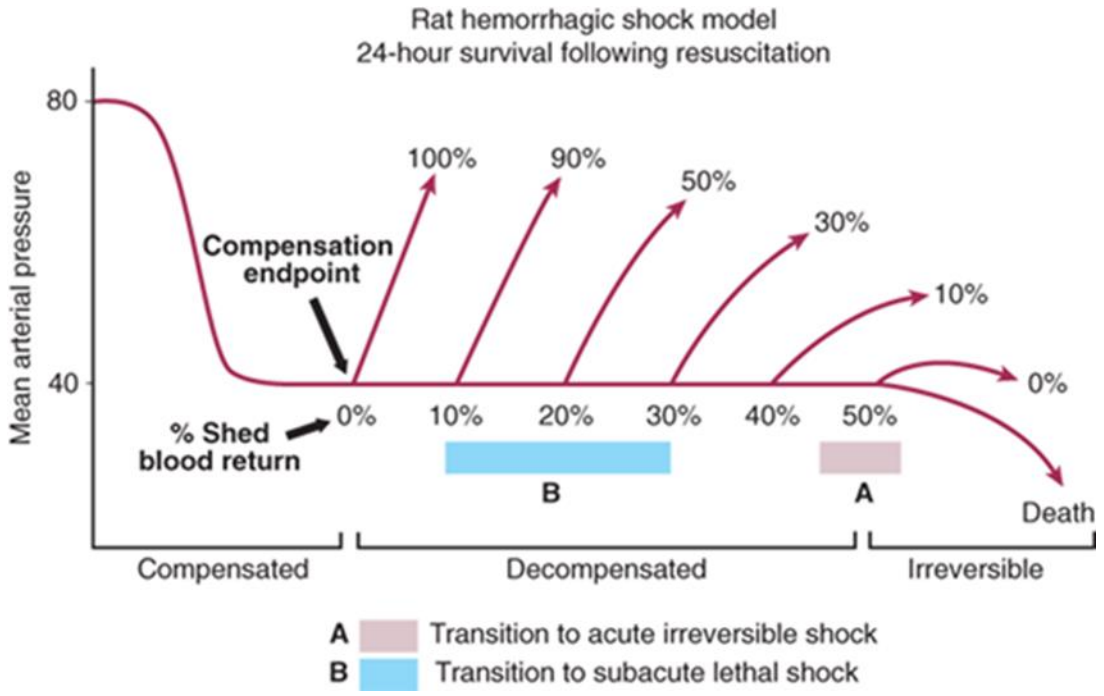
Hemodynamic Monitoring Truth

No monitoring device will improve outcome, unless coupled to a *treatment*, which improves outcome.


Rat hemorrhagic shock model
24-hour survival following resuscitation
Mean arterial pressure
80
40
Compensation endpoint
100%
90%
50%
30%
10%
0%
% Shed blood return
0%
10%
20%
30%
40%
50%
B
A
Death
Compensated
Decompensated
Irreversible
A Transition to acute irreversible shock
B Transition to subacute lethal shock

COMPENSATORY RESERVE INDEX- CONCEPT

Humans are able to compensate for significant hemorrhage through various neural and hormonal mechanisms, allowing their vital signs to remain relatively stable until these adaptive compensatory mechanisms are gradually overwhelmed, resulting in hemodynamic compromise and the onset of hemorrhagic shock.



COMPENSATORY RESERVE INDEX

- One of the most challenging aspects of providing effective treatment of shock is an inability to recognize its early onset.
- Blood pressures, arterial oxygen saturation (Spo2), and heart rate measurements collected in the early prehospital setting were similar 30 to 45 minutes after traumatic injury in hemorrhaging patients who went on to die compared with those who survived.
- These results emphasize that current physiologic monitoring can be grossly misleading, and nonpredictive of hemodynamic collapse, because of the numerous compensatory mechanisms that "protect" these vital signs from significant clinical change.
- In other words, current vital sign monitoring lacks sensitivity and specificity to predict impending hemodynamic collapse and shock during the early compensatory stage of hemorrhage.

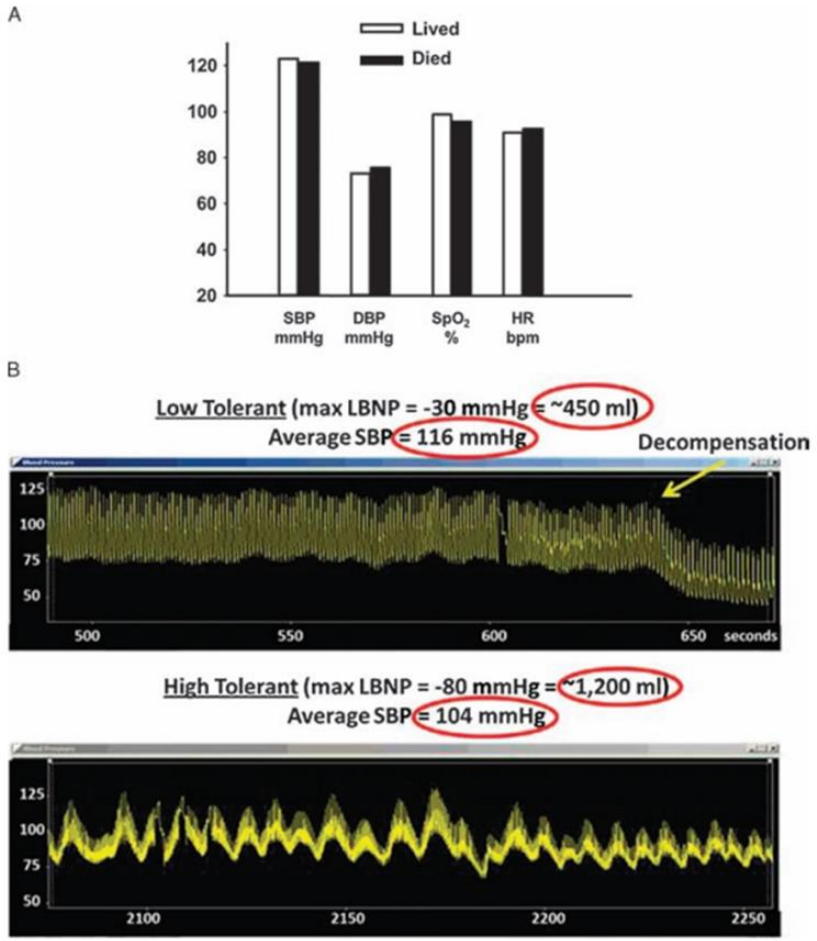
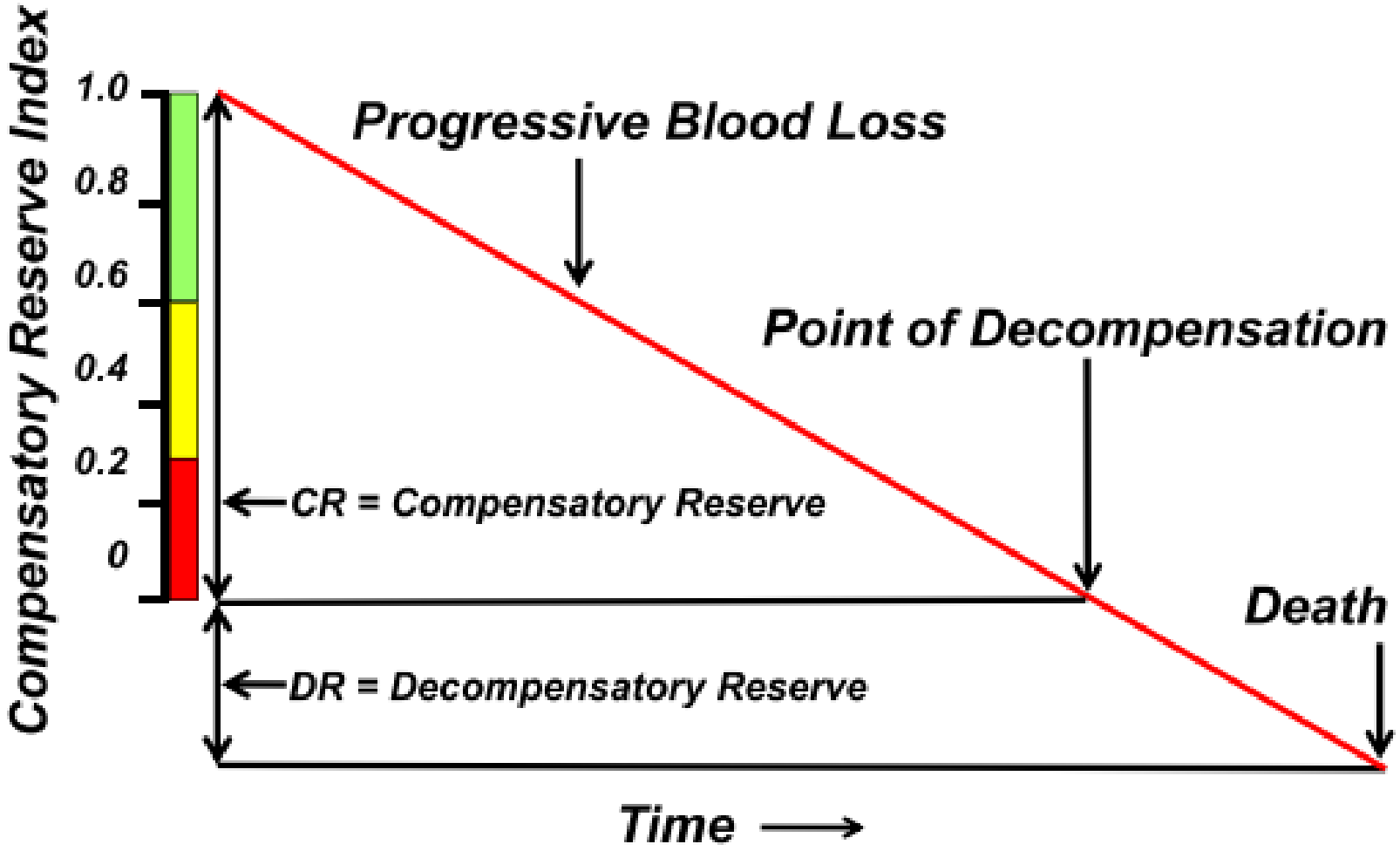


