Sepsis in obstetrics and gynecology-recent views

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Dedicated to my mother
who died due to
Severe sepsis

SEPSIS.. THE LEADING CAUSE OF DEATH

Sepsis arises when the body's response to an infection damages its own tissues and organs.

- ***It can lead to shock,*** ***------*** multiple organ failure, ---------death
- . 60-80% of all deaths all over world.
- ***6 million*** infants and young children, and ***100,000*** new mothers every year.
- Every few seconds, someone in the world dies of sepsis.
- despite advances in modern medicine like vaccines, antibiotics, and intensive care.

ALARMING RISE

- **Incidence is increasing dramatically**
  Hospitalizations for sepsis have more than doubled over the last 10 years, and
- more people are hospitalized each year for sepsis than for heart attack.
- International studies show that 20-40% of sepsis patients requiring intensive care treatment developed sepsis outside the hospital.
- In the United States, the incidence of post-surgical sepsis tripled between 1997 and 2006.

Reasons behind rise

1. Increased use of invasive surgery
2. More immuno-suppressed patients
3. New immunomodulating therapy
4. Increased use of invasive devices
5. Increase antibiotic resistance

Sepsis can affect healthy people at any age

PREVALENCE AND MORTALITY RATE IN PREGNANCY

- 0.1 to 0.6 per 1000 deliveries.

1. Young age and
2. less co morbid conditions
3. microorganisms(pelvis) are sensitive

significant factor of maternal morbidity and mortality r

- 7.6% of maternal deaths in the United States
- 15-20% of maternal deaths in developing countries

PUERPERAL SEPSIS

- ***DEFINITION BY WHO :***

  Puerperal sepsis as infection of the genital tract occurring at any time between the onset of the rupture of membranes or labour and the 42nd day postpartum.

- FEVER WITH ONE OF FOLLOWING
- PELVIC PAIN
- ABNORMAL VAGINAL DISCHARGE/
- ABNORMAL ODOUR OF DISCHARGE/
- DELAY IN RATE OF REDUCTION OF SIZE OF UTERUS.

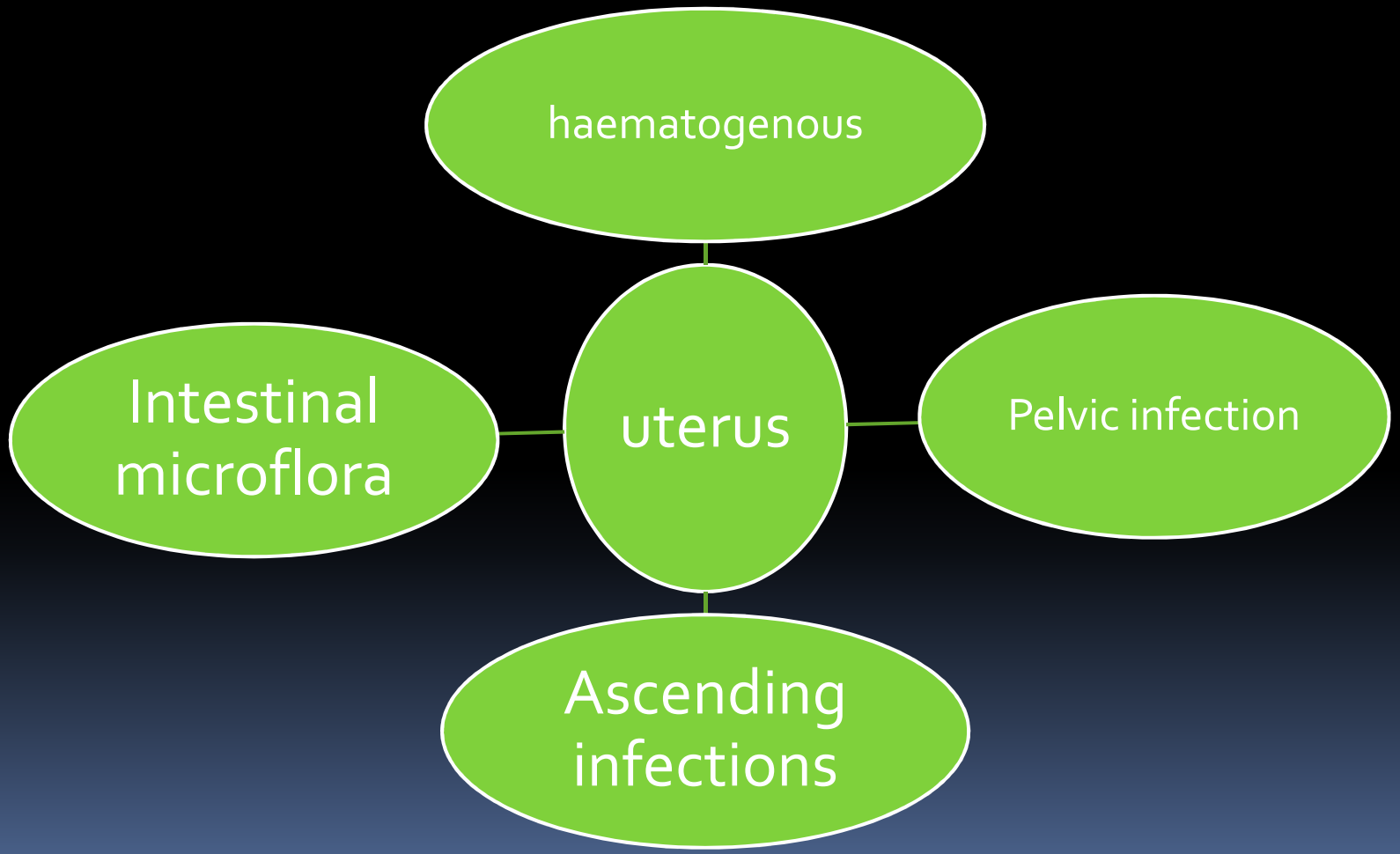
- 75,000 maternal deaths every year- low-income countries.
- high-income countries - maternal morbidity 0.1-0.6 / 1000 deliveries.

RISK FACTORS AND ROUTES OF INFECTION IN PREGNANCY

- ***RISK FACTORS:***

1. home birth in unhygienic conditions,
2. low socioeconomic status,
3. poor nutrition,
4. primiparity, anaemia,
5. prolonged rupture of membranes,
6. prolonged labour,
7. multiple vaginal examinations in labour ,
8. caesarean section,
9. multiple pregnancy,

Routes of infection:



ARE PREGNANT WOMEN MORE PRONE TO INFECTIONS AND SEPSIS

- Pregnancy represents the most important period for the ***conservation of the species***, thus, it is fundamental to strengthen all the means to protect the mother and the fetus.
- Therefore, it is appropriate to refer to pregnancy as a unique immune condition that is modulated but not suppressed.

REASONS FOR INFECTION AND SEPSIS DURING PREGNANCY

- Physiologic changes in the lower genital tract.

