SEMESTER VI

17BTU602A MEDICAL MICROBIOLOGY 4H - 4C

Total hours/week: L:4 T:0 P:0 Marks: Internal: 40 External: 60 Total: 100

Scope: To impart knowledge on micro-flora of human body, mode action, classification of microbes, function and biochemical reaction going on inside the microbial cell.

Objective: This paper deals with various types of clinical pathogens and their harmful aspects. The paper also throws light on multifarious habitats of microbes and provides information about all the microbial cellular functions and various metabolic pathways in microbes.

UNIT- I

Introduction: Normal microflora of human body, nosocomial infections, carriers, septic shock, septicemia, pathogenicity, virulence factors, toxins, biosafety levels. Morphology, pathogenesis, symptoms, laboratory diagnosis, preventive measures and chemotherapy of gram positive bacteria: *S.aureus, S.pyogenes, B.anthracis, C.perferinges, C.tetani, C.botulinum, C.diphtheriae M.tuberculosis, M. leprae.*

UNIT-II

Pathology: Morphology, pathogenesis, symptoms, laboratory diagnosis, preventive measures and chemotherapy caused by gram negative bacteria: *E.coli, N. gonorrhoea, N. meningitidis, P. aeruginosa, S. typhi, S. dysenteriae, Y. pestis, B. abortus, H. influenzae, V. cholerae, M. pneumoniae, T. pallidum M. pneumoniae, Rickettsiaceae, Chlamydiae.*

UNIT- III

Diseases caused by viruses: Picornavirus, Orthomyxoviruses, Paramyxoviruses, Rhabdoviruses, Reoviruses, Pox virus, Herpes virus, Papova virus, Retro viruses (including HIV/AIDS) and Hepatitis viruses.

UNIT- IV

Fungal and Protozoan infections:. Dermatophytoses (*Trichophyton, Microsporun and Epidermophyton*) Subcutaneous infection (*Sporothrix, Cryptococcus*), systemic infection (*Histoplasma, Coccidoides).*

UNIT- V

Opportunistic fungal infections (*Candidiasis, Aspergillosis*), Gastrointestinal infections (Amoebiasis, Giardiasis), Blood-borne infections (Leishmaniasis, Malaria).

References

1. Brooks, G.F., Carroll, K.C., Butel, J.S., & Morse, S.A. (2007). *Jawetz, Melnick and Adelberg's Medical Microbiology* (24th ed.). McGraw Hill Publication.
2. Goering, R., Dockrell, H., Zuckerman, M., & Wakelin, D. (2007). *Mims' Medical Microbiology* (4th ed.). Elsevier.
3. Willey, J.M., Sherwood, L.M., & Woolverton, C.J. (2008). *Prescott, Harley and Klein's Microbiology* (7th ed.). McGraw Hill Higher Education.

LECTURE PLAN-UNIT-1			
S.NO	Lecture duration hour	Topics	Supporting materials
1	1	Introduction	T3-599-602
2	1	Normal microflora of human body	T1-636-638-
3	1	Nosocomial infections, septic shock, septicemia	T1 20-23
4	1	Pathogenicity,Virulence factors, Toxins, biosafety levels	T2-35-37 T3-195-197
5	1	Morphology, Pathogenesis, symptoms, laboratory diagnosis, preventive measures and chemotherapy of Gram positive bacteria: *S.aureus,*	T2-46-57 T3-193-200
6	1	*S.pyogenes, B.anthracis*	T3-203-215
7	1	*C.perferinges, C.tetani*	T3-263-265
8	1	*C.botulinum, C.diphtheriae*	T3-351-364
9	1	*M.tuberculosis, M.leprae*	T3-370-374 T3-351-364
10	1	Revision	
11	1	Unit test	
		TOTAL HOURS	11 h
Textbooks:		T1- Brooks,Carroll,K.C,Butel & Morse S.A (2007) Jawetz, Medical Microbiology (24th edi). T2- Goering R., Dockrell,H., Zuckerman & Wakelin, D(2007) Mim's medical Microbiology (4th ed) Elsevier. T3-Ananthanarayan and Paniker's textbook of Microbiology (2005) 7thedi 9orient Longman Pri Ltd).	
Journals:		-	
Website:			

LECTURE PLAN-UNIT-2			
S.NO	Lecture duration hour	Topics	Supporting materials
1	1	Morphology, Pathogenesis, symptoms, laboratory diagnosis, preventive measures and chemotherapy of Gram negative bacteria: *E.coli*, *N.gonorrhoea*	T1-36-39
2	1	*N.meningitidis, P.aeruginosa*	T3-222-229
3	1	*S.typhi, S.dysenteriae*	T3-286-289
4	1	*Y.pestis,B.abortus*	T3-324-332
5	1	*H.influenzae, V.cholerae*	T3-329-330
6	1	*M.pneumoniae, T.pallidum*	T2-69-71
7	1	*Rickettsiaceae, Chlamydiae*	T3-412-429
8	1	Unit Revision-1	
9	1	Unit test	
		TOTAL HOURS	9 h
Textbooks:		T1- Brooks,Carroll,K.C,Butel & Morse S.A (2007) Jawetz, Medical Microbiology (24th edi). T2- Goering R., Dockrell,H., Zuckerman & Wakelin, D(2007) Mim's medical Microbiology (4th ed) Elsevier. T3-Ananthanarayan and Paniker's textbook of Microbiology (2005) 7thedi 9orient Longman Pri Ltd).	
Journals:		-	
Website:			

LECTURE PLAN-UNIT-3			
S.NO	Lecture duration hour	Topics	Supporting materials
1	1	**Diseases caused by viruses:** Picornavirus,Orthomyxoviruses	T3- 490-511
2	1	Paramyxoviruses,Rhabdoviruses, Reoviruses	T3-535-46
3	1	Pox virus, Herpes virus	T4-474-485
4	1	Papova virus, Retro viruses (including HIV/AIDS)	T4-84-89
5	1	Hepatitis viruses	T3-547-561
6	1	Revision	
7	1	Unit test	
		TOTAL HOURS	7 h
Textbooks:		T3-Ananthanarayan and Paniker's textbook of Microbiology (2005) 7thedi 9orient Longman Pri Ltd). T4-Willey, J.M Sherwood L.M., & Woolverton, C.J (2008).Prescott, Harley and Klen's Microbiology (7th ed).	
Journals:		-	
Website:			

LECTURE PLAN-UNIT-4			
S.NO	Lecture duration hour	Topics	Supporting materials
1	1	Fungal and Protozoan infections: Dermatophytoses (*Trichophyton)*	T3-614 T4-112-120
2	1	*Microsporum* and *Epidermophyton*	T2-109-112
3	1	Subcutaneous infection	T2-113-116
4	1	*Sporothrix, Cryptococcus*	T4-619-620
5	1	Systemic infection (*Histoplasma, Coccidoides*).	T3-123-130 T3-623, 616-617
6	1	Revision	
		TOTAL HOURS	6 h
Textbooks:		T2- Goering R., Dockrell,H., Zuckerman & Wakelin, D(2007) Mim's medical Microbiology (4th ed) Elsevier. T3-Ananthanarayan and Paniker's textbook of Microbiology (2005) 7thedi 9orient Longman Pri Ltd). T4-Willey, J.M Sherwood L.M., & Woolverton, C.J (2008).Prescott, Harley and Klen's Microbiology (7th ed).	
Journals:		-	
Website:			

LECTURE PLAN-UNIT-5			
S.NO	Lecture duration hour	Topics	Supporting materials
1	1	Opportunistic fungal infections *Candidiasis*	T3-616-617
2	1	*Aspergillosis*	T2117-119
3	1	Gastrointestinal infections	T4-120-126
4	1	*Amoebiasis, Giardiasis*	T4-123-126 T3-605
5	1	Blood-borne infections	T4-128-132
6	1	*Leishmaniasis,Malaria*	T4-160-165
7	1	Revision	
		TOTAL HOURS	7 h
Textbooks:		T1- Brooks,Carroll,K.C,Butel & Morse S.A (2007) Jawetz, Medical Microbiology (24th edi). T2- Goering R., Dockrell,H., Zuckerman & Wakelin, D(2007) Mim's medical Microbiology (4th ed) Elsevier. T3-Ananthanarayan and Paniker's textbook of Microbiology (2005) 7thedi 9orient Longman Pri Ltd).	
Journals:		-	
Website:			

Unit I

Normal micro flora of the human body: Nosocomial infections, carriers, septic shock, septicemia, Pathogenicity, Virulence factors, Toxins, Biosafety levels: Morphology,pathogenesis,symptoms,laboratory diagnosis, preventive measures and chemotherapy caused by gram positive bacteria: S.aureus, S.pyogenes, B.anthracis, C.perferinges, C.tetani, C.botulinum, C.diphtheriae, M.tuberculosis, M.leprae.

NORMAL FLORA OF HUMAN BODY

INTRODUCTION

In a healthy human, the internal tissues, e.g. blood, brain, muscle, etc., are normally free of microorganisms. However, the surface tissues, i.e., skin and mucous membranes, are constantly in contact with environmental organisms and become readily colonized by various microbial species. The mixture of organisms regularly found at any anatomical site is referred to as the **normal flora.** The normal flora of humans consists of a few eucaryotic fungi and protists, but bacteria are the most numerous and obvious microbial components of the normal flora. A healthy foetus in utero is free from microorganisms. During birth the infant in exposed to vaginal flora. Within a few hours of birth oral and nasopharyngeal flora develops and in a day or two resident flora of the lower intestine appears

NORMAL MICROBIAL FLORA

The term “normal microbial flora” denotes the population of microorganisms that inhabit the skin and mucous membranes of healthy normal persons. The skin and mucous membranes always harbor a variety of microorganisms that can be arranged into two groups:

1. The resident flora consists of relatively fixed types of microorganisms regularly found in a given area at a given age; if disturbed, it promptly reestablishes itself.

2. The transient flora consists of nonpathogenic or potentially pathogenic microorganisms that inhabit the skin or mucous membranes for hours, days, or weeks; it is derived from the environment, does not produce disease, and does not establish itself permanently on the surface. Members of the transient flora are generally of little significance so long as the normal resident flora remains intact. However, if the resident flora is disturbed, transient microorganisms may colonize, proliferate, and produce disease.

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RESIDENT FLORA

It consists of organisms which are regularly present in a particular area and when disturbed it reestablishes itself like *Esch.coli* is a normal inhabitant of the intestine.

Role of Resident flora

Microorganisms that are constantly present on body surfaces are commensals. Their growth in a given area depends upon physiologic factors like temperature, moisture, and the presence of certain nutrients and inhibitory substances. Resident flora of certain areas plays a definite role in maintaining health and normal function. Members of the resident flora in the intestinal tract synthesize vitamin K and aid in the absorption of nutrients. On mucous membranes and skin, the resident flora may prevent colonization by pathogens and possible disease through "bacterial interference." The mechanism of bacterial interference is not clear. It may involve competition for receptors or binding sites on host cells, competition for nutrients, mutual inhibition by metabolic or toxic products, mutual inhibition by antibiotic materials or bacteriocins, or other mechanisms. Suppression of the normal flora tends to be filled by organisms from the environment or from other parts of the body and such organisms behave as opportunists and may become pathogens.

On the other hand, members of the normal flora may themselves produce disease under certain circumstances and if removed from the restrictions of that environment and introduced into the bloodstream or tissues, these organisms may become pathogenic. For example, streptococci of the viridans group are the most common resident organisms of the upper respiratory tract and if large numbers of them are introduced into the bloodstream (eg, following tooth extraction or tonsillectomy), they may settle on deformed or prosthetic heart valves and produce infective endocarditis. Small numbers occur transiently in the bloodstream with minor trauma (eg, dental scaling or vigorous brushing). Bacteroides species are the commonest resident bacteria, if introduced into the free peritoneal cavity or into pelvic tissues along with other bacteria as a result of trauma, they cause suppuration and bacteremia. There are many other examples, but the important point is that microbes of the normal resident flora are harmless and may be beneficial in their normal location in the host and in the absence of coincident abnormalities. They may produce disease if introduced into foreign locations in large numbers and if predisposing factors are present.

It has both advantages as well as disadvantages.

Advantages

(i) They prevent or suppress the entry of the pathogens.

(ii) These synthesize the vitamins especially Vit.-K and several B Group vitamins.

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(iii) The normal flora evokes the Antibodies production. These Antibodies cross react with pathogens having related or shared antigens, thus raising the immune status of the host against the invading pathogen.

(iv) Colonies produced by some organisms of normal flora have a harmful effect on the pathogens.

(v) Endotoxins liberated by normal flora may help the defense mechanism of the body.

Disadvantages

(i) They become pathogenic when the immunity is lowered.

(ii) They may act as pathogens in different issue (other than their normal habitat) e.g. normal flora of intestine may cause urinary tract infection (UTI).

(iii) Normal flora may cause confusion in diagnosis due to their ubiquitous presence in the body and their resemblance to some of the pathogens.

Some Resident Microbiota

TRANSIENT FLORA

It consists of both non-pathogenic and potentially pathogenic bacteria that inhabit the body surface or mucous membranes for a limited period. They can be removed from the body surface by mechanical means like Pneumococcus and Meningococcus can be removed from nasopharynx of the human beings from time to time. Members of the normal flora form part of the host and include: saprophytes, commensals, facultative pathogens and true pathogens.

Normal Flora of the Skin

Skin is constantly exposed to and is in contact with the environment, the skin is particularly apt to contain transient microorganisms. The predominant resident microorganisms of the skin are aerobic and anaerobic diphtheroid bacilli (eg, corynebacterium, propionibacterium); nonhemolytic aerobic and anaerobic staphylococci (*Staphylococcus epidermidis*, occasionally *S aureus*, and peptostreptococcus species); gram-positive, aerobic, spore-forming bacilli that are ubiquitous in air, water, and soil; alphahemolytic streptococci (viridians streptococci) and enterococci (enterococcus species); and gram-negative coliform bacilli and acinetobacter. Low pH, fatty acids in sebaceous secretions and presence of lysozymes are important factors for eliminating non-resident microorganisms from the skin. Normal skin inhabits 102 - 104 organisms/sq. cm.

MICROBIOLOGY

Microorganisms present on the skin surface are *Staph.epidermidis* and Diphtheroids are the most common. Less common are Peptococcus, *Strept.viridens*, *Enterococcus*, *Micrococcus*, *Esch.coli*, *Candida*, etc.

Normal flora of Conjunctiva

The conjunctiva is relatively free from bacteria due to the presence of lysozyme in the tears which flushes the bacteria. Predominant organisms of the eyes are:

Moraxella sp

Diphtheroids

Straph epidermidis

Moraxella sp

Non hemolytic streptococci

Normal Flora of Nose and Nasopharynx

The nasopharynx of the infant is sterile at birth but in 2-3 days time it acquires the flora carried by the mother and attendants. The nasopharynx is a natural habitat of the common pathogenic bacteria causing infection of the nose, throat, bronchi and lungs.

The flora of nose harbours

Diptheroids

Straphylococcus

Streptococcus

Haemophilus, and

Moraxella lacunata

Normal Flora of the Mouth

The mouth contains micrococci, gram positive aerobic spore bearing bacilli, coliforms, proteus and lactobacilli. The gums pockets between the teeth and crypts of the tonsils have a wide spectrum of anaerobic flora like fusiform bacilli, treponemes, lactobacilli, etc. Candida is also found. The mouth of infant is not sterile at birth. It generally contains the same types of organisms as found in mother's vagina. These bacteria diminish in number and are replaced by similar bacteria present in the mouth of mother and nurse.

Normal Flora of Upper Respiratory Tract

Within 12 hours of birth alpha hemolytic streptococci are found in upper respiratory tract and become the dominant organism of the oropharynx and remains so for the whole life. In the pharynx and trachea, similar flora is established. Smaller bronchi and alveoli are normally sterile.

Normal Flora of Gastrointestinal Tract:

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The GI Tract of the foetus in utero is sterile. It becomes contaminated with organisms shortly after birth. In breast fed infants, the intestine contains lactobacilli, enterococci, colon bacilli and staphylococci. In bottle fed infants the intestine contains anaerobic lactobacilli, colon bacilli and aerobic and anaerobic spore bearing organisms. With the change of food, flora changes. Diet has a marked influence on the composition of the intestinal and fecal flora.

In the stomach as pH is low, the stomach is sterile but as the pH increases in small intestine the number of bacteria increases progressively beyond the duodenum to the colon. The bacterial count is low in small intestine as compared to large intestine. Lactobacilli and entrococci predominate in the duodenum and proximal ileum. The bacterial flora is similar in lower ileum, caecum and rectum. The anaerobic condition of colon is maintained by aerobic bacteria which utilizes the free oxygen.

Normal Flora of the Genitourinary Tract

Mycobacterium smegmatis a harmless commensal is found in the secretions (smegma) of both males and females genitalia. They may pose the confusion with the tubercle bacilli. Strains of mycoplasma and ureaplasma are frequently present as part of normal flora. *Gardnerella vaginalis*, *bacteroides* and *alpha streptococci* have been found in penile urethra. Female urethra is either sterile or contains *staphylococcus epidermidis*. The vagina of newly borne child is sterile and within 24 hours it colonizes with micrococci, entrococci. In 2-3 days time doderlien's bacillus appears. So the flora keeps on changing depending upon the pH of the vagina. Doderlien bacilli remain in the vagina till menopause. After menopause flora resembles that before puberty.

Septic shock

Sepsis is the result of an infection, and causes drastic changes in the body. It can be very dangerous and potentially life-threatening. It occurs when chemicals that fight infection by triggering inflammatory reactions are released into the bloodstream.Three stages of sepsis:

- Sepsis is when the infection reaches the bloodstream and causes inflammation in the body.
- Severe sepsis is when the infection is severe enough to affect the function of your organs, such as the heart, brain, and kidneys.
- Septic shock is when you experience a significant drop in blood pressure that can lead to respiratory or heart failure, stroke, failure of other organs, and death.

It is thought that the inflammation resulting from sepsis causes tiny blood clots to form. This can block oxygen and nutrients from reaching vital organs.

The inflammation occurs most often in older adults or those with a weakened immune system. But both sepsis and septic shock can happen to anyone.

Septic shock is the most common cause of death in intensive care units in the United States.

Symptoms of septic shock

Early symptoms of sepsis should not be ignored. These include:

- fever usually higher than 101˚F (38˚C)
- low body temperature (hypothermia)
- fast heart rate
- rapid breathing, or more than 20 breaths per minute

Severe sepsis is defined as sepsis with evidence of organ damage that usually affects the kidneys, heart, lungs, or brain. Symptoms of severe sepsis include:

- noticeably lower amounts of urine
- acute confusion
- dizziness
- severe problems breathing
- bluish discoloration of the digits or lips (cyanosis)

People who are experiencing septic shock will experience the symptoms of severe sepsis, but they will also have very low blood pressure that doesn't respond to fluid replacement.

Causes of septic shock

A bacterial, fungal, or viral infection can cause sepsis. Any of the infections may begin at home or while you are in the hospital for treatment of another condition.

Sepsis commonly originates from:

- abdominal or digestive system infections

- lung infections like pneumonia
- urinary tract infection
- reproductive system infection

Risk factors

Certain factors such as age or prior illness can put you at greater risk for developing septic shock. This condition is common in newborns, older adults, pregnant women, and those with suppressed immune systems caused by HIV, rheumatic diseases such as lupus and rheumatoid arthritis, or psoriasis. And inflammatory bowel diseases or cancer treatments could cause it.

The following factors could also make it more likely that a person develops septic shock:

- major surgery or long-term hospitalization
- diabetes type 1 and type 2 injection drug use
- hospitalized patients that are already very sick
- exposure to devices like intravenous catheters, urinary catheters, or breathing tubes, which can introduce bacteria into the body
- poor nutrition

Diagnosis of septic shock

If you have symptoms of sepsis, the next step is to conduct tests to determine how far along the infection is. Diagnosis is often made with a blood test. This type of test can determine if any of the following factors are present:

- bacteria in the blood
- problems with clotting due to low platelet count
- excess waste products in the blood
- abnormal liver or kidney function
- decreased amount of oxygen
- electrolyte imbalance

Depending on your symptoms and the results of the blood test, there are other tests that a doctor may want to perform to determine the source of your infection. These include:

- urine test
- wound secretion test if you have an open area that looks infected
- mucus secretion test to see what type of germ is behind the infection
- spinal fluid test

In cases where the source of the infection is not clear from the tests above, a doctor could also apply the following methods of getting an internal view of your body:

- X-rays
- CT scan
- ultrasound
- MRI

Complications of septic shock

Septic shock can cause a variety of very dangerous and life-threatening complications that can be fatal. Possible complications include:

- heart failure
- abnormal blood clotting
- kidney failure
- respiratory failure
- stroke
- liver failure
- loss of a portion of the bowel
- loss of portions of the extremities

The complications you may experience, and the outcome of your condition can depend on factors such as:

- age
- how soon treatment is started
- cause and origin of sepsis within the body
- preexisting medical conditions

Treatment of septic shock

The earlier sepsis is diagnosed and treated, the more likely you are to survive. Once sepsis is diagnosed, you will most likely be admitted to an Intensive Care Unit (ICU) for treatment. Doctors use a number of medications to treat septic shock, including:

- intravenous antibiotics to fight infection
- vasopressor medications, which are drugs that constrict blood vessels and help increase blood pressure
- insulin for blood sugar stability
- corticosteroids

Large amounts of intravenous (IV) fluids will be administered to treat dehydration and help increase blood pressure and blood flow to the organs. A respirator for breathing may also be necessary. Surgery may be performed to remove a source of infection, such as draining a pus-filled abscess or removing infected tissue.

Septicemia

Septicemia is a serious bloodstream infection. It's also known as blood poisoning.

Septicemia occurs when a bacterial infection elsewhere in the body, such as the lungs or skin, enters the bloodstream. This is dangerous because the bacteria and their toxins can be carried through the bloodstream to your entire body.

Septicemia can quickly become life-threatening. It must be treated in a hospital. If left untreated, septicemia can progress to sepsis.

Septicemia and sepsis aren't the same. Sepsis is a serious complication of septicemia. Sepsis causes inflammation throughout the body. This inflammation can cause blood clots and block oxygen from reaching vital organs, resulting in organ failure.

The National Institutes of Health estimates that over 1 million Americans get severe sepsis each year. Between 28 and 50 percent of these patients may die from the condition.

When the inflammation occurs with extremely low blood pressure, it's called septic shock. Septic shock is fatal in many cases.

Causes of septicemia

Septicemia is caused by an infection in another part of your body. This infection is typically severe. Many types of bacteria can lead to septicemia. The exact source of the infection often can't be determined. The most common infections that lead to septicemia are:

- urinary tract infections
- lung infections, such as pneumonia
- kidney infections
- infections in the abdominal area

Bacteria from these infections enter the bloodstream and multiply rapidly, causing immediate symptoms.

People already in the hospital for something else, such as a surgery, are at a higher risk of developing septicemia. Secondary infections can occur while in the hospital. These infections are often more dangerous because the bacteria may already be resistant to antibiotics. You're also at a higher risk of developing septicemia if you:

- have severe wounds or burns
- are very young or very old
- have a compromised immune system, which can occur from conditions, such as HIV or leukemia, or from medical treatments such as chemotherapy or steroid injections
- have a urinary or intravenous catheter
- are on mechanical ventilation

Symptoms of septicemia

The symptoms of septicemia usually start very quickly. Even in the first stages, a person can look very sick. They may follow an injury, surgery, or another localized infection, such as pneumonia. The most common initial symptoms are:

- chills
- fever
- breathing very fast
- rapid heart rate

More severe symptoms will begin to emerge as septicemia progresses without proper treatment. These include the following:

- confusion or inability to think clearly

- nausea and vomiting
- red dots that appear on the skin
- reduced urine volume
- inadequate blood flow
- shock

It's crucial to get to the hospital right away if you or someone else is showing signs of septicemia. You shouldn't wait or try to treat the problem at home.

Complications of septicemia

Septicemia has a number of serious complications. These complications may be fatal if left untreated or if treatment is delayed for too long.

Sepsis

Sepsis occurs when your body has a strong immune response to the infection. This leads to widespread inflammation throughout the body. It's called severe sepsis if it leads to organ failure.

People with chronic diseases are at a higher risk of sepsis. This is because they have a weakened immune system and can't fight off the infection on their own.

Septic shock

One complication of septicemia is a serious drop in blood pressure. This is called septic shock. Toxins released by the bacteria in the bloodstream can cause extremely low blood flow, which may result in organ or tissue damage.

Septic shock is a medical emergency. People with septic shock are usually cared for in a hospital's intensive care unit. You may need to be put on a ventilator, or breathing machine, if you're in septic shock.

Acute respiratory distress syndrome (ARDS)

A third complication of septicemia is acute respiratory distress syndrome (ARDS). This is a life-threatening condition that prevents enough oxygen from reaching your lungs and blood. It often results in some level of permanent lung damage. It can also damage your brain, leading to memory problems.

Diagnosis of septicemia

Diagnosing septicemia and sepsis are some of the biggest challenges facing doctors. It can be difficult to find the exact cause of the infection. Diagnosis will usually involve a wide range of tests.

Your doctor will evaluate your symptoms and ask your medical history. They'll perform a physical examination to look for low blood pressure or body temperature. The doctor may also look for signs of conditions that more commonly occur along with septicemia, including:

- pneumonia
- meningitis
- cellulitis

Your doctor may want to perform tests on multiple types of fluids to help confirm a bacterial infection. These may include the following:

- urine
- wound secretions and skin sores
- respiratory secretions
- blood

Your doctor may check your cell and platelet counts and also order tests to analyze your blood clotting.

Your doctor may also look at the oxygen and carbon dioxide levels in your blood if septicemia is causing you to have breathing issues.

If signs of infection aren't obvious, your doctor may order test to look more closely at specific organs and tissue, such as:

- X-ray
- MRI
- CT scan
- ultrasound

Treatment for septicemia

Septicemia that has started to affect your organs or tissue function is a medical emergency. It must be treated at a hospital. Many people with septicemia are admitted for treatment and recovery.

Your treatment will depend on several factors, including:

- your age
- your overall health
- the extent of your condition
- your tolerance for certain medications

Antibiotics are used to treat the bacterial infection that's causing septicemia. There isn't typically enough time to figure out the type of bacteria. Initial treatment will usually use "broad-spectrum" antibiotics. These are designed to work against a wide range of bacteria at once. A more focused antibiotic may be used if the specific bacteria is identified.

You may get fluids and other medications intravenously to maintain your blood pressure or to prevent blood clots from forming. You may also get oxygen through a mask or ventilator if you experience breathing issues as a result of septicemia.

Prevention of septicemia

Bacterial infections are the underlying cause of septicemia. See a doctor right away if you think you have this condition. If your infection can be effectively treated with antibiotics in the early stages, you may be able to prevent the bacteria from entering your bloodstream.

Parents can help protect children from septicemia by ensuring they stay up to date with their vaccinations.

If you already have a compromised immune system, the following precautions can help prevent septicemia:

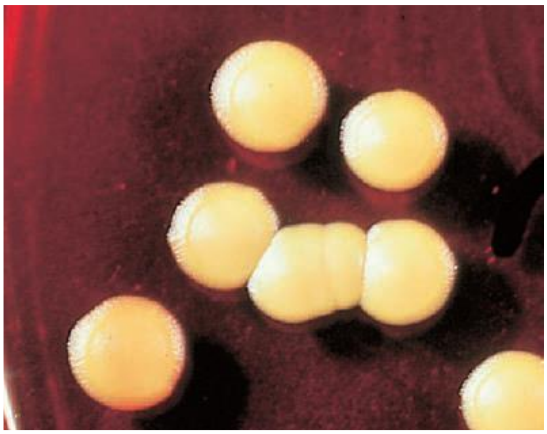
- avoid smoking
- avoid illegal drugs
- eat a healthy diet
- exercise
- wash your hands regularly
- stay away from people who are sick

S. aureus

Epidemiology

S. aureus is a relatively common human commensal: nasal carriage occurs in 30–50% of healthy adults, faecal carriage in about 20% and skin carriage in 5–10%, particularly the axilla and

perineum. S. aureus is spread via droplets and skin scales, which contaminate clothing, bed linen and other environmental sources.



S. aureus colonies on a blood agar plate
(2–3mm diameter).

Morphology and identification

On microscopy, S. aureus is seen as typical Grampositive cocci in 'grape-like' clusters. It is both coagulase and DNAase positive. Other biochemical tests can be performed for full identification.

Pathogenicity

S. aureus causes disease because of its ability to adhere to cells, spread in tissues and form abscesses, produce extracellular enzymes and exotoxins combat host defences and resist treatment with man antibiotics.