Figure 1. (*A*) Trauma patients with severe hemorrhage who lived (*open bars*) and died (*closed bars*) could not be differentiated by standard vital signs obtained 30 to 45 minutes after injury. Modified from Cooke et al.[27] (*B*) Arterial waveform recordings demonstrate pronounced oscillatory patterns in individuals with high tolerance to a progressive reduction in central blood volume (*bottom recording*) compared to low tolerance individuals (*top recording*). Modified from Convertino et al.[28]

Compensatory Reserve Index (CRI)



USAISR

- The use of lower-body negative pressure (LBNP) that has proven to produce repeatable tolerance times to *HYPOVOLEMIA*
- The integrated total of all mechanisms that compose the reserve to compensate for blood loss (the compensatory reserve):
  - Hemodynamic response
  - Metabolic response
  - Coagulation response
  - Respiratory response
  - Neuroendocrine response
  - Mental status responses

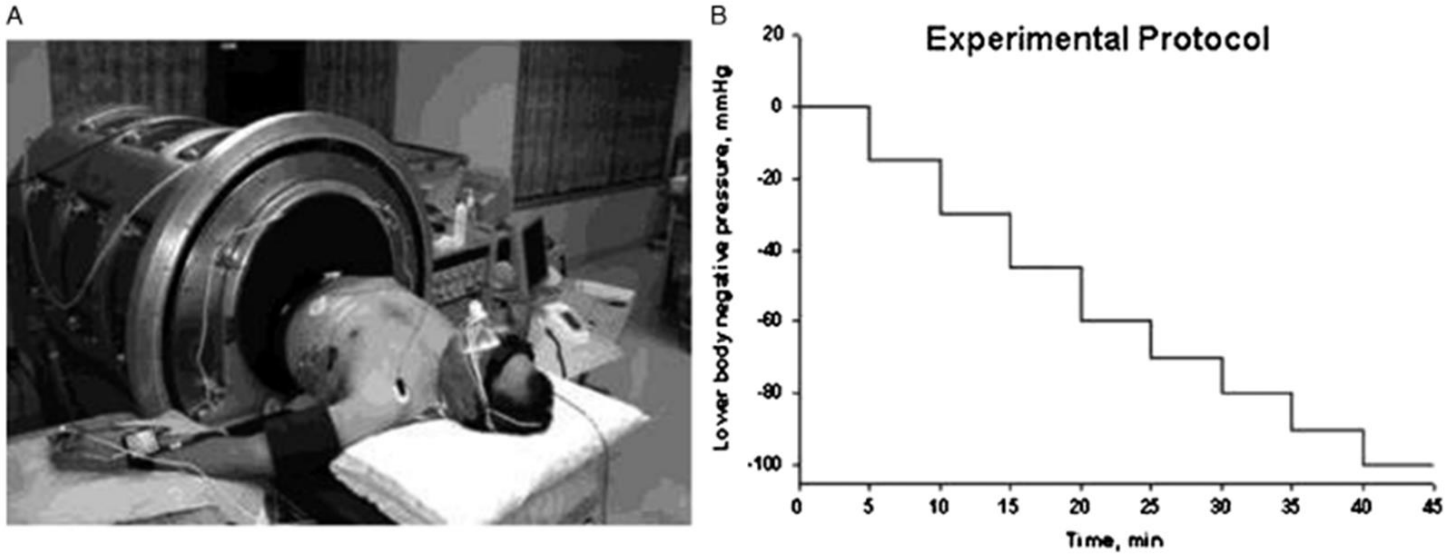
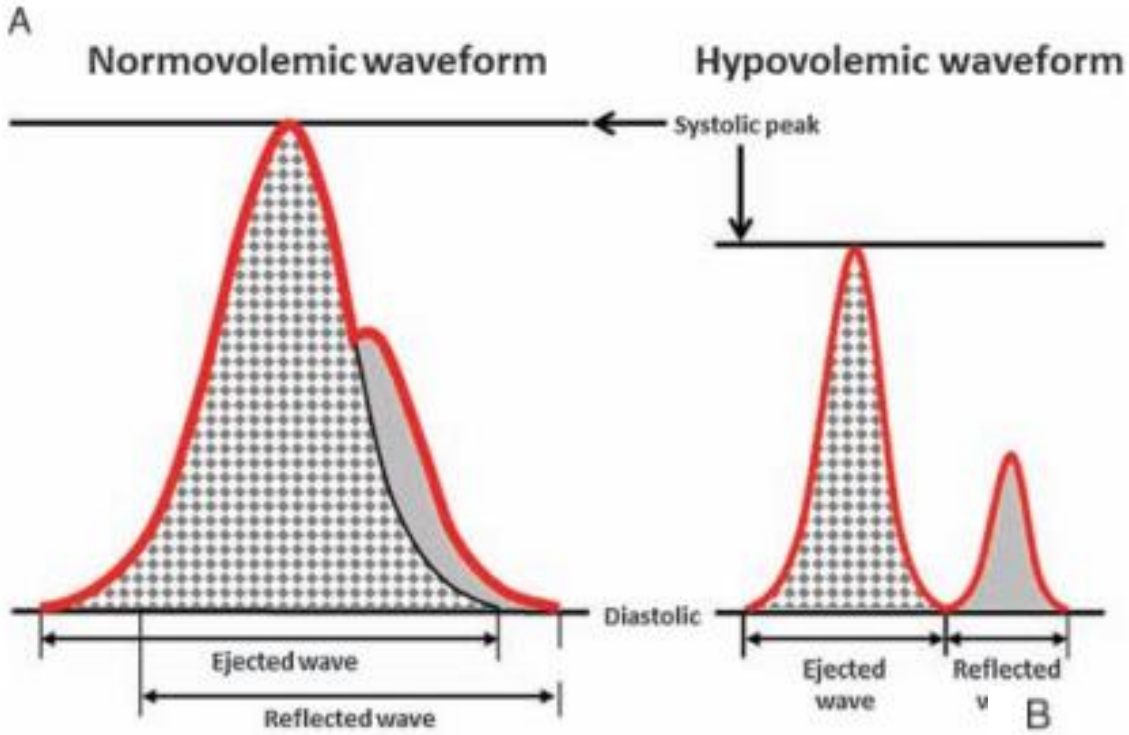