- Changes in urinary system
- .
- Changes in haemostatic system.:
- An elevated leukocyte count,
  Increased c-reacting protein,
- Increased heart rate by 15-20 bpm, may mask early signs and symptoms of infection favouring the dissemination of bacteria into the blood-stream.

CHORIOAMNIONITIS AND INTRA-AMNIOTIC INFECTION:

- before 1970 was a major cause of maternal mortality.
- :
- 1) fever,
- 2) uterine fundal tenderness,
- 3) maternal tachycardia (>100/min),
- 4) fetal tachycardia (>160/min),
- 5) purulent or foul amniotic fluid.
- Polymicrobial in nature.

- SPONTANEOUS RUPTURE OF MEMBRANES
- SEPSIS
- SHOCK

DOES THE MODE OF DELIVERY AFFECT THE INCIDENCE OF SEPSIS AND SEPTIC SHOCK?

- ENOURMOUS RISE IN RATE OF CAESAREAN SECTION.
- MORBIDITY- ENDOMETRITIS
- URINARY TRACT INFECTION.
- SURGICAL SITE INFECTION.
- EMERGENCY CAESAREAN SECTION.
- RATE OF INFECTION
  - CAESEREAN SECTION- 1.1 TO 25%
  - NORMAL DELIVERY - 2.0 TO 5.5%

- ANTEPARTUM- MOSTCOMMON INFECTION IS ASYMPTOMATIC BACTERURIA
- PRE-INCISION BROAD SPECTRUM ANTIBIOTICS ARE MORE EFFECTIVE IN PREVENTING POST-CS INFECTIONS THAN POST-CLAMPING OF THE CORD NARROWRANGE ANTIBIOTICS.

Amniocentesis, chorionic villsampling(CVS):

invasive procedures with serious complications for

- both the mother and the fetus
- the incidence of chorioamnionitis is
- 5 per 1,000 cases after CVS;
- 3.7 per 1,000 cases after amniocentesis;
- 8.8 per 1000 cases after cordocentesis,
- Sporadic reports of *Clostridium infections are seen in the literature.*

Septic abortion

- an abortion related with infection-- fever, endometritis,and parametritis, -the most serious threats
- illegal, criminal or non-medical abortions
- legalization of abortion and introduction of broad spectrum antibiotics.
- Abortion remains a primary cause of maternal death in Third World countries.
-

septic abortion

- woman of reproductive age
- presents with vaginal bleeding, lower abdominal pain, and fever.
- symptoms for several days, a generalized, serious illness may be present.
- Bacteremia----septic shock -- adult respiratory distress syndrome.

Management of septic abortion

- eradication of the infection and supportive care
- evacuation of uterus
- antibiotic therapy and fluid resuscitation .
- hysterectomy
- laparotomy – uterine perforation with a suspected bowel injury
- pelvicabscess,
- clostridial myometritis.

- Cervical dilation with laminaria tent
- mifepristone and misoprostol.
- The incidence of uterine infection very low.
- However, severe and fatal infections have been reported in certain cases; most ofthem were associated with *Clostridium infections and development of toxic shock* syndrome
- . Klebsiella pneumoniae has also been reported as the cause of septic shockafter medical termination of pregnancy with misoprostol-only

Non-obstetric causes of septic shock

Urinary tract infection

- Pyelonephritis
- . All pregnant women should be screened for the presence of bacteriuria at t heir first prenata
- 25% of women experiencing acute pyelonephritis have untreated UTI
- a

Genital tract infection/others

- Post-partum endometritis
- pelvic abscess, wound infection,
- necrotizing fasciitis,
- appendiceal abscess, acute cholecystitis, septic pelvic vein thrombosis, pneumonia, pancreatitis, .
-

Septic shock in gynecologic patients

Sepsis-related situations in Gynecology can be found

1. intra uterine devices (IUD)
2. untreated PID
3. toxic shock syndrome- use of tampons
4. gynecological cancer

Rising incidence due to

1. an aging population
2. an increase in the number of invasive procedures
3. resistance to the current antibiotic treatment.

the American College of Chest Physicians and the Society of Critical care
(1991)

SYSTEMIC INFLAMATORY RESPONSE SYNDROME [SIRS]:

Two or more of the following conditions:

1. Fever(oral temperature>38c)/hypothermia(<36c)
2. Tachypnoea (>24 breaths/min)
3. Tachycardia (heart rate> 90 beats/min)
4. Leucocytosis (>12,000/L) leucopenia(<4000/L) or 10% bands; immature forms

May have non infectious etiology. SIRS can be caused by infection, trauma, burns, pancreatitis, and other insults which result in tissue damage

definitions

- SEPSIS: SIRS that has a proven or suspected microbial etiology.
- SEVERE SEPSIS(similar to SEPSIS SYNDROME):

Sepsis with one or more signs of organ dysfunction- for example:

1] CARDIOVASCULAR: arterial systolic blood pressure<90 mmHg or mean arterial pressure<70 mmHg that responds to administration of intravenous fluids.

2] RENAL: urine output < 0.5 ml/kg per hour for 1 hr despite adequate fluid resuscitation.

3] RESPIRATORY: PaO_2/FIO_2 < 250 or if the lung is the only dysfunctional organ

4] HAEMATOLOGIC: platelet count < 80,000/L or 50% decrease in platelet count from highest value recorded over previous 3 days.

5] UNEXPLAINED METABOLIC ACIDOSIS: A pH< 7.30 or a base deficit > 5.0 mEq/L and plasma lactate level> 1.5 times upper limit of normal for reporting lab.

definitions

- SEPTIC SHOCK: Sepsis with hypotension (arterial blood pressure<90 mmHg systolic,or 40 mmHg less than patient's normal pressure) for at least 1 hr despite adequate fluid resusitation;

  OR

  Need for vasopressors to maintain systolic blood pressure> 90 mmHg or mean arterial pressure> 70 mmHg.

  REFRACTORY SEPTIC SHOCK: Septic shock that lasts for 1 hr and does not respond to fluid or pressor administration.

  MULTI ORGAN DYSFUNCTION SYNDROME[MODS]: Dysfunction of more than one organ , requiring intervention to maintain homeostasis.

