BACTEREMIA AND SEPSIS

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Outline

- History and Definitions
- Classification
- Epidemiology
- Microbiology
- Pathogenesis
- Clinical aspects of bacteremia
- Laboratory diagnosis
- Management
- Prevention

Sepsis

History

- From Greek word for “decomposition” or “decay” (Homers poems)
- First case of bacteremia (1899)*Bacillus pyocyaneus*
- The first definition Hugo Schottmüller 1914

“sepsis is present if a focus has developed from which pathogenic bacteria, constantly or periodically, invade the blood stream in such a way that this causes subjective and objective symptoms.”

Sepsis

Definitions

- In 1991, first consensus definition of sepsis.
- 2nd definition in 2001
- 3rd definition in 2016

Table 1. Definitions of sepsis.

Sepsis 1 (1991)[6]	Sepsis 2 (2001)[7]	Sepsis 3 (2016)[8]
Systemic inflammatory response syndrome (SIRS): systemic inflammatory response to a variety of severe clinical insults: Temperature >38°C or <36°C; heart rate >90 beats per min; respiratory rate >20 breaths per min or $PaCO_2$ <32 mmHg; and white blood cell count >12,000/cu mm, <4000/cu mm, or >10% immature (band) forms Sepsis is a systemic response to infection, manifested by two or more of the SIRS criteria as a result of infection. Severe sepsis: Sepsis associated with organ dysfunction, hypoperfusion, or hypotension; hypoperfusion and perfusion abnormalities may include, but not limited to, lactic acidosis, oliguria, or an acute alteration in mental status Septic shock: Sepsis-induced, with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but not limited to, lactic acidosis, oliguria, or an acute alteration in mental status; patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.	Infection: Documented or suspected and some of the following: **General parameters:** Fever (core temperature >38.3°C); hypothermia (core temperature <36°C); heart rate >90 beats per min or >2 SD above the normal value for age; tachypnea: respiratory rate >30 breaths per min; altered mental status; significant edema or positive fluid balance (>20 mL kg^{-1} over 24 h) Hyperglycemia (plasma glucose >110 mg dL^{-1} or 7.7 mM L^{-1}) in the absence of diabetes **Inflammatory parameters:** Leukocytosis (white blood cell count >12,000/μL); leukopenia (white blood cell count <4000/μL); normal white blood cell count with >10% immature forms; plasma C-reactive protein >2 SD above the normal value; and plasma procalcitonin >2 SD above the normal value **Hemodynamic parameters:** Arterial hypotension (systolic blood pressure <90 mmHg, MAP <70 mmHg, or a systolic blood pressure decrease >40 mmHg in adults or <2 SD below normal for age, mixed venous oxygen saturation >70%, cardiac index >3.5 L min^{-1} m^{-2}) Organ dysfunction parameters: Arterial hypoxemia (PaO_2/FIO_2 <300); acute oliguria (urine output <0.5 mL kg^{-1} h^{-1} or 45 mM L^{-1} for at least 2 h); creatinine increase ≥0.5 mg dL^{-1}; coagulation abnormalities (international normalized ratio >1.5 or activated partial thromboplastin time >60 s); ileus (absent bowel sounds); thrombocytopenia (platelet count <100,000 μL^{-1}) Hyperbilirubinemia (plasma total bilirubin >4 mg dL^{-1} or 70 mmol L^{-1}) **Tissue perfusion parameters:** Hyperlactatemia (>3 mmol L^{-1}); decreased capillary refill or mottling	**Clinical criteria for sepsis:** Suspected or documented infection and an acute increase of ≥2 SOFA points (Table 2) The task force considered that positive qSOFA (quick SOFA) criteria should also prompt consideration of possible infection in patients not previously recognized as infected. qSOFA criteria: Altered mental status (GCS score <15); systolic blood pressure <100 mmHg; respiratory rate >22 breaths per min Septic shock is defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality. Septic shock can be identified with a clinical construct of sepsis with persisting hypotension, requiring vasopressor therapy to elevate MAP ≥65 mm Hg and lactate >2 mmol L^{-1} (18 mg dL^{-1}) despite adequate fluid resuscitation

Sepsis

Definitions 1991

Systemic inflammatory response syndrome

Criteria include at least two of the following:

- Temperature >38°C or <36°C
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min, or $PaCO_2$ <32 mm Hg
- White blood cell count >12,000/mm3 or <4000/mm3, or >10% band forms

SIRS

- Systemic Inflammatory Response Syndrome
  - A constellation of abnormal signs
  - Many triggers, infection is most common
  - EMS uses a version of SIRS that doesn't rely on blood test results (WBC count, ABG)
  - Temp, HR, RR, glucose, mental status

Sepsis

Definitions 1991

Septicemia

Bacteremia plus a clinical presentation of bacterial invasion and toxin production.

Sepsis

Infection with a systemic inflammatory response

Severe sepsis

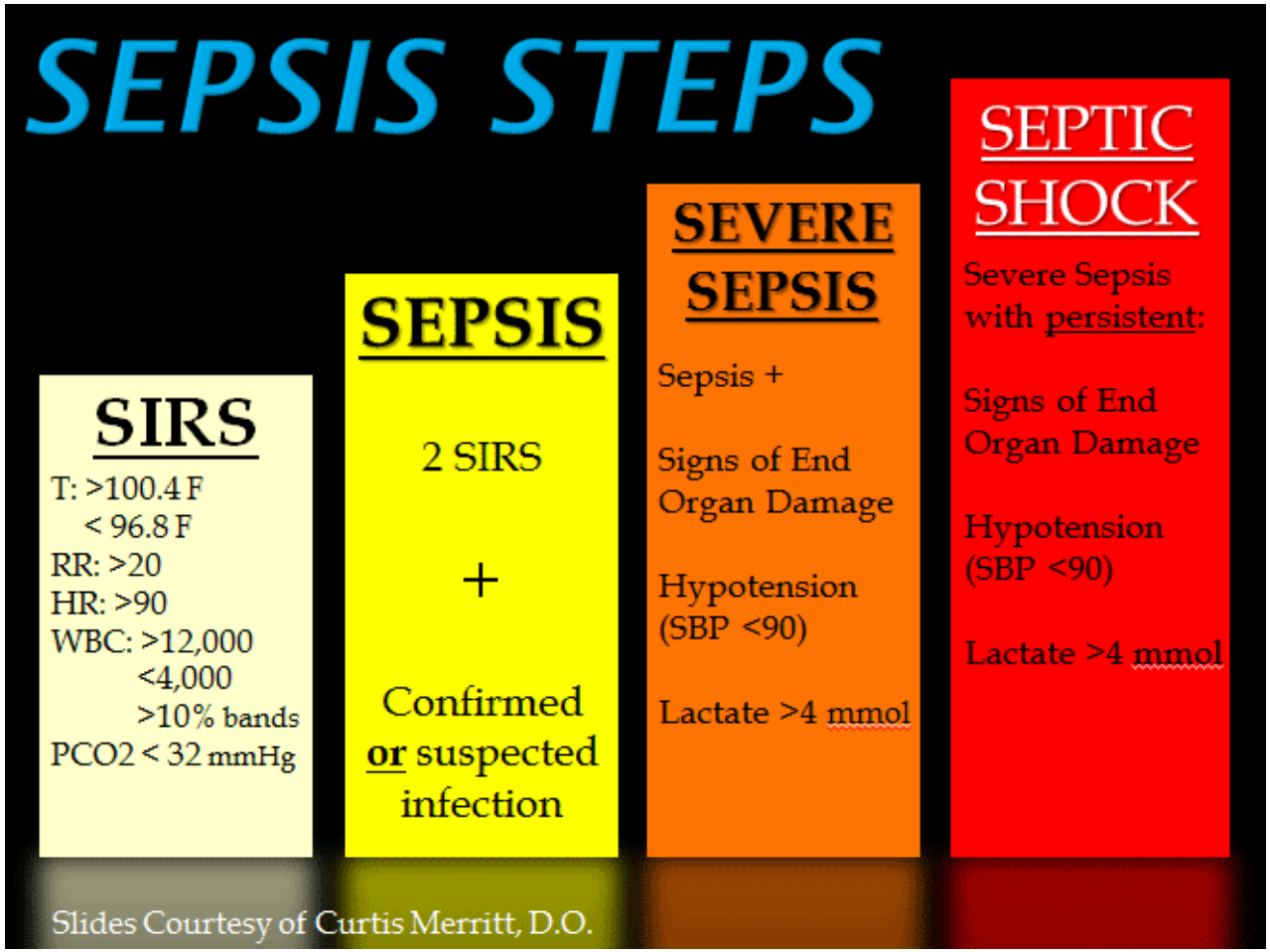
Sepsis accompanied by organ dysfunction, hypotension, or tissue hypoperfusion

