核心課程編號：B20

敗血症

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知識

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Definitions

- Systemic inflammatory response syndrome (SIRS)
  - Two or more of the following conditions:

  (1) fever (oral temperature >38°C) or hypothermia (<36°C)

  (2) tachypnea (>24 breaths/min)

  (3) tachycardia (heart rate >90 beats/min)

  (4) leukocytosis (>12,000/ L), leukopenia (<4,000/ L), or >10% bands
  - may have a noninfectious etiology
- Sepsis
  - SIRS that has a proven or suspected microbial etiology

Crit Care Med. 2013;41(2):580

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Clinical definition of sepsis

Sepsis	**Systemic response to infection, manifested by 2 or more of the conditions mentioned under SIRS(SIRS+ evidence of infection)**
Severe Sepsis	**Sepsis associated with organ dysfunction, hypoperfusion, or hypotension including lactic acidosis, oligouria, or acute alteration in mental status**
Septic shock	**Sepsis-induced hypotension (e.g., systolic blood pressure <90 mmHg or a reduction of >40mmHg from base line) despite adequate fluid resuscitation,**
MODS	**The presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.**

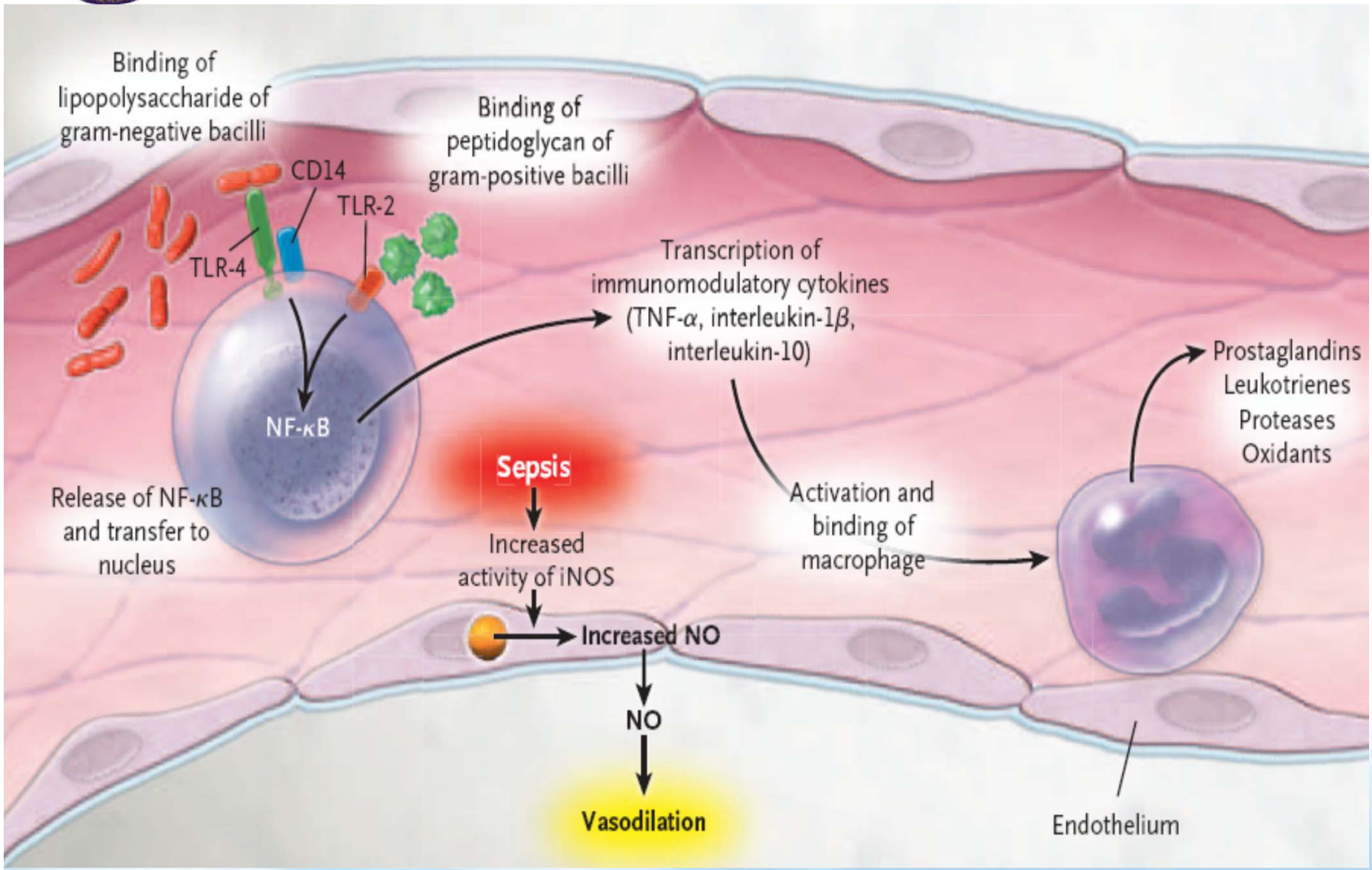
Definitions

- Bacteremia
  - Presence of bacteria in blood, as evidenced by positive blood cultures
- Septicemia
  - Presence of microbes or their toxins in blood

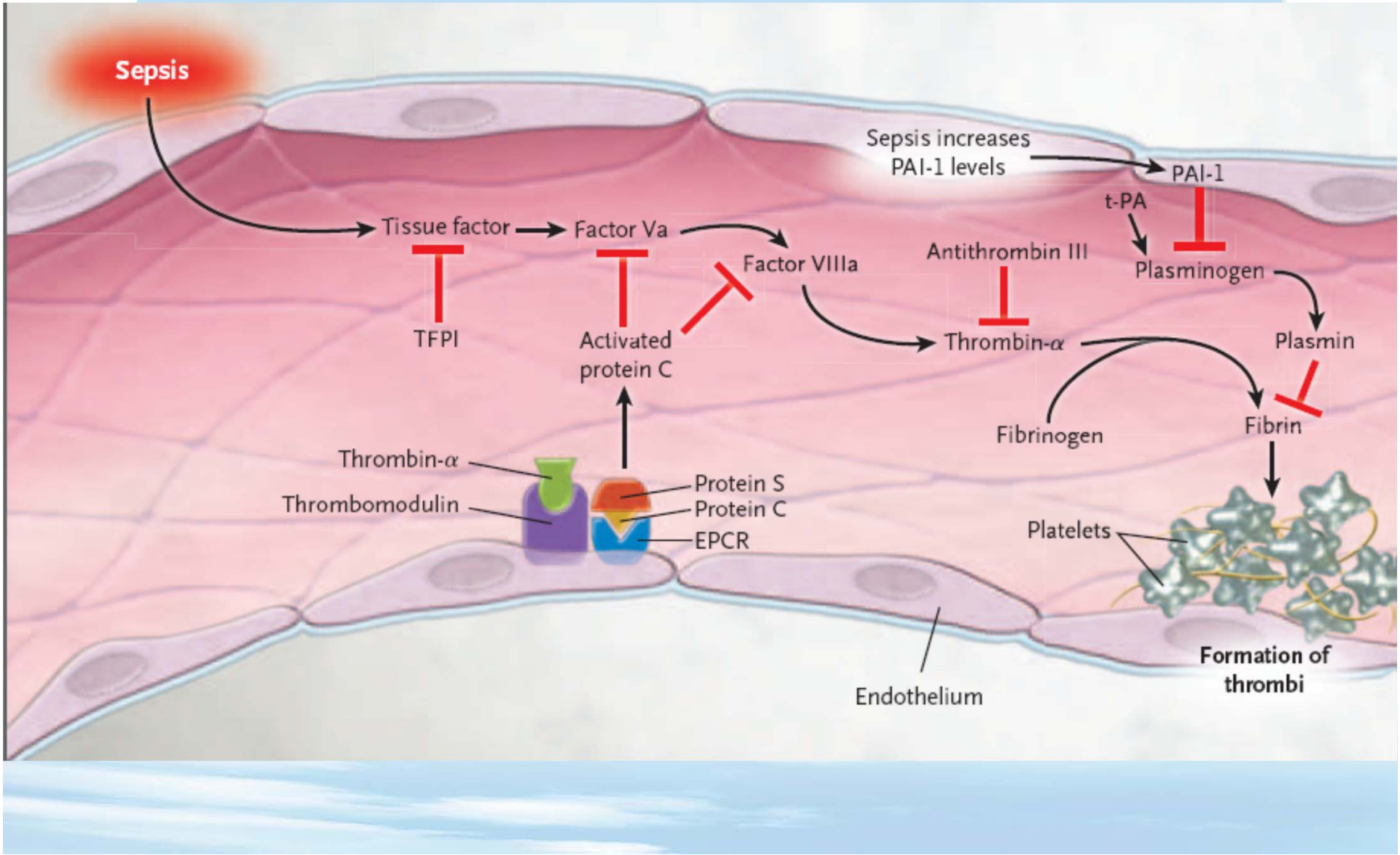
Extended criteria for diagnosis of sepsis