Expanded signs of SIRS

General signs & symptoms

Rigor– fever
Tachypnea
Positive fluid balance – edema

General inflammatory reaction

Altered WBC count
Increased CRP,

PCT concentrations

Hemodynamic alterations

Arterial hypotension
Tachycardia
Altered skin perfusion
Decreased U.O
Hyperlactatemia –

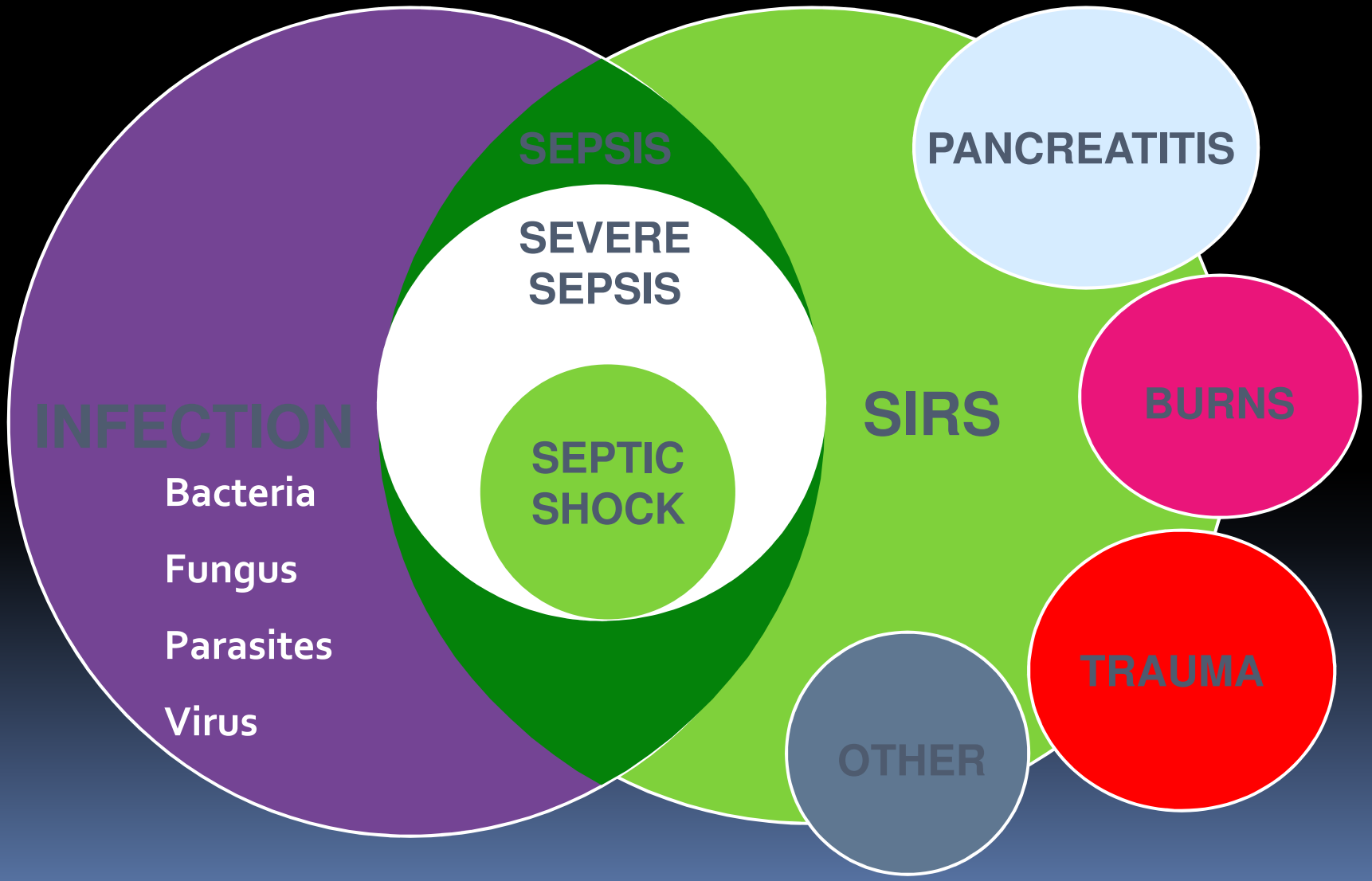
Signs of organ dysfunction

Hypoxemia
Coagulation abnormalities
Altered mental status

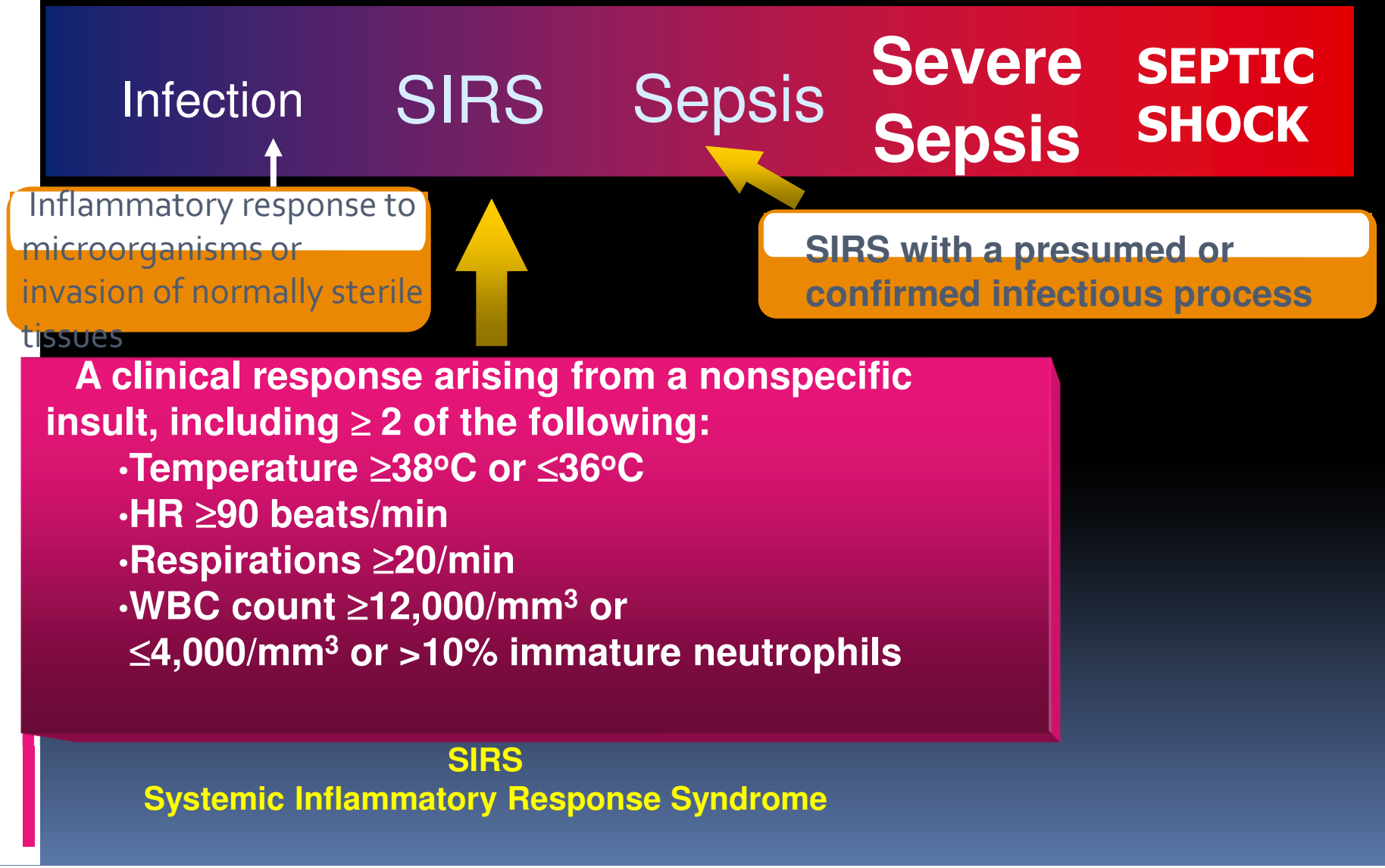
Sepsis - SCCM Definitions: The Update

- Altered mental status
- Edema or increased fluid balance
- Hyperglycemia (absent diabetes)
- Increased CRP or procalcitonin
- Hypotension
- Increased SvO_2
- CI > 3.5 L/min/m^2