Septic shock

Sepsis accompanied by refractory hypotension

Sepsis

Defintions



Sepsis

Definitions 2001

Infection: Documented or suspected and some of the following

General parameters
Inflammatory parameters
Hemodynamic parameters
Tissue perfusion parameters

Sepsis 2 (2001)[7]
Infection: Documented or suspected and some of the following:
General parameters:
Fever (core temperature > 38.3°C); hypothermia (core temperature < 36°C); heart rate > 90 beats per min or > 2 SD above the normal value for age; tachypnea: respiratory rate > 30 breaths per min; altered mental status; significant edema or positive fluid balance (> 20 mL kg^{-1} over 24 h)
Hyperglycemia (plasma glucose > 110 mg dL^{-1} or 7.7 mM L^{-1}) in the absence of diabetes
Inflammatory parameters:
Leukocytosis (white blood cell count > 12,000/μL); leukopenia (white blood cell count < 4000/μL); normal white blood cell count with > 10% immature forms; plasma C-reactive protein > 2 SD above the normal value; and plasma procalcitonin > 2 SD above the normal value
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Arterial hypotension (systolic blood pressure < 90 mmHg, MAP < 70 mmHg, or a systolic blood pressure decrease > 40 mmHg in adults or < 2 SD below normal for age, mixed venous oxygen saturation > 70%, cardiac index > 3.5 L min^{-1} m^{-2})
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Arterial hypoxemia (PaO_2/FIO_2 < 300); acute oliguria (urine output < 0.5 mL kg^{-1} h^{-1} or 45 mM L^{-1} for at least 2 h); creatinine increase ≥ 0.5 mg dL^{-1}; coagulation abnormalities (international normalized ratio > 1.5 or activated partial thromboplastin time > 60 s);
ileus (absent bowel sounds);
thrombocytopenia (platelet count < 100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin > 4 mg dL^{-1} or 70 mmol L^{-1})

Tissue perfusion parameters:
Hyperlactatemia (> 3 mmol L^{-1}); decreased capillary refill or mottling

Sepsis

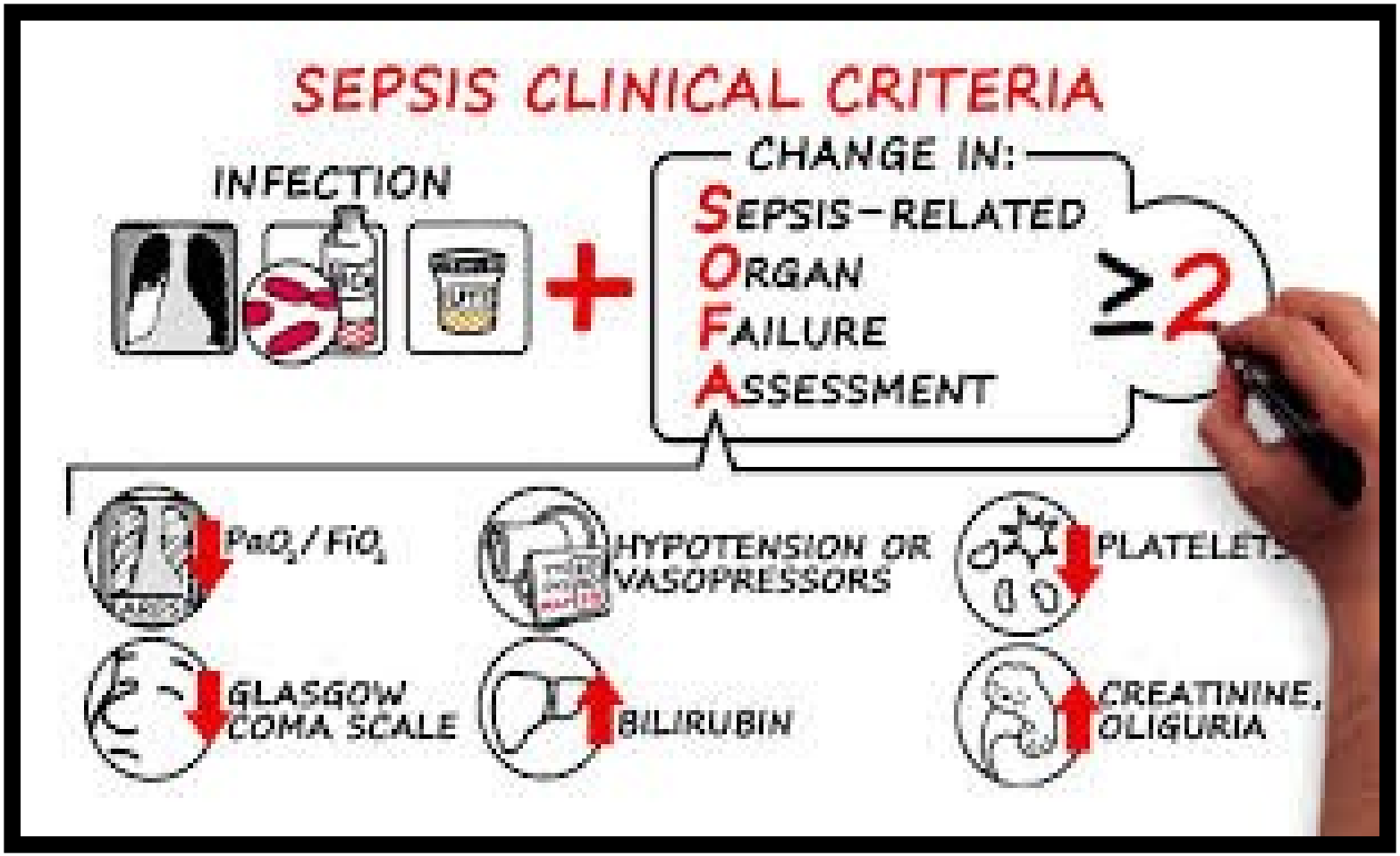
Definitions 2016

Sepsis is a life-threatening organ dysfunction caused by dysregulated host response to infection.