Organ dysfunction	**Arterial hypoxemia(PaO2/FiO2<300)**
	Acute oliguria (urine output <0.5ml/kg/hr or 45 mmol/l for at least 2 h)
	Creatinine increase > 0.5mg/dl
	Coagulation abnormalities(INR>1.5 or aPTT>60s)
	Ileus (absence bowel sound)
	Thrombocytopenia (PLT count <100,000/ul)
	Hyperbilirubinemia (plasma total bilirubin >4mg/dl or > 70 mmol/l)
Tissue perfusion	**Hyperlactatemia (>1 mmol/l)**
	Decrease capillary refill

敗血症的病生理


Binding of
lipopolysaccharide of
gram-negative bacilli
CD14
TLR-2
TLR-4
Binding of
peptidoglycan of
gram-positive bacilli
NF-κB
Release of NF-κB
and transfer to
nucleus
Transcription of
immunomodulatory cytokines
(TNF-α, interleukin-1β,
interleukin-10)
Sepsis
Increased
activity of iNOS
Increased NO
NO
Vasodilation
Activation and
binding of
macrophage
Prostaglandins
Leukotrienes
Proteases
Oxidants
Endothelium

敗血症的病生理


Sepsis
Sepsis increases PAI-1 levels
PAI-1
t-PA
Tissue factor
Factor Va
Factor VIIIa
Antithrombin III
Plasminogen
TFPI
Activated protein C
Thrombin-α
Plasmin
Fibrinogen
Fibrin
Thrombin-α
Thrombomodulin
Protein S
Protein C
EPCR
Platelets
Endothelium
Formation of thrombi

Severe sepsis (similar to "sepsis syndrome")

- Sepsis with one or more signs of organ dysfunction—for example:
  1. **Cardiovascular***:* Arterial systolic blood pressure $\leqq$ 90 mmHg or mean arterial pressure $\leqq$ 70 mmHg that responds to administration of intravenous fluid
  2. **Renal***:* Urine output <0.5 mL/kg per hour for 1 h despite adequate fluid resuscitation
  3. **Respiratory***:* PaO2 /FI O2 $\leqq$ 250 or, if the lung is the only dysfunctional organ, $\leqq$ 200
  4. **Hematologic***:* 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 $\leqq$ 7.30 or a base deficit $\geqq$ 5.0 mEq/L and a plasma lactate level >1.5 times upper limit of normal for reporting lab
  6. **Adequate fluid resuscitation***:* Pulmonary artery wedge pressure $\geqq$ 12 mmHg or central venous pressure $\geqq$8 mmHg

❖ Septic shock

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

or

- Need for vasopressors to maintain systolic blood pressure $\leqq$ 90 mmHg *or* mean arterial pressure $\leqq$ 70 mmHg

❖ Refractory septic shock

- Septic shock that lasts for >1 h and does not respond to fluid or vasopressor administration

❖ Multiple-organ dysfunction syndrome (MODS)

- Dysfunction of more than one organ, requiring intervention to maintain homeostasis

Etiology

- Any class of microorganism
- Microbial invasion of the bloodstream: not essential for severe sepsis
- Local inflammation can also elicit distant organ dysfunction and hypotension.
- Positive blood cultures
  - severe sepsis: ~20–40% of cases
  - septic shock: 40–70% of cases
  - Gram positive and negative bacteria
- Negative blood cultures: local site culture

Table 265-2 Microorganisms Involved in Episodes of Severe Sepsis at Eight Academic Medical Centers

Microorganisms	Episodes with Bloodstream Infection, % (*n* = 436)	Episodes with Documented Infection but No Bloodstream Infection, % (*n* = 430)	Total Episodes, % (*n* = 866)
Gram-negative bacteria[a]	35	44	40
Gram-positive bacteria[b]	40	24	31
Fungi	7	5	6
Polymicrobial	11	21	16
Classic pathogens[c]	<5	<5	<5

敗血症相關病史詢問

- 職業
- 嗜好
- 居住環境
- 接觸史
- 動物接觸
- 旅遊
- 性生活
- 食物
- 藥物：中藥、草藥
- 輸血史
- 病史：手術、牙科
- 家族史

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock, 2012

Intensive Care Med (2013) 39:165–228
DOI 10.1007/s00134-012-2769-8

GUIDELINES

Early management

- **Stabilize respiration**
- **Assess perfusion**
- **Interventions to restore perfusion**
- **Additional therapies**

Early goal

(a) CVP 8–12 mmHg
(b) MAP ≥65 mmHg
(c) Urine output ≥0.5 mL kg h^{-1}
(d) Superior vena cava oxygenation saturation ($ScvO_2$) or mixed venous oxygen saturation (SvO_2) 70 or 65 %, respectively.