Adhesins

S. aureus has a wide repertoire of adhesins known as MSCRAMMs (microbial surface components

recognizing adhesive matrix molecules), which mediate adherence to host cells; these include protein A, fibrinogen and fibronectin-binding and collagen-binding protein.

Exotoxins and enzymes

Coagulase: S. aureus produces coagulase, an enzyme that coagulates plasma. Coagulase results in fibrin deposition, which interferes with phagocytosis and increases the ability of the microorganism to invade tissues. Other enzymes: S. aureus may also produce staphylokinase (results in fibrinolysis), hyaluronidase (dissolves hyaluronic acid), proteases (degrades proteins) and lipases (solubilises lipids). Haemolysin, leukotoxin and leukocidin: several exotoxins are produced by S. aureus; a-toxin (haemolysin) lyses erythrocytes and damages platelets; b-toxin degrades sphingomyelin and is toxic for many types of cell, including erythrocytes; leukocidin (Panton Valentine leukocidin, PVL) lyses white blood cells and damages membranes and susceptible cells. Enterotoxins: there are six soluble enterotoxins that are produced by almost half of all S. aureus strains. They are heat stable (resistant at 100°C for 30 min), unaffected by gastrointestinal enzymes and are a cause of food poisoning, principally associated with vomiting. Exfoliative/epidermolytic toxin: some strains produce a toxin that can result in generalized desquamation of the skin (staphylococcal scalded skin syndrome). Toxic shock syndrome toxin (TSST): this is associated with shock and desquamation of skin, and is usually related to an underlying S. aureus infection. Staphylococcal enterotoxins, TSSTs and exfoliative toxin are ‘superantigens’, all of which bind non-specifically to specific white cells, resulting in over production of cytokines, giving rise to a toxic shock-like presentation.

Cell envelope

Over 90% of all clinical isolates of S. aureus strains possess a polysaccharide capsule that interferes with opsonisation and phagocytosis. S. aureus also possesses a cell-wall protein (protein A) that binds the Fc component of the antibody, preventing complement activation.

Antibiotic resistance

Many strains of S. aureus are resistant to the antibiotic meticillin and are termed 'meticillinresistant S. aureus' (MRSA).Most resistance depends on the productionof anadditional penicillin-binding protein, which is encoded by an acquired mecA gene. Many strains of MRSA are now resistant to multiple antibiotics.

Laboratory diagnosis

Laboratory diagnosis isbymicroscopicdetection of the microorganism in clinical samples, direct isolation from the infected site or blood cultures, and detection of serum antibodies to staphylococcal haemolysin and DNAase. S. aureus strains can be typed ('fingerprinted') by conventional methods, including biotype and antibiogram. S. aureus can also be genotyped by molecular methods, including pulsed field gel electrophoresis (PFGE). Typing of S. aureus is useful in epidemiological studies.

Treatment and prevention

Antimicrobial agents, such as flucloxacillin, remain the first-line treatment for sensitive strains of S.aureus;however,the increase in infections caused by MRSA has required the use of glycopeptide antibiotics such as vancomycin. Resistance to vancomycin has been reported but is still rare. MRSA can cause sepsis, ranging from wound infections to urinary tract infections and severe sepsis and septic shock. Epidemic strains of MRSA(EMRSA)have also been recognised. Prevention of spread through effective infection control procedures, including MRSA decolonisation, is therefore important.

Associated infections

Skin: boils, impetigo, furuncles, wound infections, staphylococcal scalded skin syndrome;

Respiratory: pneumonia, lung abscesses, exacerbations of chronic lung disease;

Skeletal: most common cause of osteomyelitis and septic arthritis;

Invasive: bloodstream infection, infective endocarditis, deep abscesses (brain, liver, spleen),

toxic shock syndrome;

Gastrointestinal: toxin-mediated food poisoning;

Device related: indwelling catheters, prosthetic joints and heart valves.

Streptococcus pyogenes

Epidemiology

S. pyogenes is an upper respiratory tract commensal.

Morphology and identification

Group A streptococci will not grow on media containing bile. The identity of S. pyogenes is normally confirmed by Lancefield grouping and biochemical testing. Strains of S. pyogenes can be further differentiated according to the presence of surface proteins M, R and T (Griffith types). Epidemiological typing can be carried out, based on the possession of different M-proteins.

Pathogenicity

S. pyogenes produces a wide range of virulence factors including: A capsule composed of hyaluronic acid: provides protection against phagocytosis.

Fimbriae/pili: facilitate adherence to host cells. They consist of lipoteichoic acid (an adherence factor) and M-protein.

M-proteins: surface proteins which are antiphagocytic and also bind host proteases.

F-proteins: surface proteins that bind to fibronectin.

Streptolysins (haemolysins): streptolysins O and S lyse erythrocytes and are cytotoxic to leukocytes and other cell types.

Other enzymes: include streptokinase (prevents the formation of a fibrin mesh), hyaluronidase (breaks down hyaluronic acid in connective tissue), deoxyribonucleases (DNAases), nicotinamide adenine dinucleotidase (NADase) and C5a peptidase (inactivates the C5a component of the complement system).

Streptococcal pyrogenic exotoxins (erythrogenic toxins): responsible for the rash of scarlet fever. Streptococci and enterococci. These are 'superantigens', which facilitate release of cytokines, potentially leading to shock.

Associated infections

Respiratory tract: pharyngitis, sinusitis, tonsillitis, otitis media, pneumonia;

Musculoskeletal: septic arthritis;

Gastrointestinal: spontaneous bacterial peritonitis;

Skin and soft tissue: cellulitis, impetigo, erysipelas, scarlet fever, wound infection, necrotising fasciitis;

Genitourinary: puerperal sepsis;

Cardiovascular: infective endocarditis.

Post-infection complications

Antibodies produced as a result of infection with S. pyogenes may cause non-pyogenic complications at other anatomical sites post-infection. Indeed,rheumatic fever and acute glomerulonephritismay develop up to 3 weeks after the streptococcal infection. Inflammation of the cardiac muscle occurs in rheumatic fever, whilst acute glomerulonephritis is characterised by inflammation of the renal glomerulus.

Laboratory diagnosis

Diagnosis is by isolation of the microorganism from infected sites (e.g. throat, skin, blood). The detection of serum antibodies to streptolysin O (ASOT: anti-streptolysin O titre) is particularly useful for the diagnosis of post-infection complications, such as rheumatic fever or acute glomerulonephritis. This is because the microorganism is often no longer present at the time of clinical presentation.

Treatment

S. pyogenes is sensitive to many antibiotics. Penicillin remains the drug of choice for treatment of infection with this microorganism.

Bacillus anthracis

Epidemiology

Anthrax is principally a zoonotic disease and is common in some parts of the developing world. Human infections can be classified as: non-industrial (direct human contact with infected animals) or industrial (processing of animal products by humans). Spores can survive in the soil for long periods of time and are relatively resistant to chemical disinfectants and heat. Infection with B. anthracis in theUKis rare but is normally associated with handling imported animal products. Recent UK cases have occurred in intravenous drug users, probably as a result of contaminated heroin. Anthrax has been used as a biological weapon.

Morphology and identification

Can grow under anaerobic conditions; its non-motility allows it to be distinguished from other Bacillus species; virulent strains are capsulate; do not produce a zone of haemolysis on blood nor a zone of precipitation on egg yolk agar (i.e. does not produce lecithinase). Identification is normally confirmed by morphological and biochemical tests.

Pathogenicity

Virulent strains of B. anthracis possess a protein capsule, which prevents phagocytosis. This microorganism also produces a plasmid-encoded exotoxin, which is composed of three proteins: protective antigen, oedema factor and lethal factor. Protective antigen is concerned with receptor binding and therefore the attachment and translocation of oedema factor and lethal factor into the cell. Oedema factor causes impairment of macrophage function and lethal factor lysis of macrophages.

Associated infections

Types of anthrax infection include: Skin and soft tissues: cutaneous anthrax is the predominant clinical manifestation. Development of a necrotic skin lesion (malignant pustule) occurs. Respiratory: ('wool-sorter's disease'): spores are inhaled (often from wool fibres) causing pulmonary oedema, haemorrhage and commonly, death. Gastrointestinal: consumption of contaminated meat results in haemorrhagic diarrhorea. This type of anthrax can also result in death.

Laboratory diagnosis

Normally by direct isolation of the microorganism from infected sites, i.e. sputum or specimens from skin lesions. A safety cabinet should be used to handle such specimens.

Treatment and prevention

B. anthracis is sensitive to many antibiotics. Common therapeutic agents used are penicillin, erythromycin, ciprofloxacin or doxycycline. Ciprofloxacin or doxycyclinemaybe given for post-exposure prophylaxis. Anthrax vaccinations are available for individuals at high risk, e.g. military personnel, veterinary practitioners and farm workers. Livestock in endemic areas may also be vaccinated.

Clostridium perfringens

Epidemiology

C. perfringens is widely present in the environment, in the intestine of humans and domestic animals and can contaminate meat during preparation for consumption. Small numbers of microorganisms may survive subsequent cooking particularly in large pieces of meat, and multiply during the cooling down and storage resulting in food poisoning. A more serious but rare illness (necrotising enteritis or pig-bel disease) is caused by ingesting food contaminated with Type C strains.

Clinical features

The incubation period is 8–24 hours. The common form of the disease associated with diarrhoea and abdominal cramps is self-limiting and usually over in 24 hours. Necrotising enteritis (caused by ingestion of large numbers of the causative microorganism of Type C) is often fatal.

Diagnosis

Detection of toxin in faeces. Bacterial confirmation by isolating the causative microorganism in foods and/or faeces of patients.

C. tetani

Morphology and identification

Motile; terminal spore (‘drumstick’ appearance); produces a thin spreading film of growth without discrete colonies on blood agar; motile via numerous peritrichous flagella.

Epidemiology

C. tetani is present in mammalian intestines and the environment (particularly manured soil). Spores are ubiquitous in nature. Incidence of tetanus varies worldwide; more common in developing tropical and subtropical countries; infection is inversely related to living standards, preventative medicine and wound management.

Pathogenicity

Many strains are highly toxigenic, producing oxygen-labile haemolysin (tetanolysin) and a potent neurotoxin (tetanospasmin). Tetanospasmin blocks neurotransmitter release, resulting in the

characteristic motor spasms associated with tetanus (e.g. lockjaw, arching of the back).

Associated infections

Neurological: tetanus.

Laboratory diagnosis

Demonstration of characteristic 'drumstick' bacilli in clinical samples, followed by anaerobic culture on selective or blood agar; serological detection of circulating neurotoxin by enzyme immunoassay.

Treatment and prevention

Treatment includes administration of human tetanus immunoglobulin and benzylpenicillin or metronidazole. Surgical debridement and cleansing of wounds is important in successful treatment. Prevention includes administration of the tetanus toxoid vaccine.

Clostridium botulinum

Epidemiology

Spores of C. botulinum are widespread and heat resistant and can survive in foods that have been incorrectly or minimally processed. Canned foods are often implicated. The spores produce a potent neurotoxin which is heat-labile and can be destroyed if food is heated to 80°C for 10 minutes.

Clinical features

Food-borne botulism is a rare but severe type of food poisoning caused by the ingestion of food containing the neurotoxin. After an incubation period of 18–36 hours there is marked lassitude weakness and vertigo followed by lower motor neuron dysfunction affecting first the cranial nerves (diplopia, dysphagia, dysarthria) and progressing caudally.

Diagnosis

The detection of botulinum toxin in serum, faeces and suspected food.

Treatment

Early administration of botulinum antitoxin and supportive treatment, which may require a period of assisted ventilation in an intensive care setting.

Corynebacterium diphtheriae

C. diphtheriae is the cause of diphtheria, an upperrespiratory tract infection with cardiac and neurological complications.

Epidemiology

Infection is normally spread via nasopharyngeal secretions from people who are infected or who are carriers of the microorganism. Diphtheria is rare in developed countries.

Morphology and identification

Microbiological medium containing tellurite, e.g. Hoyle's tellurite, is often used for culture of throat swabs from patients with suspected diphtheria. This selective medium allows the growth of Corynebacterium spp. whilst suppressing commensals of the upper respiratory tract. Colonies of C. diphtheriae are grey-black in colour. C. diphtheriae canbe differentiated into four subspecies: var. gravis,var.mitis,var.intermedius and var. belfanti. This and differentiation from other species can be achieved by colonial morphology, biochemical tests and haemolytic activity. Toxigenic strains can be confirmed by the Elek test (a precipitation reaction in agar), enzyme immunoassay (EIA) or polymerase chain reaction (PCR)-based techniques.

Pathogenicity

All subspecies, except var. belfanti, may produce the diphtheria exotoxin. It is a heat-stable polypeptide comprised of fragment A and fragment B. Fragment A is involved with the translocation of fragment B into the cell, the latter fragment then causes cell death by inhibiting protein synthesis. The gene which codes for production of this toxin is carried on a bacteriophage and is then integrated into the bacterial chromosome. Toxin-producing strains of C. diphtheriae multiply in the pharynx and the exotoxin produced causes necrosis of the epithelial cells.

Associated infections

Respiratory: Diphtheria: the main clinical symptoms are a sore throat, thick pharyngeal pseudomembrane, bullneck (oedema of the neck), fever, fatigue and headache. Bloodstream infection: The toxin may then cause damage to myocardial, neural and renal cells. Skin and soft tissue: Diphtheria toxin can also cause cutaneous ulceration.

Laboratory diagnosis

Direct isolation of the microorganism from throat swabs; however, laboratories in the developed world do not routinely culture throat swabs for C. diphtheriae, as cases are increasingly rare.

Treatment and prevention

Penicillin or erythromycin can be used to eradicate the microorganisms. Diphtheria antitoxin is used for passive immunisation of suspected cases of diphtheria only. In developed countries, children are routinely immunised with a toxoid vaccine. Contacts should be given antibiotic prophylaxis and a reinforcing dose of vaccine if previously vaccinated (a full immunisation course is required if not vaccinated). Travellers to areas of the world affected by diphtheria should also receive a reinforcing dose of vaccine (again, a full immunization course is required if not previously vaccinated).

Mycobacterium tuberculosis

May mimic bacterial pneumonia, but patients usually have a longer duration of symptoms.

Viral causes of community-acquired pneumonia

Primary viral pneumonia occurs mainly in children, elderly people and immune compromised patients, with an increased incidence in winter. Underlying cardiopulmonary diseases are recognized risk factors for viral pneumonia in children and adults.

Clinical manifestations in children vary considerably, but typically include fever, difficulty in breathing or apnoeic episodes in young infants, non-productive cough, wheezing or increased

breath sounds. Common viral causes include Respiratory syncytial virus (RSV), Parainfluenza viruses, Influenza A and B, Adenoviruses, Measles and Human metapneumovirus. Influenza A subtype H1N1 presents with symptoms similar to those of seasonal influenza. Primary viral pneumonia in adults is characterized by non-productive cough, cyanosis and hypoxia, fever, rhinitis, increased respiratory rate, wheezes and diffuse bilateral interstitial infiltrates on chest radiograph. Consider Varicella-zoster virus (VZV), if vesicular rash.

Diagnosis of viral pneumonia is by PCR or culture of viral agents in, e.g. nasopharyngeal aspirates, throat and nasal swabs and BALs. Viral antigens can be detected by immunofluorescence techniques. Specific antiviral therapy is available for some of the viruses associated with viral pneumonia. Ribavirin is used for the treatment of some cases of RSV and Parainfluenza infections, and for Adenovirus infections in immune compromised patients. The neuraminidase inhibitors (oseltamivir and zanamivir) are available for the treatment of Influenza A (includingH1N1 subtype) and B infections.

Hospital-acquired pneumonia (HAP) Aetiology

Commonly Streptococcus pneumoniae and Haemophilus influenzae in early-onset infections (first Lower respiratory tract infections 4 days of admission), thereafter Gram-negative bacteria (e.g. Escherichia coli, Klebsiella and Serratia spp.) and in ventilator-associated pneumonia especially meticillin-resistant *Staphylococcus aureus* (MRSA) and multiresistant Gramnegative bacteria, including *Acinetobacter* and *Pseudomonas aeruginosa*.

Epidemiology

HAP is a pneumonia presenting two or more days after admission to hospital. Pneumonia is one of the most common nosocomial infections, affecting about 0.5% of hospitalised patients. Risk factors include endotracheal intubation and ventilation, immune compromise and pre-existing pulmonary disease. Ventilator-associated pneumonia (VAP) is a subtype of hospital acquired pneumonia, which occurs in people who are on mechanical ventilation through an endotracheal or tracheostomy tube for at least 48 hours.

Investigations

Sputum and blood cultures. For VAP, bronchoscopically-collected respiratory secretions or blind bronchoalveolar lavage.

Treatment

Broad spectrum antimicrobial therapy usually required, because of large number of potential pathogens. Treatment usually guided by local antibiotic policies.

M. tuberculosis

Commonly called the tubercle bacillus (primary host humans), is the usual causative agent for tuberculosis (TB).

Epidemiology

One-third of the world's population is infected with M. tuberculosis. Increase in incidence is related to poverty, population displacement, HIV and drug resistance, mostly in Asia and Africa. In Western Europe and North America, the incidence had declined over the last 30 years as a result of improvements in nutrition, housing and preventive measures, including Bacille Calmette–Gu_erin (BCG) immunisation. More recently, this decline has reached a plateau, and in some developed countries there has been an increase. In the UK, about 8,400 new cases, with about 270 associated deaths, are recognised each year; infection is more common in Asian and African immigrants, drug addicts, alcoholics, HIV-infected and other

immune compromised patients. M. tuberculosis infections are spread usually by inhalation of 'droplet nuclei' (droplets containing mycobacteria, aerosolised by coughing or sneezing, dry in the air and remain suspended for long periods) and rarely by ingestion. Incubation period is 4–16 weeks. TB is highly infectious and outbreaks may occur. Mycobacteria are able to survive for long periods in the environment, because they withstand drying.

Pathogenesis

Primary TB: inhalation of M. tuberculosis results in a mild acute inflammatory reaction in the lung parenchyma, with phagocytosis of bacilli by alveolar macrophages. M. tuberculosis, in common with other mycobacteria, is an intracellular pathogen; its survival within macrophages is related to its ability to prevent phagosomelysosome fusion. Bacilli survive and multiply within the macrophages and are carried to the hilar lymph nodes,which enlarge. The local lesion and enlarged lymph nodes are called the primary complex (referred to as the 'Ghon focus'). The host response to mycobacterial infection is via the cell-mediated immune system and results in the formation of granulomata. Histologically, granulomas consist of epithelial cells and giant cells, which eventually undergo caseous necrosis. In many individuals, the immune system kills the bacteria and the complex becomes fibrotic and calcified. In a small number of cases, a defensive barrier is built round the infection but

the TB bacteria are not killed and lie dormant. This is called latent tuberculosis; the person is not ill and is not infectious. In some patients, particularly immunocompromised individuals, microorganisms spread locally and via the bloodstream to other organs, causing widespread disease (miliary TB). Some sites become dormant and may reactivate years later. Secondary TB: may arise in two ways:

1 Dormant mycobacteria may reactivate, often as a result of lowered immunity in the patient; reactivation occurs most commonly in the lung apex, but may occur in other organs (e.g. kidney, bone).

2 A patient may become re-infected after further exposure to an exogenous source. As with primary TB, local and distant dissemination may occur.

Clinical features

Pulmonary TB: chronic cough, haemoptysis, weight loss, malaise and night sweats. Chest radiograph: apical shadowing, often with cavities.

Extrapulmonary TB: pleural tuberculosis: pleural effusion, tuberculous empyema; lymph glands: the most common site of nonpulmonary TB, typically cervical lymph nodes, particularly in children; genitourinary: sterile pyuria, with haematuria, pyrexia and malaise; meningitis: insidiousonset,withhighmortality; bone and joints: most commonly affects the

lumbar spine; abdominal: pain and ascites; miliary: multisystem involvement.

Laboratory diagnosis

Diagnosis of active infection: Microscopy of relevant specimens, including sputum, bronchoscopy material, pleural fluid, urine, joint fluid, biopsy tissue and cerebrospinal fluid. ZN stain – appearance as thin bacilli with beads (positive in <60% pulmonary; <25% extrapulmonary). A fluorescent rhodamine-auramine dye can also be used. Culture on special media for up to 12 weeks, e.g. Lowenstein–Jensen medium, which contains egg yolk, glycerol and mineral acids plus inhibitors, such as malachite green, to reduce growth of other bacteria. Specimens, e.g. sputum, contaminated with normal flora, are pre-treated with alkali to reduce microbial contamination.

Liquid cultures are now preferred due to shorter turn around time. Antibiotic sensitivity can be obtained in about 2 weeks using radiometric and non-radiometric automated systems. Biochemical tests, pigment production or DNA probes are used to confirm species identification and for rifampicin and isoniazid resistance detection.

Diagnosis of latent infection

1. Tuberculin skin test (e.g. Mantoux test): based on the inoculation of purified protein derivative (PPD), derived from tubercle culture filtrate, into the patient's skin to demonstrate cell-mediated immunity toM. tuberculosis. Relatively inexpensive and easy to perform, but false positives occur with prior BCG and environmental mycobacterial exposure.

2. Interferon Gamma test: measures the release of interferon-gamma from lymphocytes in whole blood in response to stimulation by specific tuberculous bacterial antigens. More specific than skin test, but predictive value for future active disease not yet known.

Treatment and prevention

Combinations of up to four (used to prevent emergence of resistance) anti-mycobacterial drugs (e.g. rifampicin, isoniazid, pyrazinamide and ethambutol) for 2 months (initial phase), followed by 4 months (continuous phase) of rifampicin and isoniazid). However, multiple drug resistant strains of M. tuberculosis (MDRTB) are nowemerging (<5%in the UK). Second-line antimycobacterial agents include fluoroquinolones, macrolides, cycloserine, amikacin, kanamycin and capreomycin. Treatment beyond 6 months is indicated for meningitis (usually 1 year), resistant strains and where any break in treatment has occurred. Directly observed therapy for noncompliant patients may be instigated 3 times weekly. Addition of steroids indicated in central nervous system, ureteric and pericardial disease. Strategies for prevention include improving living standards (housing, nutrition); immunization with a live attenuated vaccine (BCG), and isolation plus prompt treatment of cases as appropriate, and chemoprophylaxis when latent infection is found.

M. leprae

M. leprae (Hansen's bacillus) causes leprosy.

Epidemiology

There are over 210,000 cases of leprosy worldwide, mainly in Asia, Africa and South America. Armadillos may be an animal reservoir in the USA. Transmission follows prolonged exposure to shedders of the bacilli via respiratory secretions or ulcer discharges. The incubation period is 2–10 years; without prophylaxis up to 10% develop the disease.

Morphology and identification

M. leprae is an acid-fast bacillus. It can be grown in the footpads of mice or armadillos, from tissue culture and on artificial media.

Associated infections

There are two major types of leprosy: lepromatous and tuberculoid, with various intermediate stages:

1. Lepromatous: progressive infection, resulting in nodular skin lesions (granulomata) and nerve involvement; associated with a poor prognosis.
2. Tuberculoid: a more benign, non-progressive form that involves macular skin lesions and severe asymptomatic nerve involvement. Spontaneous healing usually results after tissue and nerve destruction.

Laboratory diagnosis

Microscopy of scrapings from skin or nasal mucosa, or skin biopsies, examined by ZN staining.

Treatment and control

Treatment: combination of dapsone plus rifampicin and/or clofazimine; Chemoprophylaxis is needed for close contacts of infected individuals, and is particularly important for young children in contact with adults with leprosy.

Environmental (atypical) mycobacteria

These grow at a variety of temperatures; some are rapid growing (3–4 days), whereas others are slower (>8 weeks). Some produce pigmented colonies in light (photochromogens) or in light and dark (scotochromogens).

They are transmitted to humans primarily from environmental or animal sources. Some species, e.g. M. avium-intracellulare, are resistant to first-line anti-mycobacterial agents.

Laboratory diagnosis

ZN positive and resembleM. tuberculosis. Distinction by gene probe or culture characteristics.

Treatment

Clinical response unrelated to in vitro antibiotic resistance pattern. Usually combination of rifampicin, ethambutol and clarithromycin continued until culture negative for one year.

Unit II

Patology: Morphology,pathogenesis,symptoms,laboratory diagnosis, preventive measures and chemotherapy caused by gram negative bacteria: E.coli, N.gonorrhoea, N.meningitidis, Pseudomonas aeruginosa, S.typhi, S.dysenteriae, Y.pestis, B.abortus, H.influenzae, V.cholerae, M.pneumoniae, T.pallidum, Rickettiaceae, Chlamydiae.

Escherichia

The genus Escherichia currently contains several species. However, E. coli is the species most frequently isolated from humans.

Epidemiology and associated Infections

Although E. coli is a harmless commensal of the human intestine, some strains (identified as particular O, H, and K serotypes) can cause infections of the gastrointestinal tract, urinary tract, biliary tract, lower respiratory tract, bloodstream, haemolytic-uraemic syndrome (HUS), haemorrhagic colitis and neonatal meningitis.

Pathogenicity

Specific fimbriae facilitate adherence to mucosal surfaces and colonisation of the intestinal and urinary tracts. The lipopolysaccharide (endotoxin) in the cell wall is liberated when Gram-negative bacteria lyse, resulting in production of inflammatory mediators (cytokines and nitric oxide) and complement activation. This results in endotoxic shock and intravascular coagulopathy. The K1 capsular polysaccharide antigen is associated with neonatal meningitis. A number of distinct infections are mediated by the different protein toxins produced by E. coli. VTEC (verocytotoxin-producing E. coli, particularly the O157:H7 serotype, are an important cause of diarrhoea and HUS. These are also referred to as enterohaemorrhagic E. coli (EHEC). Most are sporadic cases and have the following key features:

T zoonotic infections mainly from cattle, but also from vegetables washed in contaminated water;

T low infecting dose;

T acquired by eating undercooked contaminated meat and vegetables;

T damage gut endothelium, resulting in haemorrhagic colitis;

T HUS occurs in about 5% of patients, which results in renal failure, oliguria, thrombocytopenia.

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Diarrhoea caused by other E. coli:

Enteropathogenic (EPEC): cause of infantile diarrhoea;

Enterotoxigenic (ETEC): travellers' diarrhoea,non-invasive;

Table Enterobacteriaceae infections

Genus/species	Common infections
Escherichia coli	Urinary tract infection
	Intra-abdomal infection
	Wound infection
Klebsiella spp	Urinary tract infection
	Pneumonia
	Intravascular catheter-related infection
Enterobacter spp	Hospital-acquired pneumonia
Serratia spp	Wound infection
Proteus spp	Urinary tract infection
Salmonella serotypes Typhi and Paratyphi	Enteric fever and bloodstream infection
Other salmonellae	Enteritis
Shigella spp	Enteritis
Yersinia enterocolitica	Enteritis
Yersinia pestis	Plague
Yersinia pseudotuberculosis	Mesenteric adenitis

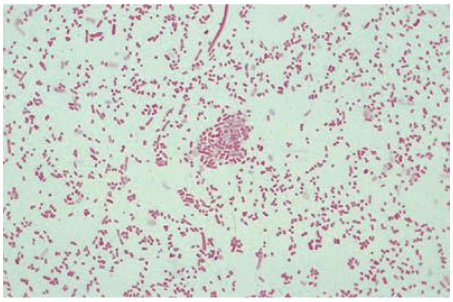


Figure Gram stain of Escherichia coli showing Gram-negative bacilli (2 mm_0.5 mm).

Laboratory diagnosis

Diagnosis is by direct isolation of the microorganism from clinical samples, e.g. faeces, urine and blood. Identification of some pathogenic strains, e.g. VTEC, EPEC, may be achieved by serotyping.

Antibacterial therapy

E. coli is commonly resistant to penicillin and ampicillin by production of b-lactamase enzymes. Production of extended spectrum b-lactamases (ESBLs), which inactivate many penicillins and cephalosporins, is an increasing problem. Antibiotics often used to treat E. coli infections include the cephalosporins, trimethoprim, ciprofloxacin and aminoglycosides; strains isolated from hospitalized patients are often more resistant to antibiotics and therefore local antibiotic sensitivity patterns need to be considered.

N. gonorrhoeae

Definition

Gram-negative kidney-shaped cocci, usually in pairs (diplococci) (Figure 7.1), aerobic.