Septic shock can be identified with a clinical construct of sepsis with persisting hypotension, requiring vasopressor therapy to elevate MAP⩾65 mm Hg and lactate>2 mmol L-1 (18 mg dL-1) despite adequate fluid resuscitation

Sepsis

Definitions 2016



Sepsis

Definitions 2016

Table 2. Sequential (sepsis-related) organ failure assessment (SOFA) score.[8,9]

System	Score				
	0	1	2	3	4
Respiration					
PaO_2/FIO_2, mmHg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3\ \mu L^{-1}$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg dL^{-1} ($\mu mol\ L^{-1}$)	<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 ≥ 70 mmHg	MAP < 70 mmHg	Dopamine < 5 or dobutamine (any dose)[a]	Dopamine 5.1–15 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1[a]	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1[a]
Central Nervous System (CNS)					
Glasgow Coma Scale score[b]	15	13–14	10–12	6–9	<6
Renal					
Creatinine, mg dL^{-1} ($\mu mol\ L^{-1}$)	<1.2 (110)	1.2–1.9 (110–170)	2.0–3.4 (171–299)	3.5–4.9 (300–440)	>5.0 (440)
Urine output, mL per day				<500	<200

Sepsis

Definitions 2016

Sepsis

Definitions

Bacteremia

Presence of viable bacteria in the blood

Pseudobacteremia

Contamination leading to false-positive results

Occult bacteremia

Bacteremia not associated with any physical signs or symptoms of severe infection

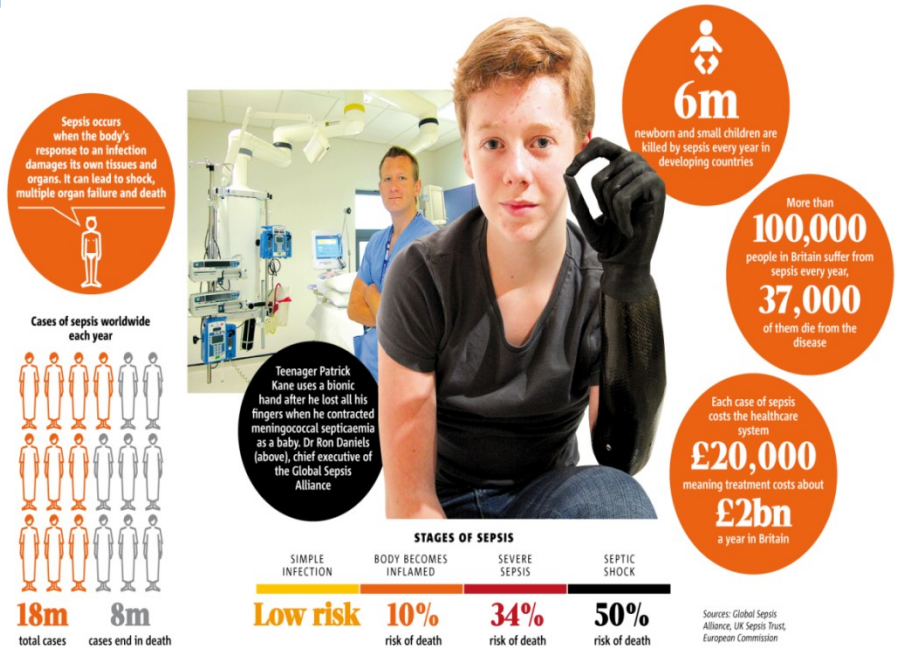
Classification of Bacteremia

- Site of Origin
  - Primary Bacteremia
  - Secondary Bacteremia
- Duration
  - Transient
  - Intermittent
  - Continuous
- Causative Agent
  - Monomicrobial
  - Polymicrobial
- Place of Acquisition
  - Community Acquired
  - Nosocomial

Sepsis

Epidemiology

- More than 30 million people affected by sepsis every year worldwide
- 6 million deaths annually



World Sepsis Day
13 September

stop sepsis save lives

Sepsis

Risk Factors

Increased incidence of Bacteremia over the last few years attributable to

- Immunocompromised state
- Increased use of invasive procedures
- Age of the patient
- Antimicrobial resistance
- Diagnostic criteria and coding practices

Increased Risk for Sepsis

- DIABETES, DIABETES, DIABETES
- Liver cirrhosis
- Autoimmune diseases (lupus, rheumatoid arthritis)
- HIV/AIDS
- Para/quadriplegics
- Sickle cell disease
- Splenectomy patients
- Compromised skin (chronic wounds, burns, ulcers)

Increased Risk for Sepsis

- Chemotherapy
- Post-organ transplant (bone marrow, solid organ)
- Chronic steroid use
- Recent antibiotic use
- Indwelling catheters of any kind (dialysis, Foley, IV, PICC, PEG tubes, etc)

Causes of Sepsis

- Pneumonia
- Urinary tract infections
- Infection after abdominal surgery
- Skin infection (cellulitis, open wounds, MRSA abscess).
- C.diff colitis
- Bacteremia from IV drug use.

Microbiology

Evolution Over the Years

Before 1980's

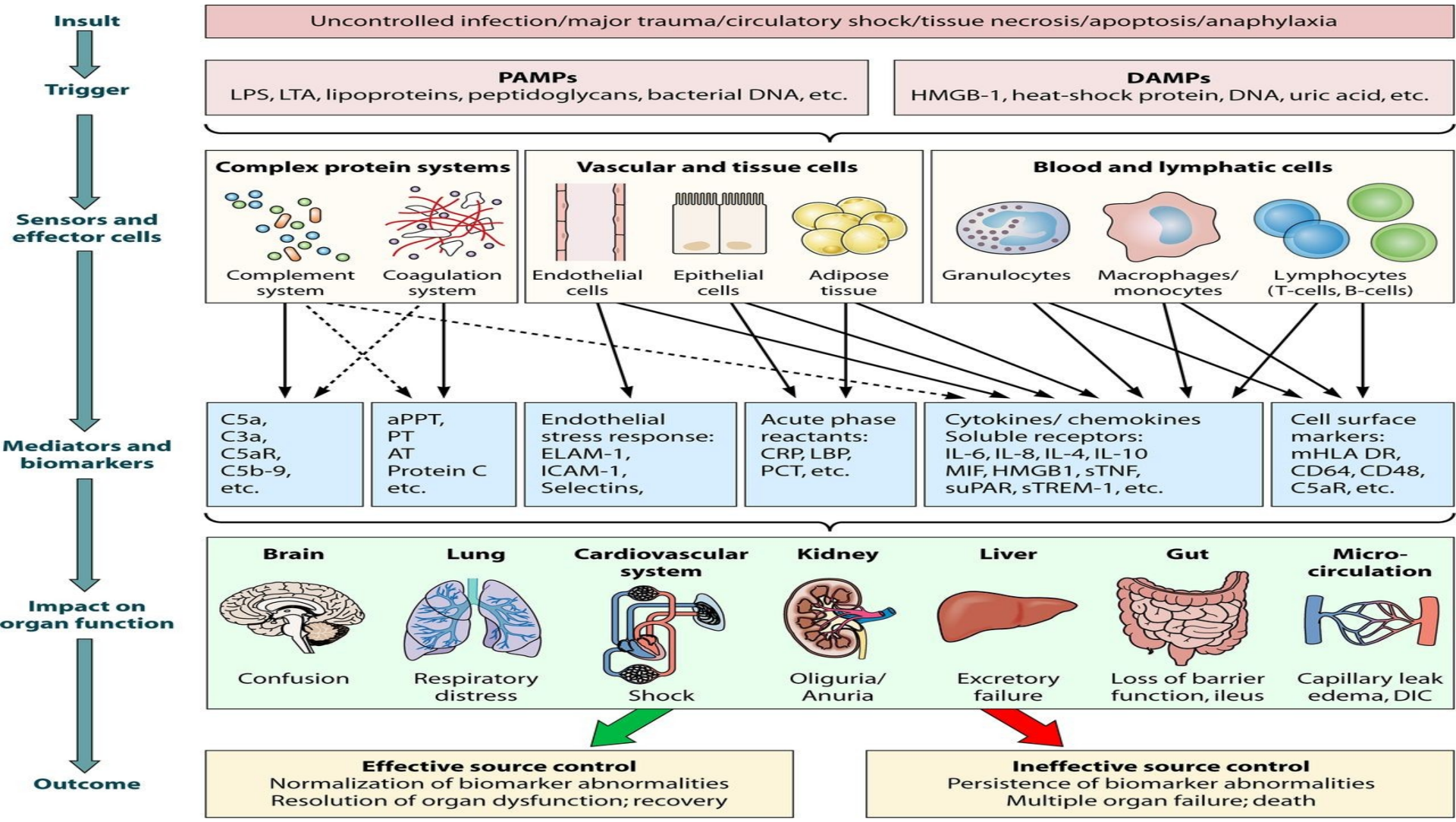
- Gram Negative aerobes
- Low incidence of MDR isolates
- Monomicrobial Seticemia
- High Incidence of *Haemophilus influenzae* and Pneumococcal bacteremia