Lab test

- **Blood tests**
  A sample of your blood can be tested for:
- Evidence of infection
- Clotting problems
- Abnormal liver or kidney function
- Impaired oxygen availability
- Electrolyte imbalances
- **Other laboratory tests**
  Depending on your symptoms, your doctor may also want to run tests on one or more of the following bodily fluids:
- **Urine.** If your doctor suspects that you have a urinary tract infection, he or she may want your urine checked for signs of bacteria.
- **Wound secretions.** If you have a wound that appears infected, testing a sample of the wound's secretions can help show what type of antibiotic might work best.
- **Respiratory secretions.** If you are coughing up mucus (sputum), it may be tested to determine what type of germ is causing the infection

Image test

- **Imaging scans**
  If the site of infection is not obvious, your doctor may order one or more of the following imaging tests:
- **X-ray.** Using low levels of radiation, X-rays are good for visualizing problems in the lungs. X-rays are painless and take only a few minutes to complete.
- **Computerized tomography (CT).** Infections in the appendix, pancreas or bowels are easier to see on CT scans. This technology takes X-rays from a variety of angles and combines them to depict cross-sectional slices of your body's internal structures. The test is painless and usually takes less than 20 minutes.
- **Ultrasound.** This technology uses sound waves to produce real-time images on a video monitor. Ultrasound may be particularly useful to check for infections in your gallbladder or ovaries.
- **Magnetic resonance imaging (MRI).** MRIs may be helpful in identifying soft tissue infections, such as abscesses within the spine. This technology uses radio waves and a strong magnet to produce cross-sectional images of your internal structures.

敗血症相關身體檢查

- Superimposed on the symptoms and signs of the patient's underlying illness and primary infection.
- Differ from patient to patient, individual variations
  - normo- or hypothermic
  - common in neonates, elderly patients, uremia or alcoholism.
- Hyperventilation: early sign
- Encephalopathy
  - Disorientation, confusion
  - Elderly, preexisting neurologic impairment
- Focal neurologic signs: uncommon
- Acrocyanosis (Livedo Reticularis) and ischemic necrosis of peripheral tissues
  - Hypotension and DIC

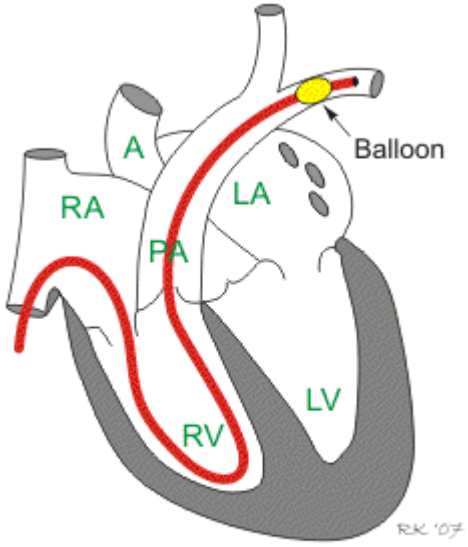
- ecthyma gangrenosum in neutropenic patients:
  - *P. aeruginosa*
  - bullous lesion, surrounded by edema that undergoes central hemorrhage and necrosis
- Hemorrhagic or bullous lesions, raw oysters: *V. vulnificus*