GRAM-NEGATIVE COCCI	
N. meningitidis	Meningitis
	Bloodstream infection
N. gonorrhoeae	Urethritis, cervicitis
	Epididymitis
	Pelvic inflammatory disease
	Neonatal ophthalmia
	Bloodstream infection
	Arthritis
Moraxella catarrhalis	Upper and lower respiratory tract infections

Epidemiology

Obligate human parasite; Manywomenare asymptomatic and may act as a reservoir of infection; Highly transmissible by sexual contact; Vertical transmission to neonates may occur during passage through an infected birth canal; Occurs worldwide; Infections are most common among sexually active young adults; Genotypic (PFGE, AFLP) typing may be undertaken to differentiate between strains of gonococci, e.g. in child abuse cases.

Laboratory identification

Provisional identification can be made by microscopy if kidney-shaped Gram-negative diplococcic are seen in pus cells. Confirmation is based on cultures: growth on gonococcal selective media, colonial morphology, Gram-stain appearance, positive oxidase reaction, catalase production, biochemical reactions (including carbohydrate fermentation) and immunological tests (for detection of specific gonococcal antigens). Gonococcal DNA can also be detected directly from clinical samples, using various molecular methods.

Pathogenicity

Gonococci have cell-surface pili, which aid adherence to mucosal surfaces of the cervix, urethra, rectum and upper respiratory tract, thus initiating infection. Other virulence factors include IgA proteases. Gonococci can survive intracellularly within polymorphonucleocytes (PMNs) and some strains are also able to resist serum lysis. Re-infections occur, because protective immunity does not develop.

Associated infections

Genitourinary: urethritis (Figure 7.2), cervicitis; complications include epididymitis, prostatitis, urethral stricture, pelvic inflammatory disease and sterility; Gastrointestinal: proctitis (asymptomatic in many); Occular: hyper-acute conjunctivitis, periorbital ‘’cellulitis; Blood: bloodstream infection, endocarditis (rare);Musculoskeletal: septic arthritis (uncommon).

Microbiological diagnosis

A diagnosis can be confirmed by microscopy, culture and/or molecular analysis of pus and secretions from various sites (depending upon the infection): cervix, urethra, rectum, conjunctiva, throat and synovial fluid. Clinical samples are cultured on enriched selective media and identified as above. Specimens should be rapidly transported to the laboratory, because gonococci die readily on drying.

Blood cultures should be sent before antimicrobial therapy is commenced when disseminated infection is suspected, e.g. in sexually active patients with septic arthritis. Serology is not helpful in the diagnosis of gonococcal infection.

Treatment and prevention

Resistance to penicillins iscommon and resistance to quinolones (e.g. ciprofloxacin) is increasing. Most strains remain susceptible to cephalosporins (e.g. ceftriaxone). Single-dose therapies are recommended to increase patient compliance.

Figure Intracellular Gram-negative diplococci (arrowed) of Neisseria gonorrhoeae (0.8 mmdiameter) in neutrophils.

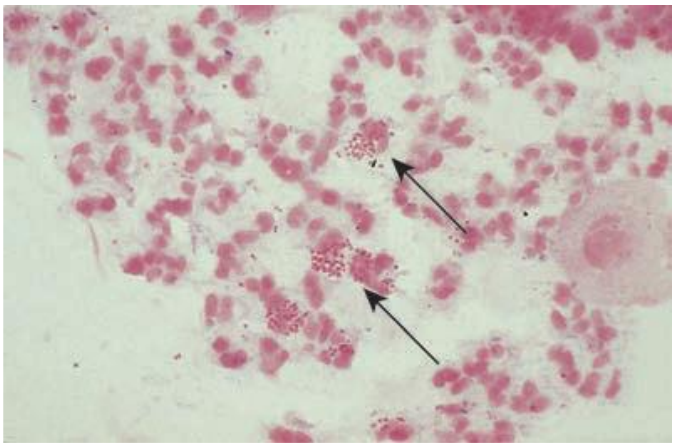
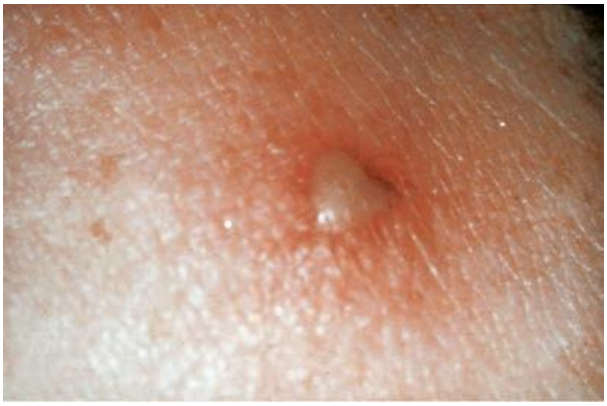


Figure Gonococcal skin lesion.



No Gram-negative cocci vaccine is available. Prevention of gonorrhea includes sex education, promotion of public awareness and the use of condoms. Contact tracing is essential in preventing further spread of disease.

N. meningitidis

Definition

Gram-negative kidney-shaped cocci, usually in pairs (diplococci); aerobic.

Epidemiology

Humans are the only natural host. Ten percent of the population are asymptomatic carriers in the upper respiratory tract. Spread from human to human is via droplets or direct contact. Sporadic cases, clusters and epidemics occur worldwide. Serotyping (performed by reference laboratories) can be used to identify outbreaks. At least 13 serogroups of meningococci have been identified. Typing is based on capsular polysaccharides; the most important groups are A, B, C, D, X, Y and W-135. In the UK, the majority of cases are caused by group B and group C is now uncommon.

Patients with genetic or drug induced defects of the later components of the complement system are predisposed to meningococcal infections. In temperate climates most infections occur in patients aged less than 5 years or 15–19 years.

Laboratory identification

Provisional identification is by microscopy when kidney-shaped, Gram-negative cocci are seen within polymorphonucleocytes. Confirmation of identification is based on cultures: colonial morphology, Gram-stain appearance, positive oxidase test and biochemical reactions (including carbohydrate fermentation).

Pathogenicity

A polysaccharide capsule protects against phagocytosis and promotes intracellular survival. Cellwall endotoxins (lipopolysaccharide) are important in the pathogenesis of severe meningococcal disease. Colonisation of nasopharynx occurs; local invasion may follow with bacteraemia and meningeal involvement.

Associated infections

Central nervous system: meningitis;

Blood: bloodstream infection (‘septicaemia’) without meningitis (less common);

Musculoskeletal: osteomyelitis, septic arthritis;

Occular: conjunctivitis;

Genitourinary: urethritis;

Respiratory: pneumonia (rare);

Cardiovascular: pericarditis (rare).

Microbiological diagnosis

Specimens: cerebrospinal fluid (CSF) or pus for microscopy, culture, antibiotic susceptibility testing and PCR;

Blood cultures: should also be sent, in addition to a blood sample for PCR;

Nasopharyngeal swabs: can determine carriage of meningococci.

Treatment

Penicillin or cefotaxime are first-line treatments, chloramphenicol is still used for patients with a true penicillin allergy; rifampicin or ciprofloxacin should also be given to eradicate nasopharyngeal carriage, except in patients treated with certain cephalosporins.

Prevention includes antibiotic prophylaxis for close contacts. Meningococcal group C vaccine (group B vaccine being developed) and tetravalent (A, C, Y, W135) polysaccharide vaccine are available for travellers to high incidence areas.

P. aeruginosa

Epidemiology

P. aeruginosa is an important microorganism in healthcare-associated infection. It is a normal commensal in the human gastrointestinal tract, but may colonise other sites when host defences are compromised, including burns and leg ulcers, the respiratory tract of patients with cystic fibrosis or bronchiectasis, and the urinary tract of patients with long-term, indwelling, urethral catheters.

P. aeruginosa, as with other members of the genus, has the ability to grow with minimal nutrients, e.g. in water and in the presence of some disinfectants; these properties are the key to its role as a hospital pathogen.

Morphology and identification

The microorganism grows on most media, producing a characteristic greenish pigment. It can be distinguished from the Enterobacteriaceae by its oxidative metabolism (oxidase-positive) and the

inability to grow anaerobically, except on nitrate. The different species of the genus Pseudomonas can be distinguished by biochemical tests.

Pathogenicity

P. aeruginosa is relatively non-pathogenic; it characteristically causes infections in hospitalized patients, particularly those who are immunocompromised. The microorganism produces several enzymes that allow spread through tissues (elastase) and a protease that breaks down IgA on mucosal surfaces. It also produces cytotoxins (exotoxin A) and other factors that inhibit host defences, including a rhamnolipid and an alginate exopolysaccharide.

Associated infections

P. aeruginosa principally causes opportunist infections including:

Skin and soft tissues: infections associated with burns and cutaneous ulcers;

Respiratory tract: ventilator-associated pneumonia and hospital acquired pneumonia and lower respiratory tract infections in cystic fibrosis and bronchiectasis patients;

Urinary tract: associated with long-term urethral catheterisation;

Invasive: bloodstream infection can follow primary infection at any site, but is more common in immune compromised patients;

Eye: contact lens-associated infections;

Ear nose and throat: otitis externa.

Laboratory diagnosis

Isolation of the microorganism from relevant body sites. The isolation of P. aeruginosa from several patients may suggest hospital cross-infection. In such circumstances, strains of P. aeruginosa can be further characterised by serotyping or molecular biological techniques.

Treatment

One of the characteristics of P. aeruginosa is resistance to antibiotics; some newer antibiotics have been designed specifically to combat P. aeruginosa. Clinically important anti-pseudomonal antibiotics include: aminoglycosides (e.g. gentamicin); broad-spectrum penicillin/beta-lactamse inhibiter combinations (e.g. piperacillin/tazobactam); third-generationcephalosporins(e.g.ceftazidime); carbapenems (e.g. imipenem and meropenem); monobactams (e.g. aztreonam); quinolones (e.g. ciprofloxacin).

In hospital units where antibiotics are used frequently (e.g. special care baby units, ICUs, cystic fibrosis clinics), P. aeruginosa isolates may become resistant to these antibiotics. Isolation of patients colonised by multi-resistant P. aeruginosa strains is an important part of controlling hospital infections.

Salmonella

The genus Salmonella contains a large number of species (more correctly, serotypes). Salmonella serotype Typhi and Salmonella serotype Paratyphi cause enteric fever (typhoid or paratyphoid); other salmonellae cause enteritis.

Classification

Over 2,000 serotypes are distinguished, most of which belong to the species S. enterica. However, many of these have been given binomial names (e.g. Salmonella typhimurium and Salmonella enteritidis), although they are not separate species. In clinical practice, laboratories identify microorganisms according to their binomial name. Salmonella spp. have both H and O antigens. There are over 60 different O antigens, and individual strains may possess several O and H antigens; the latter can exist in variant forms, termed 'phases'. Salmonella serotype Typhi also has a capsular polysaccharide antigen referred to as 'Vi' (for virulence), which is related to invasiveness.

Agglutination tests with antisera for different O and H antigens form the basis for the serological classification of Salmonella spp. Further strain differentiation of Salmonella spp. for epidemiological purposes can be achieved by phage typing.

Epidemiology

Salmonella spp. are commensals of many animals, including poultry, domestic pets, birds and humans. Transmission is via the faecal-oral route. The infective dose is relatively high and multiplication in food is important Enterobacteriaceae for effective transmission. A chronic carrier state can occur.

Morphology and identification

Salmonella spp. are motile and produce acid, and occasionally gas, from glucose and mannose. They are resistant to sodium deoxycholate, which inhibits many other Enterobacteriaceae. Deoxycholate agar is used as a selective media to isolate Salmonella spp. from stool specimens. Salmonella spp. do not ferment lactose and form pale colonies on MacConkey's medium; on xylose lysine deoxycholate (XLD) agar, many Salmonella spp. form pale colonies with black centres as a result of H2S production. This aids recognition of Salmonella colonies in mixed cultures. Further biochemical tests are required for definitive identification. Serotyping of O and H antigens by slide agglutination is used for speciation.

Pathogenicity

Salmonella spp. can survive the acidic pH of the stomach and invade the gut, resulting in an inflammatory response and subsequent diarrhoea.

Associated infections

Salmonella infections: (caused by non-typhoid salmonellae;

Enterocolitis/gastroenteritis: rarely associated with bloodstream infection, osteomyelitis, septic arthritis or abscesses;

Enteric fever: caused by Salmonella serotype

Typhi and Salmonella serotype Paratyphi. Enteric fever is prevalent in Asia, South America and Africa; approximately 300 cases per year in the UK. Salmonella spp. may persist in biliary and urinary tracts after recovery.

Laboratory diagnosis

Enterocolitis: culture of stool samples on selective media, e.g. XLD, DCA (deoxycholate citrate agar), and enrichment media, e.g. selenite broth; identification of Salmonella spp. by biochemical and agglutination tests. Phage typing can be used for typing individual strains. Enteric fever: isolation of Salmonella serotypes Typhi or Paratyphi from blood cultures (first week of infection), urine (second week) or faeces (first week onwards). Serology (Widal's test) is now rarely performed, because of unreliable results.

Treatment and prevention

Enteric fever: ciprofloxacin (though resistance is increasing);

Enterocolitis: self-limiting; antibiotics (e.g. ciprofloxacin and cefotaxime) reserved for severe or invasive infection, particularly in the elderly, very young or 'immunocompromised' individuals;

Typhoid immunisation; avoidance of contaminated water/food.

Shigella

Classification

The main pathogenic species are S. sonnei, S. boydii, S. dysenteriae and S. flexneri. They are distinguished by biochemical reactions and antigenic characteristics ('O' antigens).

Epidemiology

Obligate human pathogens with no animal reservoirs; transmission via faecal-oral route with low infective dose (10–200 microorganisms). Direct person-to-person spread is common; chronic carrier state is rare.

Morphology and identification

Shigella spp. are non-motile (they have no flagella). They are resistant to sodium deoxycholate and grow on deoxycholate agar (see Salmonella). They are non-lactose or late lactose (S. sonnei) fermenters. Further biochemical tests are carried out for definitive identification and serotyping by slide agglutination is used for speciation.

Pathogenicity

Shigella spp. express an intestinal adherence factor, which aids colonisation within the gut. They cause disease by invasion and destruction of the colonic mucosa, and also produce an enterotoxin (cytotoxin) known as Shiga toxin, which can cause Enterobacteriaceae 43 microangiopathy, HUS and thrombocytopenic purpura.

Associated infections

Self-limiting diarrhoeal illness, dysentery (diarrhea with blood and pus, fever, abdominal pain) (HUS and bloodstream infection are rare).

Laboratory diagnosis

Stool culture on selective media, e.g. XLD.

Treatment

Antibiotics (e.g. ciprofloxacin) reserved for severe cases (often caused by S. dysenteriae).

Proteus

The genus Proteus contains a number of species, e.g. P. mirabilis and P. vulgaris. Characteristics include: non-lactose fermenting, produce pale colonies on MacConkey's agar; motile, tendency to 'swarm' on blood agar; important cause of urinary tract and occasionally abdominal wound infection.

Yersinia

The genus Yersinia contains three human pathogens: Y. pestis, Y. pseudotuberculosis and Y. enterocolitica; these species are identified by biochemical tests.

Y. pestis

Y. pestis is the cause of plague (black death). Although mainly of historical interest in Europe, plague remains endemic in some areas of the world. It is primarily a pathogen of rodents and is transmitted to humans via infected fleas; lymph nodes associated with the flea bite enlarge to form a bubo (bubonic plague). Bloodstream invasion and pneumonia may follow (pneumonic plague). Person-to-person spread via droplets occurs in pneumonic plague. Y. pestis can be isolated from blood, bubo aspiration, sputum, throat swabs and skin scrapings. Treatment for Y. pestis infection is with an aminoglycoside or tetracycline. Laboratory diagnosis is by microscopy and culture of clinical material.

Brucella abortus

Definition

Small, Gram-negative coccobacilli; grows slowly aerobically. The genus Brucella contains four species responsible for human infections: Brucella melitensis, B. abortus, B. suis and B. canis.

Epidemiology

Worldwide distribution, but great variation in incidence of infection; Zoonotic infection (the main reservoir is in animals and transmission occurs from animals to humans); The main reservoirs for infection are goats and sheep (B. melitensis), cattle (B. abortus), pigs (B. suis) and dogs (B. canis). In the UK, B. melitensis is the most common species isolated, but is rare. (Fewer than 20 cases are reported per year in the UK); B. melitensis is found most commonly in the Mediterranean area; Infection is

associated with close contact with farm animals, e.g. farm workers, veterinary surgeons, or occurs as a result of ingestion of unpasteurised cows' or goats' milk.

Laboratory identification

Microscopy: Gram-negative bacilli. Brucella species are aerobic; they require CO2 for growth and are slow growers, requiring 2–3 weeks for colonies to be visible. Identification is based on Gram stain, colony morphology, growth characteristics and biochemical reactions.

Pathogenicity

Brucella species are intracellular pathogens that are capable of surviving and replicating within phagocytic cells. The principal virulence factor is the cell wall lipopolysaccharide (LPS). Infection with Brucella is typical of an intracellular pathogen, with the formation of multiple granulomatous lesions in several organs.

Associated infections

Brucellosis is an infection with non-specific symptoms including fevers, sweats, general malaise, headaches, depression and anorexia. Onset can be acute or insidious. Localised infection can occur: Central nervous system: acute or chronic meningitis, brain abscess; Gastrointestinal: liver abscesses/granulomas, hepatitis; Musculoskeletal: vertebral osteomyelitis and discitis, sacroiliitis, septic arthritis; Cardiovascular: infective endocarditis; Respiratory: pneumonia, lung abscess.

Laboratory diagnosis

Diagnosis is made by direct isolation from blood cultures, CSF or culture of aspirated bone marrow after prolonged incubation. Note: routine blood cultures are normally incubated for 3–7 days, therefore it is important to inform the laboratory if brucellosis is suspected. Serological tests, including ELISA (enzymelinked immunosorbent assay) to detect serum antibodies against Brucella are available; these aid diagnosis because many patients present late in their illness.

Treatment and prevention

Prolonged treatment isnecessarywitha tetracycline (6 weeks) and an aminoglycoside (2–3 weeks), or tetracycline and rifampicin (6 weeks). This reflects the intracellular location of the microorganisms. Prevention is achieved by eradication of Brucella in the animal population and avoidance of raw milk and associated products.

Haemophilus influenzae

Description/definition

Gram-negative bacilli; fastidious growth requirements; aerobic and anaerobic growth.

Epidemiology

Common commensal in the upper respiratory tract; Capsulated (more pathogenic) strains are also carried in a small number of healthy individuals; Carriers are an important reservoir for invasive disease; Transmission is by respiratory secretions and droplets; Most infections occur in children and patients with underlying respiratory disease; Type b strains (see Pathogenicity) were a common cause of invasive infection, particularly in small children (aged 6 months to 5 years), prior to introduction of the Hib vaccine.

Laboratory identification

Gram-negative bacilli;

Variable oxidase reaction;

Nutritionally demanding and grows only on enriched media containing haemin (factor X) and nicotinamide adenine dinucleotide (factor V); Simple nutrient agar contains no X or V factor and strains of H. influenzae will only grow around paper discs containing both these factors

Grows on 'chocolate agar' but not on blood agar (blood agar contains factor X but insufficient factor V. Heat treatment of blood before incorporation in agar produces a medium known as 'chocolate agar', which contains both factors for H. influenzae to grow); Serotyping by agglutination tests can be carried out on capsulated strains, when isolated from invasive infections.

Pathogenicity

Strains may be capsulated or non-capsulated.The polysaccharide capsule of certain strains is a major virulence factor. Capsulated strains are divided into six serotypes (designated a–f) on the basis of polysaccharide capsular antigens. H. influenzae type b is particularly pathogenic. Antibodies to the type b capsule protect against invasive infections. Non-type b capsulated strains occasionally cause invasive infections. Non-capsulated strains are an important cause of respiratory tract infections. Another component of the cell wall of H.

influenzae that contributes to pathogenesis is lipopolysaccharide (LPS), which has similar biological activity to other Gram-negative endotoxins. H. influenzae also possesses pili (fimbriae) and expresses a surface protein called Hia, both of which facilitate adherence to cells of the respiratory tract. Associated infections . Respiratory: pneumonia, epiglottitis, otitis media, sinusitis, exacerbation of chronic lung disease;

Associated infections

Bordetella B. pertussis Whooping cough

B. parapertussis Whooping cough-like syndrome

Brucella B. abortus Brucellosis

B. melitensis

B. suis

B. canis

Haemophilus H. influenzae (type b) Meningitis*

Epiglottitis*

Bone and joint infections*

Exacerbations of chronic lung disease

H. parainfluenzae Exacerbations of chronic lung disease

H. ducreyi Genital ulcers (chancroid)

Pasteurella P. multocida Cellulitis after animal bites

Haemophilus influenza requires both factors for growth (arrowed). Haemophilus and other fastidious Gram-negative bacteria Central nervous system: meningitis; Musculoskeletal: osteomyelitis, septic arthritis (uncommon); Skin and soft tissues: cellulitis (including orbital cellulitis); Cardiovascular: endocarditis (rare).

Laboratory diagnosis

Respiratory: send respiratory secretions for culture and sensitivity. Epiglottitic swabs for microscopy and culture should be collected under direct vision by an ENT specialist. Sinus washout fluid can be cultured. Central nervous system: send cerebrospinal fluid (CSF) for microscopy and culture. Musculoskeletal: send bone or synovial fluid for microscopy and culture. Skin and soft tissues: skin swabs are rarely helpful in cellulitis. Cardiovascular: send 3 sets of blood cultures if endocarditis suspected.

Treatment and prophylaxis

b-lactamase production and intrinsic resistance to ampicillin and many other b-lactam antibiotics is common, so

treatment is directed by susceptibility testing. Third-generation cephalosporins, e.g. cefotaxime or ceftriaxone, are common empirical therapy for serious infections. A vaccine ('Hib') to the type b polysaccharide capsule has ledto a large reduction inthe numberof invasive H. influenzae type b infections. Rifampicin is used for the prophylaxis of contacts of cases of H. influenzae type b meningitis, and as an adjunct to therapy to reduce nasopharyngeal carriage.

V. cholerae

Classification

V. cholerae strains are subdivided according to O-antigens. V.cholerae O1 is the cause of cholera. Other V. cholerae(non-O1) strains may occasionally cause diarrhoea. V. cholerae O1 has a number of biotypes, including the 'classic' strain, which was the principal cause of cholera until the mid-1960s. The 'El Tor' biotype has been responsible for most cases of cholera over the last two decades. In the 1990s, O139 caused epidemics in Southea Asia.

Epidemiology

Found in water contaminated with human faeces; no animal reservoirs; Important cause of severe infection in developing countries, where potable water and sewage systems are poor;Transmitted via consumption of contaminated food or water.

Morphology and identification

V. cholerae is characterised by an ability to grow in alkaline conditions (pH > 8.0). Alkaline broth is used to gro the microorganism selectively from faecal samples. A special selective medium (thiosulphate–citrate–bile salt–sucrose agar) is also used. V. cholerae forms characteristic yellow colonies on this medium. 56 Campylobacter, Helicobacter and Vibrio Specific slide agglutination reactions for 'O' antigens distinguish V. cholerae from non-cholera Vibrio spp.. Biochemical tests are used for confirmation.

Pathogenicity

V. cholerae produces an enterotoxin that acts on intestinal epithelial cells, stimulating adenyl cyclase activity. This results in water and sodium ions passing into the gut lumen to produce profuse, watery diarrhoea (rice-wate appearance).

Associated infections

Acute enteritis.

Laboratory diagnosis

Isolation of microorganism from faeces on selective media.

Prevention

Avoidance of contaminated food; oral vaccines suitable for travellers.

Treatment

Rehydration; ciprofloxacin shortens duration of

illness.

Treponema pallidum

Morphology:

a. Gram negative spirochete (helically-coiled cell), motile, non-spore forming, non-encapsulated microaerophilic bacteria, 6 to 15 μm long and 0.1 to 0.2 μm wide.

b. obligate intracellular pathogen

c. Reservoirs -Humans (only reservoir, not normal flora)

d. Transmission - direct contact, sexual, perinatal

e. Too thin to be seen with light microscopy in specimens stained with Gram stain or Giemsa stain

f. Motile spirochetes can be seen with darkfield micoscopy

g. Staining with anti-treponemal antibodies labeled with fluorescent dyes

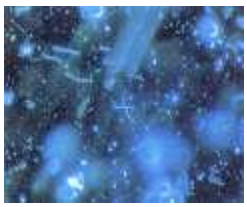


Fig: Darkfield Microscopy of *Treponema pallidum*

Cultural Characteristics:

a. The *Treponema* are motile, helically coiled organisms having a corkscrew-like shape,.

b. They stain very poorly because their thickness approaches the resolution of the light microscope.

c. *Treponema* are delicate organisms requiring pH in the range 7.2 to 7.4, temperatures in the range

30°C to 37°C and a microaerophilic environment.

d. The structure of these organisms is somewhat different: the cells have a coating of glycosamino glycans, which may be host-derived, and the outer membrane covers the three flagella that provide motility.

e. In addition, the cells have a high lipid content (cardiolipin, cholesterol), which is unusual for most bacteria. Cardiolipin elicits "Wassermann" antibodies that are diagnostic for syphilis.

f. Multiplication is by binary transverse fission.

g. Treponemes have not yet been cultured in vitro.

Antigenic structure:

- Outer membrane proteins promote adherence
- Hyaluronidase may facilitate perivascular infiltration
- Antiphagocytic coating of fibronectin
- Tissue destruction and lesions are primarily result of host's immune response (immunopathology)

Pathogenesis:

Humans are the only natural host for *T pallidum* subsp *pallidum*, and infection occurs through sexual contact. The organisms penetrate mucous membranes or enter minuscule breaks in the skin. In women the initial lesion is usually on the labia, the walls of the vagina, or the cervix; in men it is on the shaft or glans of the penis. A chancre also may occur on lips, tongue, tonsils, anus, or other skin areas. The observation, made in a number of in vitro studies, that *T pallidum* subsp *pallidum* and subsp *pertenue* specifically attach to numerous cell types is believed to reflect the ability of these bacteria to infect diverse tissues and organs. To disseminate away from the site of initial entry, organisms must traverse the viscous ground substance between tissue cells. There is evidence that *Treponema pallidum* subsp *pallidum* elaborates an enzyme capable of degrading hyaluronic acid within the ground substance, thereby potentially facilitating hematogenous dissemination of organisms.

Clinical Features:

Primary Syphilis

- a single small painless depressed ulcer with elevated margins ("chancre") at the site of initial infection, fever, headache, anorexia and local lymphadenomegaly

- primarily occurs on the external genitalia, periorally (if oral intercourse) or perianally (if anal intercourse)
- occurs 3-6 weeks after initial infection
- spontaneously resolves in 3-6 weeks
- caused by *Treponema pallidum* infection of the skin
- may progress to secondary syphilis

Secondary Syphilis

- small flat erythematous rashes of the palms and soles, small painless papules ("condyloma lata") of the groin and axilla, and generalized lymphadenomegaly
- occurs 12-18 weeks after initial infection
- spontaneously resolves in 3-6 weeks
- caused by *Treponema pallidum* septicemia
- may progress to tertiary syphilis

Tertiary Syphilis

- nodular well circumscribed caseating granulomas ("gummas") of the skin, liver and bone, obliterative endarteritis of the vasa vasorum leading to aortic aneurysm ("cardiovascular syphilis"), meningitis, obliterative endarteritis of the cerebral arteries leading to cerebral infarct, and permanent central neuronal damage leading to general paresis and tabes dorsalis ("neurosyphilis")
- occurs 3-15 years after initial infection
- occurs in 30% of untreated patients
- caused by *Treponema pallidum* accumulation in tissues

Early Congenital Syphilis

- small flat erythematous rashes of the palms and soles, condylomalata of the groin and axilla, osteitis, rhinitis (snuffles"), hepatosplenomegaly and generalized lymphadenomegaly
- occurs immediately after birth
- spontaneously resolves in 1-3 weeks
- caused by intrauterine *Treponema pallidum* infection "

***Treponema pallidum* septicemia**

- may progress to late congenital syphilis

Late Congenital Syphilis

- gummas (see above) of the cartilage of the nose, the bone of the hard palate and the teeth leading to deformation of the face ("bulldog facies"), gummas of the tibia and fibula leading to deformation of the legs ("saber shins"), and neurosyphilis
- occurs 1-3 years after birth
- caused by *Treponema pallidum* accumulation in tissues

Laboratory diagnosis:

Tests: After the examination, a blood test for syphilis will be done. Besides this you may be tested for other sexually transmitted infections, including HIV.