After 1980's

- Gram positive organisms
- High incidence of MRSA,VRE,ESBL
- Polymicrobial Septicemia
- Low Incidence of *Haemophilus influenzae* and Pneumococcal bacteremia

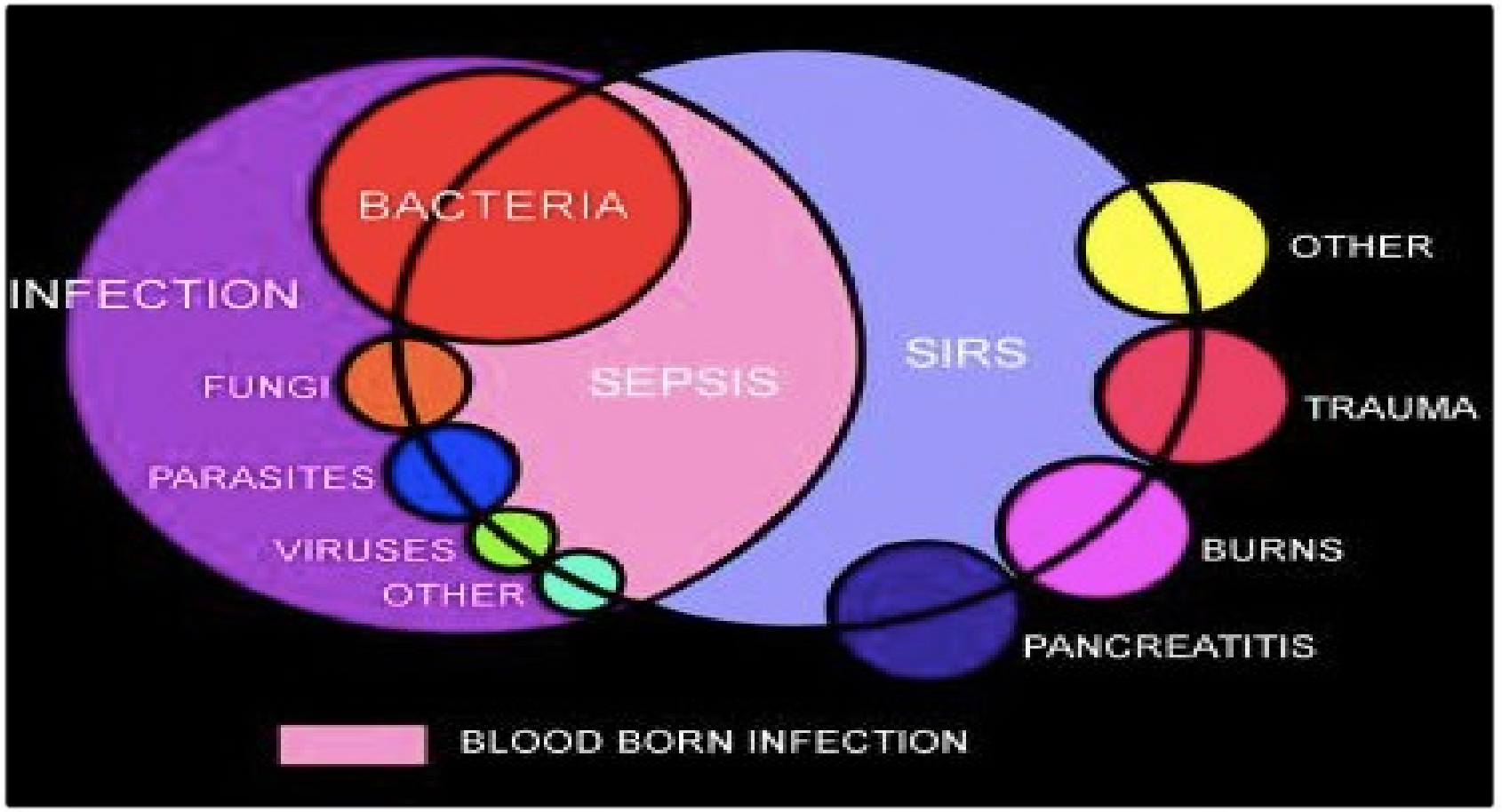
Sepsis

Pathogenesis



Pathophysiology of Sepsis

- Uncontrolled, exaggerated immune response
- Endothelium damage, cell mediator activation, disruption of coagulation system homeostasis
- Vasodilation and capillary permeability
- Systemic inflammatory response
- End-organ damage, death


BACTERIA
INFECTION
FUNGI
PARASITES
VIRUSES
OTHER
SEPSIS
SIRS
OTHER
TRAUMA
BURNS
PANCREATITIS
BLOOD BORN INFECTION

Clinical aspects of Bacteremia

Signs and Symptoms

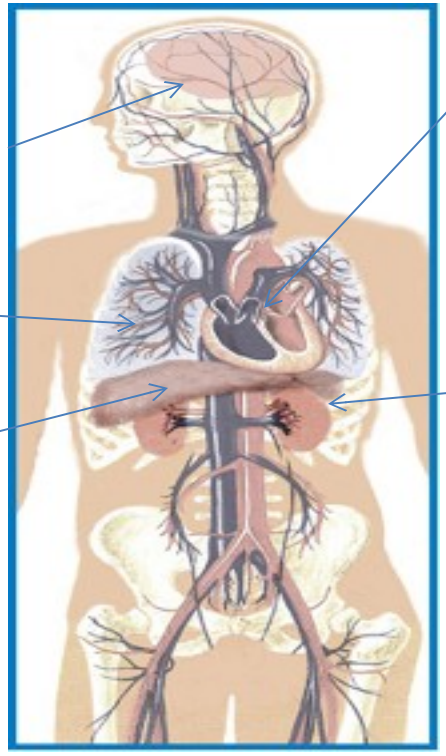
- Fever or hypothermia
- Shaking chills
- Hypotension
- Tachypnea (Early sign)
- Delirium, stupor, or agitation
- Nausea and vomiting
- Acute renal failure
- Ecthyma gangrenosum

Multiple Organ System Dysfunction

CNS
Altered mental status

Respiratory
Tachypnea
Hypoxia

Hepatic
Jaundice
Liver inflammation
Coagulopathy



Cardiovascular
Tachycardia
Hypotension

Renal
Oliguria
Anuria
Renal failure

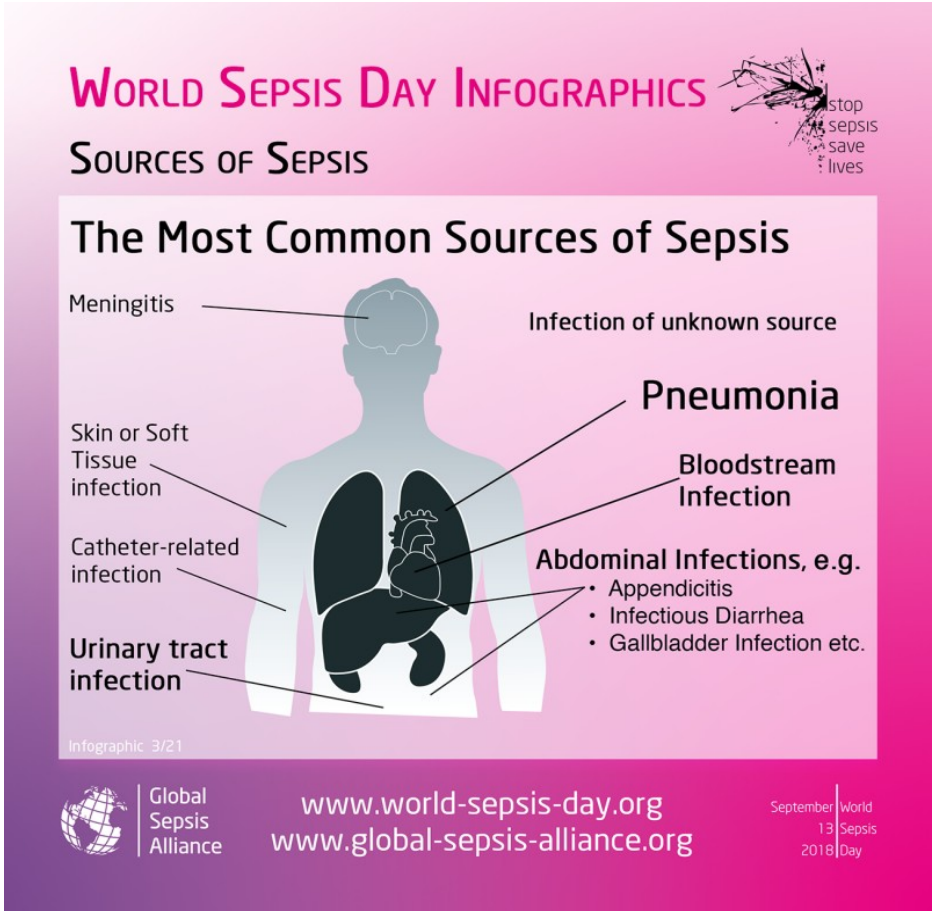
Hematologic
Consumptive coagulopathy
Petechiae
Purpura