Figure 2. Subject in the LBNP device (*A*) and the LBNP protocol (*B*). See Convertino et al.[2]


A
Normovolemic waveform
Hypovolemic waveform
Systolic peak
Diastolic
Ejected wave
Reflected wave
Ejected wave
Reflected
B

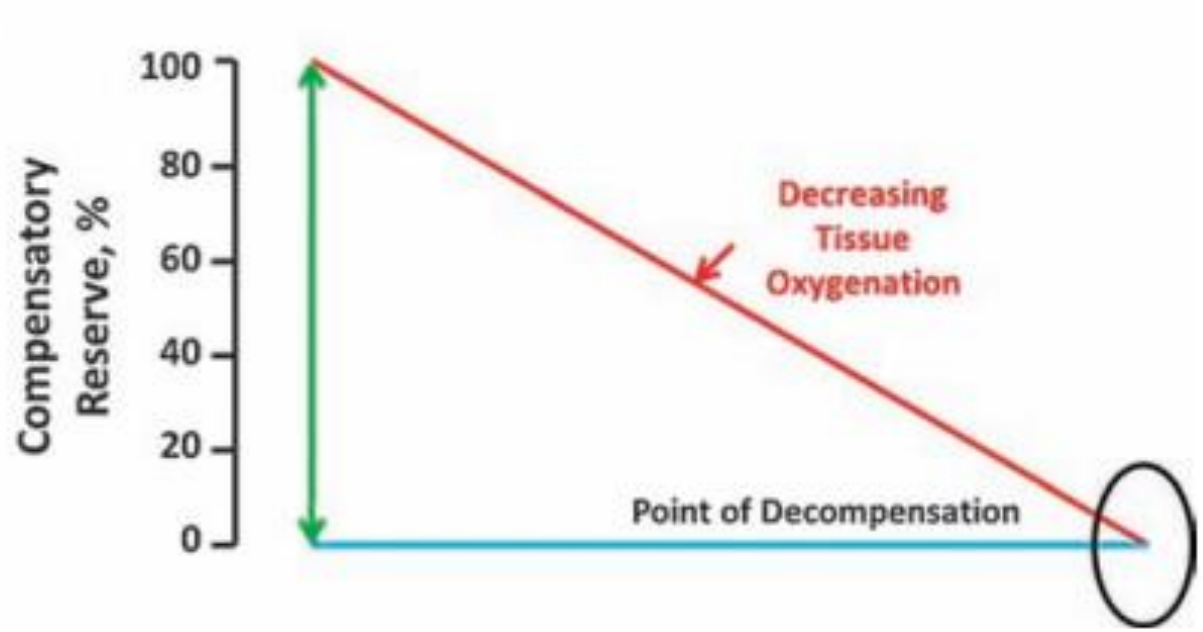

Compensatory Reserve, %
100
80
60
40
20
0
Decreasing Tissue Oxygenation
Point of Decompensation

TABLE 1. Times Course, Sensitivity and Specificity of Changes in Traditional Vital Signs and Hemodynamic Responses During Progressive Central Hypovolemia

Vital Sign	Change During Progressive Central Hypovolemia	Sensitivity	Specificity	Reference(s)
Systolic BP	Late	0.80	0.17	5,27,39–44
Diastolic BP	Late	0.40	0.53	40–44
Mean BP	Late	0.60	0.33	40–45
Heart rate	Not specific	0.80	0.02	27,39,40,45
Shock Index	Late	—	—	39,42
SpO_2	Late	0.60	0.00	40–43,45
Stroke volume	Early	0.60	0.33	31,41,42,44
Cardiac output	Late	0.80	0.02	41
Radial pulse character	Late	—	—	38
$EtCO_2$	Late			46
Respiratory rate	Late	—	—	37,46
GCS	Late	—	—	38
Blood pH	Late	—	—	4,40
Blood lactate	Late		0.03	4,40
Blood base excess	Late		0.02	4,40
Perfusion index	Late	0.71	0.29	47
Pulse pressure variability	Late	0.78	0.69	47
SmO_2	Early, but low specificity	0.65	0.63	48
Compensatory reserve	Early and specific	0.84–0.87	0.78–0.86	28,39–43,45,47–49

BP, blood pressure.