- Arterial hypoxemia (PaO_2/FiO_2 < 300)
- Acute oliguria (> 2 hours)
- Increased serum Cr (> 0.5 mg/dL)
- Coagulopathy (INR > 1.5)
- Ileus (absent bowel sounds)
- Thrombocytopenia (< 100,000/uL)
- Hyperbilirubinemia (> 40 mg/dL or 70 mmol/L)
- Hyperlactatemia (> 1 mmol/L)
- Decreased capillary refill or mottling

Relationship Of Infection, SIRS, Sepsis Severe Sepsis and Septic Shock



Sepsis: Defining a Disease Continuum



Sepsis with ≥1 sign of organ failure

Cardiovascular (hypotension)

Lungs: (ARDS):

Kidneys

Liver

Digestive

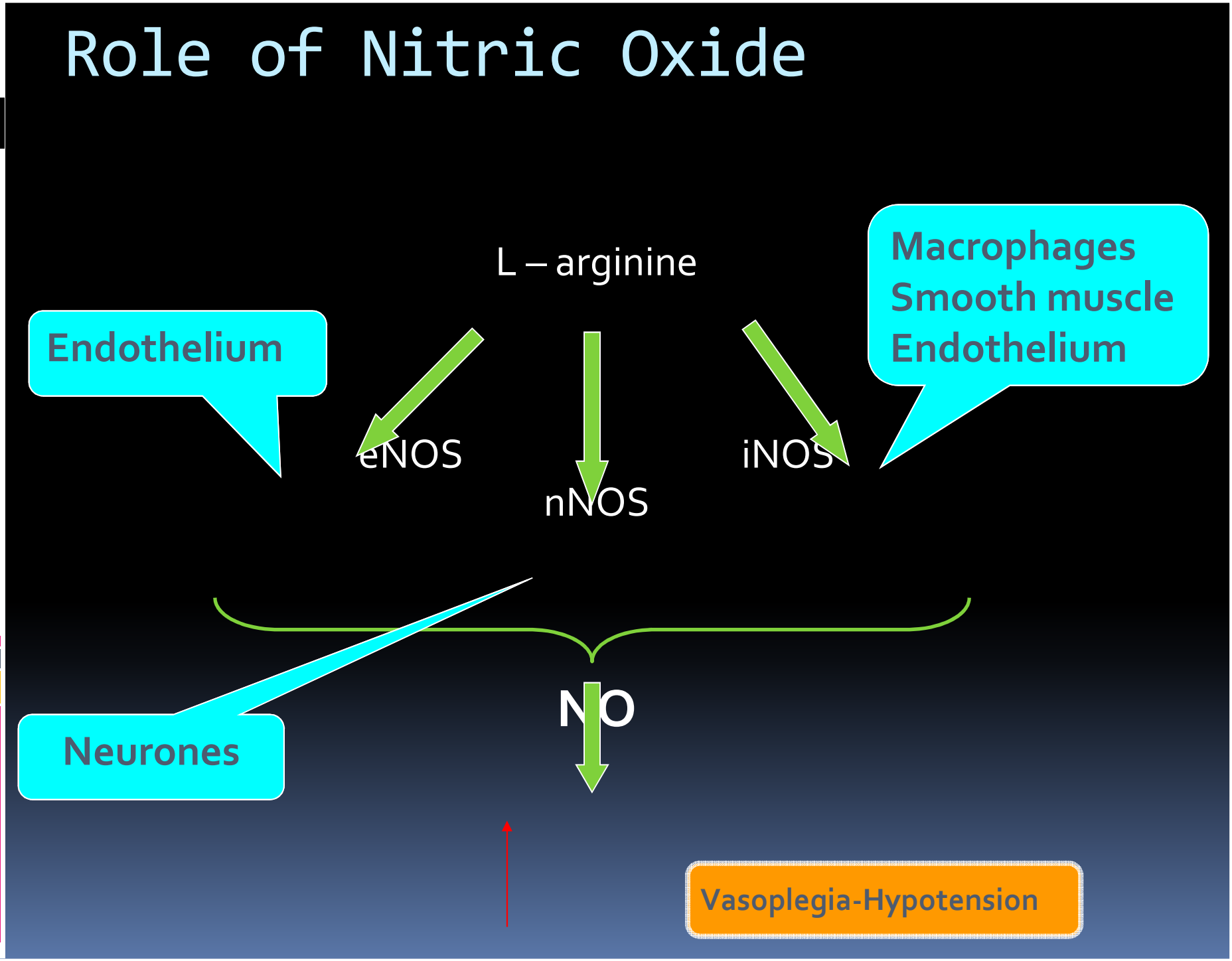
Brain - confusion

HYPOTENSION despite adequate fluid resuscitation/Requiring Vasopressors or Inotropes