Gastrointestinal manifestations

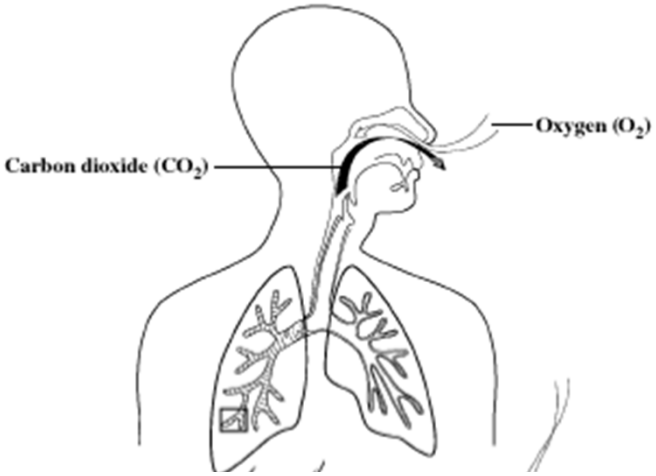
- Nausea, vomiting, diarrhea, and ileus may suggest acute gastroenteritis
- Stress ulceration: upper gastrointestinal bleeding.
- Cholestatic jaundice
  - elevated levels of serum bilirubin (mostly conjugated)
  - alkaline phosphatase
  - may precede other signs of sepsis
- Hepatocellular or canalicular dysfunction
  - return to normal with resolution of the infection
- Acute hepatic injury or ischemic bowel necrosis.

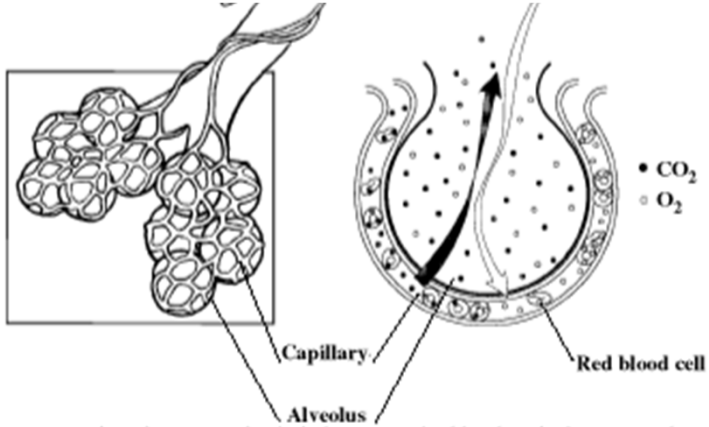
Pulmonary Complications

- Fall in arterial PO2 early in the course
  - Ventilation-perfusion mismatching
  - Increasing alveolar capillary permeability
  - increased pulmonary water content
  - decreases pulmonary compliance
  - interferes with oxygen exchange.
- Acute respiratory distress syndrome (ARDS).
  - Progressive diffuse pulmonary infiltrates
  - arterial hypoxemia (PaO2/FIO2, <200)
  - ~50% of patients with severe sepsis or septic shock.
- Respiratory muscle fatigue
  - exacerbate hypoxemia and hypercapnia.
- An elevated pulmonary capillary wedge pressure (>18 mmHg)
  - fluid volume overload or cardiac failure rather than ARDS.
- Pneumonia caused by viruses or by *Pneumocystis*
  - May be clinically indistinguishable from ARDS.

