Intravascular infections

Bacteraemia: The presence of bacteria in the bloodstream

The terms **sepsis** and **septicemia** refer to the major clinical symptom complexes generally associated with bacteremia.

The presence of bacteria in the bloodstream associated with symptoms or signs of infection. These may be systemic (e.g. tachycardia, fever, sweats, confusion, hypotension) or localised (e.g. signs of pneumonia or osteomyelitis).

Microorganism	Common focus of infection	Notes
Staphylococcus aureus	Deep abscesses, osteomyelitis, septic arthritis, intravascular catheter infection, endocarditis	
Coagulase-negative staphylococci (e.g. *Staphylococcus epidermidis*)	Intravascular catheter infection; other prosthetic device infections	Frequent contaminant of blood cultures, therefore assessment important in confirming diagnosis
	Endocarditis	Often post-cardiac valve replacement
β-haemolytic streptococci group A	Cellulitis, necrotising fasciitis (NF), puerperal sepsis, pharyngitis	NF can have a severe acute presentation; high mortality
β-haemolytic streptococci group B	Sepsis; meningitis	Important pathogen in neonatal period
β-haemolytic streptococci groups C/G	Cellulitis	
Streptococcus anginosus group	Deep abscesses	Particularly liver, intra-abdominal, lung and brain
Streptococcus pneumoniae	Pneumonia, otitis media, meningitis	More frequent in splenectomised patients
'Viridans streptococci'	Endocarditis	Often subacute presentation
Diphtheroids	Prosthetic device infection	Less common than *Staphylococcus epidermidis*
Listeria monocytogenes	Primary focus often unknown, meningitis	Important in neonates and immunocompromised patients
Clostridium perfringens	Gas-gangrene, anaerobic cellulitis	Uncommon, sometimes associated with diabetes mellitus

Neisseria meningitidis	Sepsis (without focus), meningitis	Often acute and severe with purpuric rash; endotoxic shock a common feature
Neisseria gonorrhoeae	Genital infection	Sepsis is rare (<3% of cases of gonorrhoea) associated with arthritis and skin rash
Escherichia coli and other coliforms	Urinary tract infection; intra-abdominal sepsis (e.g. appendicitis, cholangitis); nosocomial pneumonia	
Pseudomonas aeruginosa	Nosocomial infections	Pneumonia in ventilated patients
Haemophilus influenzae type b	Meningitis, epiglottitis	Formerly in children < 5 years; now uncommon with Hib immunisation
Salmonella serotypes Typhi and Paratyphi	Primary focus often unknown	Rare in UK, cases normally imported
Other *Salmonella* spp.	Enteritis	Complication of salmonella enteritis; associated with HIV infection
Brucella spp.	Primary focus often unknown, vertebral osteomyelitis	Chronic illness often presenting as a pyrexia of unknown origin

Pathogenesis and epidemiology
A bacteraemia may be transient, intermittent or constant.

Transient bacteraemias are **short-lived (> 1 h)** and can occur as a result of normal activities of daily living (such as tooth brushing); may be caused by medical investigations (e.g. colonoscopy) or as a result of infection (e.g. flushing a colonised vascular catheter).

Some infections, e.g. abscesses or pneumonia result in intermittent bacteraemia, while infections, such as endocarditis, result in a constant bacteremia.

Bloodstream infection is almost always a **complication of localised infection** (e.g. pneumonia). Invasion of bacteria from a localised focus of infection into the bloodstream is often a **marker of more severe infection**. The presence of microorganisms or their components in blood can stimulate a systemic inflammatory response.

Systemic inflammatory response syndrome (SIRS) The presence of two or more of: temperature >38 or < 36 C or
90 beats per minute
respiratory rate >20 breaths per minute
white cell count >12 10^9 /L peripheral blood.

Many conditions can cause a systemic inflammatory response, e.g. infection, myocardial infarction, pancreatitis.

Exposure **to lipopolysaccharide** (or endotoxin) can result in septic shock (also known as endotoxic shock). The presence of endotoxin leads to activation of various inflammatory cascades. Release of cytokines results in vasodilatation and increased vascular permeability, causing a fall in

blood pressure (septic shock). Activation of the clotting cascade may result in disseminated intravascular coagulopathy (DIC), with bleeding and thrombosis occurring simultaneously. Endotoxaemia can occur in the absence of culturable bacteria in the bloodstream, e.g. from Gram-negative bacteria causing infection elsewhere.