Clinical aspects of Bacteremia

Syndromes Associated with Bacteremia

-

- Catheter-Related Bloodstream Infections
- Pneumonias
- Urinary Tract Infections
- Intra-abdominal Infections
- Skin Infections
- Infective Endocarditis
- Musculoskeletal Infections
- Central Nervous System Infections



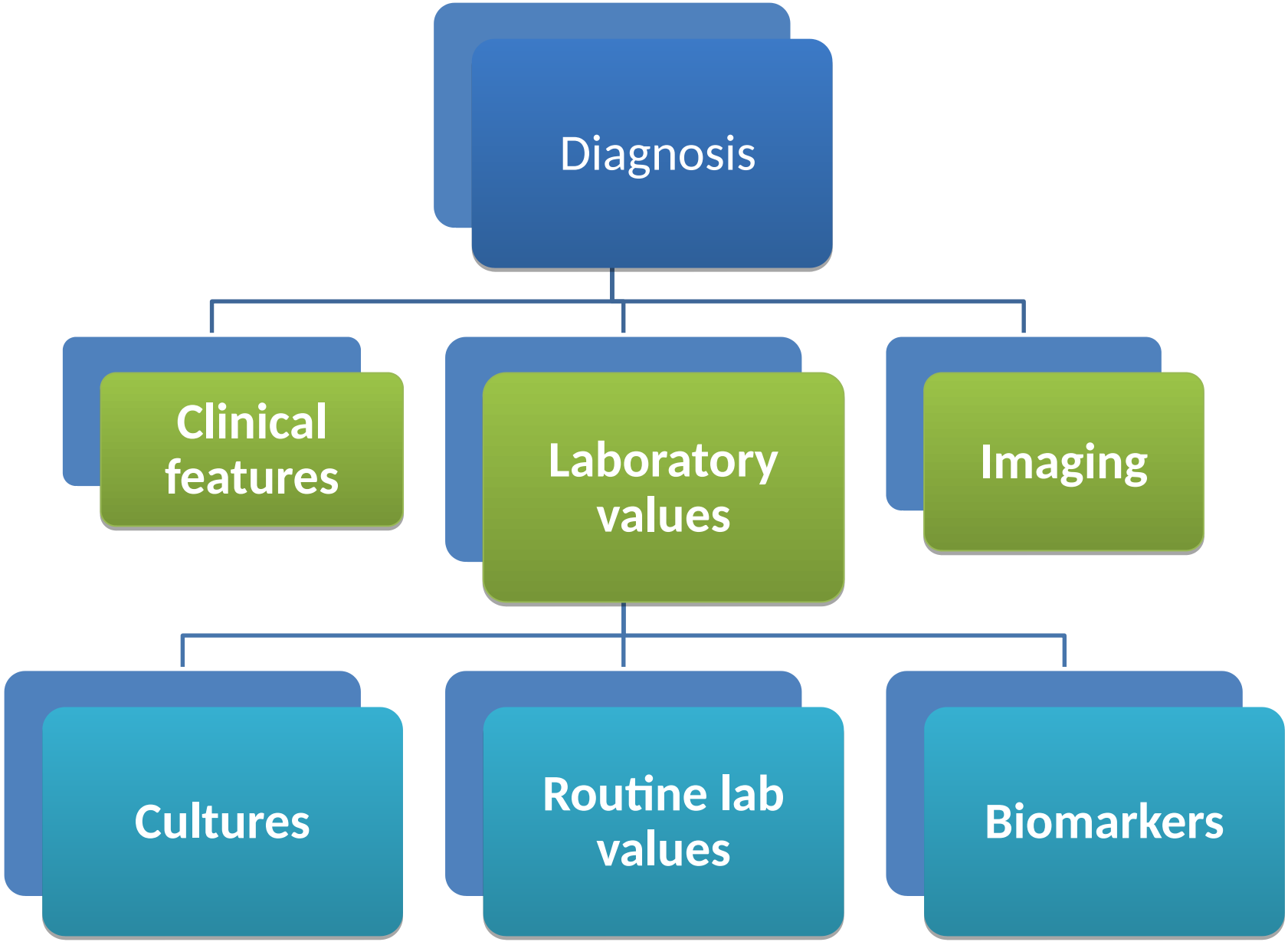
United Effort to Improve Survival from Sepsis

- Research from past 20 years is saving lives
  - Rapid identification, fluids, antibiotics
- Education to all physicians, nurses, technicians
- “Care bundles” monitored by Feds
- Sepsis alert teams in hospitals
- Chart review
- Administrative support at all levels

EMS and Sepsis

- The whole principle behind Emergency Medical Services is early identification and treatment of life and limb-threatening disease and injury. This is the fundamental reason the EMS was created. EMS has demonstrated a benefit in STEMI, stroke, and trauma. As it happens, it appears that sepsis is no different. EMS can benefit patients by early recognition and early management.

- Over the past 20 years, we have learned that we can improve survival from sepsis when we identify it faster, provide the supportive care to reverse organ hypoperfusion (IV fluids and other drugs that reverse shock), and provide antibiotics as quickly as possible. EMS can play a very important role in helping hospital staff achieve these goals even before the patient gets to the ED.


Diagnosis
Clinical features
Laboratory values
Imaging
Cultures
Routine lab values
Biomarkers

Sepsis

Laboratory diagnosis

- Thrombocytopenia
- Leukocytosis or leukopenia
- Lactic acidosis
- Hypoglycemia or hyperglycemia
- Abnormal liver function test results (hyperbilirubinemia)
- Coagulopathy
- Elevations in C-reactive protein, haptoglobin, and fbrinogen
- Deranged Renal function tests

Sepsis

Laboratory Diagnosis

Cultures

- Blood Cultures: Most Important
  - Positive blood culture is critical value
- Other cultures: according to source of infection

Sepsis

Laboratory Diagnosis

Cultures

Suspected site	Symptoms/signs*	Initial microbiologic evaluation¶
Upper respiratory tract	Pharyngeal inflammation plus exudate ± swelling and lymphadenopathy	Throat swab for aerobic culture
Lower respiratory tract	Productive cough, pleuritic chest pain, consolidative auscultatory findings	Sputum of good quality, rapid influenza testing, urinary antigen testing (eg, pneumococcus, legionella; not recommended in children), quantitative culture of protected brush or bronchoalveolar lavage
Urinary tract	Urgency, dysuria, loin, or back pain	Urine culture and microscopy showing pyuria

Sepsis

Laboratory Diagnosis

Cultures

Suspected site	Symptoms/signs*	Initial microbiologic evaluation¶
Central nervous system	Signs of meningeal irritation	CSF cell count, protein, glucose, Gram stain, and culture$^{\Delta}$
Gastrointestinal	Abdominal pain, distension, diarrhea, and vomiting	Stool culture
Intra-abdominal	Specific abdominal symptoms/signs	Aerobic and anaerobic culture of percutaneously or surgically drained abdominal fluid collections
Genital tract	Women: Low abdominal pain, vaginal discharge Men: Dysuria, frequency, urgency, urge incontinence, cloudy urine, prostatic tenderness	Women: Endocervical and high vaginal swabs onto selective media Men: Urine Gram stain and culture