Blood test:

Infection with syphilis causes your body to make antibodies against the syphilis bacteria. When your blood is tested, it may show the antibodies that are present. A positive result means that you either have the infection or have had it in the past (the antibodies persist in the body for years; even after successfully treatment of an infection). If the blood test is negative, it does not necessarily mean that you are not infected. The antibodies against syphilis bacteria may not be detected for up to three months after infection. Your doctor may advise repeat test after three months to confirm the diagnosis. Blood test for syphilis is done in every pregnant woman as the infection can affect the baby (it can result in death of the foetus or newborn baby or cause other complications). The test is usually done at weeks 11-20 of pregnancy. The common blood tests done for syphilis include:

- RPR (rapid plasma reagin).
- VDRL (venereal disease research laboratory).
- FTA-ABS (fluorescent treponemal antibody absorption) or MHA-TP (microhemagglutination assay for T pallidum).

Swab: If the patient has sores the doctor will take a sample from the sore and examine it under a microscope (perform a dark-field microscope examination). The test is useful in the primary and also sometimes in the secondary phase of infection.

Spinal fluid examination: During the tertiary phase, the examination of a sample of spinal fluid obtained by spinal puncture may be done to check for infection and to measure the success of treatment.

Treatment:

a. Recommended regimen:

i. Benzathine penicillin G 2.4 million units IM once

b. Non-pregnant penicillin-allergic adults *

c. Data to support the use of alternatives to penicillin are limited and if used, close follow-up is essential

i. Doxycycline 100mg orally twice daily for two weeks or

j. Tetracycline 500mg orally 4 times a day for two weeks or

k. Adherance is poor (i.e., dosing and gastrointestinal effects)

l. Ceftriaxone1 g IM daily x 8-10 d or

m. (Azithromycin 2 g po)…not recommended in CA

d. Efficacy in HIV + persons not studied so use with caution

Prevention and control:

a. Sanitary: As with other sexually transmitted diseases (STDs), use of a condom helps prevent infection.

b. Immunological: None are available.

c. Chemotherapeutic: Benzathine penicillin (long acting) or penicillin G are the drugs of choice. One must be aware of a possible Jarisch-Herxheimer reaction following treatment of secondary or tertiary syphilis, however. The rapid release of treponemal antigens after lysis by penicillin can cause hypersensitivity reactions in some persons.

Rickettsia

Definition

Rickettsiaceae cause a number of important human infections, including typhus and the related spotted fevers.

They are small, Gram-negative bacilli (0.2–1 mm diameter); obligate intracellular pathogens; utilise

ATP from host cell; grow only in tissue culture. The genus contains a number of species that cause human infection (Table).

Epidemiology

Rickettsial infections are zoonoses with a variety of animal reservoirs and insect vectors. Associated infections Epidemic or louse-borne typhus, murine typhus, scrub typhus and spotted fevers.

Laboratory diagnosis

This is by serology. The Weil–Felix test detects cross-reacting antibodies to Rickettsiae, which agglutinate certain strains of Proteus (OX-19 and OX-2). The test is non-specific and has now been superseded by more specific serological tests based on purified rickettsial antigens (immunofluorescence assays and ELISA).

Treatment and prevention

Treatment is with tetracycline or chloramphenicol. Infection can be prevented by avoidance of the various vectors. A vaccine to R. prowazekii is available.

Species	Principal host/reservoir	Vector	Disease
R. typhi	Rats	Fleas	Murine typhus
R. prowazekii	Humans/squirrels	Lice	Epidemic or Louse-borne typhus
R. tsutsugamushi	Rats	Mites	Scrub typhus
R. akari	Mice	Mites	Rickettsial pox
R. rickettsii[a]	Dogs	Ticks	Rocky mountain spotted fever

[a]Tick-borne spotted fevers in areas of the world outside the USA carry a variety of names and are caused by Rickettsiae very similar to *R. rickettsii* (e.g. Boutonneuse fever caused by *R. conorii* occurs in the Mediterranean region).

Vectors and infections associated with *Rickettsia*

Chlamydiae

The Chlamydiae are bacterial phylum and class whose members are a group of obligate intracellular bacteria, whose members are remarkably diverse, ranging from pathogens of humans and animals to symbionts of ubiquitous protozoa. They are ovoid in shape and stain Gram-negative.

Historically it was believed that all Chlamydiae species had a peptidoglycan-free cell wall, but recent work demonstrates a detectable presence of peptidoglycan, as well as other important proteins. Many species belonging to this order are susceptible to antimicrobial agents. All known Chlamydiae only grow by infecting eukaryotic host cells. They are as small as or smaller than many viruses. They are dependent on replication inside the host cells, thus some species are termed obligate intracellular pathogens and others are symbionts of ubiquitous protozoa. Most intracellular Chlamydiae are located in an inclusion body or vacuole. Outside cells, they survive only as an extracellular infectious form. Chlamydiae can grow only where their host cells grow, and develop according to a characteristic biphasic developmental cycle.Therefore, Chlamydiae cannot be propagated in bacterial culture media in the clinical laboratory. Chlamydiae are most successfully isolated while still inside their host cells. Chlamydiae is the most common bacterial STD in the United States and 2.86 million chlamydiae infections are reported annually.

History

Chlamydia-like disease affecting the eyes of people was first described in ancient Chinese and Egyptian manuscripts. A modern description of chlamydia-like organisms was provided by Halberstaedrrter and von Prowazek in 1907. Chlamydial isolates cultured in the yolk sacs of embryonating eggs were obtained from a human pneumonitis outbreak in the late 1920s and early 1930s, and by the mid-20th century, isolates had been obtained from dozens of vertebrate species. The term chlamydia (a cloak) appeared in the literature in 1945, although other names continued to be used, including Bedsonia, Miyagawanella, ornithosis-, TRIC-, and PLT-agents. In 1956, Chlamydia trachomatis was first cultured by Tang Fei-fan, though they were not yet recognized as bacteria.

Nomenclature

In 1966, Chlamydiae were recognized as bacteria and the genus Chlamydia was validated. The order Chlamydiales was created by Storz and Page in 1971. The class Chlamydiia was recently validly published. Between 1989 and 1999, new families, genera, and species were recognized. The phylum Chlamydiae was established in Bergey's Manual of Systematic Bacteriology.By 2006, genetic data for over 350 chlamydial lineages had been reported,

Taxonomy and molecular signatures

The Chlamydiae currently contain eight validly named genera, and 14 genera.The phylum presently consist of two orders (Chlamydiales, Parachlamydiales) and nine families within a single class (Chlamydiia).Only four of these families are validly named (Chlamydiaceae, Parachlamydiaceae, Simkaniaceae, Waddliaceae) while five are described as families (Clavichlamydiaceae, Criblamydiaceae, Parilichlamydiaceae, Piscichlamydiaceae, and Rhabdochlamydiaceae). The Chlamydiales order as recently described contains the families Chlamydiaceae, and the Clanchiamydiaceae, while the new Parachlamydiales order harbors the remaining seven families.This proposal is supported by the observation of two distinct phylogenetic clades that warrant taxonomic ranks above the family level. Molecular signatures in the form of conserved indels (CSIs) and proteins (CSPs) have been found to be uniquely shared by each separate order, providing a means of distinguishing each clade from the other and supporting the view of shared ancestry of the families within each order. The distinctness of the two orders is also supported by the fact that no CSIs were found among any other combination of families.

Molecular signatures have also been found that are exclusive for the family Chlamydiaceae. The Chlamydiaceae originally consisted of one genus, Chlamydia, but in 1999 was split into two genera, Chlamydophila and Chlamydia. The genera have since 2015 been reunited where species belonging to the genus Chlamydophila have been reclassified as Chlamydia species. However, CSIs and CSPs have been found specifically for Chlamydophila species, supporting their distinctness from Chlamydia, perhaps warranting additional consideration of two separate groupings within the family. CSIs and CSPs have also been found that are exclusively shared by all Chlamydia that are further indicative of a lineage independent from Chlamydophila, supporting a means to distinguish Chlamydia species from neighbouring Chlamydophila members.

Phylogenetics

The Chlamydiae form a unique bacterial evolutionary group that separated from other bacteria about a billion years ago, and can be distinguished by the presence of several CSIs and CSPs. The species from this group can be distinguished from all other bacteria by the presence of conserved indels in a number

of proteins and by large numbers of signature proteins that are uniquely present in different Chlamydiae species. Reports have varied as to whether the Chlamydiae are related to the Planctomycetales or Spirochaetes. Genome sequencing, however, indicates that 11% of the genes in Protochlamydia amoebophila UWE25 and 4% in the Chlamydiaceae are most similar to chloroplast, plant, and cyanobacterial genes. Cavalier-Smith has postulated that the Chlamydiae fall into the clade Planctobacteria in the larger clade Gracilicutes. However, phylogeny and shared presence of CSIs in proteins that are lineage-specific indicate that the Verrucomicrobia are the closest free-living relatives of these parasitic organisms. Comparison of ribosomal RNA genes has provided a phylogeny of known strains within Chlamydiae.

Human pathogens and diagnostics

Three species of Chlamydiae that commonly infect humans are described:

- Chlamydia trachomatis, which causes the eye-disease trachoma and the sexually transmitted infection chlamydia
- Chlamydophila pneumoniae, which causes a form of pneumonia
- Chlamydophila psittaci, which causes psittacosis

The unique physiological status of the Chlamydiae including their biphasic lifecycle and obligation to replicate within a eukaryotic host has enabled the use of DNA analysis for chlamydial diagnostics. Horizontal transfer of genes is evident and complicates this area of research. In one extreme example, two genes encoding histone-like H1 proteins of eukaryotic origin have been found in the prokaryotic genome of C. trachomatis, an obligate intracellular pathogen.

Unit III

Diseases caused by viruses: Picornavirus, Orthomyxoviruses, Rhabdoviruses, Reoviruses, Pox viruses, Herpes viruses, Papova viruses, Retro viruses (including HIV/AIDS), Hepatitis viruses.

Picornaviruses

Introduction

The picornaviruses are small (22 to 30 nm) nonenveloped, single-stranded RNA viruses with cubic symmetry. The virus capsid is composed of 60 protein subunits, each consisting of four poly-peptides VP1–VP4. Because they contain no essential lipids, they are ether resistant. They replicate in the cytoplasm. The picornaviruses that affect humans are the enteroviruses, found primarily in the gut; the rhinoviruses, found in the upper respiratory tract and hepatovirus (Hepatitis A virus) in the intestine and liver.

Structure

Each capsid is composed of 60 copies of four structural proteins of which each proto-meter consists of four polypeptides known as VP1, VP2, VP3 and PV4. VP1-VP3 are exposed on the virion surface, while VP4 lies buried in close association with the RNA core (Fig. 17.21). All the VP polypeptides originate from one protomer known as VPO that is cleaved to give the different capsid components. Immunogenic sites are located on the exposed external parts of the capsid.

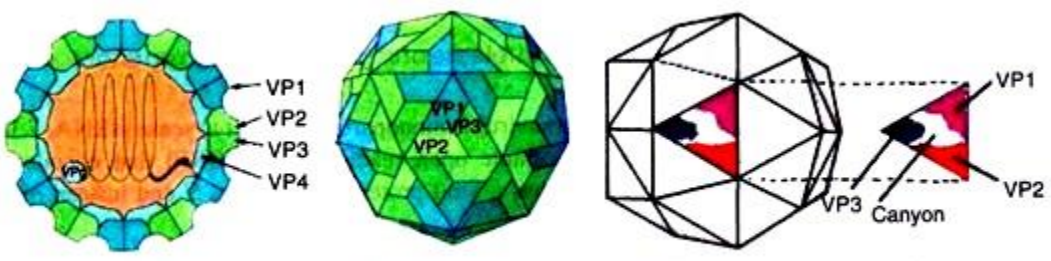


Fig. 17.21 : Structure of virion of picornavirus.

All the subgroups are structurally identical. They have icosahedral capsid of 27-30 nm which is composed of 32 capsomers. The length of viral genome is about 2500 nm; therefore it is tightly packaged within the capsid along with substances such as sodium ions which cancels out the negative charges on RNA caused by the phosphate groups. The uptake of un-enveloped viruses always considered to involve endocytosis into an endosome i.e. it is pH-dependent and sensitive to ionophores and lysosomotropic agents. Five VP1 protein subunits at the 5 fold axis of symmetry form a canyon in the capsid which is the recognition site for the receptor.

Clinical Manifestations

Enteroviruses are implicated in many diseases, including undifferentiated febrile illnesses, upper and lower respiratory tract infections, gastrointestinal disturbances, conjunctivitis, skin and mucous membrane lesions, and diseases of the central nervous system, muscles, heart, and liver. Less commonly, enteroviruses are associated with generalized neonatal infections, diabetes mellitus, pancreatitis, orchitis, and occasionally hemolytic-uremic syndrome and intrauterine infections. A new disease called wandering myoclonus was discovered in China (see below). Rhinoviruses cause mainly upper (e.g. coryza) and lower respiratory tract illnesses

Classification and Antigenic Types

The family *Picornaviridae* comprises five genera: *Enterovirus, Hepatovirus* and *Rhinovirus*, which infect humans: *Apthovirus* (foot-and-mouth disease virus), which infects cloven-hoofed animals and occasionally humans; and *Cardiovirus*, which infects rodents. At the time of writing, 67 human enterovirus serotypes and 115 rhinovirus serotypes are known.

Picornaviruses do not have a common group-specific antigen. However, antigenic sharing is observed between a few serotypes. Each serotype has a type-specific antigen, which is identifiable by neutralization tests.

Pathogenesis

When the portal of entry for a picornavirus is the mouth or nose, the virus infects and replicates in the nasopharyngeal epithelium and regional lymphoid tissues to give rise to asymptomatic infections or respiratory illnesses. Because enteroviruses can resist stomach acid and bile, they can penetrate to the lower intestine, where they infect and multiply in the intestinal epithelium and mesenteric lymph nodes. Viremia may result; this leads to further multiplication of virus in the reticuloendothelial system. From there, the virus can be carried by the bloodstream to target organs such as the spinal cord, brain meninges, heart, liver and skin. From the central nervous system the virus can travel via neural pathways to skeletal and heart muscles. It can be transferred by fingers and inanimate objects, such as handkerchiefs and towels, to the eye, where it may replicate in the conjunctival epithelium and cornea.

Host Defenses

Shortly after infection of the respiratory or alimentary tract, increasing amounts of interferon and subsequently virus-specific IgA-antibody are detected in the saliva and the respiratory and gut secretions. Interferon inhibits virus multiplication, and IgA complexes with extracellular virus. The complexing of virus by IgA not only inhibits the spread of virus to susceptible epithelial cells but also reduces the oral and fecal shedding of infectious virus.

The earliest serum antibody to appear in response to picornavirus infection is IgM. By about 2 weeks, IgM is overtaken by IgG. The IgG response peaks at about 2 to 3 weeks and remains at a plateau for a few weeks, before it begins to fall. The IgG elicited by some enterovirus infections remains detectable for several years. This neutralizing IgG confers serotype-specific immunity. Both IgG and IgM can complex with invading virus and prevent the spread of virus via the bloodstream to target organs. Virus-antibody complexes are eliminated by phagocytosis, digestion, and excretion.

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Epidemiology

Picornaviruses are found worldwide, the enteroviruses primarily in alimentary tracts of humans and animals but can be in nerve and muscle cells. Rhinoviruses are found in the respiratory tract. Although enteroviruses are transmitted mostly by the fecal-oral route, they can also be transmitted by salivary and respiratory droplets. Some serotypes are spread by conjunctival secretions and exudates from skin lesions.

In temperate countries, outbreaks of enterovirus illnesses occur most frequently in summer and autumn, whereas rhinovirus infections appear more often in autumn and spring. In the tropics, there is no apparent seasonal occurrence. Enteroviruses in excreta that contaminate the soil are carried by surface waters to lakes, beaches, vegetation, and community water supplies. These sources may serve as foci of infection. Shellfish that feed in freshwater or seawater beds contaminated by excreta harbor enteroviruses. Cockroaches in sewage pipelines and flies that settle on excreta may act as transient vectors.

Diagnosis

Enteroviruses and rhinoviruses may be isolated from feces pharyngeal swabs, saliva, and nasal aspirates, and some enteroviruses may be isolated from skin lesions, conjunctiva cerebrospinal fluid, spinal cord, brain, heart, and blood. Virus is present in respiratory and conjunctival secretions from a few days before onset of illness to about 1 week after. Virus excretion in feces may continue for several weeks or longer. However, the chance of virus isolation is greatest if appropriate specimens are sent to the laboratory at the onset of illness. Table 53-2 lists the virus isolation systems that are used. The most specific of the conventional laboratory tests used to identify picornavirus serotypes is the neutralization test. Serodiagnosis for the whole range of picornaviruses is impractical because of the multiplicity of serotypes. A serologic test is performed primarily to confirm the causative role of virus isolated from clinical specimens (i.e., to exclude the coincidental presence of a passenger virus that does not contribute to the disease

process). A fourfold or greater rise in the titer of neutralizing antibody to the isolate between sera collected during the acute and convalescent phases of the illness is regarded as diagnostic of a current or recent infection. The neutralization test is also used to determine the immune status of a person.

Control

Control of picornavirus diseases depends largely on mass education of the public on the mode of virus transmission, stressing the importance of good personal hygiene, and on provision of a good sewage disposal system and uncontaminated water supply. Fecal and pharyngeal discharges are infectious; hence, they must be handled with care and disposed of safely. Vaccine is commercially available for poliomyelitis and hepatitis A.

There is no established specific therapy. Treatment is symptomatic and supportive. Clinical studies show that ribavirin shortens respiratory illnesses and interferon nasal sprays have prophylactic value for common colds.

Orthomyxoviridae

Orthomyxoviridae is a family of RNA viruses. It includes seven genera: Influenzavirus A, Influenzavirus B, Influenzavirus C, Influenzavirus D, Isavirus, Thogotovirus, and Quaranjavirus. The first four genera contain viruses that cause influenza in vertebrates, including birds (see also avian influenza), humans, and other mammals. Isaviruses infect salmon; the thogotoviruses are arboviruses, infecting vertebrates and invertebrates, such as ticks and mosquitoes.

The four genera of Influenza virus, which are identified by antigenic differences in their nucleoprotein and matrix protein, infect vertebrates as follows:

Influenzavirus A infects humans, other mammals, and birds, and causes all flu pandemics

Influenzavirus B infects humans and seals

Influenzavirus C infects humans, pigs, and dogs.

Influenzavirus D infects pigs and cattle

Types

There are four genera of influenza virus, each containing only a single species, or type. Influenza A and C infect a variety of species, while influenza B almost exclusively infects humans, and influenza D infects cattle and pigs.

Influenza A

Influenza A viruses are further classified, based on the viral surface proteins hemagglutinin (HA or H) and neuraminidase (NA or N). Sixteen H subtypes (or serotypes) and nine N subtypes of influenza A virus have been identified.

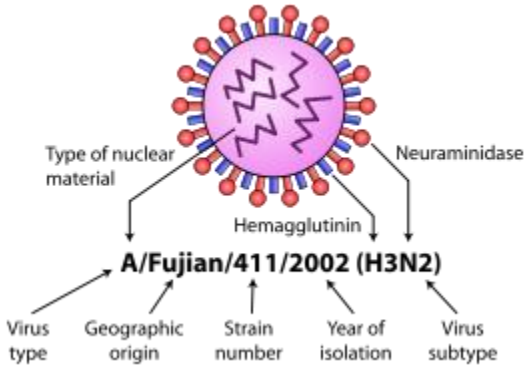


Diagram of influenza nomenclature

Further variation exists; thus, specific influenza strain isolates are identified by a standard nomenclature specifying virus type, geographical location where first isolated, sequential number of isolation, year of isolation, and HA and NA subtype.

Examples of the nomenclature are:

A/Brisbane/59/2007 (H1N1)

A/Moscow/10/99 (H3N2).

The type A viruses are the most virulent human pathogens among the three influenza types and cause the most severe disease. The serotypes that have been confirmed in humans, ordered by the number of known human pandemic deaths, are:

H1N1 caused "Spanish flu" in 1918, "Swine flu" in 2009.

H2N2 caused "Asian Flu".

H3N2 caused "Hong Kong Flu".

H5N1 is a pandemic threat.

H7N7 has unusual zoonotic potential.

H1N2 is endemic in humans and pigs

H9N2, H7N2, H7N3, H10N7.

Influenza B

Influenza B virus is almost exclusively a human pathogen, and is less common than influenza A. The only other animal known to be susceptible to influenza B infection is the seal. This type of influenza mutates at a rate 2–3 times lower than type A and consequently is less genetically diverse, with only one influenza B serotype. As a result of this lack of antigenic diversity, a degree of immunity to influenza B is usually acquired at an early age. However, influenza B mutates enough that lasting immunity is not possible.This reduced rate of antigenic change, combined with its limited host range (inhibiting cross species antigenic shift), ensures that pandemics of influenza B do not occur.

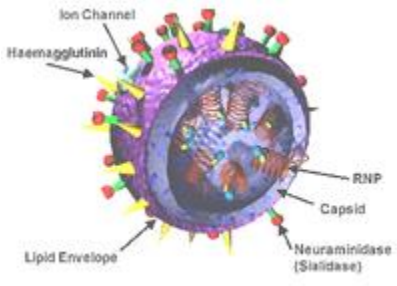
Influenza C

The influenza C virus infects humans and pigs, and can cause severe illness and local epidemics. However, influenza C is less common than the other types and usually seems to cause mild disease in children.

Influenza D

This is a genus that was classified in 2016, the members of which were first isolated in 2011. This genus appears to be most closely related to Influenza C, from which it diverged several hundred years ago.There are at least two strains of this genus in extant. The main hosts appear to be cattle, but this virus has seen to infect pigs as well.

Morphology



Structure of the influenza virion. The hemagglutinin (HA) and neuraminidase (NA) proteins are shown on the surface of the particle. The viral RNAs that make up the genome are shown as red coils inside the particle and bound to Ribonuclear Proteins (RNPs).

The virion is pleomorphic; the envelope can occur in spherical and filamentous forms. In general, the virus's morphology is ellipsoidal with particles 80 to 120 nm in diameter, or filamentous virions 80–120 nm in diameter and up to 20 µm long. There are some 500 distinct spike-like surface projections of the envelope each projecting 10 to 14 nm from the surface with varying surface densities.

The major glycoprotein (HA) is interposed irregularly by clusters of neuraminidase (NA), with a ratio of HA to NA of about 4–5 to 1.

Cholesterol-laden membranes with protruding glycoproteins enclose the nucleocapsids; nucleoproteins of different size classes with a loop at each end; the arrangement within the virion is uncertain. The ribonuclear proteins are filamentous and fall in the range of 50 to 130 nm long and 9 to 15 nm in diameter. They have a helical symmetry.

Genome

Viruses of this family contain 6 to 8 segments of linear negative-sense single stranded RNA.

The total genome length is 12000–15000 nucleotides (nt). The size of each segment is as follows:

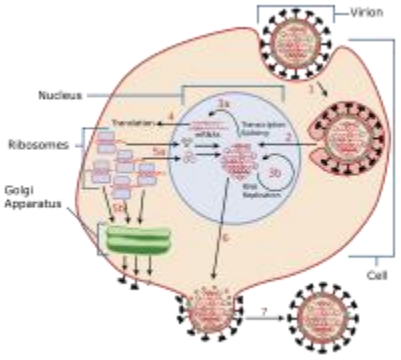
The Genome sequence has terminal repeated sequences; repeated at both ends. Terminal repeats at the 5'-end 12–13 nucleotides long. Nucleotide sequences of 3'-terminus identical; the same in genera of same family; most on RNA (segments), or on all RNA species. Terminal repeats at the 3'-end 9–11 nucleotides long. Encapsidated nucleic acid is solely genomic. Each virion may contain defective interfering copies. In Influenza A (H1N1) PB1-F2 is produced from an

alternative reading frame in PB1. The M and NS genes produce 2 different genes via alternative splicing.

Structure

The influenza A virus particle or virion is 80–120 nm in diameter, usually producing both ellipsoidal, baciliform, and filamentous particles. Unusually for a virus, the influenza A genome is not a single piece of nucleic acid; instead, it contains eight pieces of segmented negative-sense RNA (13.5 kilobases total), which encode 11 proteins (HA, NA, NP, M1, M2, NS1, NEP, PA, PB1, PB1-F2, PB2). The best-characterised of these viral proteins are hemagglutinin and neuraminidase, two large glycoproteins found on the outside of the viral particles. Neuraminidase is an enzyme involved in the release of progeny virus from infected cells, by cleaving sugars that bind the mature viral particles. By contrast, hemagglutinin is a lectin that mediates binding of the virus to target cells and entry of the viral genome into the target cell. The hemagglutinin (H) and neuraminidase (N) proteins are targets for antiviral drugs. These proteins are also recognised by antibodies, i.e. they are antigens. The responses of antibodies to these proteins are used to classify the different serotypes of influenza A viruses, hence the H and N in H5N1.

Replication cycle



Invasion and replication of the influenza virus. The steps in this process are discussed in the text.

Typically, influenza is transmitted from infected mammals through the air by coughs or sneezes, creating aerosols containing the virus, and from infected birds through their droppings. Influenza can also be transmitted by saliva, nasal secretions, feces and blood. Infections occur through contact with these bodily fluids or with contaminated surfaces. Out of a host, flu viruses can remain infectious for about one week at human body temperature, over 30 days at 0 °C (32 °F),

and indefinitely at very low temperatures (such as lakes in northeast Siberia). They can be inactivated easily by disinfectants and detergents.

The viruses bind to a cell through interactions between its hemagglutinin glycoprotein and sialic acid sugars on the surfaces of epithelial cells in the lung and throat (Stage 1 in infection figure). The cell imports the virus by endocytosis. In the acidic endosome, part of the haemagglutinin protein fuses the viral envelope with the vacuole's membrane, releasing the viral RNA (vRNA) molecules, accessory proteins and RNA-dependent RNA polymerase into the cytoplasm (Stage 2). These proteins and vRNA form a complex that is transported into the cell nucleus, where the RNA-dependent RNA polymerase begins transcribing complementary positive-sense cRNA (Steps 3a and b). The cRNA is either exported into the cytoplasm and translated (step 4), or remains in the nucleus. Newly synthesised viral proteins are either secreted through the Golgi apparatus onto the cell surface (in the case of neuraminidase and hemagglutinin, step 5b) or transported back into the nucleus to bind vRNA and form new viral genome particles (step 5a). Other viral proteins have multiple actions in the host cell, including degrading cellular mRNA and using the released nucleotides for vRNA synthesis and also inhibiting translation of host-cell mRNAs.

Negative-sense vRNAs that form the genomes of future viruses, RNA-dependent RNA transcriptase, and other viral proteins are assembled into a virion. Hemagglutinin and neuraminidase molecules cluster into a bulge in the cell membrane. The vRNA and viral core proteins leave the nucleus and enter this membrane protrusion. The mature virus buds off from the cell in a sphere of host phospholipid membrane, acquiring hemagglutinin and neuraminidase with this membrane coat (step 7). As before, the viruses adhere to the cell through hemagglutinin; the mature viruses detach once their neuraminidase has cleaved sialic acid residues from the host cell. After the release of new influenza virus, the host cell dies.

Orthomyxoviridae viruses are one of two RNA viruses that replicate in the nucleus (the other being retroviridae). This is because the machinery of orthomyxo viruses cannot make their own mRNAs. They use cellular RNAs as primers for initiating the viral mRNA synthesis in a process known as cap snatching. Once in the nucleus, the RNA Polymerase Protein PB2 finds a cellular pre-mRNA and binds to its 5' capped end. Then RNA Polymerase PA cleaves off the cellular mRNA near the 5' end and uses this capped fragment as a primer for transcribing the rest of the viral RNA genome in viral mRNA. This is due to the need of mRNA to have a 5' cap in order to be recognized by the cell's ribosome for translation.

Since RNA proofreading enzymes are absent, the RNA-dependent RNA transcriptase makes a single nucleotide insertion error roughly every 10 thousand nucleotides, which is the approximate length of the influenza vRNA. Hence, nearly every newly manufactured influenza virus will contain a mutation in its genome. The separation of the genome into eight separate segments of vRNA allows mixing (reassortment) of the genes if more than one variety of influenza virus has infected the same cell (superinfection). The resulting alteration in the genome segments packaged into viral progeny confers new behavior, sometimes the ability to infect new host species or to overcome protective immunity of host populations to its old genome (in which case it is called an antigenic shift).

Viability and disinfection

Mammalian influenza viruses tend to be labile, but can survive several hours in mucus. Avian influenza virus can survive for 100 days in distilled water at room temperature, and 200 days at 17 °C (63 °F). The avian virus is inactivated more quickly in manure, but can survive for up to 2 weeks in feces on cages. Avian influenza viruses can survive indefinitely when frozen. Influenza viruses are susceptible to bleach, 70% ethanol, aldehydes, oxidizing agents, and quaternary ammonium compounds. They are inactivated by heat of 133 °F (56 °C) for minimum of 60 minutes, as well as by low pH <2.