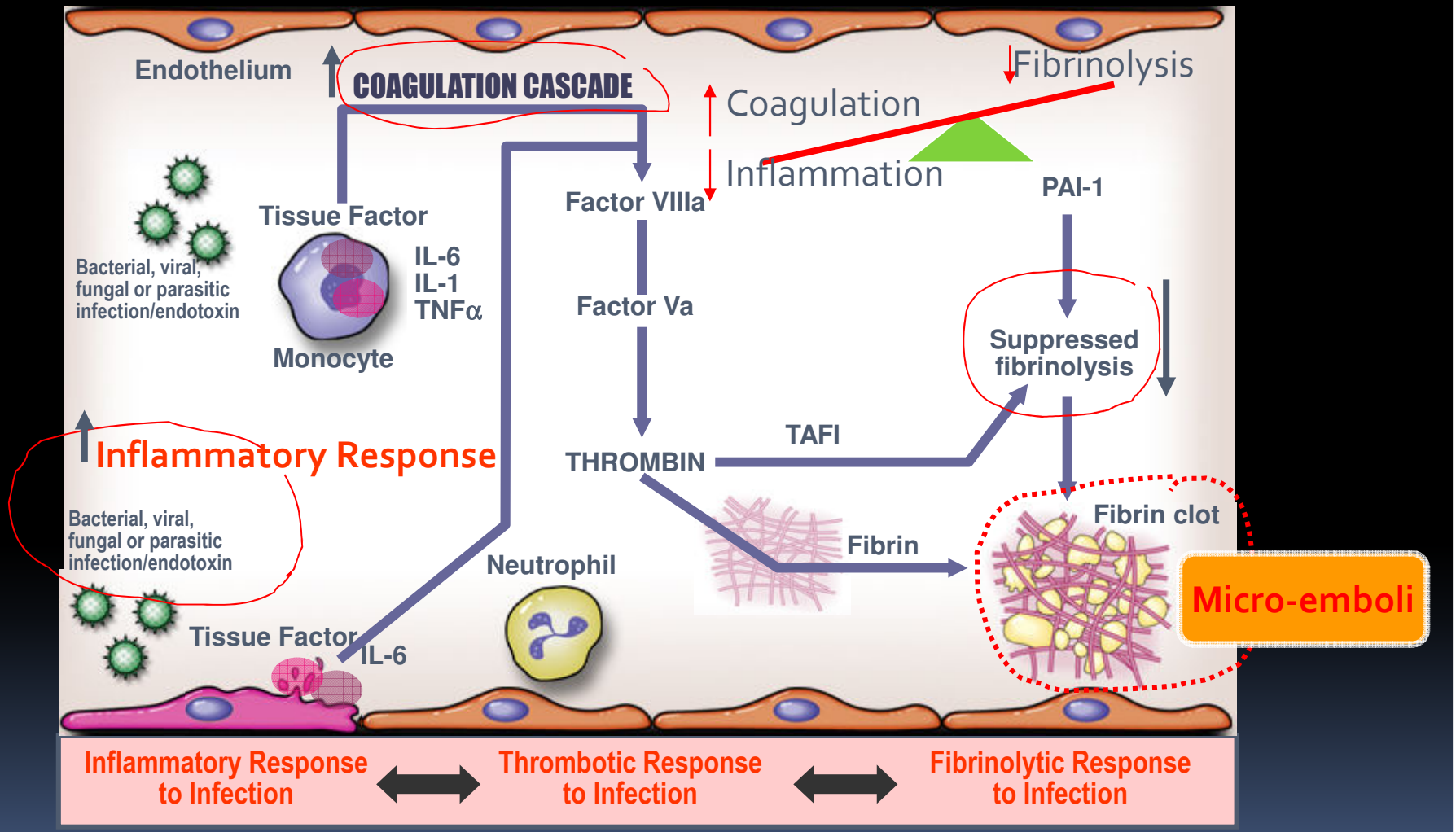
Pathogenesis of shock

- Infectious trigger
- Interaction with human cells- macrophages Monocytes, Neutrophils, Endothelial cells
- Cytokines & inflammatory mediator cascade
- Cardiac dysfunction, Microemboli, Microvasular injury, increased Nitric oxide- Vasoplegia
- Microcirculatory Mitochondrial dysfunction

Role of Nitric Oxide



Coagulation in Sepsis



Bernard GR, et al. New Engl J Med, 2001;344:699-709.

Final pathway in sepsis

Vasoplegia , Cardiac dysfunction, Capillary leak
Hypovolemia,Maldistribution Microemboli

↓

Microcirculatory Mitochondrial Dysfunction syndrome (MMDS)