The lipoteichoic acid in the cell walls of Gram-positive microorganisms, e.g. pneumococci, can also activate an inflammatory cascade to produce septic shock. Improved understanding of the immunological pathways leading to endotoxic shock have led to the design of monoclonal antibodies and drugs that may block the development of endotoxic shock.

The relative incidence of microorganisms causing bloodstream infection varies in different countries and with patients' age and circumstances, e.g.:

- Coagulase-negative staphylococci (CoNS). most frequent blood culture isolate in hospitalised patients in developed countries; related to frequent use of intravascular catheters;
- Staphylococcus aureus. usually in the top five causes of bloodstream infection in hospitalised patients;
- E. coli. frequent cause of bloodstream infection in elderly patients with urinary tract infection;
- Salmonella spp. uncommon in developed countries, but an important cause of bloodstream infection in developing countries

Laboratory diagnosis

Blood for culture should be obtained aseptically. Bacteria that are part of the normal skin flora (e.g. CoNS) may contaminate blood cultures therefore careful sampling technique is mandatory to reduce contamination. Contaminating bacteria must be distinguished from true infection by clinical assessment.

The length of time before growth is detectable depends on the **type of microorganism**, the **volume of blood cultured**, the **number of bacteria** present and whether **antibiotics were in the original sample**; most blood cultures become positive within 48 hours. Sampling the correct volume of blood is critical, to avoid both false negative and false positive results.

A variety of automated blood culture instruments are now available that detect bacterial growth by various techniques, e.g. the **detection of carbon dioxide** by **radiometric or optical methods**.

When bacterial growth is detected, **Gram staining** of the blood culture gives a presumptive indication of the likely microorganism. Further identification and **antibiotic susceptibility** testing are carried out after the microorganism has been grown.

Negative cultures may result from
(1) prior antibiotic treatment
(2) fungal endocarditis with entrapment of these relatively large organisms in capillary beds
(3) fastidious or cell wall–deficient organisms that are difficult to isolate
(4) infection caused by obligate intracellular parasites, such as chlamydiae, rickettsiae
(5) immunologic factors (eg, antibody acting on circulating organisms).

Infections of the Fetus and Newborn

- During normal development, the fetus is in a protected intrauterine environment, with **fetal membranes** serving as a physical barrier to external infection and the **placenta** contributing, with maternal immunity, for protection against many blood-borne infections. Transplacental transmission of specific immunoglobulins, particularly of the **IgG class**, continues to provide some immunologic protection to the infant for weeks to months after birth, while **cytokines** from the mother can provide transient cell-mediated immune support. If the infant is **breast-fed**, specific immunoglobulins (predominantly of the IgA class) in maternal colostrum afford some protection against pathogens that involve or invade through the infant's gastrointestinal tract.
- On the other hand, the **fetal immune system is immature**, and there is relative **suppression of maternal cell-mediated immunity** as pregnancy progresses. These immune deficiencies serve an important biological purpose; they protect fetus and mother from activation of specific immunologic recognition and response mechanisms to differences in their histocompatibility locus antigens. If these processes did not occur normally, the fetus could be immunologically rejected by the mother or the fetal immune mechanisms activated to respond against maternal antigens in a form of "graft versus host" disease.
- Specific and nonspecific immune responses begin to develop in early fetal life, perhaps as early as 8 weeks' gestation; however, a

nearly normal immunocompetent state is usually not achieved until the infant is more than 2 years of age. Deficiencies commonly seen in the early period include poor antibody response to polysaccharide antigens, decreased phagocytic capability and variability in intracellular killing of certain infectious agents, lower levels of complement components, and decreased opsonic capacity.

Definitions:
Prenatal infections include those acquired by the mother and/or fetus at any time before birth.
Natal infections are those acquired during delivery.
Postnatal infections: acquired after delivery throughout the newborn (or neonatal) period, defined as the first 4 weeks of life.
C**ongenital** infection, which describes infection occurring at any time before or at birth (prenatal or natal).

Modes of Infection and Major Agents

Mode	Bacteria
Prenatal transplacental	*Listeria monocytogenes*, *Mycobacterium tuberculosis* (rare), *Treponema pallidum*
Ascending	Group B streptococci, *Escherichia coli*, *L. monocytogenes*
Natal	Group B streptococci; *E. coli*, *L. monocytogenes*, *Neisseria gonorrhoeae*
Postnatal	E. coli, group B streptococci, *L. monocytogenes*, miscellaneous Gram-negative bacteria, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Clostridium tetani*

C. trachomatis and gonococci produce severe conjunctivitis

Chlamydia infant pneumonia syndrome occurs in infants up to 6 months of age

Postnatal infections by *S. aureus* may cause scalded skin syndrome