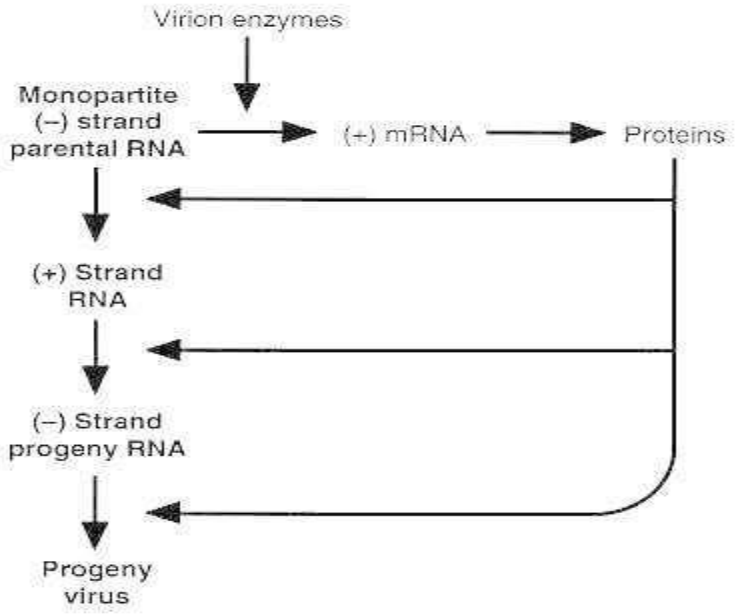
Vaccination and prophylaxis

Vaccines and drugs are available for the prophylaxis and treatment of influenza virus infections. Vaccines are composed of either inactivated or live attenuated virions of the H1N1 and H3N2 human influenza A viruses, as well as those of influenza B viruses. Because the antigenicities of the wild viruses evolve, vaccines are reformulated annually by updating the seed strains. However, when the antigenicities of the seed strains and wild viruses do not match, vaccines fail to protect the vaccinees. In addition, even when they do match, escape mutants are often generated. Drugs available for the treatment of influenza include Amantadine and Rimantadine, which inhibit the uncoating of virions by interfering with M2, and Oseltamivir (marketed under the brand name Tamiflu), Zanamivir, and Peramivir, which inhibit the release of virions from infected cells by interfering with NA. However, escape mutants are often generated for the former drug and less frequently for the latter drug.

Rhabdoviruses

Clinical Manifestations

Five general stages of rabies are recognized in humans: incubation, prodrome, acute neurologic period, coma, and death (or, very rarely, recovery). No specific antirabies agents are useful once clinical signs or symptoms develop. The incubation period in rabies, usually 30 to 90 days but ranging from as few as 5 days to longer than 2 years after initial exposure, is more variable than in any other acute infection. Incubation periods may be somewhat shorter in children and in individuals bitten close to the central nervous system (e.g., the head). Clinical symptoms are first noted during the prodromal period, which usually lasts from 2 to 10 days. These symptoms are often nonspecific (general malaise, fever, and fatigue) or suggest involvement of the respiratory system (sore throat, cough, and dyspnea), gastrointestinal system (anorexia, dysphagia, nausea, vomiting, abdominal pain, and diarrhea), or central nervous systems (headache, vertigo, anxiety, apprehension, irritability, and nervousness). More remarkable abnormalities (agitation, photophobia, priapism, increased libido, insomnia, nightmares, and depression) may also occur, suggesting encephalitis, psychiatric disturbances, or brain conditions. Pain or paresthesia at the site of virus inoculation, combined with a history of recent animal bite, should suggest a consideration of rabies.



Pathogenesis of rabies.

The acute neurologic period begins with objective signs of central nervous system dysfunction. The disease may be classified as furious rabies if hyperactivity (i.e., hydrophobia) predominates and as dumb rabies if paralysis dominates the clinical picture. Fever, paresthesia, nuchal rigidity, muscle fasciculations, focal and generalized convulsions, hyperventilation, and hypersalivation may occur in both forms of the disease.

At the end of the acute neurologic phase, periods of rapid, irregular breathing may begin; paralysis and coma soon follow. Respiratory arrest may occur thereafter, unless the patient is receiving ventilatory assistance, which may prolong survival for days, weeks, or longer, with death due to other complications.

Although life support measures can prolong the clinical course of rabies, rarely will they affect the outcome of disease. The possibility of recovery, however, must be recognized, and when resources permit, every effort should be made to support the patient. At least seven cases of human "recovery" have been documented.

Structure

The rabies virus is a negative-sense, non-segmented, single-stranded RNA virus measuring approximately 60 nm × 180 nm. It is composed of an internal protein core or nucleocapsid, containing the nucleic acid, and an outer envelope, a lipid-containing bilayer covered with transmembrane glycoprotein spikes.

Virion structure of rabies virus.

The virus genome encodes five proteins associated with either the ribonucleoprotein (RNP) complex or the viral envelope. The L (transcriptase), N (nucleoprotein), and NS (transcriptase-associated) proteins comprise the RNP complex, together with the viral RNA. These aggregate in the cytoplasm of virus-infected neurons and compose Negri bodies, the characteristic histopathologic finding of rabies virus infection. The M (matrix) and G (glycoprotein) proteins are associated with the lipid envelope. The G protein forms the protrusions that cover the outer surface of the virion envelope and is the only rabies virus protein known to induce virus-neutralizing antibody.

Genome of rabies virus (ERA strain). This contains single-stranded RNA (12 kilobases); N, NS, M, G, and L genes; a leader sequence at the 3′ end; and four intergenic regions.

Classification and Antigenic Types

The genus Lyssavirus includes rabies virus and the antigenically- and genetically-related rabies-like viruses: Lagos bat, Mokola, and Duvenhage viruses, and two suggested subtypes of European bat lyssaviruses. Cross-protection studies suggest that animals immunized with traditional rabies vaccines may not be fully protected if challenged with other lyssaviruses.

Rabies viruses may be categorized as either fixed (adapted by passage in animals or cell culture) or street (wild type). The use of monoclonal antibodies and genetic sequencing to differentiate street rabies viruses has been helpful in identifying viral variants originating in major host reservoirs throughout the world and suggesting the likely sources of human exposure when a history of definitive animal bite was otherwise missing from a patient's case history.

Multiplication

The replication of rabies virus is believed to be similar to that of other negative-stranded RNA viruses. The virus attaches to the host cell membranes via the G protein, penetrates the cytoplasm by fusion or pinocytosis, and is uncoated to RNP. The core initiates primary transcription of the five complementary monocistronic messenger RNAs by using the virion-associated RNA-dependent RNA polymerase. Each RNA is then translated into an individual viral protein. After viral proteins have been synthesized, replication of the genomic RNA continues with the synthesis of full length, positive-stranded RNA, which acts as a template for the production of progeny negative-stranded RNA.

Pathogenesis

Rabies virus is most commonly transmitted through the bite of an infected mammal, all of which may be susceptible, but to greatly varying degrees. The virus may enter the peripheral nervous system directly, or may replicate in muscle tissue after entering the host, remaining at or near the site of introduction for most of the incubation period. However, the precise sites of viral sequestration remain unknown, since neither antigen nor virus can usually be found in any organ during this phase.

Virus may enter the peripheral nervous system via the neuromuscular junctions, and moves rapidly centripetally to the central nervous system for replication; symptoms may develop shortly

thereafter. The virus then begins to pass centrifugally to many tissues and organs, such as the salivary glands.

In general, gross examination of the brain shows mild congestion of the meningeal vessels; microscopic examination usually demonstrates slight perivascular cuffing, limited tissue necrosis, acidophilic intracytoplasmic neuronal inclusions, and rarely, neuronophagia.

Host Defenses

The host animal species, viral variant, inoculum concentration, body location and severity of exposure, and host immune status have been associated with overt susceptibility to infection and with different incubation periods. The association of virus-neutralizing antibody, principally IgG, and protective immunity is well known. Production of cytokine, such as interferon, induced during rabies virus infection or vaccination, has been reported to abort the disease if it occurs shortly after viral infection. In one clinical trial, however, all subjects died despite experimental treatment with high doses of alpha interferon.

Recently it has been demonstrated that animals immunized with purified RNP complexes or recombinant nucleoprotein vaccines resisted lethal challenge with rabies virus, although the role of N protein in protection, illness, or recovery is unclear.

Epidemiology

Rabies has been recognized for over 4,000 years. Today it is found in most countries, with the exception of those regions from which it has not been naturally reported, including many Australian islands, or areas achieving secondary elimination, such as the United Kingdom. Almost all human rabies is caused by the bite of a rabid animal. The risk of rabies is highest in countries with hyperendemic canine rabies, including most of Asia, Africa, and Latin America. In the United States and Europe, domestic animal rabies was largely controlled during the 1940–50s and now represents less than 10% of all animal rabies recorded. Wildlife rabies in the United States occurs primarily among wild terrestrial carnivores, such as raccoons, skunks, foxes, and coyotes, and in insectivorous bats.

Life cycle of rabies.

Human rabies is almost always attributable to a bite (any penetration of the skin by the teeth). Nonbite exposures (contamination of an open wound or a mucous membrane via scratches, licks, and inhalation of aerosol) rarely cause rabies in humans. In the United States, nonbite exposures were reported as the source of infection for only 5 (3 %) of the 154 cases reported from 1950 through 1980. Of these five human cases, four were apparently attributable via exposure to aerosols containing highly concentrated live rabies virus: two in spelunkers (cave explorers) and two in rabies research laboratory workers. The fifth case occurred in the recipient of a cornea transplanted from a patient dying of unsuspected rabies encephalitis. An increasing proportion of current human rabies patients in the United States have had no known exposure to the virus; since 1980, 19 of 25 (90%) of the rabies patients have had no definitive rabid animal exposure. This may be attributable either to an inability of the patient to recognize actual rabies exposure at the time, or a failure to properly question the patient concerning potential animal contact. Although it is now a rare human disease in the United States, its actual incidence may be higher than generally believed. The initial suspicion of rabies only occurred at postmortem examination in five reported human cases in the United States since 1985.

Diagnosis

Differential Diagnosis

The diagnosis of human rabies is usually suggested by epidemiologic and clinical findings and confirmed in the laboratory. The diagnosis is not difficult if there is a history of animal bite exposure and if a full spectrum of symptoms and signs has appeared. Otherwise, careful but rapid assessment of the epidemiologic and clinical features of less typical cases is essential before special laboratory tests are performed. Every patient with neurologic signs or symptoms or unexplained encephalitis should be questioned about the possibility of animal exposure in a rabies-endemic area inside or outside the country of residence. The failure to suspect rabies in several of the recent human deaths in the United States may have occurred because no thorough exposure history had been sought.

Early in the course of illness, rabies can mimic numerous infectious and noninfectious diseases. Many other encephalitides, such as those caused by herpesviruses and arboviruses, resemble rabies. Other infectious diseases also may resemble rabies, such as tetanus, cerebral malaria, rickettsial diseases, and typhoid. Paralytic infectious illnesses that may be confused with rabies include poliomyelitis, botulism, and simian herpes type B encephalitis.

Noninfectious diseases that may be confused with rabies encompass a number of neurologic syndromes, especially acute inflammatory polyneuropathy (Guillain-Barre syndrome), as well as allergic postvaccinal encephalomyelitis secondary to vaccination with nervous-tissue rabies vaccines, intoxication with poisons or drugs, withdrawal from alcohol, acute porphyria, and rabies hysteria. Guillain-Barre syndrome may be mistaken for the paralytic form of rabies, and vice versa.

Laboratory Diagnosis

The detection of rabies antigen, antibody, viral RNA, or the isolation of virus establishes a diagnosis of rabies. Because any individual test may not be positive in a patient with rabies, serial serum specimens for detection of rabies antibodies, saliva specimens for culture of virus, and skin biopsies for direct immunofluorescence testing for virus antigen are sometimes necessary, especially when rabies is strongly suspected.

One of the most rapid methods to diagnose rabies antemortem in humans is to perform a direct immunofluorescence test on a skin biopsy from the nape of the neck for evidence of rabies antigen. The direct immunofluorescence test is the most sensitive and specific method of detecting rabies antigen in skin and other fresh tissue (e.g., brain biopsy), although the results may occasionally be negative in early stages of the disease. If fresh tissue is unavailable, enzyme digestion of fixed tissues may enhance the reactivity of the immunofluorescence test; however, sensitivity may be unacceptably low.

The diagnosis can also be established if virus is isolated from saliva after inoculation of neuroblastoma cells or laboratory rodents; this is generally most successful during the first 2 to 3 weeks of illness. The detection of rabies virus-neutralizing antibody, as typically performed by the rapid fluorescent focus inhibition test (RFFIT), in the serum of unvaccinated individuals is also diagnostic. The presence of antibody in the cerebrospinal fluid confirms the diagnosis, but it may appear 2 to 3 days later than serum antibody and may therefore be less useful early in the disease. Whereas the serological response after vaccination cannot be generally differentiated from that due to disease, vaccination does not typically produce cerebrospinal fluid antibody.

Only seven “recoveries” from rabies, all in the past 25 years, have been well documented. Although rabies virus was not isolated in any of the patients, the high rabies-neutralizing antibody titer in serum samples and the presence of neutralizing antibodies in cerebrospinal fluid strongly supported the diagnoses.

Control

Animal rabies is prevented by vaccinating susceptible species, particularly dogs and cats. Mass dog vaccination programs in the United States and Europe were largely responsible for a dramatic reduction in canine and human rabies during the 1940's and 1950s. In these countries, the number of reported cases in wildlife is currently about 10-fold greater than that in domestic animals; wildlife therefore constitute the greatest risk to human beings. Oral vaccination of wildlife with attenuated and recombinant rabies vaccines by the use of vaccine-containing bait offers hope of controlling the disease in susceptible wild free-ranging animal populations.

Human rabies is best prevented by avoiding exposures to the disease. When an exposure is suspected, the patient's physician and local health department authorities should determine whether an exposure actually occurred and whether a risk of rabies exists in the geographic area. If treatment (postexposure prophylaxis) is necessary, it should be initiated promptly. Postexposure prophylaxis consists of the combination of local wound cleansing, human rabies immune globulin (HRIG) and rabies vaccine. Two cell culture products currently licensed in the United States include the human diploid cell vaccine (HDCV) and rabies vaccine adsorbed (RVA). Postexposure treatment will abort the infection, but there is no cure for clinical disease.

Preexposure immunization may be offered to persons at high risk, such as veterinarians, animal handlers, certain laboratory workers, and persons spending time (e.g., 1 month or more) in foreign countries where rabies is a constant threat. Persons, such as spelunkers, whose vocational or recreational pursuits bring them into frequent contact with potentially rabid animals should also be considered for preexposure prophylaxis. The schedules for preexposure prophylaxis.

Reovirus

Reoviruses (family Reoviridae) is the family of viruses that can affect the gastrointestinal system (such as Rotavirus) and respiratory tract. Reoviruses have genomes consisting of 8–11 segmented, dsRNA.

In fact, reoviruses are dsRNA viruses rather than negative-strand RNA viruses. For the sake of brevity, reoviruses are included in this chapter. Since only one strand (ie, negative-strand) out of

the two stands is utilized as the template for the viral RNA replication, reoviruses can be regarded as negative-strand RNA virus in molecular point of view.

***Classification*:** Family Reoviridae is composed of two genera: reovirus and rotavirus. Reovirus causes respiratory infection to children but its associated symptom is mild or subclinical.

***Epidemiology*:** In contrast to reovirus, rotavirus is the main cause of gastroenteritis in the winter. Rotavirus infection leads to diarrhea and vomiting, resulting in dehydration. Rotavirus is estimated to cause about 40% of all hospital admissions due to diarrhea among children under 5 years of age worldwide—leading to some 100 million episodes of acute diarrhea each year that result in 350,000 to 600,000 child deaths. The infection episode can be life-threatening, unless properly treated. Rotavirus vaccine is available. However, no therapeutic antiviral drug is available for the treatment.

***Virion* Structure:** Rotavirus virions are naked, nucleocapsid particles, 70–90 nm in diameter, containing 11 segments of dsRNA genome (Fig. 16.11). One peculiarity is that the nucleocapsid is double-shelled so that inside the outer shell is another layer of shell, the inner shell. Twelve spikes project from the inner layer at each of the 12 vertices.

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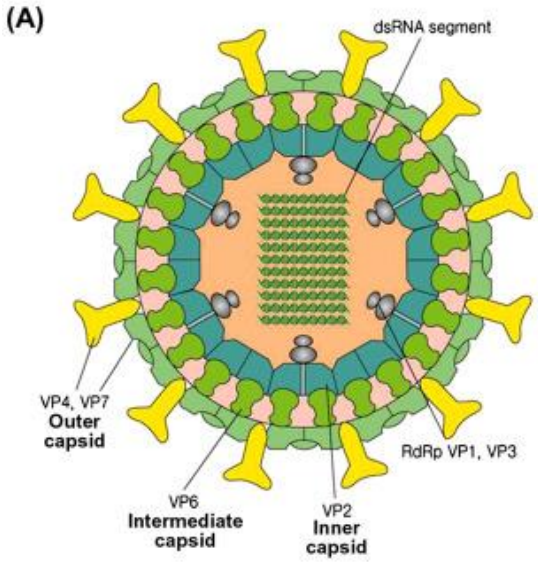
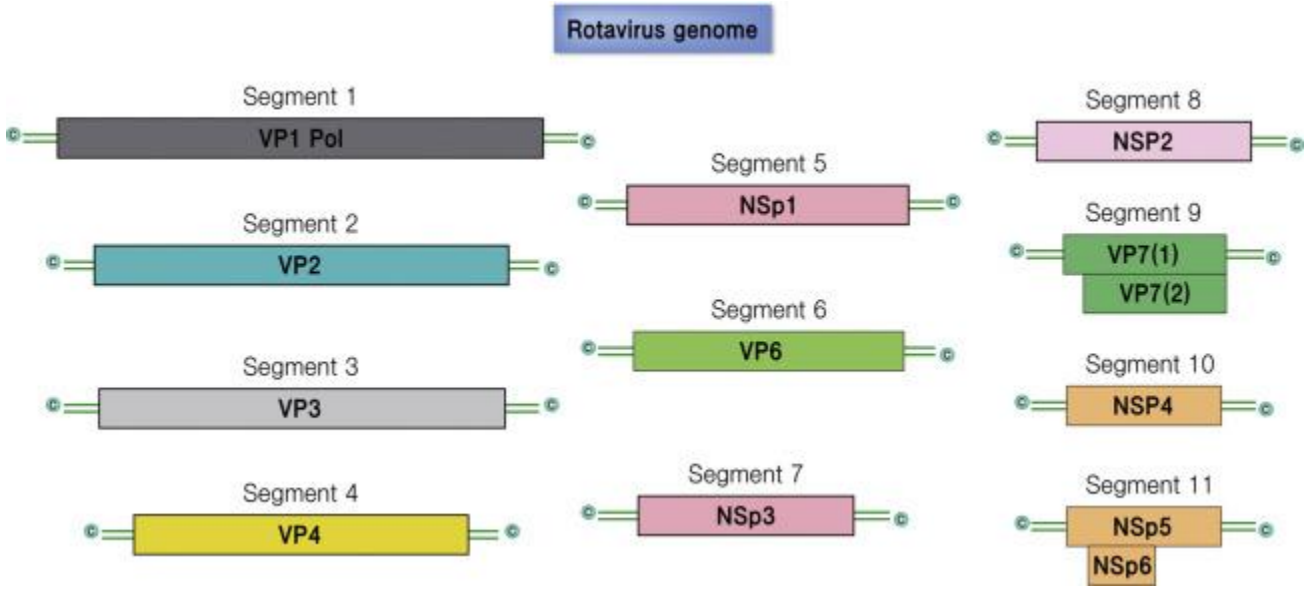


***Genome Structure*:** Rotavirus possesses 11 RNA segments, which are dsRNA (Fig. 16.12). The replication strategy is similar to that of negative-strand RNA virus, where only one strand (ie, negative-strand) is copied during replication (see Fig. Part III-2). Each RNA segment encodes one protein (open reading frame, ORF), except that two segments (Segments 9 and 11) express an additional related protein by using the second AUG codon.



Reoviruses are nonenveloped, double-stranded, segmented RNA viruses. Currently, the strains known to infect reptiles have been placed in the genus *Orthoreovirus*. Experimental infection with clinical isolates of reovirus from beauty snakes and Moellendorff's ratsnakes induced severe clinical disease in juvenile black ratsnakes, confirming their pathogenic properties in these species and likely other species of reptiles (Lamirande *et al*., 1999).

Epizootiology and Transmission

Reports of reovirus infection have been documented in various species of reptiles, including emerald tree boas, rough green snakes, Chinese vipers, rat snakes, iguanas, leopard geckos, green lizards, tortoises, and chameleons (Landolfi *et al*., 2010; Marschang, 2011). Numerous strains of reovirus have been identified and appear to cause different clinical manifestations among different reptile species. While certain viral strains appear to be nonpathogenic, some strains are associated with high morbidity and mortality. Mode of transmission has not been clearly delineated in reptiles. However, in birds, transmission occurs via direct or indirect contact with contaminated feces. Interspecies infection may occur.

Pathogenesis

The precise pathogenic mechanisms of reoviruses in reptiles are unclear. As an RNA virus, reoviruses replicate in the cytoplasm of the infected cells. Reptilian reoviruses appear to mediate cell fusion to form syncitia from a small type III protein (Corcoran and Duncan, 2004).

Clinical Signs

Neurological signs, including incoordination, proprioceptive deficits, and convulsion, as well as pneumonia, stomatitis, and gastrointestinal signs, have been reported in animals infected with reoviruses (Vieler *et al*., 1999; Lamirande *et al*., 1999; Marschang and Divers, 2014). Infected green snakes were reported to develop papillomas (Marschang, 2011), while ratsnakes experimentally inoculated with reovirus were found dead 26 days post-inoculation (Lamirande *et al*., 1999). In tortoises, infection can result in the development of tongue lesions, and animals can become cachectic.

Necropsy Findings

Proliferative tracheitis and interstitial pneumonia were the prominent lesions observed in experimentally inoculated ratsnakes. Microscopically, affected tissues can form syncytia. However, inclusions are not a distinct feature associated with reovirus infection. Some strains of reovirus are associated with hepatitis and pancreatitis. In snakes, reovirus infection is associated with the development of papillomas.

Differential Diagnosis

Differentials for CNS and respiratory signs include paramyxovirus infection and IBD, toxin exposure, as well as both bacteria (mycoplasmosis and mycobacteriosis) and fungal infection. PCR-based assays, virus isolation, and viral detection via electron microscopy can be used to determine the presence of the virus in tissues and feces.

Treatment

No effective treatment has been reported for reovirus infection. In severe cases, euthanasia is recommended.

Control

In birds, vertical transmission has been reported for reovirus, making eradication very difficult in an affected colony. A similar scenario may be expected for reovirus infection in reptiles. Consistent with their nonenveloped characteristic, reoviruses are stable in the environment and are resistant to many disinfectants, including pH3, 2% Lysol®, 3% formaldehyde, 1% hydrogen peroxide, quaternary ammonium, and heating to 56°C for 120 min. However, paracetic acid fogging has been shown to be effective in inactivating the virus in laboratories and facilities (Gregersen and Roth, 2012).

Prevention

As with other viral agents previously discussed, strict biosecurity, quarantine, and implementation of good hygiene practices should reduce the possibility of introducing the virus into the existing colony.

Therapeutic applications

Although reoviruses are mostly nonpathogenic in humans, these viruses have served as very productive experimental models for studies of viral pathogenesis. Newborn mice are exquisitely sensitive to reovirus infection and have been used as the preferred experimental system for studies of reovirus pathogenesis.

The reoviruses have been demonstrated to have oncolytic (cancer-killing) properties, encouraging the development of reovirus-based therapies for cancer treatment.

Reolysin is a formulation of reovirus (reovirus serotype 3-dearing strain) that is currently in clinical trials for the treatment of various cancers, including studies currently developed to investigate the role of Reolysin combined with other immunotherapies.

Poxvirus

Poxviruses are brick or oval-shaped viruses with large double-stranded DNA genomes. Poxviruses exist throughout the world and cause disease in humans and many other types of animals. Poxvirus infections typically result in the formation of lesions, skin nodules, or disseminated rash.

Infection in humans usually occurs due to contact with contaminated animals, people, or materials. While some poxviruses, such as smallpox (variola virus), no longer exist in nature, other poxviruses can still cause disease. These include monkeypox virus, orf virus, molluscum contagiosum, and others.

Poxviruses (members of the Poxviridae family) can infect both humans and animals. The orthopoxviruses include smallpox (variola), monkeypox, vaccinia, cowpox, buffalopox, cantagalo, and aracatuba viruses. The parapoxviruses include orf virus, bovine papular stomatitis virus, pseudocowpox virus, deerpox virus, and sealpox virus. Yatapoxviruses include tanapox virus and yabapoxviruses, which are found primarily in Africa. Molluscipoxviruses include the human poxvirus, molluscum contagiosum virus.

Smallpox and molluscum contagiosum are specific to humans. The other viruses cause rare zoonotic infections in humans.

Introduction

The last endemic case of smallpox occurred in 1977, total eradication was confirmed in 1980, and the official account of the disease and its eradication has appeared. Consequently, smallpox is not discussed below. However, its importance should not be forgotten. It helped to shape history, and it made history by being the first disease to be controlled by immunization and the first to be eradicated. The remaining poxvirus infections of humans are relatively insignificant. Furthermore, even such important animal diseases as sheeppox and camelpox are less important than animal infections caused by other pathogens.

Clinical Manifestations

Poxvirus infections are characterized by the production of skin lesions. With most poxviruses there is typically just a primary lesion, but generalized lesions develop with human monkeypox and molluscum. In human cowpox and parapox infections the lesion develops at the site of inoculation (usually the hand), and infection may be spread to other sites such as the face and/or genitals by scratching. When seen by the physician, cowpox and parapox lesions are usually hemorrhagic crusting ulcers, but early in infection the former are usually vesicular and the latter nodular. The lesions of molluscum, usually multiple, are firm, pearly, flesh-colored nodules.

Parapox and molluscum infections are relatively painless and cause very little constitutional disturbance. Human cowpox is very painful, particularly in young children, usually causes pyrexia and marked lymphadenopathy; patients often require hospitalization. Rare encephalitic complications of cowpox have been reported, and erythema multiforme is a complication of parapox infections. Infection in immunocompromised or eczematous individuals is more severe and usually results in generalized illness, and in cowpox has caused deaths.

Smallpox vaccination has been associated with serious complications. However, routine use of smallpox vaccine has been discontinued, and any future use of recombinant vaccinia virus vaccines will involve attenuated strains, thus reducing the chances of complications.

Although human monkeypox is rare and geographically localized, it is a serious generalized infection, which clinically resembles mild smallpox. A febrile prodrome precedes the development of a vesicular or pustular rash, typically centrifugal in distribution. Detailed examination of more than 300 cases in Zaire showed an overall mortality of 10 percent, reaching 15 to 20 percent in unvaccinated children. Respiratory complications were seen in about 12 percent of unvaccinated patients.

Structure

Poxvirus virions are large and brick shaped. Orthopoxviruses are approximately 240 nm by 300 nm, with short surface tubules 10 nm wide. Parapoxviruses are narrower (160 nm) and have one long tubule that winds around the virion; in electron micrographs, superimposition of the top and bottom surfaces gives a characteristic criss-cross appearance. Virions extracted artificially from infected cells are infectious and are generally used in studies on poxviruses. However, virions released naturally from infected cells acquire an additional envelope, which is easily lost during manipulation. These naturally released virions possess extra antibody neutralization sites not

present on the artificially extracted forms. Internally, virions have a dumbbell-shaped core and two lateral bodies. The genome consists of one molecule of double-stranded DNA, from 130 kb (parapox) to 260 kb (fowlpox), and the core contains enzymes for virus uncoating and genome replication. Linear maps of the genomes of various poxviruses have been prepared, and the entire genome of a strain of vaccinia virus has been sequenced.

Classification and Antigenic Types

Poxviruses are assigned to genera on the basis of close genetic and serologic relationships. The viruses are antigenically complex. Surface and soluble antigens show extensive cross-reaction between species in a genus but not between genera. This means that antigenic typing, as used for other virus groups, is not appropriate. Poxviruses have traditionally been assigned to species on the basis of biologic criteria. Genome analysis is now used and has generally confirmed biologic work, although some strains (e.g., rabbitpox and buffalopox viruses) are now regarded as variants of vaccinia virus. Isolates of molluscum virus can be typed by DNA restriction enzyme analysis.