Laboratory Diagnosis
Blood Cultures

- Specimen Collection
- Specimen transport
- Blood Culture Systems
- Processing of positive blood cultures
- Rapid Identification of Microorganisms from Blood Cultures
- Interpretation and reporting

Laboratory Diagnosis
Blood Cultures

Specimen Collection

Skin Preparation

Multiple blood cultures

Increase yield

Recognize true pathogen

Timing

Volume

Blood to Broth ratio 1:5 to 1:10

Labeling

Patient details

Date and time of collection

Site of collection

Patient weight (kg)	Recommended blood per culture (ml)	Total blood volume for 2 cultures (ml)
Less than 8	1	2
8 to 14	3	6
14 to 27	5	10
28 to 41	10	20

Laboratory Diagnosis
Blood Cultures

Specimen Transport

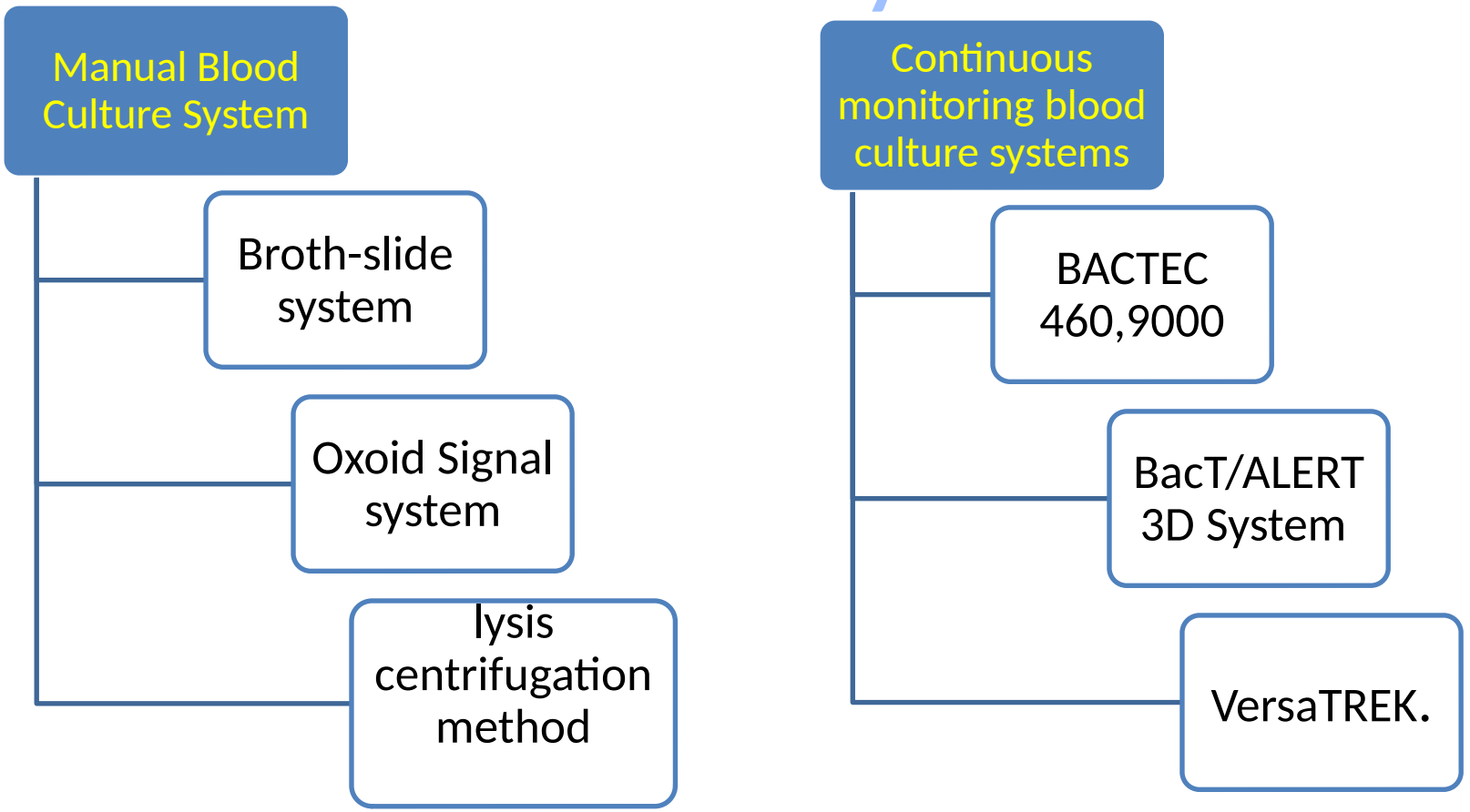
- Do not refrigerate blood cultures
- Ensure that bottles are not broken in transit

Rejection Criteria

- Reject blood cultures that are received unlabeled.
- Do not process if the tube or bottle is cracked or broken.
- Labeled blood cultures are not rejected even if medium is expired

Laboratory Diagnosis
Blood Cultures

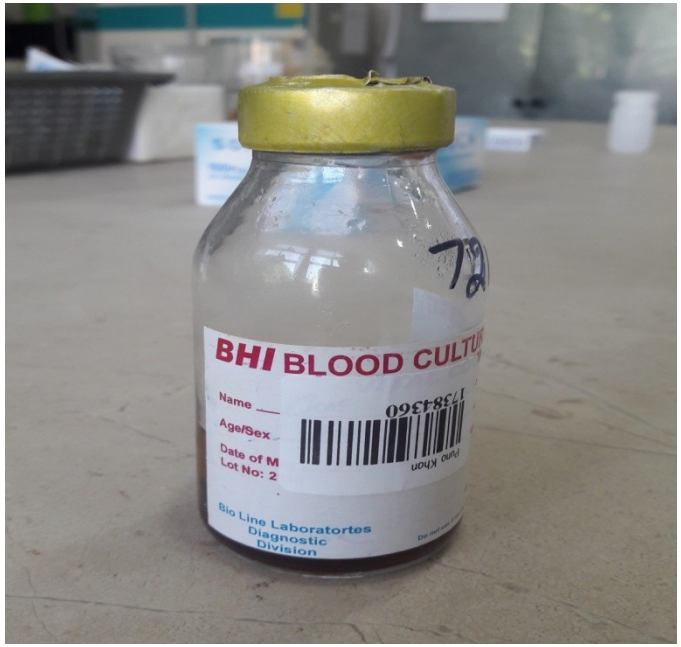
Blood Culture systems



Laboratory Diagnosis
Blood Cultures

Culture Media Used in Conventional Broth Systems

- Brain-heart infusion
- Soybean casein broth
- Peptone broth
- Trypticase soy broth
- Brucella broth
- Columbia broth base



Laboratory Diagnosis
Blood Culture Additives

Neutralization of Inhibitors: Antimicrobial removal device (ARD), Resins

Anticoagulants and Other Additives.