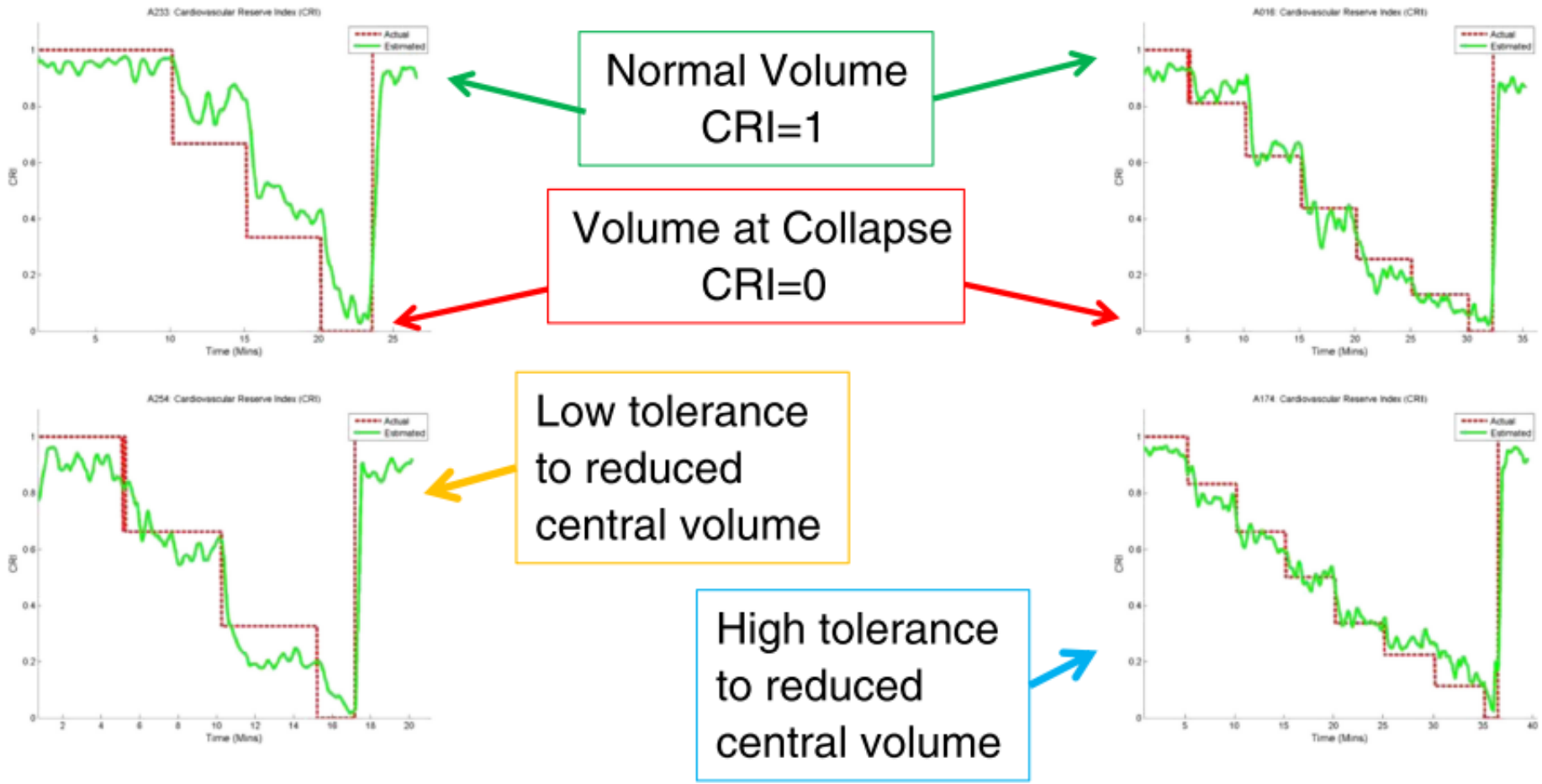
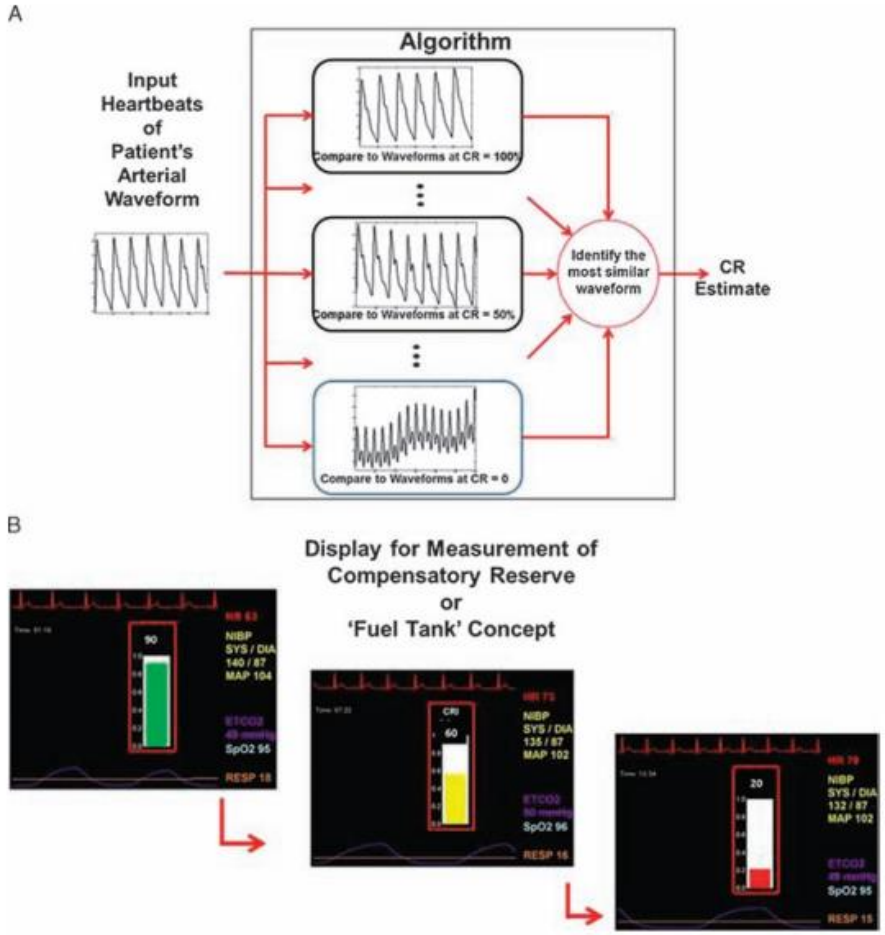
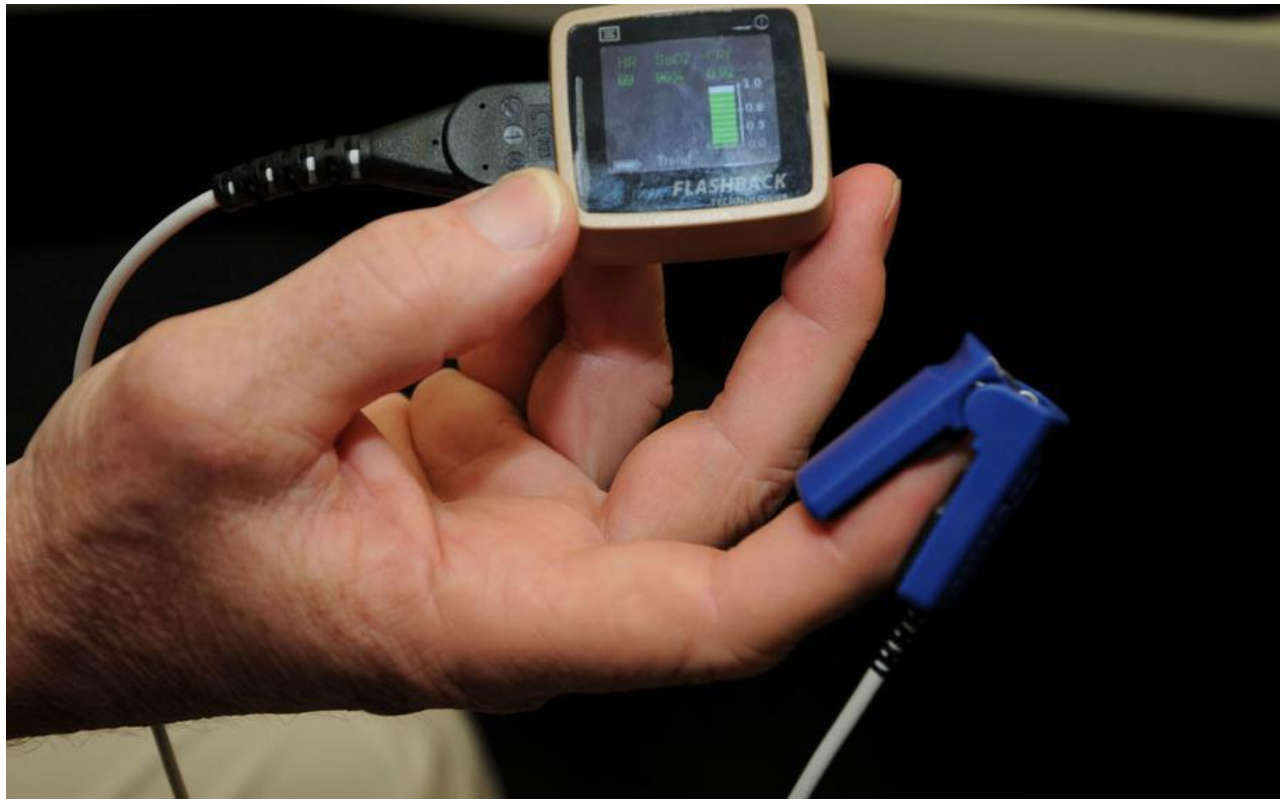