Multiplication

Poxvirus replication takes place in cytoplasmic inclusions. Infecting virions are partly uncoated by cellular enzymes and then fully uncoated by viral enzymes released from the virion core. The viral DNA is not infectious per se, and other core enzymes (including a DNA-dependent RNA polymerase) play essential roles in the replication cycle. The replication cycle can be divided into functions controlled by early (prereplicative) gene products and those controlled by late (postreplicative) gene products. Most virions (80 to 90 percent) remain within cells and therefore lack the outer envelope found on naturally released virions.

Knowledge of the molecular biology of poxvirus replication has led to the development of recombinant vaccinia virus strains that code for the products of foreign genes inserted into the vaccinia virus genome. Such recombinants are infectious and are being widely used to study gene expression, as candidate vaccines (e.g., against rabies and rinderpest), and for the production of biopharmaceuticals such as factor VIII. An extension of these studies has led to the development of canarypox recombinants which express foreign genes in mammals without causing productive infection. The use of such non-replicating vectors may overcome objections to the use of vaccinia virus as a vector.

Pathogenesis

The pathogenesis of localized poxvirus infections is simple. Virus invades through broken skin, replicates at the site of inoculation, and causes dermal hyperplasia and leukocyte infiltration. With cowpox, and to a lesser extent with parapox, there is limited lymphatic spread; this causes lymphadenopathy and elicits an immune response. The lesion of molluscum is circumscribed by a connective tissue capsule, and the dermis, although distorted, is not usually broken. Some poxviruses express an epidermal growth factor and host range genes which play a role in pathogenesis and cell tropism.

Human monkeypox is usually acquired via the respiratory tract, and during a 12-day incubation period viremia distributes infection to internal organs, which are damaged by virus infection. Spread to the skin initiates the clinical phase, and the lesions progress through the classic stages of macule to papule to vesicle to pustule to crust. Lymphadenopathy, usually involving the cervical and inguinal areas, is often marked.

Host Defenses

With the exception of human monkeypox, which is usually acquired via the respiratory route, human poxvirus infections are acquired by inoculation into the skin or contact with broken skin. Consequently, unbroken skin presents the first line of defense. Interferon, nonspecific inflammation, and probably pyrexia play a role in limiting infection during the early stages.

Infection induces humoral and cellular immune responses to naturally released virions and to viral antigens on the surface of virus-infected cells. Responses to the extra antigens on the envelope of naturally released virions are particularly important, determining the speed and extent of recovery and the prevention or attenuation of future infection.

In general, the immune response is related to the severity of infection; the immunity elicited by a mild infection may be insufficient to prevent reinfection, as is often the case with human parapox infections.

Epidemiology

With the exception of molluscum, which is a specifically human disease, human poxvirus infections are acquired from animal reservoirs. In some cases the reservoir is known and distributed worldwide, as in the case of ovine and bovine parapoxviruses. Human infection with these viruses is an occupational hazard of those working with the infected reservoir hosts.

Monkeypox is restricted to West Africa, and squirrels are more important as reservoir hosts than monkeys. Cowpox virus is restricted to Europe and western parts of the former USSR. Bovine cowpox is rare, and the domestic cat is the most commonly reported host. Conclusive information about the reservoir host of cowpox virus is lacking, but it is probably small wild rodents. Cases occur without known contact with cats or cattle, and indirect spread via barbed wire or brambles is possible.

Limited natural person-to-person spread of monkeypox has been observed, but not further than four or five generations. Parapox and cowpox infections rarely, if ever, spread from person to person. Person-to-person spread of molluscum is traditionally associated with physical contact sports (e.g., wrestling) and the sharing of towels. There is increasing evidence, however, that sexual transmission of molluscum is important.

Vaccinia virus is traditionally regarded as a laboratory virus with no natural reservoir. However, buffalopox virus, now considered a variant of vaccinia virus, appears to have established itself in India, although information about its reservoir host is lacking. Because of the potential use of recombinant vaccinia virus vaccines, it is important to remember that such strains may become established in animal populations and/or interact with genetically related viruses circulating in them.

Diagnosis

In many cases, the nature of the lesions and a careful history that establishes contact with an infected reservoir animal or another infected person will permit a satisfactory diagnosis; difficulties may arise if no such contact is established. This is perhaps most common with human cowpox, since most cases are not traced to a particular source and a clinical diagnosis of anthrax is sometimes made.

Electron microscopy of vesicle or scab material is an effective means of rapid diagnosis; poxviruses and herpesviruses are readily distinguished, and the characteristic morphology of parapoxviruses can be recognized. Cowpox was diagnosed in this way in 23/24 cases where suitable material was available. Immunofluorescence of infected cell cultures will differentiate morphologically similar poxviruses from different genera (e.g. Orthopoxvirus and Yatapoxvirus). Although molluscum virus has yet to be cultivated, the other poxviruses are easily isolated in tissue culture and/or chicken embryos. Cultivation then allows identification by biologic and serum neutralization tests. Precise identification by

antibody detection is compromised by close antigenic relationships within genera, but knowledge of host and geographic range will help to confirm a presumptive diagnosis.

Control

Control of the common human poxvirus infections depends on knowledge of their epidemiology. In particular, persons caring for sick livestock should take precautions, but the extent of occupational exposure is such that infection and reinfection are inevitable. Control of infections such as cowpox which has an unknown reservoir, is virtually impossible. Person-to-person transmission is reduced by improving hygiene. Monkeypox is a special case. The World Health Organization considers that the benefits of vaccination do not outweigh the risks and expense. Control of this disease depends on health education and on breaking the link with the animal reservoir; this last should be achieved by the use of forest land near villages for agriculture.

In conclusion, it is significant that the strategies used for smallpox eradication are being assessed for the control and eradication of other diseases such as measles and that smallpox recombinant poxviruses may play an important role in the control of other infections.

Herpes viruses

Of the more than 100 known herpes viruses, 8 routinely infect only humans: herpes simplex virus types 1 and 2, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, human herpes virus 6 (variants A and B), human herpes virus 7, and Kaposi's sarcoma virus or human herpes virus 8. A simian virus, called B virus, occasionally infects humans. All herpes viruses can establish latent infection within specific tissues, which are characteristic for each virus.

Structure

Herpes viruses have a unique four-layered structure: a core containing the large, double-stranded DNA genome is enclosed by an icosapentahedral capsid which is composed of capsomers. The

capsid is surrounded by an amorphous protein coat called the tegument. It is encased in a glycoprotein-bearing lipid bilayer envelope.

Classification

Herpes viruses are divided into three groups: The α herpes viruses, herpes simplex virus types 1 and 2, and varicella-zoster virus, have a short replicative cycle, induce cytopathology in monolayer cell cultures, and have a broad host range; β herpes viruses, cytomegalovirus, and human herpes viruses 6 and 7, with a long replicative cycle and restricted host range; and γ herpes viruses, Epstein-Barr virus and human herpes virus 8, with a very restricted host range.

Multiplication

Transcription, genome replication, and capsid assembly occur in the host cell nucleus. Genes are replicated in a specific order: (1) immediate-early genes, which encode regulatory proteins; (2) early genes, which encode enzymes for replicating viral DNA; and (3) late genes, which encode structural proteins. The tegument and envelope are acquired as the virion buds out through the nuclear membrane or endoplasmic reticulum. Virions are transported to the cell membrane via the Golgi complex, and the host cell dies as mature virions are released. Alternatively, in selected cell types, the virus may be maintained in a latent state. The latent viral genome may reactivate at any time; the mechanism of reactivation is not known.

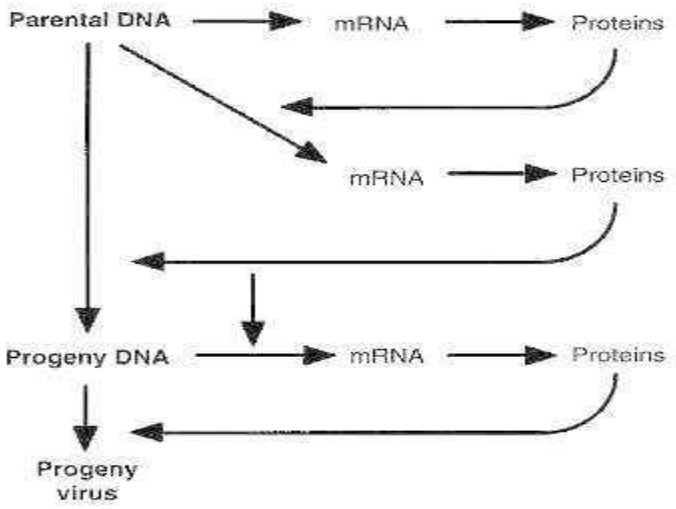
Diagnosis

Cytomegalovirus retinitis is diagnosed clinically. Diagnosis of all other herpesvirus infection relies on isolation of the virus through culturing and/or on detection of viral genes or gene products, particularly using polymerase chain reaction technology.

Control of Herpes virus Infections

Prevention: A vaccine to prevent varicella-zoster virus infections was recently licensed in the United States. Vaccines against herpes simplex virus 2, and cytomegalovirus are undergoing extensive evaluations in field trials. Passive immunization with immunoglobulin or hyperimmune globulin is used either to prevent infection or as an adjunct to antiviral therapy.

Treatment: Infections with herpes simplex virus 1 and 2 and varicella-zoster virus are currently the most amenable to therapy; acyclovir, valaciclovir and famciclovir are all licensed therapeutics. Ganciclovir is used to treat cytomegalovirus retinitis. B virus appears to respond to either of these drugs. There is as yet no treatment for Epstein-Barr virus or human herpes virus 6,7 or 8 infections.



Papovavirus

A papovavirus is any member of the former virus family of Papovaviridae. They are mainly associated with various neoplasms in mammals. The family of Papovaviridae is no longer used in recent taxonomy, but is split into the Papillomaviridae and the Polyomaviridae. The name derives from three abbreviations: Pa for papillomavirus, Po for polyomavirus, and Va for

"vacuolating" (simian vacuolating virus 40 or SV40, which is now known to be part of the polyomavirus genus).

Papovaviruses are DNA viruses containing double-stranded DNA, are icosahedral in shape, and do not have a lipoprotein envelope.

They are commonly found in humans and other species, mostly mammals. The one that most often causes disease in humans is the human papillomavirus, however clinically significant members include JC virus (causative agent of progressive multifocal leukoencephalopathy) and BK virus (causative agent of hemorrhagic cystitis in immunocompromised patients).

The Papovaviridae family is comprised of two genera: papillomaviruses and polyomaviruses. The family name is derived from the names of three prototypical members: rabbit papilloma virus, mouse polyoma virus, and simian virus 40 (SV40), originally called vacuolating virus. The family has several general features in common:

Genome:

It consists of single molecules of supercoiled, circular (covalently closed), double-stranded DNA that are replicated in the nucleus and bound to histones H2a, H2b, H3, and H4. Genome lengths vary slightly by genus; polyoma viruses are 5 kilobases, while papilloma viruses are 8 kilobases. The virions are spherical in shape and have non-enveloped, icosahedral capsids with a triangulation number, T=7. The genome does not encode a viral polymerase; instead, it uses the host's polymerase during replication. The virally encoded T antigen acts to direct the host DNA polymerase to the viral genome. Interestingly, while the reading frames of papillomaviruses are encoded on a single strand of DNA, for polyomaviruses both DNA strands encode functional proteins.

- Most of the species have a narrow host range.
- Replication and assembly occur in the nucleus.
- Virions are released via cell destruction.
- Some infections are characterized by oncogenesis or host cell transformation.

- Transmission usually occurs through direct contact, including sexual contact.
- The family is resistant to inactivation by heat or formalin.
- The viruses encode 5-7 structural proteins and 3 capsid proteins (VP1-3).

Significant Diseases

- Warts (papilloma), including condyloma acuminata (genital warts)
- Progressive Multifocal Leukoencephalopathy (PML)
- Cervical carcinoma (HPV 16, 18, 31, 33)
- Squamous cell carcinoma
- Epidermodysplasia verruciformis

The Papovavirus Family is one of the many virus families associated with human disease. The Papovavirus is divided into two subfamilies or genera, Polyomavirus and Papillomavirus. However, the family name is more indicative of the history of the virus, than of its component subsets. Papova is derived not from the combination of the subfamilies, but from the first described viruses used to define the family:

Rabbit Papilloma virus

Mouse Polyoma virus

Simian Vacuolating virus

For centuries,it had been suspected that warts were caused by some infectious agent. The transmissibility of the condition from person to person had long been recognized. But it wasn't until 1933 that the first papillomavirus was scientifically described. The Shope papillomavirus of the rabbit soon became the first specific experimental example of viral association with warts.

In the late 1950s, a poliovirus vaccine prepared in monkey cultures was contaminated with an oncogenic polyomavirus of Asian macaques, later termed Simian Virus 40 (SV40). This vaccine was administered to millions of U.S. residents. No apparent disease was induced, but the incident unsurprisingly sparked major research on the nature and pathogenesis of polyomaviruses.

The biology of papovavirus has shown to be truly fascinating. Relatively speaking, it is a small, unenveloped virus with an icosahedral capsid and a triangulation number of 7. All papovaviruses contain double-stranded DNA and replicate in the nucleus.

Perhaps the most perplexing aspect of papova biology is its gene expression. The genomes of papovaviruses such as SV40 employ differential splicing, overlapping and nested gene organizations. And to make matters even more complex, varying reading frames are used to transcribe sets of genes and "early genes" and "late genes" which insure the initial activation of the more crucial viral processes and developments.

Of the several dozen members of the papovavirus family, only a handful are associated with human disease. These viruses are human papillomavirus (HPV), and two members of the polyoma subgroup JC virus and BK virus. In recent years, HPV, in particular, has become a major source of concern as it has been consistently linked to genital cancer. Also, HPVs recent prevalence and epidemic status poses additional questions regarding future medical implications and impact. Primarily, the concern surrounds the fact that there is a continuing prevalence among adolescents and young adults despite widespread condom use, and there is uncertainty as to the existence and magnitude of a future rise or epidemic of genital cancers.

Genus Papillomavirus:

Human Papillomavirus

HPV is currently the most important papovavirus. Seventy strains of Human Papillomavirus have been identified so far. These viruses are known for their role in causing warts (both common warts and genital warts) as well as their association with cancer. Most people are infected with some strain of HPV in their lives.

Human retroviruses

Human immunodeficiency virus (HIV)

A member of the Lentivirinae subfamily of the Retroviridae family. Enveloped RNA viruses with 100–150nm in diameter virion. Replicates through DNA intermediates utilizing the RNA-directed DNA polymerase (reverse transcriptase) There are two types: HIV-1 and HIV-2 (40% sequence homology). HIV-1 is divided into three groups:M(11 subtypes A–K), and O and N groups. Group M subtypes include 95% of the global virus isolates and have worldwide distribution, whereas Major virus groups 89 groups O and N are confined to parts of West and

Central Africa. Generally HIV isolates, even from a single individual, show a high level of variation. The term quasi-species is used to describe this pool of diverse and changing viruses present in an individual.

Epidemiology

There has been worldwide spread of HIV since 1981. Estimates of prevalence worldwide vary greatly. By the end of 2010, 60 million people worldwide were estimated to be living with HIV (25 million in Africa and 7.5 million in Asia); 20 million people have died of HIV since the epidemic started in 1981.

The main risk groups for HIV infection are: men who have sex with men (MSM); intravenous drug users; people with haemophilia and blood transfusion recipients before 1985; sexually promiscuous individuals; children born to HIV-infected mothers; heterosexual contacts of HIV-infected individuals.

Pathogenesis and immune response

Transmission is mainly through sexual intercourse, via blood or blood products or from mother to child during delivery and/or breast feeding. HIV directly infects and kills cells that are essential for an effective immune response. The virus attaches to the cellular receptor CD4 and chemokine coreceptor CCR5 or CXCR4. By infecting the key cells of the adaptive immune response, this explains the main clinical feature of disease as being profound immune suppression. This results in early impairment of various CD4-cell functions followed by a decrease in CD4-cell numbers. A humoral antibody response against most HIV-specific proteins develops. In later stages, deficiency of both the humoral and the cellular immune responses leads to the development of AIDS.

Associated diseases

Immune system: Acquired immunodeficiency syndrome (AIDS) is characterised by severe disease resulting from generalised infections with bacteria including: mycobacteria, viruses (e.g. HSV, CMV and VZV), fungi (e.g. Pneumocystis, Candida, Aspergillus and Cryptococcus), protozoa including Toxoplasma and with associated tumours (Kaposi's sarcoma, lymphomas).

Diagnosis

Clotted blood: detection of HIV-specific antibody and antigen by passive particle agglutination tests (PPAT), fourth generation EIA and western blotting (WB).

EDTA-blood: molecular techniques for detecting HIV, quantifying viral load; typing and drug resistance genotyping have become a significant part of patient diagnosis and clinicalmanagement.

Treatment

Five classes of drugs are available:

1 nucleoside reverse transcriptase inhibitors (e.g.

zidovudine, lamivudine);

2 non-nucleoside reverse transcriptase inhibitors

(e.g. nevarapine and delavirdine);

3 protease inhibitors (e.g. indinavir, atazanavir);

4 fusion inhibitors (enfuvirtide);

5 integration inhibitors (raltegravir).

A combination of three drugs (highly active antiretroviral therapy or HAART) is the accepted standard form of treatment. Antiretroviral drug resistance is a continuing problem and patients require follow-up to monitor HIV load and CD4 counts.

Prevention and control

There is no antiviral cure. No effective vaccine has been developed; there are problems as a result of viral variability, latency and evasion to immune response. Testing of all blood and organ donors prevents transmission from those sources. Information campaigns, needle exchange programmes and condom use. Post-exposure prophylaxis with HAART is recommended after sexual exposure or exposure in healthcare settings.

Human T-cell lymphotropic viruses (HTLV-I and HTLV-II) Virus Members of the delta-retroviruses genus of the Retroviridae family. 90 Major virus groups The RNA genome is less variable than that of HIV; HTLV-II shows 60–70% sequence homology with HTLV-I.

Epidemiology

HTLV-I is endemic in Japan, the Caribbean, Melanesia, part of sub-Saharan Africa and Brazil.

HTLV-II is endemic among Native American Indians in North, Central and South America. A high proportion of intravenous drug users in North America are seropositive.

Pathogenesis

Transmission is by blood exposure, sexual intercourse and from mother to child through breastfeeding. HTLV-I can immortalise T lymphocytes in vitro and can transactivate T cells in vivo, but no oncogenes have been identified. No similar characteristics have been proved for HTLV-II. Most infected individuals remain asymptomatic carriers for life. Only 2–4% of infected people develop adult T-cell leukemia and lymphoma (ATLL) after many decades of infection. HTLVI can invade the CNS and the resulting inflammatory immune response is responsible for the pathogenesis of HTLV-associated myopathy (HAM).

Associated diseases

Blood: adult T-cell leukemia and lymphoma; Central nervous system: HTLV-associated myopathy; Eye: uveitis.

Diagnosis

Clotted blood: detection of HTLV-I-specific antibody is made by EIA, particle agglutination assays and western blotting; EDTA-blood: nucleic acid detection methods.

Prevention and control

Testing of all blood donors is undertaken in countries, such as the USA and the UK.

Treatment

No antiviral drugs are available.

HIV viral anatomy

Each viral particle contains two short viral RNA chains and at least three viral enzymes; reverse transcriptase, integrase and protease. Viral particles contain an outer layer that is penetrated by

pin-like viral structures. These structures are glycoproteins (gp) and are a combination of gp-120

(as the head of the pin) and gp-41 (as the stem of the pin), which play an important role in HIV attachment to target cells. HIV only infects cells that express CD4 and one type of chemokine receptor (CCR5 or CXCR4) on their surface. Attachment of gp-120 to CD4 receptor leads to a structural re-configuration of gp-120; exposing gp-41 to the cell membrane. This results in the formation of a tunnel in the membrane, through which HIV genome (RNA) and enzymes cross and enter into the cytoplasm. Agents that prevent HIV attachment to its host (target) cells are called entry inhibitors. Some may block gp-41 (e.g. enfuvertide) while others may

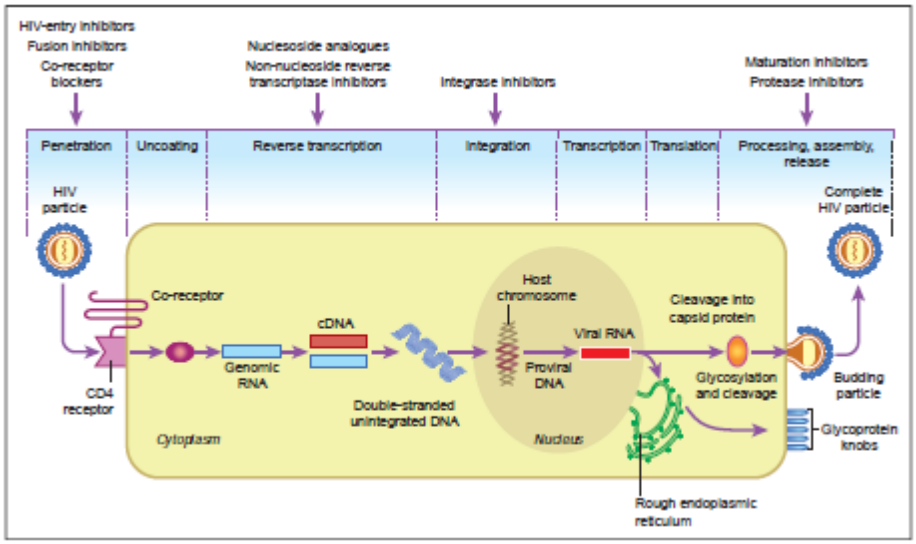


Figure 41.1 The replication cycle of HIV-1. The sites of action for the existing and investigational antiretroviral agents are shown. cDNA – complementary DNA; mRNA – messenger RNA. From Veldkamp, P. et al. Antiretroviral

Once inside the cytoplasm, reverse transcription occurs, the viral RNA acting as a template for a complementary DNA molecule utilising the HIV-specific enzyme reverse transcriptase. Therapeutic agents, synthetic nucleotides (phosphorylated nucleoside) and non-nucleotide inhibitors can be used to interfere with this process. In the absence of antiretroviral agents, the completed HIV DNA chain migrates inside the host cell's nucleus and through a complex process becomes integrated into the cell's DNA. The process involves viral integrase amongst other factors. Agents that block viral integrase can stop HIV's life cycle at this stage and are called integrase inhibitors. In the absence of integrase inhibitors, viral DNA is transcribed into chains of RNA that cross the nucleus and enter host cell's cytoplasm. Translation of

viralRNAinto its building blocks takes place in the cell's endoplasmic reticulum and free ribosomes inside the cytoplasm. The viral product of endoplasmic reticulum is gp-160 that is cleaved in the Golgi apparatus by cellular proteases into gp-41 and gp-120. Viral maturation involves a complex process in which two viral RNA chains become enclosed in the host cell's membrane and bud off from its surface into the blood. During this process HIV protease is involved in cleaving reverse transcriptase, integrase and protease from a single transcribed protein containing each of these viral enzymes. At the end of the maturation process, the new viral particle is capable of infecting new cells. Protease inhibitors stop HIV protease and prevent maturation of new viral particles, making them incapable of infecting new cells.

Epidemiology

World Health Organisation data show that in 2008, 33.4 million people had HIV, 2 million died of HIV related illnesses and 2.7 million (including 430,000 children younger than 15 years) became infected with the virus. In the UK, it has been estimated that 83,000 individuals had HIV and 27% were unaware of their diagnosis in 2009.

Routes of HIV transmission

HIV is a blood borne virus that can be transmitted sexually, which is the main route of ongoing epidemics. Historically, sexual transmission of HIV was mostly reported amongst men who have sex with men (MSM) in developed nations. Heterosexual transmission of HIV has been the main route of its transmission amongst developing nations. In the UK, heterosexual transmission of HIV has been the main route of transmission since 2000. This trend has been mostly (but not exclusively) related to immigration of people from sub-Saharan African countries.

HIV can also be transmitted during pregnancy and delivery from an infected mother to the child. However, successful antenatal screening programmes in many countries have significantly reduced the rate of mother to child transmission. Because of robust screening programmes and inactivation processes, transmission of HIV through blood products in the UK has also been extremely low since 1993. Sharing of injection equipment between intravenous drug users (IVDU) is another identified route of HIV transmission.

Pathogenesis

HIV infected CD4-containing lymphocytes are no longer able to function, leading to severe disruption in the immune response to infections, especially those requiring cellular immunity.

Table 41.1 AIDS defining illnesses

Bacterial Infections	Mycobacterium avium complex
	Disseminated Tuberculosis
	Disseminated or extrapulmonary Mycobacterial (other species) infection
	Recurrent *Salmonella* septicaemia
Fungal Infections	*Pneumocystis jiroveci* pneumonia (formerly *Pneumocystis carinii*)
	Candidiasis of bronchi, trachea or lungs
	Oesophageal candidiasis
	Disseminated or extrapulmonary coccidioidomycosis.
	Extrapulmonary cryptococcosis, extrapulmonary
Protozoal infections	Chronic intestinal cryptosporidiosis (for >1 month)
	Disseminated or extra-pulmonary histoplasmosis
	Toxoplasmosis of the brain
	Chronic intestinal isosporiasis (for >1 month)
Viral infections	Cytomegalovirus disease (other than liver, spleen or lymph nodes)
	Chronic ulcer(s) (for >1 month); bronchitis, pneumonitis or oesophagitis caused by Herpes Simplex Virus
	Progressive multifocal leukoencephalopathy
Malignancy	Invasive cervical cancer
	Kaposi's sarcoma (Figure 41.3)
	Immunoblastic or primary brain Burkitt's Lymphoma,
Others/general	HIV-related encephalopathy
	Recurrent pneumonia
	Wasting syndrome due to HIV

Prophylaxis

Correctly and consistently used male latex condoms are the most effective method for prevention of sexual transmission of HIV. Prevention of mother to child (MTC) HIV transmission relies on early diagnosis of HIV infected mothers, early commencement of highly active antiretroviral therapy (HAART), caesarean section for mothers with detectable plasma HIV viral load at the time of delivery, and avoidance of breast feeding of the infant.

Hepatitis viruses

Hepatitis viruses (includes DNA and RNA viruses)
Hepatitis A virus (HAV)
Virus
Member of Picornaviridae family of viruses, genus Hepatovirus. Small non-enveloped RNA virus 28–32nm (previously enterovirus 72); only one serotype.
Epidemiology
Most infections in endemic areas (developing world) occur before 5 years of age and the majority are asymptomatic. In the developed world, most

clinical cases occur in adults. Common source outbreaks result from contamination of drinking water and food. Infections acquired frequently by travellers from non-endemic to endemic areas. Antibody prevalence in young adults is 30–60%, higher in lower socioeconomic groups.

Pathogenesis

Transmission is via the faecal-oral route. The incubation period is 2–6 weeks (mean 30 days). All age groups are susceptible to hepatitis A infection and disease severity increases with age. In most cases, there is complete recovery and a specific antibody response persists lifelong. There is no chronic disease or carrier state.

Associated disease

Liver: Acute hepatitis.

Diagnosis

Clotted blood: serology (EIA), testing for specific HAV IgM (acute infection) or IgG (immune status); EDTA-blood: reverse-transcription PCRis carried out at a few reference laboratories to confirm difficult to interpret serology results.

Treatment

Symptomatic care. Major virus groups 87

Prevention

A killed HAV vaccine is available and recommended for high risk groups.

Hepatitis B virus (HBV)

Virus

Member of the Hepadnaviridae family of viruses. DNA virus, 42nm in diameter, consisting of: Core: DNA, partially circular genome; Nucleocapsid (hepatitis B core antigen,HBcAg); 'e' antigen (HBeAg) is a cleavage product of the core antigen found on infected cells or free in serum; Envelope (hepatitis B surface antigen, HBsAg); Also exists as 22nm spherical or filamentous particle consisting of hepatitis B surface antigen, HBsAg.

Epidemiology

Hepatitis B virus has a worldwide distribution, withmore than 360million carriers (prevalence in north and mid-Europe and North America 0.1–0.5%; southern Europe 2–5%; Africa and Southeast Asia 6–20%).