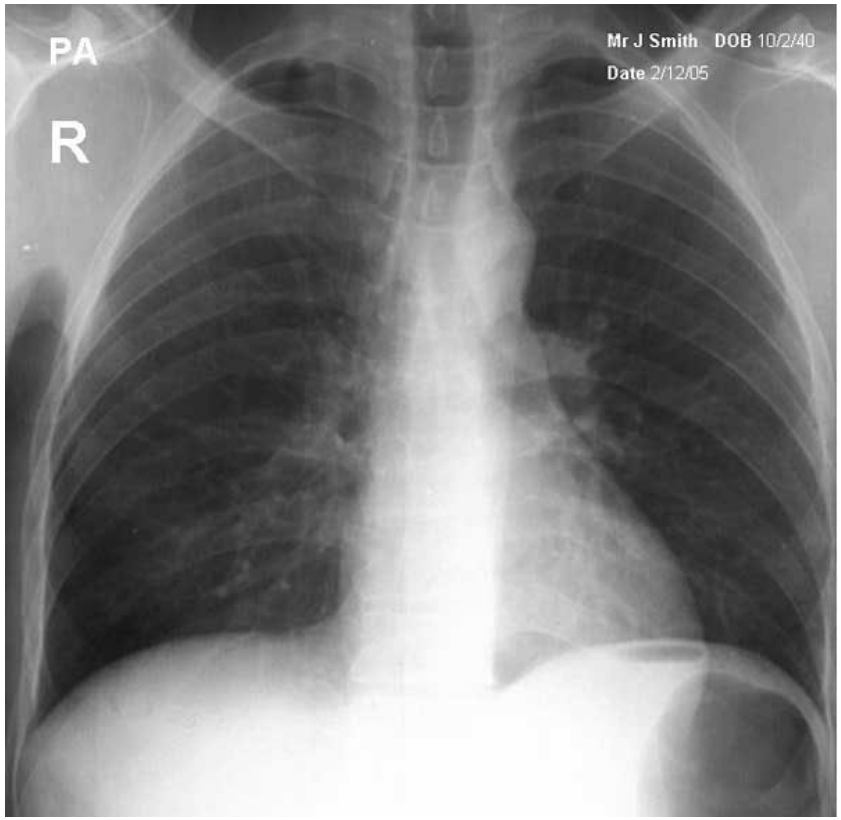


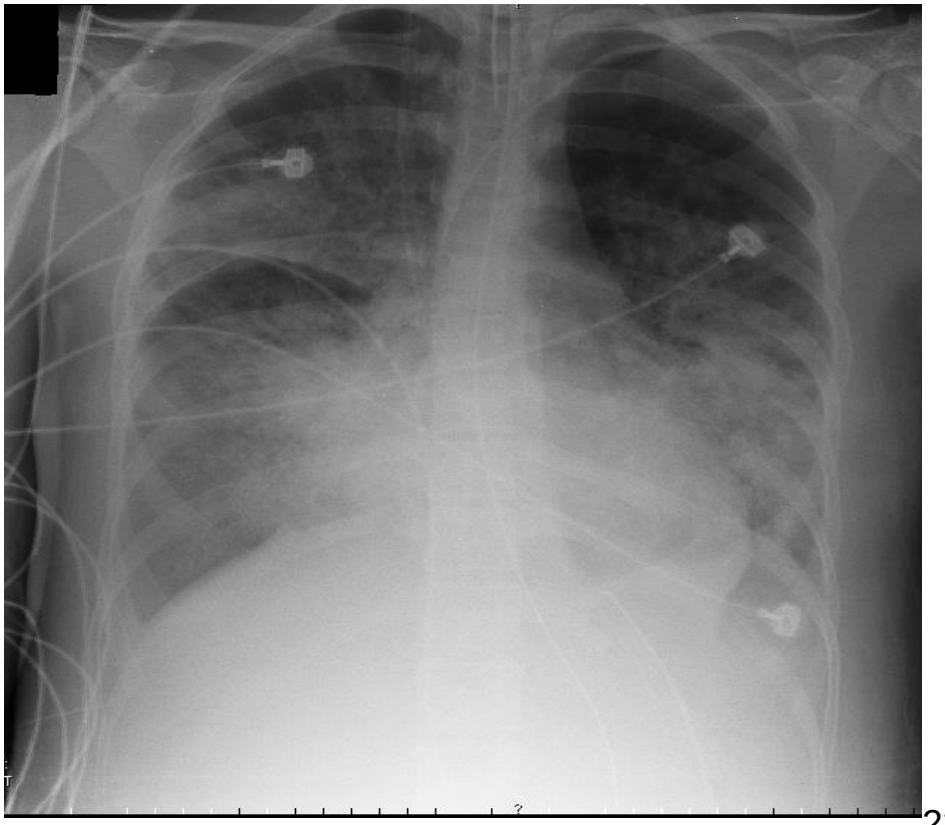
Balloon-tipped, Swan-Ganz catheter for measuring pulmonary capillary wedge pressure (PCWP).





Transfer of oxygen of inhaled air into the blood and of waste carbon dioxide of blood into the lungs occur in the alveolus.