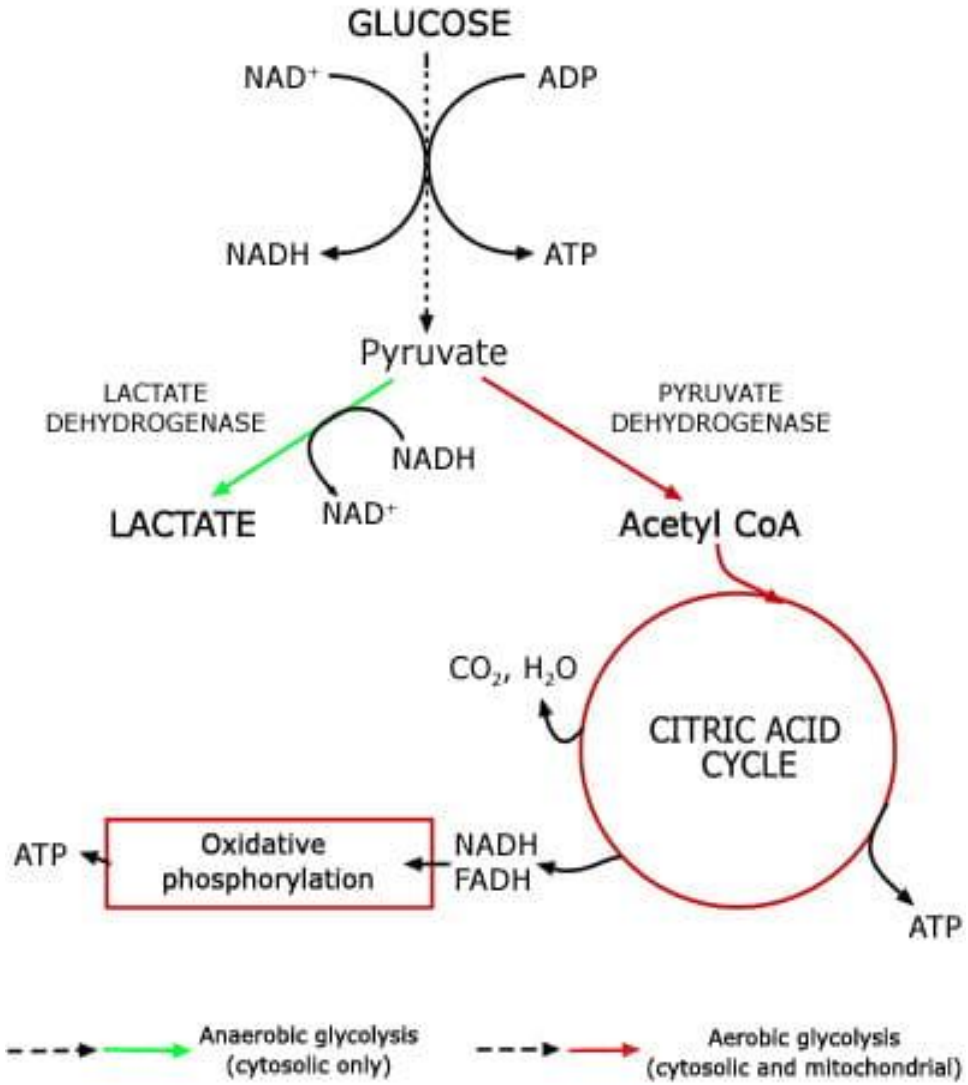
Figure 3. CRI estimation accuracy results on 4 of the 184 LBNP subjects who went to presyncope during LBNP studies. The *red line* indicates the ground truth CRI value, which can only be determined using the maximum tolerated LBNP (blood loss) after a subject achieves hemodynamic decompensation. The *green line* shows the beat-to-beat CRI estimates by CipherBP. As can be seen from the plots, there is a wide range of reserve volumes between subjects, and they can be generally classified as having low or high tolerance to blood loss. In either case, the CRI estimates by CipherBP effectively track the true CRI value.


A
Algorithm
Input Heartbeats of Patient's Arterial Waveform
Compare to Waveforms at CR = 100%
Compare to Waveforms at CR = 50%
Compare to Waveforms at CR = 0
Identify the most similar waveform
CR Estimate
B
Display for Measurement of Compensatory Reserve or 'Fuel Tank' Concept
90
NIBP
SYS / DIA
140 / 87
MAP 104
SpO2 95
RESP 18
CR
60
NIBP
SYS / DIA
135 / 87
MAP 102
SpO2 96
RESP 16
20
NIBP
SYS / DIA
132 / 87
MAP 102
SpO2 95
RESP 15