Pathogenesis

Transmission is via exposure to blood and blood products containing the virus, by sexual intercourse and vertically at birth (this is the main route of transmission in Asia and Africa); Incubation period of 6 weeks–6 months; Viral replication in liver results in lysis of hepatocytes by cytotoxic T cells in those who mount an effective immune response; Hepatic damage is reversed in 8–12 weeks in 90% cases; 2–10% become chronic carriers (persistence of HBsAg for >6 months); 95% of newborns of carrier mothers become carriers if untreated; The four phases of chronic infection include: T immune tolerance (usually infections acquired at birth); T immune clearance (many patients clear HBe antigen and covert toHBe antibody positivity); T inactive carrier (HBe antibody positive with low levels of virus present in blood); T hBeAg-

negative chronic hepatitis B (HBe antigen negative, HBe antibody positive & HBV DNA detected). Not all patients go through each of the four phases.

Associated diseases

Liver : acute, chronic carrier or rarely fulminant (rapidly progressive, with liver failure); cirrhosis; hepatocellular carcinoma.

Diagnosis

Clotted blood: serological tests are made by immunoassays detecting HBsAg, HBeAg and antibodies to HBcAg (IgM and IgG), anti-HBeAg and anti-HBsAg; EDTA-blood: for quantitative nucleic acid detection to determine viral load and genotype assessment.

Prevention

HBV vaccines and/or HBV immunoglobulin (HBIG) for post-exposure prophylaxis and babies born to carrier mothers.

Treatment

Lamivudine, adefovir, entecavir, telbivudine, clevudine and tenofovir.

Hepatitis C virus (HCV)

Virus

RNA virus, 40–50nm in diameter; Member of the Flaviviridae family of viruses. There are six main genotypes, which respond differently to antiviral treatment.

Epidemiology

HCV occurs worldwide. Antibody prevalence varies between less than 1% in the USA and Western Europe and 2% in southern Italy, Spain and central Europe. Higher prevalence rates, up to 20%, are detected in Egypt. There is high prevalence of infection among injecting drug users in most parts of the world.

Associated diseases

Liver : HCV has a similar pathogenesis to HBV; infections are followed by chronic hepatitis in 60–80% of cases; cirrhosis, hepatocellular carcinoma.

Diagnosis

Clotted blood: serology by EIA to detect HCV antibodies, antigens and by RT-PCR; EDTA-blood: to determine genotype and viral load.

Prevention

Since 1991, routine testing of all blood and organ donors for HCV antibody has been undertaken, to prevent transmission by transfusion or transplantation.

Treatment

Pegylated interferon-a, ribavirin.

Delta agent (‘hepatitis D virus’, HDV)

Virus

Defective RNA virus; 36nm in diameter, which replicates only in HBV-infected cells.

Epidemiology

Worldwide distribution; high prevalence in the Mediterranean area, Africa, South America, Japan and the Middle East. It has similar transmission and affects the same risk groups to HBV.

Associated disease

Liver: infections are either a co-infection with HBVor a superinfection of chronicHBVinfection leading to aggravation of HBV disease.

Diagnosis

Clotted blood: serology (EIA) can be used to detect HDV antibody and HDV antigen; nucleic acid detection methods are available in hepatitis reference facilities.

Prevention

HBV vaccination and subsequent immunity to HBV reduces the risk of acquiring the delta agent.

Hepatitis E virus (HEV)

Virus

Non-enveloped, positive-strand RNA virus, it represents the only species in the Hepeviridae family. There are 4 known genotypes that infect certain mammals including man.

Epidemiology

Endemic in Indian subcontinent, Southeast Asia, Middle East, North Africa and Central America. Common source outbreaks caused by contaminated water or food are common. In developed countries, sporadic cases are detected among travelers returning from endemic areas. More recently strains (genotypes 3 and 4) of hepatitis E have been detected in domestic animals in industrialized countries and are implicated in zoonotic infections.

Pathogenesis

Transmission by the faecal-oral route and rarely by blood transfusion in endemic countries Incubation period is up to 6 weeks. Specific IgG and IgM antibodies are produced.

Associated diseases

Liver: acute self-limiting hepatitis with no evidence of chronic infection. High mortality rate (10–20%) in pregnant women has been observed in India.

Diagnosis

Clotted blood: serology (detection of IgG and IgM antibodies by EIA); nucleic acid detection in reference laboratories.

Treatment

Symptomatic care.

Prevention

Vaccine under development.

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III B.Sc Biotechnology **COURSE NAME: MEDICAL MICROBIOLOGY**

COURSE CODE: 17BTU602A **UNIT: 4** **BATCH-2017-2020**

Unit 4

Fungal and Protozoan infections: Dermatophytoses (Trichophyton, Microsporun and Epidermophyton) Subcutaneous infection (Sporothrix, Cryptococcus), Systemic infection (Histoplasma, Coccidoides). Opportunistic Candidiasis.

Epidemiology

The natural habitat is humans, animals or soil; human infection results from spread from any of these reservoirs. Dermatophyte infections are found worldwide, with different species predominating in various climates.

Laboratory diagnosis

Skin scrapings, hair or nail clippings from active lesions are examined microscopically in 20–30% potassium hydroxide on a glass slide; the presence of hyphae confirms the diagnosis. Optical brighteners, such as calcofluor or blankophor, can enhance the detection of fungal elements when viewed under a fluorescence microscope. Occasionally, the dermatophyte species can be identified by typical morphology. Samples can be cultured on Sabouraud's medium at 28°C. Subsequent species identification is based on growth rate, colony appearance and microscopic morphology. Infected hair may fluoresce under ultraviolet light (Wood's light) and is characteristic of certain infections, e.g. Microsporum canis.

Treatment

Depends on the site and severity of infection. Options include topical imidazoles e.g. clotrimazole

Table 17.4 Clinically important genera of dermatophytes

Genera	Infection
Epidermophyton	*E. floccosum*, the only species. It infects the skin (tinea corporis), nails (tinea unguium), groin (tinea cruris) and feet (tinea pedis) (Plate 36)
Microsporum	*M. audouini* causes epidemic ringworm of the scalp (tinea capitis) in children. *M. canis*, which predominantly affects cats and dogs, occasionally causes ringworm in children
Trichophyton	*T. mentagrophytes* var. *interdigitale* is the most common cause of tinea pedis *T. rubrum* causes severe recurrent skin and nail infections *T. violaceum* is a common cause of tinea capitis in Asian subcontinents, North America and the West Indies *T. tonsurans* is an increasingly common cause of scalp ringworm, especially in the Afro-Caribbean population

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Trichophyton

Rippon (1988) accepted 22 species and four varieties in the genus *Trichophyton* based on morphology. DNA sequences now play a prominent role in delineating phylogenetic relationships, and as such species concepts in *Trichophyton* have changed. Sixteen species are now recognised in the genus. The descriptions and species concepts provided in this publication are based upon a combination of traditional morphological criteria and the current (2016) recognised phylogenetic species (de Hoog *et al*. 2016).

Laboratory Identification

The genus *Trichophyton* is characterised morphologically by the development of both smooth-walled macro- and microconidia. Macroconidia are mostly borne laterally directly on the hyphae or on short pedicels, and are thin- or thick-walled, clavate to fusiform, and range from 4-8 x 8-50 µm in size. Macroconidia are few or absent in many species. Microconidia are spherical, pyriform to clavate or of irregular shape and range from 2-3 x 2-4 µm in size. The presence of microconidia differentiates this genus from *Epidermophyton*, and the smooth-walled, mostly sessile macroconidia differentiates it from *Lophophyton*, *Microsporum*, *Nannizzia* and *Paraphyton*.

In practice, two groups may be recognised on direct microscopy:

1. Those species that usually produce microconidia; macroconidia may or may not be present i.e. T. *rubrum, T. interdigitale, T. mentagrophytes, T. equinum, T. erinacei, T. tonsurans*, and to a lesser extent *T. verrucosum*, which may produce conidia on some media. In these species the shape, size and arrangement of the microconidia is the most important character. Culture characteristics are also useful.

2. Those species that usually do not produce conidia. Chlamydospores or other hyphal structures may be present, but microscopy is generally non-diagnostic; i.e. *T. verrucosum, T. violaceum, T. concentricum, T. schoenleinii* and *T. soudanense*. Culture characteristics and clinical information such as the site, appearance of the lesion, geographic location, travel history, animal contacts and even occupation are most important.

Many laboratories have used growth on additional media and/or confirmatory tests to help differentiate between species of *Trichophyton*, especially isolates of *T. rubrum, T. interdigitale, T. mentagrophytes* and *T. tonsurans.* These include growth characteristics on media such as Littman oxgall agar, lactritmel agar, potato dextrose agar, Sabouraud's agar with 5% Salt, 1% peptone agar, bromocresol purple-milk solids glucose agar (BCP), Trichophyton agars No. 1-5, hydrolysis of urea and hair perforation tests.

Microsporum

Microsporum is a genus of fungi that causes tinea capitis, tinea corporis, ringworm, and other dermatophytoses (fungal infections of the skin). *Microsporum* forms both macroconidia (large asexual reproductive structures) and microconidia (smaller asexual reproductive structures) on short conidiophores. Macroconidia are hyaline, multiseptate, variable in form, fusiform, spindle-shaped to obovate, 7–20 by 30–160 um in size, with thin or thick echinulate to verrucose cell walls. Their shape, size and cell wall features are important

characteristics for species identification. Microconidia are hyaline, single-celled, pyriform to clavate, smooth-walled, 2.5–3.5 by 4–7 um in size and are not diagnostic for any one species.

The separation of this genus from *Trichophyton* is essentially based on the roughness of the macroconidial cell wall, although in practice this may sometimes be difficult to observe. Seventeen species of *Microsporum* have been described; however, only the more common species are included in these descriptions.

The genus *Microsporum* is now restricted to just three species: *M. audouinii, M. canis* and *M. ferrugineum*. The remaining geophilic and zoophilic species, previously considered *Microsporum* species, have been transferred to the genera *Lophophyton, Nannizzia* and *Paraphyton.*

Laboratory Identification

Microsporum species may form both macro- and microconidia, although they are not always present. Cultures are mostly granular to cottony, yellowish to brownish, with a cream-coloured or brown colony reverse. Macroconidia are hyaline, multiseptate, with thick rough cell walls, and are clavate, fusiform or spindle-shaped. Microconidia are single-celled, hyaline, smooth-walled, and are predominantly clavate in shape.

Epidermophyton floccosum

Epidermophyton floccosum is an anthropophilic dermatophyte with a worldwide distribution which often causes tinea pedis, tinea cruris, tinea corporis and onychomycosis. It is not known to invade hair *in vivo* and no specific growth requirements have been reported.

Morphological Description

Colonies are usually slow growing, greenish-brown or khaki-coloured with a suede-like surface, raised and folded in the centre, with a flat periphery and submerged fringe of growth. Older cultures may develop white pleomorphic tufts of mycelium. A deep yellowish-brown reverse pigment is usually present. Microscopic morphology shows characteristic smooth, thin-walled macroconidia which are often produced in clusters growing directly from the hyphae. Numerous chlamydospores are formed in older cultures. Microconidia are not formed.

Subcutaneous Mycoses

These are chronic, localized infections of the skin and subcutaneous tissue following the traumatic implantation of the aetiologic agent. The causative fungi are all soil saprophytes of regional epidemiology whose ability to adapt to the tissue environment and elicit disease is extremely variable.

Sporothrix

Sporotrichosis is primarily a chronic mycotic infection of the cutaneous or subcutaneous tissues and adjacent lymphatics characterized by nodular lesions which may suppurate and ulcerate.

Infections are caused by the traumatic implantation of the fungus into the skin, or very rarely, by inhalation into the lungs. Secondary spread to articular surfaces, bone and muscle is not infrequent, and the infection may also occasionally involve the central nervous system, lungs or genitourinary tract.

Fixed cutaneous sporotrichosis:

Primary lesions develop at the site of implantation of the fungus, usually at more exposed sites mainly the limbs, hands and fingers. Lesions often start out as a painless nodule which soon become palpable and ulcerate often discharging a serous or purulent fluid. Importantly, lesions remain localised around the initial site of implantation and do not spread along the lymphangitic channels. Isolates from these lesions usually grow well at 35C, but not at 37C.

Lymphocutaneous sporotrichosis:

Primary lesions develop at the site of implantation of the fungus, but secondary lesions also appear along the lymphangitic channels which follow the same indolent course as the primary lesion ie they start out as painless nodules which soon become palpable and ulcerate. No systemic symptoms are present. Isolates from these lesions usually grow well at both 35C and 37C.

Pulmonary sporotrichosis:

This is a rare entity usually caused by the inhalation of conidia but cases of haematogenous dissemination have been reported. Symptoms are nonspecific and include cough, sputum production, fever, weight loss and upper-lobe lesion. Haemoptysis may occur and it can be massive and fatal. The natural course of the lung lesion is gradual progression to death.

Osteoarticular sporotrichosis:

Most patients also have cutaneous lesions and present with stiffness and pain in a large joint, usually the knee, elbow, ankle or wrist. Osteomyelitis seldom occurs without arthritis; the lesions usually confined to the long bones near affected joints.

Other rare forms of sporotrichoisis include endophthalmitis, chorioretinitis and meningitis.

Laboratory diagnosis:

1. **Clinical material:**

   A tissue biopsy is the best specimen.

2. **Direct Microscopy:**

   Tissue sections should be stained using PAS digest, Grocott's methenamine silver (GMS) or Gram stain.

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Interpretation:
Look for small narrow base budding yeast cells (2-5um). **Note** they are often present in very low numbers and may be difficult to find. PAS and GMS stains are essential.

3. Culture:

Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood.

Interpretation:
A positive culture from a biopsy should be considered significant.

3. **Serology:**

   Serological tests are of limited value in the diagnosis of Sporotrichosis.
4. **Identification:**

   Hyphomycete characterized by thermal dimorphism and clusters of ovoid, denticulate conidia produced sympodially on short conidiophores.
5. **Causative agents:**

   Sporothrix schenckii complex.

Cryptococcus
C. neoformans, C. grubii and C. gattii are encapsulated yeasts that cause cryptococcal meningitis. The first two are found worldwide, whilst C. gattii is associated with Eucalyptus and is most common in Australia and parts of Africa. Their natural habitat is soil, particularly soil contaminated with pigeon droppings, which due to the presence of high molecular weight nitrogenous compounds, act as a natural selective medium.
Cryptococcal species have polysaccharide capsules that can be visualised in clinical specimens, such as cerebrospinal fluid, bymixing the fluid with Indian ink. They can be isolated from sputum, bronchoalveolar lavage fluid, tissue biopsies and other clinical specimens, or the capsular antigen can be detected by sensitive and specific latex agglutination tests on CSF or serum.
Infection is thought to be acquired by inhalation of yeast cells, which become desiccated and are blown on air currents.Humaninfections are rare; most occur in immunocompromised individuals, including those with HIV.
Primary infection occurs in the lungs and is usually asymptomatic. Acute pneumonia may occur with fungaemia and infection in various organs, particularly the brain and meninges. Treatment of cryptococcal meningitis is with amphotericin and flucytosine in combination, followed by fluconazole.

Systemic infection

Fever, often low grade (38.5°C), rigors on flushing catheter, no other obvious focus of infection. The clinical diagnosis of intravascular catheter related infection may be difficult to establish as a result of the non-specific clinical presentation.

Laboratory diagnosis

Localised infection: culture of exit site swab (high negative predictive value); Systemic infection: semi-quantitative/quantitative culture of explanted CVC tip. If systemic CVC infection is suspected, paired blood cultures (via separate peripheral venepuncture and CVC) should be taken for analysis.

Treatment

Depends on causative microorganism; if *Staphylococcus aureus*, *Candida albicans* or coliforms, then appropriate antimicrobial therapy and catheter removal; if coagulase-negative staphylococci (CoNS), may attempt antibiotic treatment without catheter removal.

Prevention

Good aseptic technique pre- and post-insertion aids in reducing intravenous catheter infection.

Histoplasmosis

Histoplasmosis is a type of lung infection. It is caused by inhaling *Histoplasma capsulatum* fungal spores. These spores are found in soil and in the droppings of bats and birds. This fungus mainly grows in the central, southeastern, and mid-Atlantic states.

Most cases of histoplasmosis don't require treatment. However, people with weaker immune systems may experience serious problems. The disease may progress and spread to other areas of the body. Skin lesions have been reported in 10 to 15 percent of cases of histoplasmosis that has spread throughout the body.

Possible symptoms include:

- fever
- dry cough
- chest pain
- joint pain
- red bumps on your lower legs

In severe cases, symptoms may include:

- excessive sweating
- shortness of breath

- coughing up blood

Widespread histoplasmosis causes inflammation and irritation. Symptoms may include:

- chest pain, caused by swelling around the heart
- high fever
- stiff neck and headaches, from swelling around the brain and spinal cord

Causes

Fungal spores can be released into the air when contaminated soil or droppings are disturbed. Breathing the spores may lead to an infection.

The spores that cause this condition are commonly found in places where birds and bats have roosted, such as:

- caves
- chicken coops
- parks
- older barns

You can get histoplasmosis more than once. However, the first infection is generally the most severe.

The fungus doesn't spread from one person to another and it's not contagious.

Types of Histoplasmosis

Acute

Acute, or short-term, histoplasmosis is typically mild. It rarely leads to complications.

The Centers for Disease Control and Prevention (CDC) estimate that between 60 and 90 percentTrusted Source of people who live in areas where the fungus is common have been exposed. Many of these people probably did not have any symptoms of infection.

Chronic

Chronic, or long-term, histoplasmosis occurs far less often than the acute form. In rare cases, it can spread throughout the body. Once histoplasmosis has spread throughout your body it is life-threatening if it isn't treated.

Widespread disease usually occurs in people with impaired immune systems. In areas where the fungus is common, the CDC says that it may occur in up to 30 percentTrusted Source of people with HIV.

There are two major risk factors for developing this disease. The first is working in a high-risk occupation and the second risk factor is having a compromised immune system.

Occupations

You are more likely to be exposed to histoplasmosis if your job exposes you to disturbed soil or animal droppings. High-risk jobs include:

- construction worker
- farmer
- pest control worker
- demolition worker
- roofer
- landscaper

Weakened Immune Systems

Many people who have been exposed to histoplasmosis do not get noticeably sick. However, your risk of severe infection is higher if you have a compromised immune system. Conditions associated with weakened immunity include:

- being very young or very old
- having HIV or AIDS

- taking strong anti-inflammatory medications like corticosteroids
- undergoing chemotherapy for cancer
- taking TNF inhibitors for conditions such as rheumatoid arthritis
- taking immunosuppressant drugs to prevent a transplant rejection

Potential Long-Term Complications of Infection

In rare cases, histoplasmosis can be life-threatening. Therefore, it is extremely important to get treatment.

Histoplasmosis can also cause a number of complications.

Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome can develop if your lungs fill with fluid. This can lead to dangerously low levels of oxygen in your blood.

Heart Function Issues

Your heart might not be able to function normally if the area around it becomes inflamed and full of fluid.

Meningitis

Histoplasmosis can cause a serious condition called meningitis. Meningitisoccurs when the membranes surrounding your brain and spinal cord become infected.

Adrenal Glands and Hormone Problems

Infection can damage your adrenal glands and this may cause problems with hormone production.

Testing for and Diagnosing Histoplasmosis

If you have a mild case of histoplasmosis, you may never know that you were infected. Testing for histoplasmosis is usually reserved for people who both have a severe infection and live or work in a high-risk area.

To confirm a diagnosis, your doctor may conduct blood or urine tests. These tests check for antibodies or other proteins that indicate prior contact with histoplasmosis. Your doctor might also take urine, sputum, or blood cultures to make an accurate diagnosis. However, it can take up to six weeks to get results.

Depending on what parts of your body are affected, you may need other tests. Your doctor might take a biopsy(tissue sample) of your lung, liver, skin, or bone marrow. You might also need an X-ray or computerized tomography (CT) scan of your chest. The purpose of these tests is to determine if additional treatments are needed to address any complications.

Treatments for Histoplasmosis

If you have a mild infection, you probably won't need treatment. Your doctor might instruct to you rest and take an over-the-counter medication for symptoms.

If you have trouble breathing or are infected for longer than one month, treatment may be necessary. You will likely be given an oral antifungal medication, but you may also require IV treatment. The most commonly used drugs are:

- ketoconazole
- amphotericin B
- itraconazole

If you have a severe infection, you might need to take your medication intravenously (through a vein). This is how the strongest medications are delivered. Some people may have to take antifungal medication for up to two years.

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Prevention

You can reduce your risk of infection by avoiding high-risk areas. These include:

- construction sites
- renovated buildings
- caves
- pigeon or chicken coops

If you can't avoid high-risk areas, there are steps you can take to help keep spores from getting into the air. For example, spray sites with water before working or digging in them. Wear a respirator mask when there is a high risk of exposure to spores. Your employer is obligated to provide you with appropriate safety equipment if it's needed to protect your health.

Coccidioides

Coccidioides is a genus of dimorphic ascomycetes in the family Onygenaceae. Member species are the cause of coccidioidomycosis, also known as San Joaquin Valley fever, an infectious fungal disease largely confined to the Western Hemisphere and endemic in the Southwestern United States.[2] The host acquires the disease by respiratory inhalation of spores disseminated in their natural habitat. The causative agents of coccidioidomycosis are *Coccidioides immitis* and *Coccidioides posadasii*. Both *C. immitis* and *C. posadasii* are indistinguishable during laboratory testing and commonly referred in literature as *Coccidioides*.

Clinical Presentation

Both Coccidioides species share the same asexual life cycle, switching between saprobic (on left) and parasitic (on right) life stages.

Coccidioidomycosis is amazingly diverse in terms of its scope of clinical presentation, as well as clinical severity. About 60% of *Coccidioides* infections as determined by serologic conversion are asymptomatic. The most common clinical syndrome in the other 40% of infected patients is an acute respiratory illness characterized by fever, cough, and pleuritic pain. Skin manifestations, such as erythema nodosum, are also common with *Coccidioides* infection. *Coccidioides* infection can cause a severe and difficult-to-treat meningitis in AIDS and other immunocompromised patients, and occasionally in immunocompetent hosts. Infection can sometimes cause acute respiratory distress syndrome and fatal multilobar pneumonia. The risk of symptomatic infection increases with age.

Epidemiology

The primary coccidioidomycosis-endemic areas are located in Southern California and southern Arizona, and northern Mexico, in Sonora, Nuevo León, Coahuila, and Baja California, where it resides in soil. Both *C. immitis* and *C. posadasii* were viewed as desert saprophytes, but recent genomic research revealed *Coccidioides* species to have evolved interacting with their animal hosts.

Etymology

The soil fungus *Coccidioides* was discovered in 1892 by Alejandro Posadas, a medical student, in an Argentinian soldier with widespread disease. Biopsy specimens revealed organisms that resembled the protozoan Coccidia (from the Greek kokkis, "little berry"). In 1896, Gilchrist and Rixford named the organism *Coccidioides* ("resembling Coccidia") *immitis* (Latin for “harsh,” describing the clinical course). Ophüls and Moffitt proved that *C. immitis* was a fungus rather than a protozoan in 1900. In 2002, *C. immitis* was divided into a second species, *C. posadasii*, after Alejandro Posadas.

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KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III B.Sc Biotechnology **COURSE NAME: MEDICAL MICROBIOLOGY**
COURSE CODE: 17BTU602A **UNIT: 5** **BATCH-2017-2020**

Unit 4
Opportunistic fungal infections (Candidiasis, Aspergillosis), Gastro intestinal infections (Amoebiasis, Giardiasis), Blood-borne infections (Leishmaniasis, Malaria).

Opportunistic Systemic Mycoses

These are fungal infections of the body which occur almost exclusively in debilitated patients whose normal defence mechanisms are impaired.
The organisms involved are cosmopolitan fungi which have a very low inherent virulence. The increased incidence of these infections and the diversity of fungi causing them, has parallelled the emergence of AIDS, more aggressive cancer and post-transplantation chemotherapy and the use of antibiotics, cytotoxins, immunosuppressives, corticosteroids and other macro disruptive procedures that result in lowered resistance of the host.

Candidiasis

Candidiasis is a primary or secondary mycotic infection caused by members of the genus *Candida* and other related genera. The clinical manifestations may be acute, subacute or chronic to episodic. Involvement may be localized to the mouth, throat, skin, scalp, vagina, fingers, nails, bronchi, lungs, or the gastrointestinal tract, or become systemic as in septicemia, endocarditis and meningitis. In healthy individuals, *Candida* infections are usually due to impaired epithelial barrier functions and occur in all age groups, but are most common in the newborn and the elderly. They usually remain superficial and respond readily to treatment. Systemic candidiasis is usually seen in patients with cell-mediated immune deficiency, and those receiving aggressive cancer treatment, immunosuppression, or transplantation therapy.

Candidiasis

There are many kinds of fungus that live in the human body. One type is called candida. It's a type of yeast that normally lives in small amounts in places like your mouth and belly, or on your skin without causing any problems. But when the environment is right, the yeast can multiply and grow out of control.
The infection it causes is called candidiasis. There are several different types of it. Most can be easily treated with over-the-counter or prescription medications.

Thrush (Oropharyngeal Candidiasis)
When the candida yeast spreads in the mouth and throat, it can cause an infection called thrush. It's most common in newborns, the elderly and people with weakened immune systems. Also more likely to get it are adults who:

- Are being treated for cancer
- Take medications like corticosteroids and wide-spectrum antibiotics
- Wear dentures

- Have diabetes

The symptoms include:

- White or yellow patches on the tongue, lips, gums, roof of mouth, and inner cheeks
- Redness or soreness in the mouth and throat
- Cracking at the corners of the mouth
- Pain when swallowing, if it spreads to the throat

Thrush is treated with antifungal medicines like nystatin, clotrimazole, and fluconazole. Rinsing the mouth with chlorhexidine (CHX) mouthwash may help prevent infections in people with weakened immune systems.

Genital Yeast Infection (Genital Candidiasis)

Three out of four adult women will get at least one yeast infection during their lifetime. This occurs when too much yeast grows in the vagina. (Men also can get a genital yeast infection, but it's much less common).

A yeast infection typically happens when the balance in the vagina changes. This can be caused by pregnancy, diabetes, use of some medicines, lubricants, or spermicides, or a weakened immune system. Occasionally, the infection can be passed from person to person during sex.

The symptoms include:

- Extreme itchiness in the vagina
- Redness and swelling of the vagina and vulva (the outer part of the female genitals)
- Pain and burning when you pee
- Discomfort during sex
- A thick, white “cottage cheese” discharge from the vagina

A man with a yeast infection may have an itchy rash on his penis.

Candidiasis

The genus Candida contains a large number of species, about eight of which are regularly found causing infection. C. albicans remains the most frequently isolated pathogen, although infection with C. glabrata appears to be increasing and C. parapsilosis and C. tropicalis are also frequently encountered. C. albicans is a commensal of the mouth and gastrointestinal tract.

Superficial Candida infections are common and include vaginal and oral candidiasis (thrush), skin and nail infections, which can arise in warm, moist areas such as skin folds or because hands are immersed in water for long periods, and as a complication of antibiotic therapy that temporarily reduces the bacterial flora.

Invasive Candida infections usually arise from the patients own commensal flora following surgery, use of broad spectrum antibiotics or intravascular catheters and can affect any organ of the body. Candidaemia may result in abscesses in various organs (e.g. brain, liver, spleen). These infections

occur primarily in immunocompromised patients. Endophthalmitis is another potential consequence of candidaemia.

Candida can also colonise prosthetic materials, e.g. intravascular catheters and peritoneal dialysis catheters, resulting in bloodstream infection and peritonitis, respectively. Candida spp. are a rare cause of endocarditis.

Laboratory diagnosis

By direct microscopy of appropriate clinical material for oval Gram-positive cells, some of which may be budding or producing pseudohyphae (a string of elongated cells produced as a result of budding in some yeasts); culture; and serology for Candida antibodies or antigen in patients with deep-seated infections. Budding yeast and pseudomycelia (a mycelium-like mass of pseudohyphae) may also be seen with appropriate stains in histopathological specimens.

Treatment

Topical with an azole, nystatin or amphotericin; parenteral therapy is with fluconazole, flucytosine, itraconazole, voriconazole, posaconazole, caspofungin, anidulafungin, micafungin or amphotericin

Overview

Aspergillosis is an infection caused by a type of mold (fungus). The illnesses resulting from aspergillosis infection usually affect the respiratory system, but their signs and severity vary greatly.

The mold that triggers the illnesses, aspergillus, is everywhere — indoors and outdoors. Most strains of this mold are harmless, but a few can cause serious illnesses when people with weakened immune systems, underlying lung disease or asthma inhale their fungal spores.

In some people, the spores trigger an allergic reaction. Other people develop mild to serious lung infections. The most serious form of aspergillosis — invasive aspergillosis — occurs when the infection spreads to blood vessels and beyond.