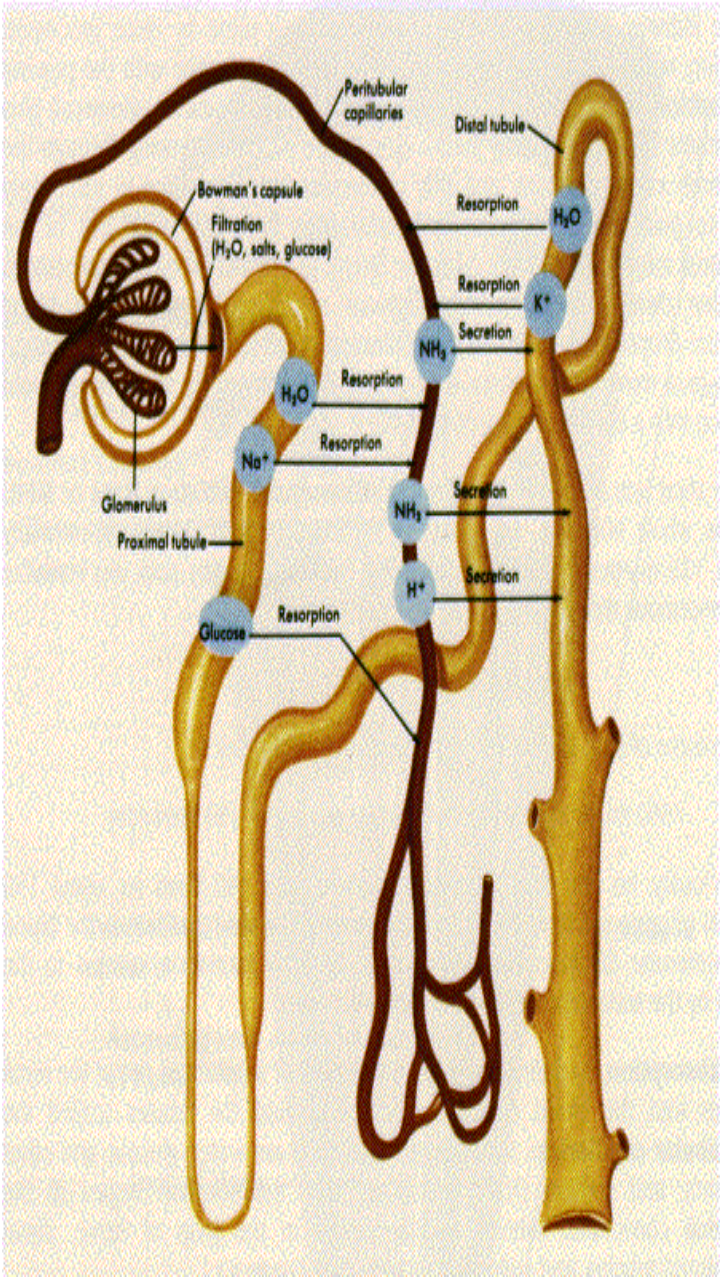


Cardiovascular Complications

- Sepsis-induced hypotension
  - generalized maldistribution of blood flow and blood volume
  - Hypovolemia: diffuse capillary leakage of intravascular fluid
  - dehydration: antecedent disease, insensible fluid losses, vomiting or diarrhea, and polyuria
- Normal or increased cardiac output and decreased systemic vascular resistance:
- Depression of myocardial function
  - increased end-diastolic and systolic ventricular volumes
  - decreased ejection fraction
  - Maintained cardiac output, normal stroke volume.
- Refractory hypotension

Renal Complications

- Oliguria, azotemia, proteinuria, and nonspecific urinary casts
- Inappropriately polyuria
  - Hyperglycemia
- Renal failure
  - Acute tubular necrosis (ATN)
  - Glomerulonephritis
  - Renal cortical necrosis
  - Interstitial nephritis
- Drug-induced renal damage
  - Hypotensive patients are given aminoglycoside antibiotics.



Coagulopathy

- Thrombocytopenia
  - 10–30% of patients
  - very low (<50,000/ L) in DIC

Neurologic complications

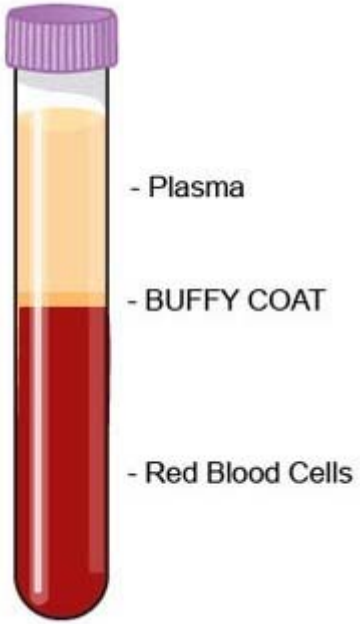
- "critical-illness" polyneuropathy
  - septic illness lasts for weeks or months
  - prevent weaning from ventilatory support
  - produce distal motor weakness
  - Electrophysiologic studies are diagnostic
  - d/d Guillain-Barré syndrome, metabolic disturbances, and toxin activity

Diagnosis

- No specific diagnostic test
- Diagnostically sensitive findings
  - fever or hypothermia (36% normal temperature)
  - Tachypnea (40% normal respiratory rate)
  - Tachycardia (10% normal pulse rate)
  - leukocytosis or leukopenia (33% normal WBC counts)
  - acutely altered mental status
  - Thrombocytopenia
  - Elevated blood lactate level
  - Hypotension
- Noninfectious etiologies of SIRS
  - pancreatitis, burns, trauma, adrenal insufficiency, pulmonary embolism, dissecting or ruptured aortic aneurysm, myocardial infarction, occult hemorrhage, cardiac tamponade, post–cardiopulmonary bypass syndrome, anaphylaxis, and drug overdose.