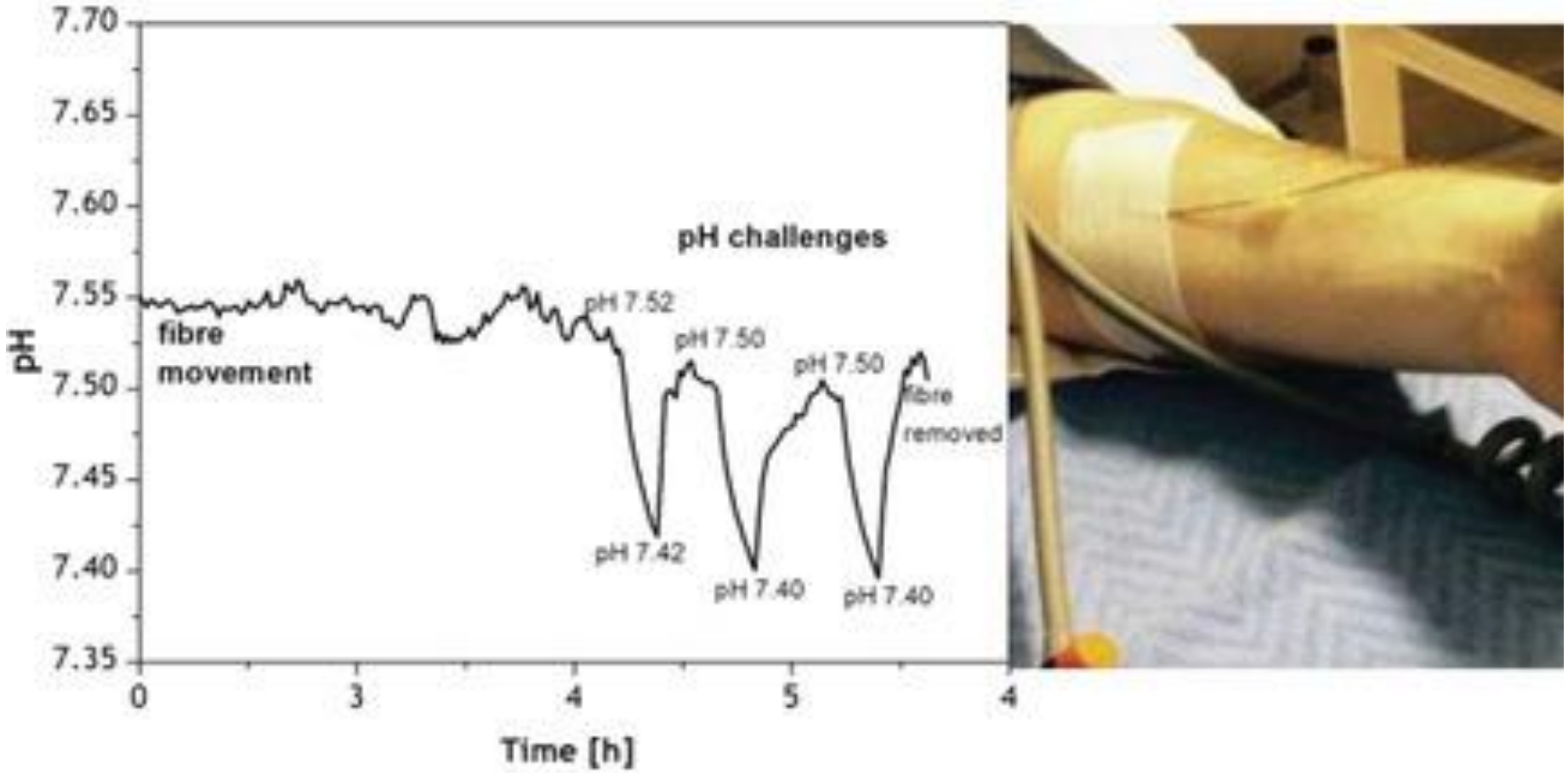

FLASHBACK

LACTATE & BASE DEFICIT

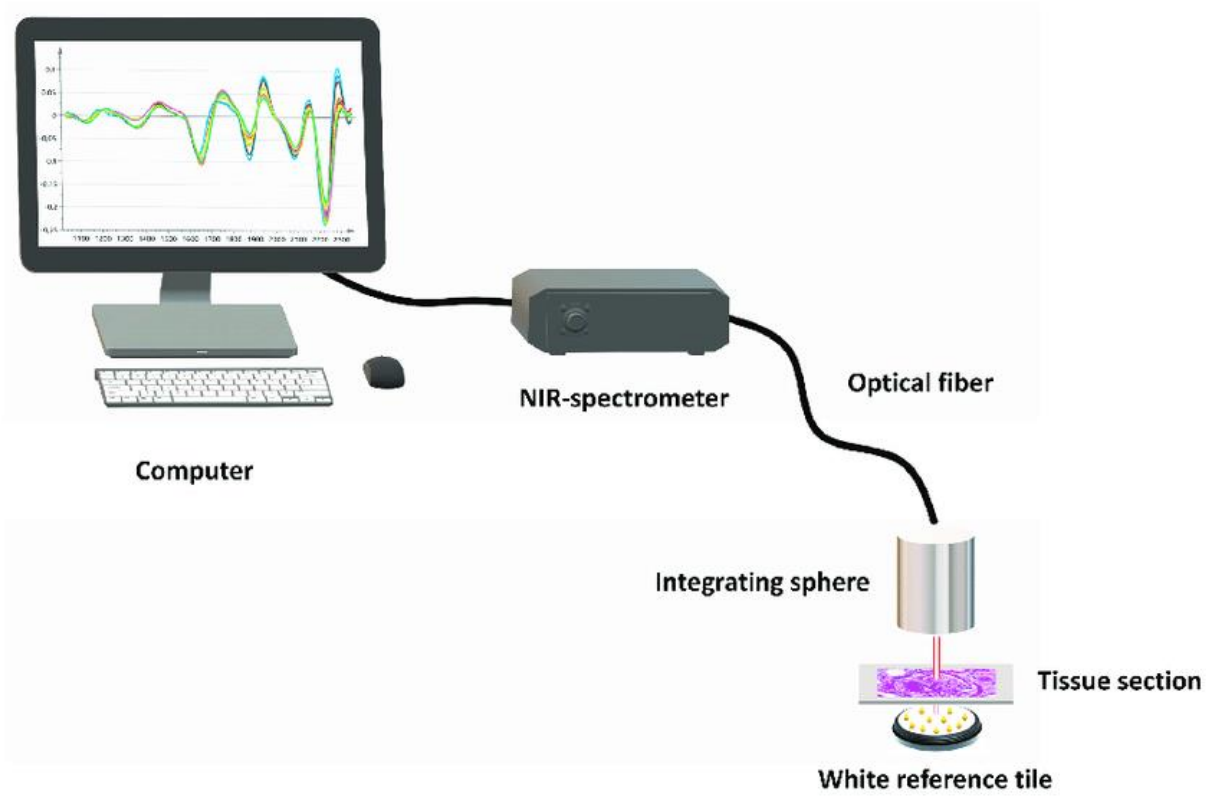
- BD :
  - ✓Mild= 3-5mmol/L
  - ✓Moderate= 6-14mmol/L
  - ✓Severe= >15mmol/L
- LA & BD at admission and time required for correction correlates with outcome
  - ✓ Normalization W/I 24 Hrs= 100% Survival
  - ✓ Normalization W/I 24-48 Hrs= 100% Survival
  - ✓ Persitance beyond 48Hrs= 14% Survival
- NB: Ethanol, Ketoacidois, HCO3, Hypercapnia, Hypothermia & Heparin may compromise utility of BD in estimation of O2 dept