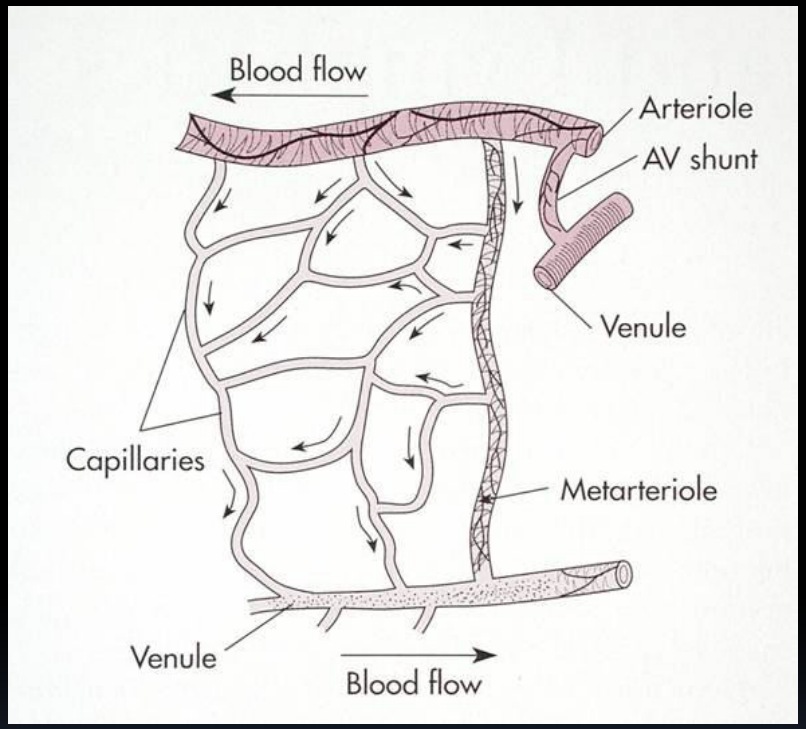
↓

Cell death-Organ injury –MODS- Death

Sepsis is a disease of the microcirculation

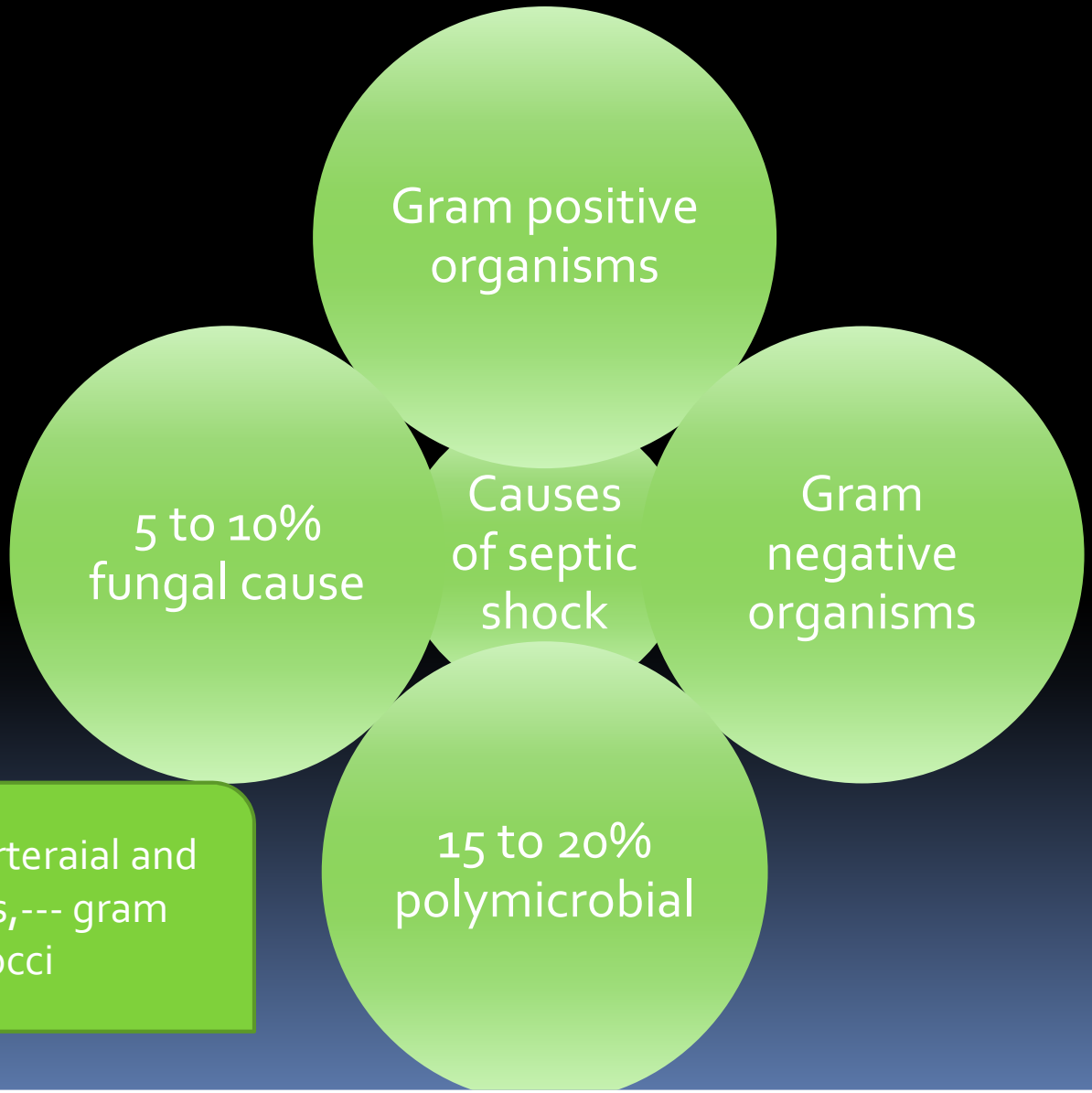
Why the microcirculation is important in shock.

- It is where oxygen exchange takes place.
- It plays a central role in the immune system.
- During sepsis and shock it the first to go and last to recover.



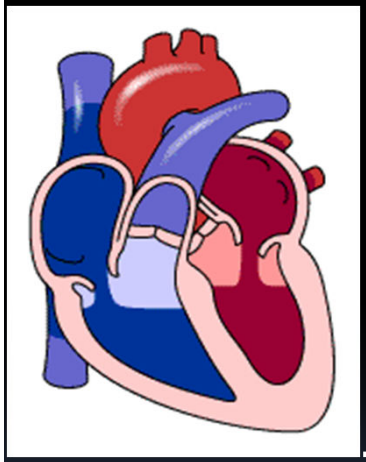
Rescue of the microcirculation = resuscitation end-point

etiology



Increased use of arteraial and venous catheters,--- gram positive cocci

Heart



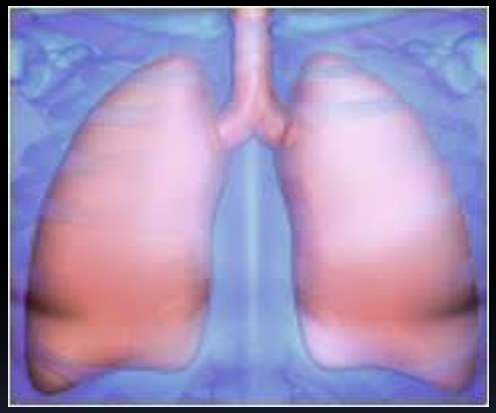
Vasodilatation (nitric oxide release)
Hypovolemia
Myocardial dysfunction
Cell metabolism alteration
Decrease vascular resistance

Tachycardia, Hypotension, Hypoperfusion

lungs

- pulmonary vascular effects-
- diffuse pulmonary infiltrates,-
- complience redused maldistribution of blood flow ——

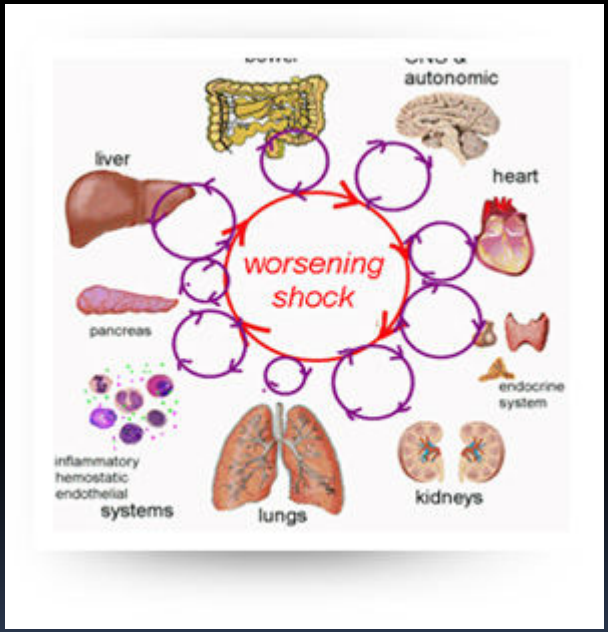
- Endothelial cell injury
- Bronchodilatation /bronchoconstriction
- Pulmonary edema/ARDS
- Pulmonary hypertension



KIDNEY

- severe renovascular spam--Injury to Endothelial cell - decrease in glomrrular capillary filtration
- Renovascular thrombosis

Multisystem involvement



- Subtle changes in mental acuity to confusion,lethargy,obtundation,and coma
- Cold,pale,dusky,mottled,may bc cynotic
-
- capillary reffill
- Liver-increased bilirubin– hymolysis and hepatocelluiar dysfunction
- Gastrointestinal –stress bleeding
- ,

Physiological basis of signs

Symptom/sign	
Subtle Brain—subtle mental changes, septic encephalopathy—	1/-decreased cerebral perfusion 2/ cytokine induced endothelial cell damage- leaky blood brain barrier
Tachycardia,bounding pulse	Myocardial ischimia,depressed cardiac function,cardiac output more or less,decreased SVR
Normotensive/hypotensive,widened pulse pressure	Decreased circulatory volume
oliguria	Afferrent arteriolar vasoconstriction
tachycardia	Pulmonary edema,acidosis,muscle fatigue
warm	Increased cardiac output,perepheral vasodilatation,febrile responce
Fever/hypothermia	Infections,endotoxins,cytokines

Septic Shock Hemodynamics

Warm (hyperdynamic) shock

- hypotensive
- tachycardia
- tachypnea
- bounding pulse
- warm, well perfused extremities
- skin flushed, moist

Cold (hypodynamic) shock

- hypotensive
- tachycardia
- tachypnea
- narrow, thready pulse
- cold, poorly perfused extremities
- skin pale, dry

management

- The net result of these changes is to cause a combination of:
- • hypoxaemia
- • hypovolaemia
- • vasodilation and capillary leak
- • impaired tissue oxygen utilisation

Respiratory changes --tachypnea

The earliest clinical sign of sepsis is often a rapid respiratory rate

- lactic acidosis , pyrexia,
- cytokine-mediated effects on the respiratory centre.
- pulmonary pathology,
- shunting of deoxygenated blood through the lungs (cytokine mediated) or pulmonary oedema secondary to capillary leak.