Etiologic diagnosis

- Blood cultures
  - At least two blood samples (10 mL each) from different venipuncture sites)
- Negative blood cultures
  - prior antibiotic administration
  - slow-growing or fastidious organisms
  - absence of microbial invasion of the bloodstream
- Primary site of infection
  - Gram's staining and culture
- Buffy coat smears of peripheral blood.



Treatment of sepsis

Optimal management of sepsis

- early, goal-directed therapy
- lung-protective ventilation
- antibiotics
- possibly activated protein C.
- The use of corticosteroids, vasopressin, and intensive insulin therapy requires further study.

Later in the course of sepsis :

- appropriate management necessitates organ support and prevention of nosocomial infection.

Removal of the Source of Infection

- Removal or drainage of a focal source of infection
- Nasal intubation: paranasal sinusitis
- neutropenic patient: perianal abscess
- sacral or ischial decubitus ulcers: pelvic or other soft tissue pus collections
- Urinary tract: ureteral obstruction, perinephric abscess, and renal abscess.

Hemodynamic Support

- Adequate oxygen and substrate delivery
- Initial management of hypotension
  - 1–2 L of normal saline over 1–2 h.
- Vasopressor therapy
- Avoid pulmonary edema
  - pulmonary capillary wedge pressure: 12–16 mmHg
  - central venous pressure at 8–12 cm H_2O.
- Urine output rate
  - >0.5 mL/kg per hour
- reasonable goal
  - mean arterial blood pressure of >65 mmHg
  - systolic pressure, >90 mmHg
  - cardiac index of 4 L/min per m2.

Respiratory Support

- Ventilator therapy is indicated
- Effects
  - ensure adequate oxygenation
  - divert blood from muscles of respiration
  - prevent aspiration of oropharyngeal contents
  - reduce the cardiac afterload
- Cautions
  - Low tidal volumes
  - careful sedation,
  - elevation of the head of the bed
  - stress-ulcer prophylaxis

Metabolic Support

- Adrenal insufficiency
  - Hydrocortisone (50 mg IV every 6 h)
- Erythrocyte transfusion to 30% hematocrit: debated.
- Bicarbonate
- DIC complicated by major bleeding
- Hypercatabolic and have acute renal failure

GENERAL SUPPORT

- Nutritional supplementation
- Prophylactic heparinization: prevent deep venous thrombosis
- Preventing skin breakdown, nosocomial infections, and stress ulcers.
- Intensive glucose control

Antibiotics use

Classification of cephalosporin

	GPC	Mixed	GNB	NGFB	Anaerobe
1 º Ceph (Veterin, Cephalothin)	+++	-	+	-	-
2 º Ceph (Cefoxin)	++	++	++	-	++
3 º Ceph (Ceftriaxone, Ceftazidime)	+	-	+++	- ++	-
4 º Ceph (Maxipime, Cefrom)	++	-	+++	++	-

NGFB: only P. aeruginosa, except the A. baumannii and S. maltophilia

Classification of penicillin group

	GPC	Mixed	GNB	Anaerobe
1 º Penicillin Amoxicillin Ampicillin	+++	+	+	+
2 º Augmentin (Clavulanic acid) Unasyn (Sulbactam)	+++	++	+++	++
3 º Timentin (Clavulanic acid)	+	++	+++	++
4 º Penicillin Tazocin (tazobactam)	+	++	+++	+++

Classification of quinolones

Drug/Pathologen	GPC	GNB	NFGNB	Atypical	Anaerobes
1st generation	-	+	-	-	-
Pipemidic acid (Dolcol), Nalidixic acid (Nagacide)					
2nd generation	+	+++	+	++	-
Ciprofloxacin (Ciproxin), Norfloxacin (Baccidal), Ofloxacin (Tarivid)					
3nd generation	++	+++	+/-	++	+
Levofloxacin (Cravit), Gatifloxacin, Sparfloxacin					
4th generation	+++	+++	-	++	++
Trovafloxacin, Moxifloxacin (Avelox)					

NFGNB: *P. aeruginosa*, *A. baumannii*, *Steno. maltophilia*

Classification of Quinolones

- Cipro
- Levo
- Moxi

G (+)	G (-) (especially *Pseudomonas*)	Atypical pathogens	Anaerobes