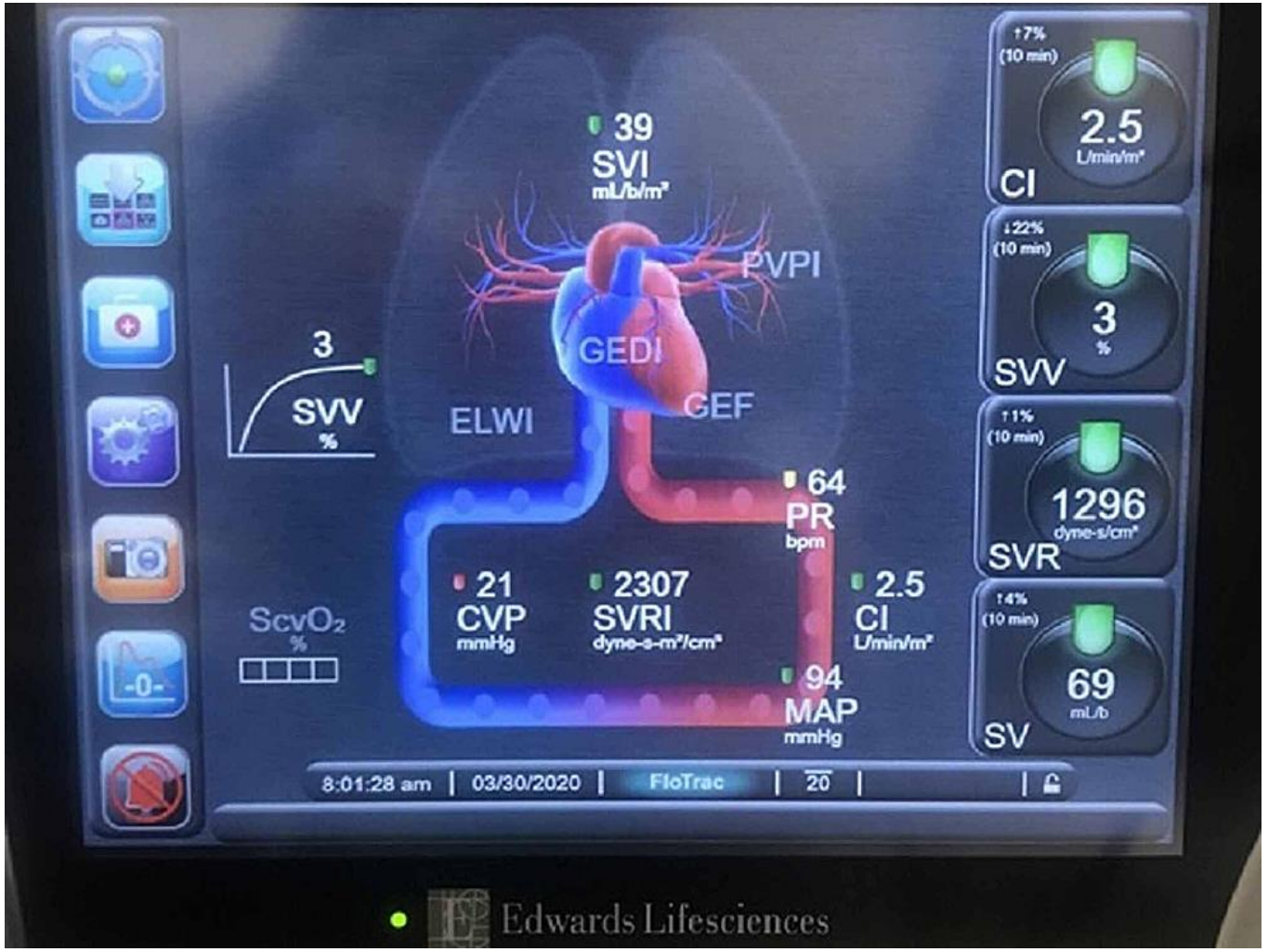
TISSUE PH, O2 & CO2 LEVELS



NEAR INFRARED SPECTROSCOPY (STO2)



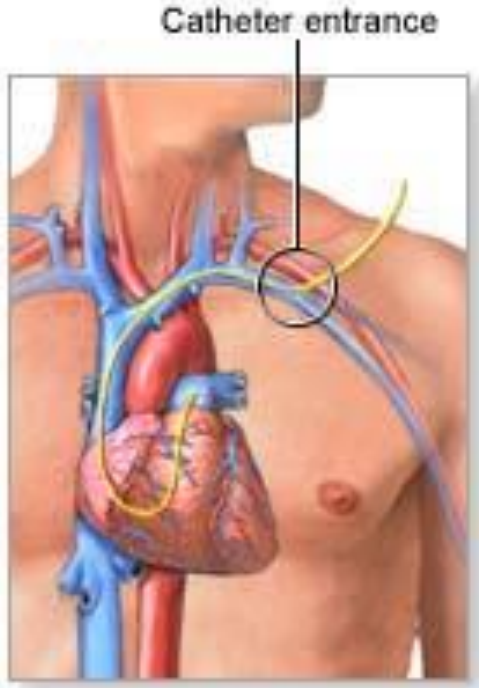
CO MONITORING

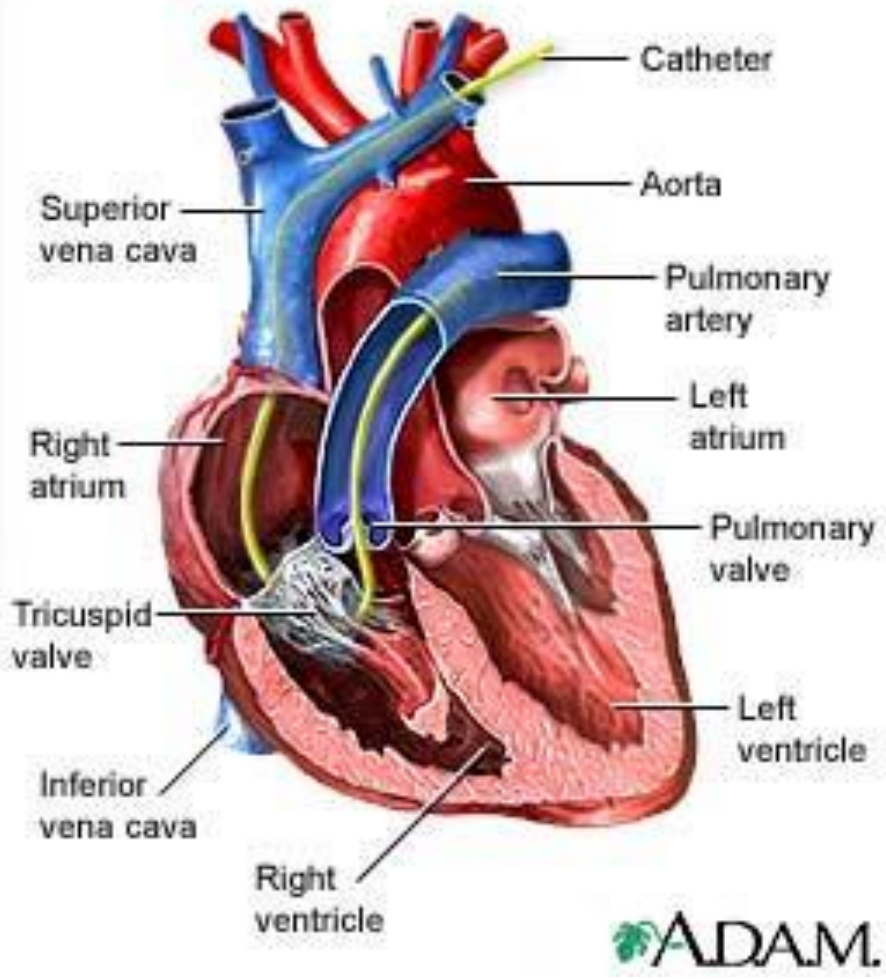


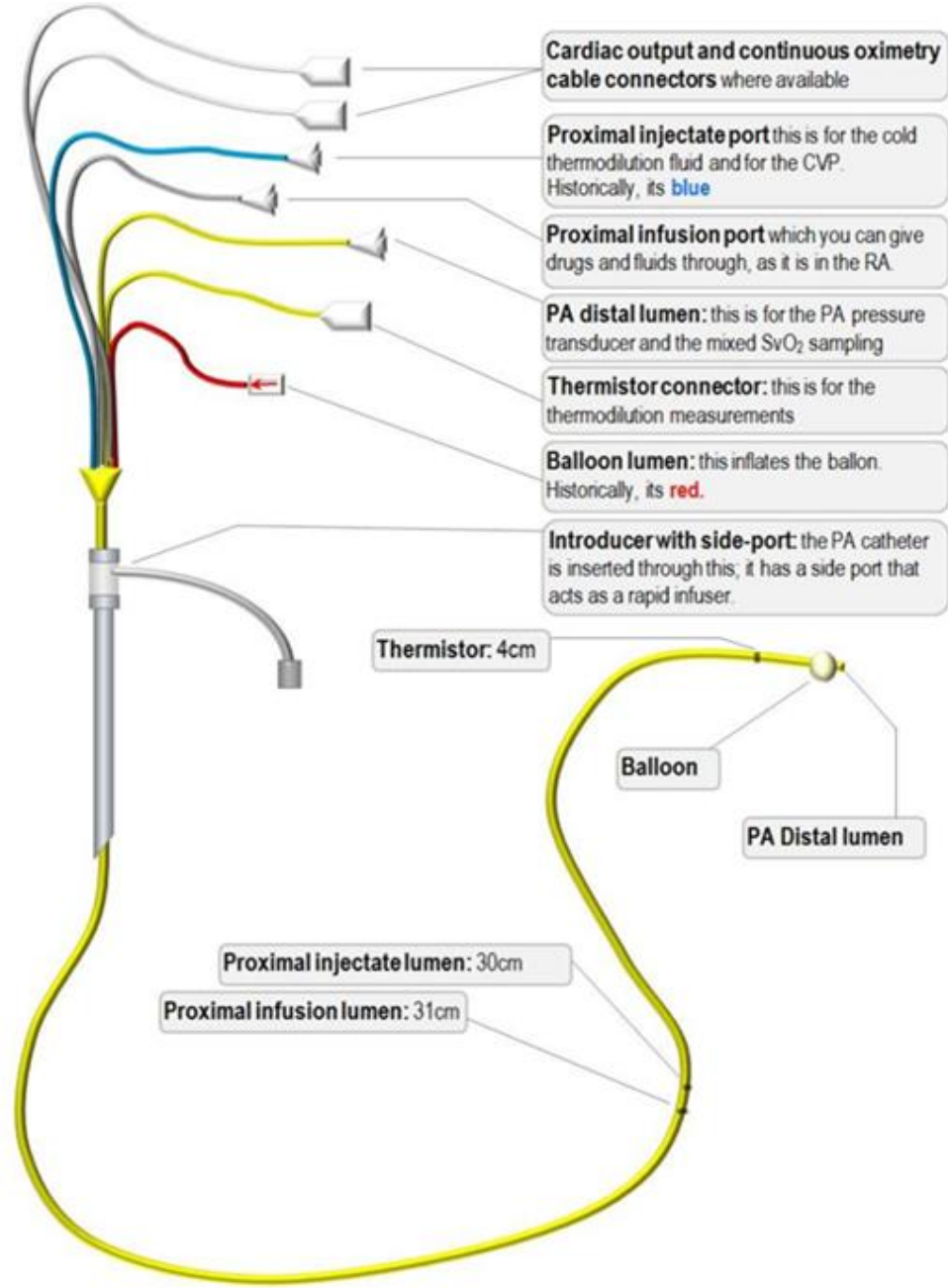
Swan-Ganz - right heart catheterization (PAWP)