Sodium polyanetholsulfonate (SPS) functions

Anticoagulation

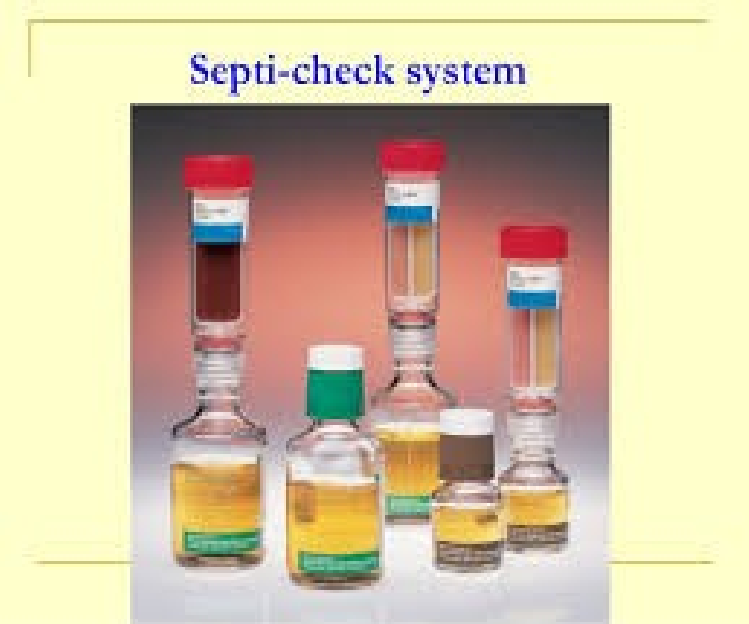
Neutralization of the bactericidal activity

Prevention of phagocytosis

Inactivation of certain antimicrobial agents

Laboratory Diagnosis
Manual Blood Culture Systems

Broth Slide system



- Biphasic (solid agar and broth combination)
- Slide paddle (agars) attached to the top of a standard broth bottle.
- Tipped daily or twice weekly to bathe the slide paddle with the broth medium, allowing frequent blind subcultures

Laboratory Diagnosis
Manual Blood Culture Systems

Oxoid Signal system

- Blood is inoculated into broth
- Plastic signal device is then attached to the top of the bottle
- Signal device has a long needle extending down below the level of the liquid
- Growth: CO_2 generation, increases pressure on the liquid
- The presence of fluid in the signal device indicates the growth of bacteria

Laboratory Diagnosis
Manual Blood Cultures Systems

Lysis centrifugation

- Fastidious bacteria, yeasts, dimorphic fungi and mycobacteria
- Mixture of saponin, propylene glycol, SPS, and EDTA.
- Lysis of white and red blood cells, releasing intracellular organisms
- Concentration through high-speed centrifugation
- Sediment inoculated onto culture medium (fungal and mycobacterial media)

Blood Cultures

Examination of Blood Culture Bottles in a Manual System

Microscopic observation	Associated microorganism(s)
Hemolysis	Streptococci, staphylococci, *Listeria* spp., clostridia, *Bacillus* spp.
Turbidity	Aerobic Gram-negative bacilli, staphylococci, *Bacteroides* spp.
Gas formation	Aerobic Gram-negative bacilli, anaerobes
Pellicle formation	*Pseudomonas* spp., *Bacillus* spp., yeast cells
Clotting	*Staphylococcus aureus*

Laboratory Diagnosis

Continuous-Monitoring Blood Culture Systems

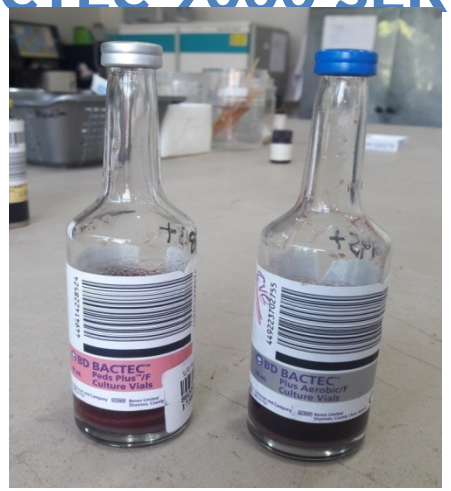
BACTEC 460

- First automated blood culture system
- Radiolabeled carbon (14C) in the broth medium: Growth leading to $^{14}CO_2$ production
- Gas aspiration into an ionization chamber using sterile needles injected into the bottle.
- Amount of $^{14}CO_2$ produced measured as a growth index and compared with threshold level.
- Advantage: Early detection
- Disadvantage: high cost , high contamination rate ,radiation hazard

Laboratory Diagnosis

Continuous-Monitoring Blood Culture Systems

BACTEC 9000 SERIES



Three models are currently available
9240 (holds 240 bottles/module)
9120 (holds 120 bottles/module)
9050 (holds 50 bottles/module)

- Based on **Fluorescence**
- Growth Detected by a gas-permeable sensor on the bottom of each vial
- Carbon dioxide produced by an organism diffuses into the sensor, generating hydrogen ions
- Increase hydrogen ion concentration increases fluorescence output of the sensor.
- Photodetectors measures the fluorescence every 10 minutes

Laboratory Diagnosis

Continuous-Monitoring Blood Culture Systems

BacT/ALERT 3D System

- Bottles with pH-sensitive membranes placed in the bottom of the bottles.
- Microbial growth,release of CO2, pH change indicated by a change in color from gray to yellow. The color change is measured by reflected light.
- Measures CO2 production **colorimetrically**
- Gas-impermeable plastic blood culture bottles safer and lighter,do not interfere with microorganism growth

Laboratory Diagnosis

Continuous-Monitoring Blood Culture Systems

VERSA TREK

- Detects the consumption or production of multiple gases
- Gases are detected by monitoring changes in head space pressure.
- Internal computer algorithm monitors the changes in pressure, plots a growth curve to flag the bottle as positive.
- Advantage: Earlier detection of growth

Laboratory Diagnosis
Blood Cultures

PROCESSING OF BLOOD CULTURES

Safety

- keep culture bottles within a biosafety cabinet or wear face mask.
- Always wear gloves
- Needleless transfer devices or safety needles, and never recap them
- Dispose of needles and syringes in a puncture-proof container

Incubation

- Continuous-monitoring blood culture systems include an incubator
- Temperature: 35℃ ±2° C for 5 to 7 days

Laboratory Diagnosis
Blood Cultures

PROTOCOLS FOR POSITIVE BLOOD CULTURES

- Gram stain
- Inform physician
- Subculture and biochemical tests based on Gram stain
- Direct identification
- Direct AST: For disk method, add 10 drops of the blood culture and inoculate Mueller Hinton agar.

Laboratory Diagnosis
Rapid Identifcation of Microorganisms Growing in Blood Cultures

- **Direct Tube Coagulase:**
- **Fluorescence in situ Hybridization:**
- **Nucleic Acid Amplifcation Methods:**
- **Other Rapid Diagnostic Tests:**
  i. Thermonuclease
  ii. Oxidase
  iii. Bile solubility
  iv. Quellung capsule stain
  v. Modifed Kinyoun stain

Laboratory Diagnosis
Blood Cultures

Gram stain result	BAP	BAP with disks	CHOC	AN 1	Other tests	Report
Positive cocci in clusters	X	Cefoxitin, penicillin, vancomycin	X	X	1 or 2 drops to coagulate plasma at 35'C. Add AST *if* coagulase positive	"**Probable *Staphylococcus* spp.**"; update to "Probable ***Staphylococcus aureus***
Positive cocci in chains or pairs	X	Penicillin, vancomycin, optochin, CAMP test	X		1 drop to bile-esculin slant at 35C; AST if bile-esculin positive	**Probable *Streptococcus* spp.**"; update to "**Probable *Enterococcus*"** if bile-esculin positive or "Probable ***Streptococcus pneumoniae***" if Quellung positive or bile soluble

Laboratory Diagnosis
Blood Cultures

Gram stain result	BAP	BAP with disks	CHOC	AN 1	Other tests	Report
positive rods	X	Penicillin, vancomycin, CAMP test	X	X	1 drop to bile-esculin slant at 35C; wet mount	"Gram-positive rods"; ***Listeria*** " if tumbling motile or bile-esculin positive
Negative rods	X	Polymyxin B or colistin disk			MAC or EMB; kit; AST.	"**Gram-negative rods**"
Yeast	X		X		CHROMagar; germ tube read at 2 h; India ink if round; 2 drops to urea slant at 35'C	Yeast"; update to "Probable ***Cryptococcus***" if urease positive or capsules present. "***Candida albicans*****"** if germ tube positive.