EARLY MANAGEMEment

Stabilize respiration

pulse oximetry.

Supplemental oxygen

Intubation and mechanical ventilation

Chest radiographs and arterial blood analysis should be obtained following initial stabilization.

These studies are used in combination with other clinical parameters to diagnose acute respiratory distress syndrome (ARDS), which frequently complicate sepsis. distress syndrome:

Fluid therapy

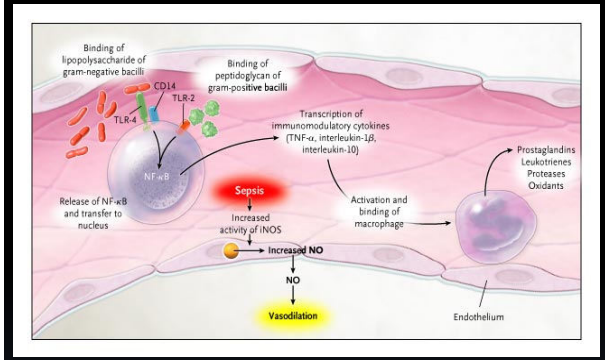
- Fluid therapy is considered the first step in the resuscitation of most patients with hypotension and shock

- . Uncorrected hypovolemia---- inappropriate infusions of vasopressor agents--- may increase organ hypoperfusion and ischemia.
- overzealous fluid resuscitation - increased complications,-- increased length of ICU

Fluids -- critical role in the pathogenesis and treatment of early resuscitation of severe sepsis and septic shock.

- The type, composition, titration, management strategies and complications of fluid administration
- early titrated fluid administration
- 1/modulates inflammation,
- 2/improves microvascular perfusion,
- 3/impacts organ function and outcome.
  - Fluid administration has limited impact on tissue perfusion during the later stages of sepsis and excess is deleterious to outcome.

The pathogenesis of hypovolemia in sepsis



1/maldistributive defect with vasodilatation,

2/ extravasation of fluid in interstitial space

3/increased capillary endothelial Permeability

4/ vomiting,diarrhea, sweating, edema peritonitis or other exogenouslosses.

quantitating volume status/perfusion

Common signs of hypoperfusion

- cool, vasoconstricted skin
- tachycardia >90/min,
- obtundation or restlessness
- oliguria / anuria.
- modified by preexisting disease or medications. beta-blockers .
- The clinical assessmentof hypovolemia is historically nonsensitive and nonspecific .

reliable?

- findings of an ineffective circulation (capillary refill time
- >2 s, skin mottling, and cool extremities) were compared
- to parameters obtained from a pulmonary artery catherter,
- it was found that they are not useful predictors of a
- low cardiac index (CI) or low SvO_2

Titrating fluid therapyThe goal is to infuse adequate volume

1/ Achieving A Predetermined Value

.

2/Optimizing Systemic Oxygen Delivery -Cardiac Preload-afterload-arterial Oxygen Content.

3/ Ultimately Balancing Tissue Oxygen Demands

Volume status/Preload accessment

1. blood pressure
2. heart rate
   urine output
3. central venous pressure
4. pulmonary artery occlusion pressure (PAOP).

Invasive monitoring--uses

CVP

- **Establish central venous access** — 1/to infuse intravenous fluids, infuse medications
- 2/, infuse blood products,
- 3/ draw blood
- 4/ central venous pressure (CVP) and the central venous oxyhemoglobin saturation $(ScvO)_2$

CVP

- The CVP describes the pressure of blood in the thoracic vena cava near the right atrium of the heart.---- CVP is a good indicator of right ventricular preload--left ventricular preload Preload is best defined as left ventricular end-diastolic volume
-

CVP- How much useful

- because of the
- 1/ changes in venous tone,
- 2/ intrathoracic pressures (positive end expiratory pressure, etc.),
- 3/ left and right ventricular compliance and
- 4/ geometry that occur in critically ill patients, there is a poor relationship between the CVP and right ventricular end-diastolic volume.
- Furthermore, the right ventricular end-diastolic volume may not reflect the patients' position on the Frank–Starling curve and therefore his/her preload reserve.

preload
Frank–Starling principle

-).
- As preload increases left ventricular stroke volume increases until the optimal preload is achieved at which point the stroke volume remains relatively constant (see Figure 1
- maximal overlap of the actin-myosin myofibrils.
- . functioning near the 'flat' part - fluid loading has little effect on cardiac output
- a functional reserve to the heart in situations of acute stress.
-

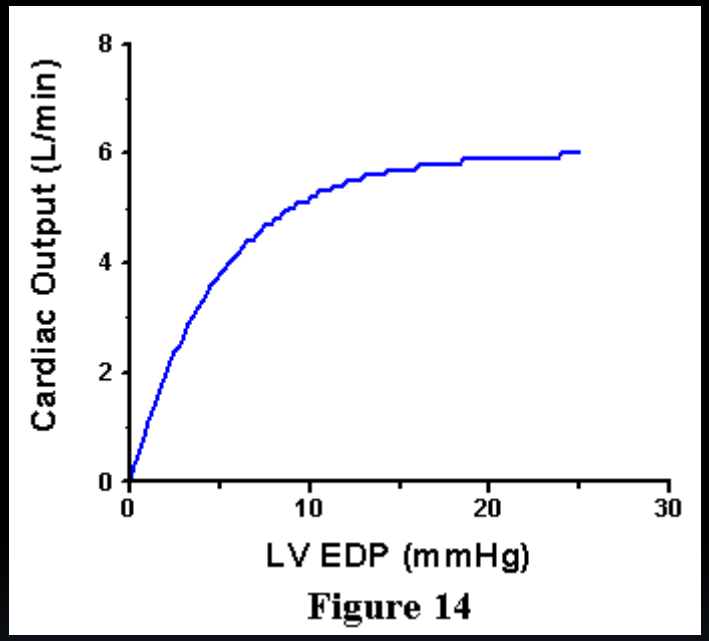


Figure 14

fluid responsiveness

- 50% of patients with circulatory failure will respond to a fluid challenge.
- altered left ventricular compliance and function, the position of an acutely ill patient on his/her Frank–Starling curve cannot be predicted from their preload (LVEDV) alone
- . In critically ill patients it is therefore important not only to determine the patients' preload (LVEDV)
- but their fluid responsiveness, i.e. to whether the patient will increase his/her stroke volume or cardiac output with fluid loading (i.e. have recruitable cardiac output).

CVP- conclusion??