- Risks
  - Bruising around the area where the catheter was inserted
  - Injury to the vein
  - Pneumothorax
  - Infarction
  - Cardiac arrhythmias requiring treatment
  - Cardiac tamponade
  - Embolism caused by blood clots at the tip of the catheter
  - Infection
  - Low blood pressure

- Normal results for this test are:
  - Cardiac index is 2.8 to 4.2 liters per minute per square meter (of body surface area)
  - Pulmonary artery systolic pressure is 17 to 32 millimeters of mercury (mm Hg)
  - Pulmonary artery mean pressure is 9 to 19 mm Hg
  - Pulmonary diastolic pressure is 4 to 13 mm Hg
  - Pulmonary capillary wedge pressure is 4 to 12 mm Hg
  - Right atrial pressure is 0 to 7 mm Hg


Catheter entrance


Catheter
Aorta
Superior vena cava
Pulmonary artery
Left atrium
Right atrium
Pulmonary valve
Tricuspid valve
Left ventricle
Inferior vena cava
Right ventricle
A.D.A.M.


Cardiac output and continuous oximetry cable connectors where available
Proximal injectate port this is for the cold thermodilution fluid and for the CVP. Historically, its blue
Proximal infusion port which you can give drugs and fluids through, as it is in the RA
PA distal lumen: this is for the PA pressure transducer and the mixed SvO_2 sampling
Thermistor connector: this is for the thermodilution measurements
Balloon lumen: this inflates the ballon. Historically, its red.
Introducer with side-port: the PA catheter is inserted through this; it has a side port that acts as a rapid infuser
Thermistor: 4cm
Balloon
PA Distal lumen
Proximal injectate lumen: 30cm
Proximal infusion lumen: 31cm

Pulse index Contour Continuous Cardiac Output (PiCCO)

Stewart–Hamilton equation

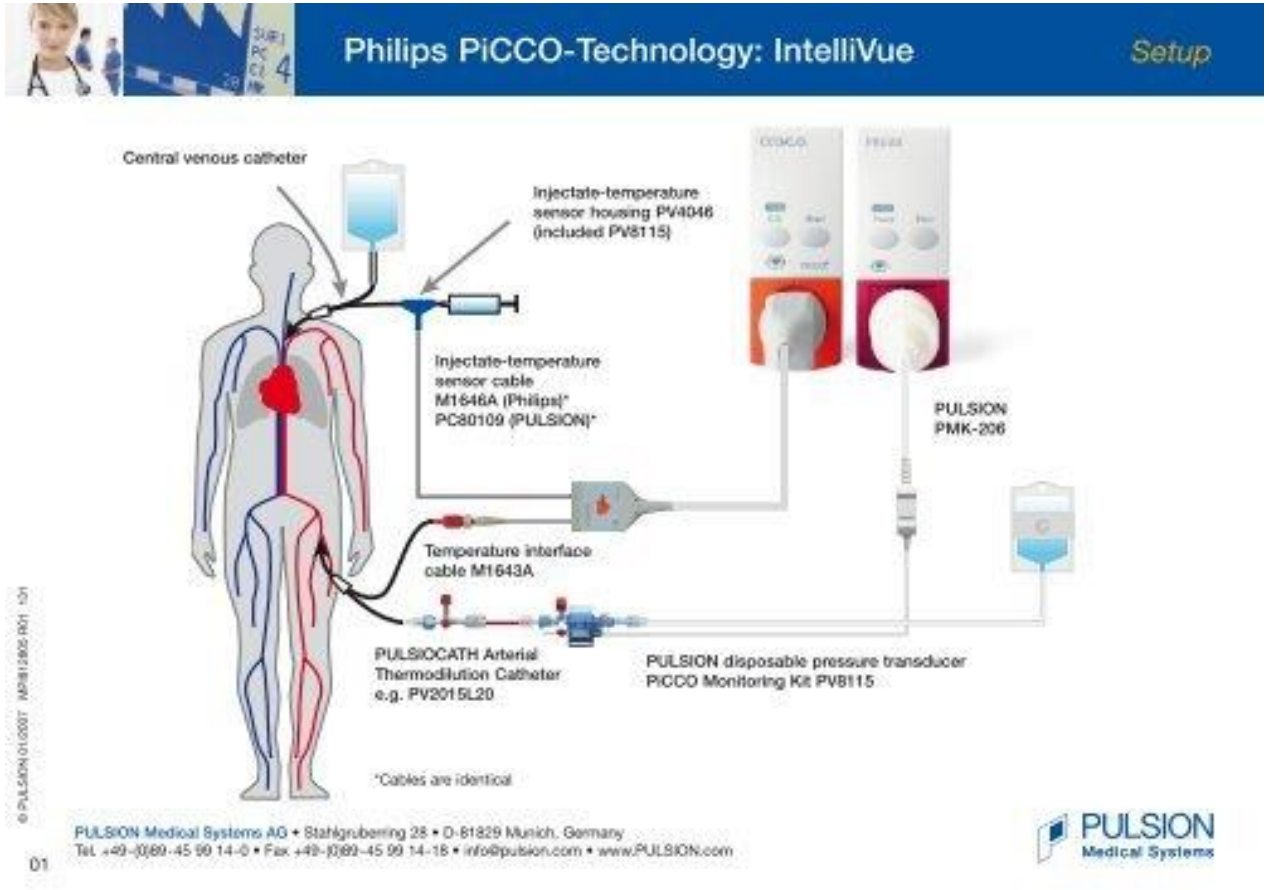
$$CO = \left(\frac{k \times (T_{blood} - T_{injectate}) \times V_{injectate}}{\int \Delta T_B \times dt} \right)$$

Or modified to suit dye-dilution techniques:

$$CO = \frac{\text{amount of injected indicator}}{\text{area under dilution curve}}$$

Definition of terms used

CO = cardiac output
$V_{injectate}$ = volume of injectate
k = correction factor
T_{blood} = temperature of blood
$T_{injectate}$ = temperature of injectate
$\int \Delta T_B \times dt$ = integral of area under temperature/time curve



THANK YOU

I hope you are still awake at the end of this lecture !