Laboratory Diagnosis
Blood Cultures

Interpretation

- Members of Enterobacteriaceae, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Candida albicans* almost always indicate infection

- Coagulase negative *Staphylococci*, Diphtheroids, *Viridans Streptococci*, *Bacillus* species and other skin microbiota should be questioned when isolated

Laboratory Diagnosis
Blood Cultures

Interpretation

- **More than one blood culture bottle** growing the same organism usually indicates that the isolate is signifcant

- Isolation of the **same organism in** the **blood** and from a **normally sterile site** usually indicates that the organism isolated from the blood is a pathogen

Laboratory Diagnosis
Blood Cultures

QUALITY CONTROL

Contamination rate

- Dividing the number of cultures containing skin contaminants by the total number of cultures collected by venipuncture.
- **1-3%**

True-positive blood culture rates

- Dividing the number of cultures positive by the total number of blood cultures received
- 6 to 12%
- If too low, too many samples might have been drawn; if it is too high, not enough samples may have been collected

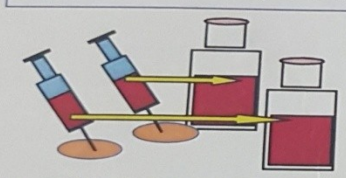
Monitor compliance with volume and number of bottles

Laboratory Diagnosis
Blood Cultures

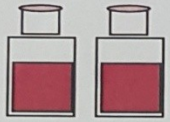
Blood Culture

Primary pathogens: Salmonella, Brucella, Other Gram – rods, Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae

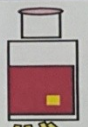
NOT pathogens unless recovered from >1 separate blood culture: Bacillus sp., coagulase – staph, viridans streptococci, coryneform Gram + rods



#1 Collect 10 ml per bottle from 2 separate skin sites

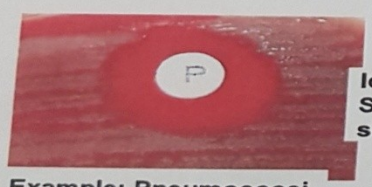


#2 Incubate at 35°C in air up to 5 days
Check & invert bottles daily



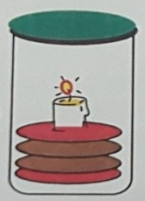
#3 Subculture at 18 h
Make Gram stain & subculture when bottle shows growth

Gram + cocci → BAP + Optochin disk

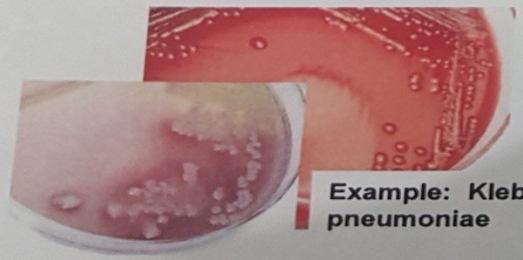


#6 Identify & perform Susceptibilities on significant pathogens

Example: Pneumococci

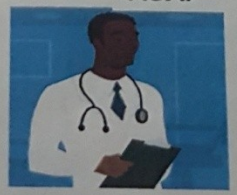


#5 Incubate up to 72 hours in CO_2



Example: Klebsiella pneumoniae

#4 Call significant Gram stain results to Doctor ASAP



Gram – rods → BAP + Mac

Gram – diplococci or coccobacilli → Choc & BAP

Sepsis

Laboratory Diagnosis

Biomarkers

"Objectively measured characteristic that indicates a normal biologic or pathogenic process, or pharmacologic response to therapy "

- The goal of such a marker is to distinguish between sepsis and any other SIRS

Sepsis
Laboratory Diagnosis
Biomarkers

BOX 36-2 Biomarkers for Sepsis

Some of the more commonly used diagnostic and/or prognostic biomarkers for sepsis:

- (1-3)-β-D-Glucan*
- Lactate
- Procalcitonin
- C-reactrive protein
- D-dimer
- Endocan
- Inducible protein 10
- Group IV phospholipase A2 type II
- Neutrophil gelatinase-associated lipocalin
- Lipopolysaccharide-binding protein
- Macrophage migration inhibitory factor
- Mature adrenomedullin
- Mer receptor
- Mid-regional pro-adenomedullin
- Natriutetic peptides
- Copeptin
- Thrombopoietin
- Soluble triggering receptor expressed on myeloid cells-1
- Soluble urokinase-type plasminogen activator

*Marker for invasive fungal infection.

Management of Sepsis

Initial Resuscitation Therapy	Monitoring Response	Source identification and control

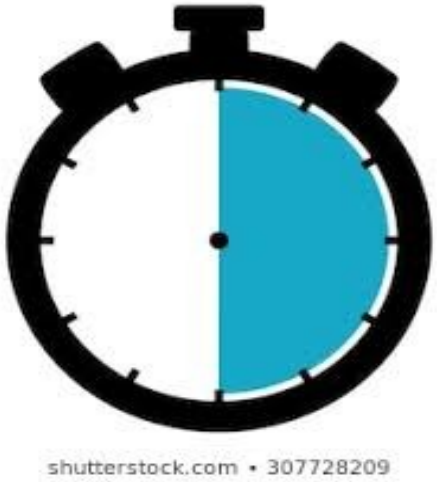
Sepsis

Management

- Give high-flow oxygen
- Take blood culture
- Give IV antibiotics according to local protocol
- Start IV fluid resuscitation
- Check lactate
- Monitor hourly urine output

Sepsis

Management



- Repeat serum lactate
- After initial fluid resuscitation administer vasopressor
- Re-assess volume status and tissue perfusion

Sepsis

Management

- Establish source control
- Re-assess volume status and tissue perfusion
- For Unresponsive patients consider: **Hydrocortisone and fludrocortisone**
- **Insulin** to control blood glucose

Sepsis

Management

- **Antimicrobial Therapy**
- **Antisepsis Therapy**
  Physiologic Support
  Anticoagulation Agents
  Glucocorticoids
  Anticytokine Therapies

Sepsis

Emperic Antimicrobial Therapy

Expected Organism	Regimen
Suspected Methicillin-resistant *Staphylococcus aureus* (MRSA)	
Suspected Extended-Spectrum Beta-lactamase (ESBL) Producing GNRs	
Suspected Carbapenem-resistant GNRs	

Sepsis

Emperic Antimicrobial Therapy

Expected Organism	Regimen
Suspected *Pseudomonas aeruginosa*	
Polymicrobial aerobic-anaerobic infection	
Unknown source < 15% MDR prevalence > 15% MDR prevalence	

Sepsis

Management

THERAPIES BEING INVESTIGATED

Inhibition of innate immunity : Inhibition of TLRs

Intravenous immune globulin: Polyclonal, IgA, IgM ; binds endotoxin

Cytokine and endotoxin inactivation or removal :Hemoperfusion, plasma exchange

Granulocyte-macrophage colony stimulating factor: Promotes maturation of the progenitor cells of granulocytes

Interferon-gamma: Restoration of monocytic cell function

Sepsis

Management

THERAPIES BEING INVESTIGATED

Stem cell therapy: Reprogram the immune system

Immunostimulation: IL-7, IL-15, or anti-PDL1

Hemofiltration: Remove proinflammatory molecules

Anticoagulants: Heparin has anti-thrombotic and immunomodulating effects

Beta-blockade: Attenuate the deleterious effects of the sympathetic adrenergic response

Vitamin C: Hydrocortisone and vitamin C act synergistically on the inflammatory cascade

Targeting bioenergetic failure: Activating mitochondrial biogenesis

Sepsis

Prevention

- Community-acquired bacteremia Immunizations
- Nosocomial bacteremias

Minimizing iatrogenic infections

Infection control practices

PAST QUESTIONS?

Past Questions?

- A 26 year old female presents to ER, diagnosed with Gram negative sepsis and multi-organ failure

A) Define sepsis with respect to vital parameters

B) Enlist important points for pathophysiology of sepsis

C) Three important strategies for sepsis with justification

D) Give 3 novel therapeutic strategies for sepsis

Past Questions?

- Define sepsis, severe sepsis and septic shock
- What is SIRS? How is it different from sepsis?
- What is bacterial translocation? Enumerate risk factors


Thank
You