- there is no association between the CVP and circulating blood volume,
- that the CVP is a poor indicator of left and right ventricular preload and that the
- CVP does not predict fluid responsiveness. Based on these results it is stated that the **CVP should no longer be routinely measured in the ICU, operating room or emergency room**

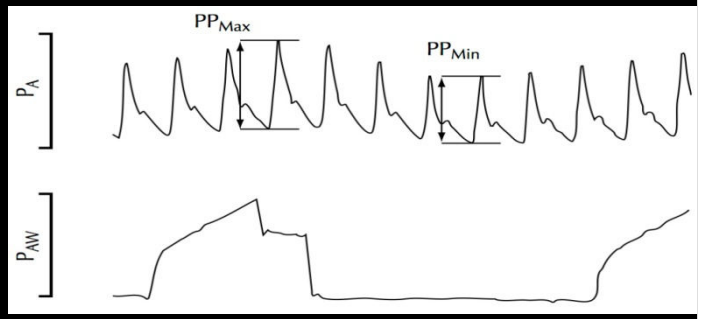
PAOP

- The PAOP suffers many of the limitations of the CVP.
- The PAOP is a measure of left ventricular end-diastolic pressure or LV preload.. ,
- alterations in left ventricular compliance
- Factors that alter left ventricular compliance include left ventricular preload, left ventricular afterload, left ventricular mass and ventricular fiber stiffness
- . Myocardial ischemia, sepsis, diabetes, obesity, aging, sustained tachycardia, dialysis, alter myocardial fiber stiffness.

PPV - the best predictor of preload responsiveness

- PPV is defined as the difference between the maximal pulse pressure and the minimum pulse pressure divided by theaverage of these two pressures

  preload responsive if their CI increased by at least
- 10–15% after rapid infusion of standard volume of intravenousfluid
-



Atrial arrhythmias and spontaneous breathing can interfere with the usefulness of this technique

PPV in mechanically ventilated patients remains a useful approach for assessing preload

Type of fluids

crystalloid

- Crystalloid therapy

- 0.9% sodium chloride solution (normal saline or NaCl)
- and Ringer's lactate solution..
- the use of large volumesof normal saline, promotesthedevelopment of hyperchloremic metabolicacidosis

- ,

colloids

- Colloids are higher-molecular-weight solutions that
- increase plasma oncotic pressure. Due to their higher molecular weight, colloids stay in the
- intravascular space significantly longer than crystalloids
- with an intravascular half-life for albumin of 16 h versus
- 30–60 min for normal saline and lactated Ringer's
- solution [41,42]. When titrated to the same PAOP

The optimal hemoglobin (macrovascular and microvascular hematocrite)

- Appropriate hemoglobin levels in shock remain controversial
- Blood transfusion to be given very carefully
- May be associated with increased infection
- Allogenic leukocytes—immunosuppresion
- Pts in septic shock are known to tolerate low HB
- 8—10 gm –recommonded range

Hemoglobin concentrations may vary in the central, peripheral and microvascular circulations.

- . Anemia may also result from hemodilution
- The risks and benefits of RBC transfusionshould be assessed in every patient before transfusion.

Resuscitation end points

Macro circulation

CVP 8–12 mm Hg

(MAP) >=65 mm Hg

Urine output >=to 0.5 mL/kg/hr

SCVO2(superior vena cava) >=70% or SVO2 >= 65%,

Micro circulation

Lactate < 2 mmol/L

SCVO2 > 70%

Tissue hypoperfusion can persist despite normal vital sign.

Pregnancy perspective

- In pregnant patients pulmonary edema can occur at low CVP-Differencial behaviour of sytemic and pulmonary vascular systems.
- Deterioration in mother is associated with dangerous sequele to foetus .
- Early recognition,aggressive treatment ,timely decisions and aggressive perioperative support—key to success

Operating in sick patients

- Labour may set in—decide mode of delivery
- Foetal distress is commonest indication of CS
- Heavy and prolonged trial for normal delivery are not advocated against the background of thrombocytopenia,metabolic acidosis and DIC
- Intraoperative losses has to be carefully replaced as pts are volume contracted
- DIC may worson-PPH,intraperitonal haematomas ,abdominal wound haematomas,vulval haematomas

- Timely decisions,skilled surgery,careful fluid therapy,judicious use of componants-very imp
- Minimal level of thrombocytes needed to go ahead with surgery is debatable
- Thombocytopenia- underlying grave disease (severe sepsis) where coagulation factors are depleted-FFPs/cryoprecipites infusions are more helpful

- Extreme causiosness in using antihypertensive drugs Diuretics,analgesics and uterine relaxants in presence of volume depleted states.

- Intrapartum fever is a grave sign
- Non-immune fetal hydrops –one of sequele in acutly ill mothers

- Viral haemorragic fever,dengue fever may progress to MODS

goals

- within 4 hours of the onset of septic shock:
- **Fluid resuscitation** is initiated to achieve
- 1/ right atrial pressure of 8 to 12 mm H g 2/ assessment for volume responsiveness
- .
- **Vasoactive drugs** are then used to achieve a mean arterial pressure of 65 to 70 mm Hg
- .
- **Inotropic agents** are used to achieve a physiologically appropriate cardiac output (about 1 to 1.5 times normal) if myocardial function is depressed, and/or a right atrial or mixed venous oxygen saturation of at least 70%

Antibiotic policy

Therapy be pathogen- and susceptibility-directed,

vancomycin with

1/Cephalosporin,3rdge

2/Beta-lactam/beta-lactamase inhibitor

3/Carbapenem(piparacillin)

Fluoroquinolone (ciprofloxacin)

Aminoglycoside (eg, gentamicin, amikacin)

Monobactam (eg, aztreonam

Antibiotics

- Selection of two agents from the same class, for example, two beta-lactams, should be avoided.
- local susceptibility patterns when choosing an empiric antibiotic regimen

  Gram-negative pathogens have historically been covered with two agents from different antibiotic classes.

- Observation for toxicity presence of response, and the development of nosocomial superinfection .
- The duration of therapy is typically 7 to 10 days, although longer courses may be appropriate in patients who have a slow clinical response, an undrainable focus of infection, or immunologic deficiencies

Protocols/monitoring

1. **Protocols** — Sepsis treatment protocols may improve outcome Implementation of a standardized hospital order set .
2. **INFORMATION FOR PATIENTS** —

- **Hemodynamic monitoring**
- **Metabolic monitoring** includes serial measurements of serum lactate, glucose, electrolytes, ionized calcium every 8 hours initially. C-reactive protein is measured daily.
- **Coagulation monitoring** includes INR, aPTT, D-dimer, and fibrinogen every 8 hours initially.
- **Fluid monitoring** includes total protein (to estimate plasma

ADDITIONAL THERAPIES

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- **Glucocorticoids —**
- **Nutrition —**
- **Intensive insulin therapy —**
- **External cooling**
- DVT profilaxis
- Sress ulcer profilaxis
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PREVENTION

Thank You