Depending on the type of aspergillosis, treatment may involve observation, antifungal medications or, in rare cases, surgery.

Symptoms

The signs and symptoms of aspergillosis vary with the type of illness you develop:

Allergic reaction

Some people with asthma or cystic fibrosis have an allergic reaction to aspergillus mold. Signs and symptoms of this condition, known as allergic bronchopulmonary aspergillosis, include:

- Fever
- A cough that may bring up blood or plugs of mucus
- Worsening asthma

Aspergilloma

Certain chronic lung (pulmonary) conditions, such as emphysema, tuberculosis or advanced sarcoidosis, can cause air spaces (cavities) to form in the lungs. When people with lung cavities are also infected with aspergillus, fungus fibers may find their way into the cavities and grow into tangled masses (fungus balls) known as aspergillomas.

Aspergillomas may produce no symptoms or cause only a mild cough at first. Over time and without treatment, however, aspergillomas can worsen the underlying chronic lung condition and possibly cause:

- A cough that often brings up blood (hemoptysis)
- Wheezing
- Shortness of breath
- Unintentional weight loss
- Fatigue

Invasive aspergillosis

This is the most severe form of aspergillosis. It occurs when the infection spreads rapidly from the lungs to the brain, heart, kidneys or skin. Invasive aspergillosis occurs only in people whose immune systems are weakened as a result of cancer chemotherapy, bone marrow transplantation or a disease of the immune system. Untreated, this form of aspergillosis may be fatal.

Signs and symptoms depend on which organs are affected, but in general, invasive aspergillosis can cause:

- Fever and chills
- A cough that brings up blood (hemoptysis)
- Shortness of breath
- Chest or joint pain
- Headaches or eye symptoms
- Skin lesions

Other types of aspergillosis

Aspergillus can invade areas of your body other than your lungs, such as your sinuses. In your sinuses, the fungus can cause a stuffy nose sometimes accompanied by drainage that may contain blood. Fever, facial pain and headache may also occur.

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If you have asthma or cystic fibrosis, see your doctor whenever you notice a change in your breathing. Although aspergillosis may not be the cause, it's important to have breathing problems evaluated.

If you have a weakened immune system and develop an unexplained fever, shortness of breath or a cough that brings up blood, get immediate medical care. In the case of invasive aspergillosis, prompt treatment is crucial. In some cases, treatment with antifungal medication begins as soon as aspergillosis is suspected, even before testing has confirmed the diagnosis.

Causes

Aspergillus mold is unavoidable. Outdoors, it's found in decaying leaves and compost and on plants, trees and grain crops.

Everyday exposure to aspergillus is rarely a problem for people with healthy immune systems. When mold spores are inhaled, immune system cells surround and destroy them. But people who have a weakened immune system from illness or immunosuppressant medications have fewer infection-fighting cells. This allows aspergillus to take hold, invading the lungs and, in the most serious cases, other parts of the body. Aspergillosis is not contagious from person to person.

Risk factors

Your risk of developing aspergillosis depends on your overall health and the extent of your exposure to mold. In general, these factors make you more vulnerable to infection:

- **Weakened immune system.** People taking immune-suppressing drugs after undergoing transplant surgery — especially bone marrow or stem cell transplants — or people who have certain cancers of the blood are at highest risk of invasive aspergillosis. People in the later stages of AIDS also may be at increased risk.
- **Low white blood cell level.** People who have had chemotherapy, an organ transplant or leukemia have lower white cell levels, making them more susceptible to invasive aspergillosis. So does having chronic granulomatous disease — an inherited disorder that affects immune system cells.
- **Lung cavities.** People who have air spaces (cavities) in their lungs are at higher risk of developing aspergillomas.
- **Asthma or cystic fibrosis.** People with asthma and cystic fibrosis, especially those whose lung problems are long-standing or hard to control, are more likely to have an allergic response to aspergillus mold.

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- **Long-term corticosteroid therapy.** Long-term use of corticosteroids may increase the risk of opportunistic infections, depending on the underlying disease being treated and what other drugs are being used.

Complications

Depending on the type of infection, aspergillosis can cause a variety of serious complications:

- **Bleeding.** Both aspergillomas and invasive aspergillosis can cause severe, and sometimes fatal, bleeding in your lungs.
- **Systemic infection.** The most serious complication of invasive aspergillosis is the spread of the infection to other parts of your body, especially your brain, heart and kidneys. Invasive aspergillosis spreads rapidly and may be fatal.

Prevention

It's nearly impossible to avoid exposure to aspergillus, but if you have had a transplant or are undergoing chemotherapy, try to stay away from places where you're likely to encounter mold, such as construction sites, compost piles and buildings that store grain. If you have a weakened immune system, your doctor may advise you to wear a face mask to avoid being exposed to aspergillus and other airborne infectious agents.

Gastrointestinal infection

There are a number of bacteria, viruses, and parasites that cause gastrointestinal (GI) infections. According to the U.S. Centers for Disease Control and PreventionTrusted Source, diarrheal diseases account for 1 in 9 child deaths worldwide. It affects 2,195 children every day — more than AIDS, malaria, and measles combined.

Symptoms of gastrointestinal infection

Although they can continue for as long as 14 days, GI infections usually last a few days. They're characterized by abdominal cramps and discomfort followed by diarrhea. Other symptoms might include:

- nausea
- vomiting
- fever
- loss of appetite

- muscle aches
- dehydration
- headache
- mucus or blood in the stool
- weight loss

Common causes of gastrointestinal infections

Here are a few common types of GI infections.

Bacterial

- ***E. coli.*** *E. coli bacteria* are found in the intestines of people and animals. Most varieties are harmless, but some strains — such as *E. coli* O157:H7 — secrete a toxin that can cause abdominal cramps, vomiting, and bloody diarrhea. *E. coli* spread through contaminated water or food that came into contact with animal manure. *E. coli* can also spread through direct person-to-person contact.
- ***Salmonella***. Salmonella infection is commonly caused by eating raw or undercooked poultry, meat, and eggs. The majority of salmonella infections can be classified as gastroenteritis.

Viral

- **Norovirus.** Noroviruses are the most common cause of foodborne illness worldwide. It's especially likely to spread among people in confined spaces. Although in most cases the virus is spread through contaminated food or water, person-to-person transmission is also possible.
- **Rotavirus.** According to the Mayo Clinic, rotavirus is the leading cause of viral gastroenteritis in children worldwide. Children are commonly infected when they touch objects contaminated with the virus and then put their fingers in their mouths. There's a rotavirus vaccine available in some countries.

Parasite

- **Giardiasis.** *Giardia* is a parasite that spreads easily through human contact and contaminated water. It's resistant to chlorine and can spread in public swimming pools. Infection can occur from drinking water from and bathing in contaminated lakes and streams.
- **Cryptosporidiosis.** A leading cause of waterborne disease in the United States, *Cryptosporidium* is a microscopic parasite which causes cryptosporidiosis. It has an outer shell that helps it survive outside of a host and tolerate chlorine disinfection.

Adults

See your doctor right away if you:

- have a fever above 104°F (40°C)
- have an inability to keep liquids down for 24 hours
- are vomiting for more than 48 hours
- are vomiting blood
- are becoming dehydrated: excessive thirst, dry mouth, little or no urine (or deep yellow urine), extreme weakness, lightheadedness or dizziness
- have blood in your bowel movements

Children

See your pediatrician right away if your child:

- has a fever of above 102°F (39°C)
- is experiencing a lot of discomfort or pain
- appears lethargic
- is very irritable
- has bloody diarrhea
- appears dehydrated

To tell if your child is dehydrated, you can monitor how much they're drinking and urinating and compare to their typical amount.

Infants

Get your baby to their pediatrician right away if they:

- have been vomiting (not just normal spitting up) for more than several hours
- have a dry mouth
- haven't had a wet diaper in six hours
- cries without tears
- has severe diarrhea
- has bloody stools
- is unresponsive
- is unusually drowsy or sleepy
- has a sunken soft spot on the top of their head

Treatment for gastrointestinal infections

In most cases, self-care measures are the recommended treatment. Antibiotics will not help GI infections from viruses or parasites.

Although antibiotics can help with complicated cases of bacterial infection, in uncomplicated cases, antibiotics may actually prolong the condition and increase risk of relapse.

Additionally, in certain infections, antibiotics may lead to dangerous complications. Your doctor can help determine if you or your child need antibiotics.

Your doctor might recommend that you stay away from high-fiber foods that could make diarrhea worse. They might also recommend over-the-counter medications that neutralize stomach acid or that treat nausea, abdominal pain, and diarrhea.

The most important self-care treatment for adults and children with a GI infection is to stay hydrated.

Amebiasis

Amebiasis is a parasitic infection of the intestines caused by the protozoan *Entamoeba histolytica,* or *E. histolytica*. The symptoms of amebiasis include loose stool, abdominal cramping, and stomach pain. However, most people with amebiasis won't experience significant symptoms.

Risk for amebiasis

Amebiasis is common in tropical countries with underdeveloped sanitation. It's most common in the Indian subcontinent, parts of Central and South America, and parts of Africa. It's relatively rare in the United States.

People with the greatest risk for amebiasis include:

- people who have traveled to tropical locations where there's poor sanitation
- immigrants from tropical countries with poor sanitary conditions
- people who live in institutions with poor sanitary conditions, such as prisons
- men who have sex with other men
- people with compromised immune systems and other health conditions

Causes

E. histolytica is a single-celled protozoan that usually enters the human body when a person ingests cysts through food or water. It can also enter the body through direct contact with fecal matter.

The cysts are a relatively inactive form of the parasite that can live for several months in the soil or environment where they were deposited in feces. The microscopic cysts are present in soil, fertilizer, or water that's been contaminated with infected feces. Food handlers may transmit the cysts while preparing or handling food. Transmission is also possible during anal sex, oral-anal sex, and colonic irrigation.

When cysts enter the body, they lodge in the digestive tract. They then release an invasive, active form of the parasite called a trophozite. The parasites reproduce in the digestive tract and migrate to the large intestine. There, they can burrow into the intestinal wall or the colon. This causes bloody diarrhea, colitis, and tissue destruction. The infected person can then spread the disease by releasing new cysts into the environment through infected feces.

Symptoms of amebiasis

When symptoms occur, they tend to appear 1 to 4 weeks after ingestion of the cysts. According to the Centers for Disease Control and PreventionTrusted Source (CDC), only about 10 to 20 percent of people who have amebiasis become ill from it. Symptoms at this stage tend to be mild and include loose stools and stomach cramping.

Once the trophozites have breached the intestinal walls, they can enter the bloodstream and travel to various internal organs. They can end up in your liver, heart, lungs, brain, or other organs. If trophozites invade an internal organ, they can potentially cause:

- abscesses
- infections
- severe illness
- death

If the parasite invades the lining of your intestine, it can cause amebic dysentery. Amebic dysentery is a more dangerous form of amebiasis with frequent watery and bloody stools and severe stomach cramping.

The liver is a frequent destination for the parasite. Symptoms of amebic liver disease include fever and tenderness in the upper-right part of your abdomen.

Diagnosis

A doctor may suspect amebiasis after asking about your recent health and travel history. Your doctor may test you for the presence of *E. histolytica*. You may have to give stool samples for several days to screen for the presence of cysts. Your doctor may order lab tests to check liver function to help determine if the ameba has damaged your liver.

When the parasites spread outside the intestine, they may no longer show up in stool. So your doctor may order an ultrasound or CT scan to check for lesions on your liver. If lesions appear, your

doctor may need to perform a needle aspiration to see if the liver has any abscesses. An abscess in the liver is a serious consequence of amebiasis.

Finally, a colonoscopy may be necessary to check for the presence of the parasite in your large intestine (colon).

Treatments

Treatment for uncomplicated cases of amebiasis generally consists of a 10-day course of metronidazole (Flagyl) that you take as a capsule. Your doctor may also prescribe medication to control nausea if you need it.

If the parasite is present in your intestinal tissues, the treatment must address not only the organism but also any damage to your infected organs. Surgery may be necessary if the colon or peritoneal tissues have perforations.

Amebiasis generally responds well to treatment and should clear up in about 2 weeks. If you have a more serious case where the parasite appears in your internal tissues or organs, your outlook is still good as long as you get appropriate medical treatment. If amebiasis is left untreated, however, it can be deadly.

Prevention

Proper sanitation is the key to avoiding amebiasis. As a general rule, thoroughly wash hands with soap and water after using the bathroom and before handling food.

If you're traveling to places where the infection is common, follow this regimen when preparing and eating food:

- Thoroughly wash fruits and vegetables before eating.
- Avoid eating fruits or vegetables unless you wash and peel them yourself.
- Stick to bottled water and soft drinks.
- If you must drink water, boil it or treat it with iodine.

- Avoid ice cubes or fountain drinks.
- Avoid milk, cheese, or other unpasteurized dairy products.
- Avoid food sold by street vendors.

Giardiasis

Giardiasis is an infection in your small intestine. It's caused by a microscopic parasite called *Giardia lamblia*. Giardiasis spreads through contact with infected people. And you can get giardiasis by eating contaminated food or drinking contaminated water. Pet dogs and cats also frequently contract giardia.

This condition can be found all over the world, according to the Centers for Disease Control and Prevention (CDC). However, it's more common in overcrowded developing countries that lack sanitary conditions and water quality control.

Causes of giardiasis

G. lamblia are found in animal and human feces. These parasites also thrive in contaminated food, water, and soil, and can survive outside a host for long periods of time. Accidentally consuming these parasites can lead to an infection.

The most common way to get giardiasis is to drink water that contain *G. lamblia*. Contaminated water can be in swimming pools, spas, and bodies of water, such as lakes. Sources of contamination include animal feces, diapers, and agricultural runoff.

Contracting giardiasis from food is less common because heat kills the parasites. Poor hygiene when handling food or eating produce rinsed in contaminated water can allow the parasite to spread.

Giardiasis also spreads through personal contact. For example, unprotected anal sex can pass the infection from one person to another.

Changing a child's diaper or picking up the parasite while working in a day care center are also common ways to become infected. Children are at high risk for giardiasis because they're likely to encounter feces when wearing diapers or potty training.

Symptoms of giardiasis

Some people can carry giardia parasites without experiencing any symptoms. Symptoms of giardiasis generally show up one or two weeks after exposure. Common symptoms include:

- fatigue
- nausea
- diarrhea or greasy stools
- loss of appetite
- vomiting
- bloating and abdominal cramps
- weight loss
- excessive gas
- headaches
- abdominal pain

Diagnosis

You may have to submit one or more stool samples for testing. A technician will check your stool sample for giardia parasites. You could have to submit more samples during treatment. Your doctor may also perform an enteroscopy. This procedure involves running a flexible tube down your throat and into your small intestine. This will allow your doctor to examine your digestive tract and take a tissue sample.

Treatments for giardiasis

In most cases, giardiasis eventually clears up on its own. Your doctor might prescribe medication if your infection is severe or prolonged. Most doctors will recommend treatment with antiparasitic drugs, rather than leaving it to clear up on its own. Certain antibiotics are commonly used to treat giardiasis:

- Metronidazole is an antibiotic that needs to be taken for five to seven days. It can cause nausea and leave a metallic taste in your mouth.
- Tinidazole is as effective as metronidazole, and often treats giardiasis in a single dose.
- Nitazoxanide is a popular option for children because it's available in liquid form and only needs to be taken for three days.
- Paromomycin has a lower chance of causing birth defects than other antibiotics, although pregnant women should wait until after delivery before taking any medication for giardiasis. This medication is given in three doses over the course of 5 to 10 days.

Complications

Giardiasis can lead to complications such as weight loss and dehydration from diarrhea. The infection can also cause lactose intolerance in some people. Children under 5 years old who have giardiasis are at risk for malnutrition, which can interfere with their physical and mental development.

Prevention

You can't prevent giardiasis, but you can lower your risk of getting it by thoroughly washing your hands, especially if you work in places where germs spread easily, such as day care centers.

Ponds, streams, rivers, and other bodies of water can all be sources of giardia. Don't swallow water if you go swimming in one of these. Avoid drinking surface water unless it's been boiled, treated with iodine, or filtered. Bring bottled water with you when you go hiking or camping.

When traveling in a region where giardiasis occurs, don't drink tap water. You should also avoid brushing your teeth with tap water. Keep in mind that tap water can also be present in ice and other beverages. Avoid eating uncooked local produce.

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Be cautious about sexual practices associated with the spread of this infection, such as anal sex. Use a condom to reduce the chance of contracting giardiasis.

Giardiasis infections usually last about six to eight weeks, but problems such as lactose intolerance can persist after the infection clears up.

	Opt 1	Opt 2	Opt 3	Opt 4
Unit I				
The sputum specimen must be stored	10°C	5°C	4°C	8°C
the blood samples should be collecte	late	early	before diagnosis	after symptom
When a parasite is growing and multi	pathogen	infection	organism	diagnose
For microbiological examination urin	good	sterile	normal	clean catch mid-strea
Cary-Blair medium is used for the tra	blood	CSF	stool	urine
a parasite organism or agent that proc	pathagon	parasite	bacteria	virus
the ability of an organism to cause di	diagnosis	symptoms	pathogenicity	disease
The most important step in the diagn	Specimen	Organism	Symptoms	Prophylaxis
In case of meningeal irritation or affe	blood	cerebrospinal	urine	pus
in blood specimens is seperat	haemoglobin	serum	iron	protein
The collected CSF should be stored a	room temperat	4C	2C	5C
is a good transport medi	agar medium	peptone water	Cary-Blair medi	alkaline medium
An alternate transport medium for stc	alkaline-pepto	peptone water	alkaline medium	water
A sterile is used for transport	container	plastic contain	screw-cap conta	metal container
Specimens must be collected before a	Vaccines	Antimicrobial	Symptoms	Culturing
To eliminate normal flora skin surfac	Germicide	Soap	Vaseline	Cotton
Pus swabs collected in transport med	2	4	6	8
During blood collection the skin shou	Isopropyl alcol	Antiseptic	Soap	Antibiotic
About _____ ml of blood should	10	20	30	40
the blood samples should be incubate	25°C	37°C	4°C	10°C
_____ ml of urine sample should be c	10	40	30	20
In case of _____ only few millilit	Arthritis	Gas gangrene	Renal failure	Paralysis
If the urine sample is delayed for mo	Amino acid	Boric acid	Sodium chllorid	Calcium chloride
In case of suspected renal tuberculosi	1	2	3	4
The CSF should be collected from __	Cerebrum	Cerebellum	Ventricle	Arachnoid space
In case of infants the CSF should be c	Ventricle	Arachnoid spa	Cerebrum	Cerebellum
About _____ ml of CSF should b	10	30	40	20
For collecting nasopharyngeal aspirat	Sterile catheter	Syringe	Swab	Cotton
_____ is collected in case of eye s	Pus	Mucous	Conjuctival scra	Conjunctival tissue
Respiratory secretions should be tran	1	2	3	4
The natural secretions of eye contain	Antibiotic	Toxins	Antibacterial	Amylase
If not possible to obtain faeces a spec	Cotton woll sw	Syringe	Catheter	Cotton
Salmonella, Shigella and Vibrio survi	24	48	32	76
Campylobacter can survive in C-B m	2	4	6	8
If cholera is suspected the stool samp	1	3	5	8
_____ is the transportation mediu	CB medium	Boric acid	Alkaline pepton	Phosphate buffered s
For suspected viral enteritis the stool	Phosphate buf	Alkaline pepto	CB medium	Boric acid
About _____ ml of sterile phospha	3	6	9	12
_____ is the transportation mediun	Trisodium citr	Sodium chllor	Boric acid	Calcium chloride
About _____ ml of synovial, pleur	2 to 3	5 to 6	3 to 5	4 to 6
Synovial, pleural and ascitic fluids sh	Antibiotic	Antiseptic	Anticoagulant	Antibacterial
In case of sputum sample the sample	morning	Evening	Mid night	Noon
_____ bacilli requires entirely diff	Rod shaped	Spindle shape	Club shaped	Acid-fast
In suspected anthrax the pus sample s	Lesions	Scrapings	Edema	Necrosis

For darkfield examination pus from s	Salt solution	Saline solutio	Anticoagulant	Antiseptic
In case of tuberculosis _____ spe	Stool	Urine	Blood	Sputum
The sputum sample collected in pape	Saline solution	Anticoagulant	Formalin solutio	Salt solution
_____ technique is used to stain aci	Ziehl Neelsen	Gram staining	Endospore staini	Quellung
In bacilliary dysentry _____ yields	Smears	Swabs	Rectal swabs	Renal smears
In case of salmonellosis _____ sa	Urine	Stool	Sputum	Blood
In case of thyphoid _____ sample sl	Sputum	Blood	Faeces	CSF
In order to avoid drying of stool samp	Thioglycollate	Sodium citrate	Buffered glycer	Para amino benzoic a
A n alternative for Thioglycollate sen	Sodium citrate	Buffered glyc	Para amino benz	Thioglycollate semis
_____ should be incorporated in a	Trisodium citra	Formalin solu	Sodium citrate	Para amino benzoic a
_____ is added to the blood samp	Sodium citrate	Thioglycollate	Antiseptic	Antibacterial
Once the specimen is collected the cc	Labelled	Opened	Diluted	Defined
Samples of blood and CSF for cultur	Labelled	Refrigerated	Processed	Incubated
The sputum sample should be free fr	Blood	Pus	Saliva	Tissue
when the patient has symptoms of cy	blood	Pus	Sputum	urine
In case of suspected septicemia ____	blood	Pus	Sputum	urine

Unit II

In Greek 'pathos means _____	Suffering	violence	disease	infection
The lodgement and multiplication	disease	infection	immunity	parasitism
Initial infection with a parasite in a	primary	secondary	re-infection	nosocomial
Subsequent infection by the same	Primary	Secondary	Re-infection	Iatrogenic
When a new parasite sets up an in	Primary	Secondary	Re-infection	Iatrogenic
Infection or sepsis at localized site	Primary	Secondary	Focal	Iatrogenic
In a patient already suffering from	Cross	Focal	Re-infection	Nosocomial
Cross infection occurring in hospi	Cross	Focal	. Re-infection	
Physicians induced infections are t	Iatrogenic	Focal	Nosocomial	Re-infection
When clinical effects are not appa	Atypical	Inapparent	Subclinical	Clinical
_____ infection is the one in w	Endogenous	Exogenous	Inapparent	Clinical
Some parasites, following infectio	Endogenous	Exogenous	Latent	Atypical
A person who arbours the pathoge	Patient	Carrier	Healthy person	Immunodeficient pe
A person one who harbours the pa	Healthy carrie	Convalescent	Contact carrier	Paradoxical carrier
A person who have recovered fron	Healthy	Convalescent	Contact	Paradoxical
The _____ carrier state lasts th	Acute	Temporary	Chronic	Healthy
The term _____ carrier is appli	Acute	Temporary	Contact	Paradoxical
The _____ carrier state lasts for s	Acute or chro	Temporary	Contact	Paradoxical
The term _____ carrier refers to a	Healthy	Convalescent	Contact	Paradoxical
Infectious diseases transmitted fro	Zoonosis	Anoosis	Xanthosis	Phytosis
When the pathogen multiplies in t	Mechanical	Biological ve	Healthy	Contact
Some pathogens are able to cross t	Congenital	Intracelaine	Vertical	Horizontal
_____ is generally employed t	Infection	Immunity	Pathogenicity	Virulence
_____ is applied to the same	Infection	Immunity	Pathogenicity	Virulence
_____ is the science that eval	Epidemiology	Oncology	Infection	Physiology
An individual who practices epide	Epidemiologi	Scientist	Investigator	Environmentalist
A _____ is an impairement of the	Health	Disease	Infection	Immunity
_____ is the condition in which t	Health	Disease	Infection	Immunity

When a disease occurs occasionall	Epidemic	Endemic	Sporadic	Pandemic
When the disease occurs at a stead	Epidemic	Endemic	Sporadic	Pandemic
_____ disease gradually inc	hyperendemic	Epidemic	Endemic	Pandemic
An_____is a sudden incre	Epidemic	Endemic	sporadic	Pandemic
The first case in an epidemic is cal	index case	infection	disease	outbreak
A sudden unexpected occurrence c	index case	Infection	disease	outbreak
A_____is an increase in di	epidemic	Endemic	Pandemic	Sporadic
The factors that influence the freq	epizootiology	Zootiology	Epidemiology	Entamology
Moderate prevalance of a disease i	epizootic	enzootic	panzootic	zoonoses
A sudden outbreak of disease in ar	epizootic	enzootic	panzotic	zoonoses
A wide dissemination of aniomals	epizoolic	enzoolic	panzootic	zoonoses
Animal disease that can be transm	epizootic	enzootic	panzootic	zoonoses
A _____ period is the period b	incubation	survival	lag	log
The _____ is the period in wl	incubatiob pe	prodromal st	survival period	death
The _____ represents the events	infectious dis	disease	infection	injury
_____ is an illness caused by a	communicabl	epidemic	epidemic	injury
The _____ is the time during v	incubation pe	the period of	predormal stag	injury
The water used in the lab is tested	Quarentum	GTL	Materials secti	Dispatch
The Goods purchased is stored at_	Dispatch sect	Materials se	Quarentum sec	Stock section
The water used in laboratory is pu	Catridge	Pad	Sinted glass	Earthern ware
The monitoring of the lab environ	QA	QC	GTL	QB
The microbial load of lab environr	Settle plate	Pour plate	Spread plate	Streak plate.
The AHU stands for_____	Aerosol hand	Air handling	Atmosphere ha	Auto handling unit
_____ controls the microbes	Air pressure	a. Aerosol	Atmosphere	oxygen
The circulating air is filtered in lat	Pad	Candle	HEPA	Catridge
The discard materials to be_____	Dissuaded	Dispenced	Decontaminate	sterilized
Quality control checks the quality	QA	QC	GTL	QB
The proper disposal of biologicals	Epidemic	Endemic	Pandemic	Randamic
There is no single reliable test ava	Antibiotics	Antiseptics	Disinfectants	Diluent.
In the Rideal walker test typhoid b	Phenol	Boron	Acid	Alcohol
_____ is a product ketan	. HCL	BPL	TNT	SDS
QA stands for _____	Quality assur	Quality assoc	Quality accepta	Quality abolision.

Unit III

species often resemble Staph	micrococcus	streptococcus	lactococcus	staphylococcus
established the pathogenic	pasteur	emil von behri	jenner	alexander ogston
staphylococci can grow in the presen	peptone	beef extract	NaCl	lactose
is the selective medium for isolatio	blood agar	PLET	nutrient agar	crystal violet blood a
local infection of superficial layers o	impetigo	pustule	hemorrhage	meningitis
The test is used for the identi	slide coagulase	tube coagulase	Grams test	serum test
Streptococcus pyogenes are more sen	amoxycillin	penicillin	erythromycin	bacitracin
the disease common in dockworkers	hide porter's di	gas gangrene	edeme	toxemia
_____ strains usually secrete bot	micrococcus	streptococcus	staphylococcus a	E.coli
Vegetative cells of Bacilli are destroy	60°C	40°C	20°C	10°C
The spores of Bacillus anthracis were	20	30	40	60

Lepra bacilli have been found to rema	100	80	46	20
The Lepra bacilli seen in large numb	Common disea	Multibaciliry (	Gas gangrene	Symptomatic disease
was the first effective chemoth	rifampicin	clofazimine	ethionamide	dapsone
_____ vaccine was used to preven	BCG	Polio vaccine	Leprosy vaccine	Rabies vaccine
The Lepra bacillus was first observed	Jenner	Behring	Pasteur	Hansen
The diphtheria bacillus was first obse	Pasteur	Hansen	Klebs	Loeffler
Typing in Pneumococcus may be can	serum typing	Quellung	Bamboo-stick	stickland
Corynebacterium exists in a _____	Rod	Cocci	Varied	Spindle shaped
On repeated subculture Pneumococci	smooth-rough	rough-smooth	smooth	rough
is always a secondary in	meningitis	hemorrhage	paralysis	Broncho-pneumonia
The strain used to produce the diphth	Bacillus Calme	Park Williams	Park Williams 5	Bacillus Calmette 8 s
The diagnostically important constan	Bile solubility	serum solubili	symptoms	pathogeicity
The incubation period of Lepra bacill	5 to 6	2 to 5	4 to 9	1 to 3
The BCG vaccine used to prevent lep	Fernandez	Pasteur	Jenner	Hansen
Preventation of anthrax in animals is	prophlaxix	treatment	active immuniza	antibiotics
reaction is useful for the prima	M'Fadyean's	Quellung	Nagler	immunization
Staphylococci are lysed under the inf	Penicillin	streptomycin	amoxycillin	dapsone
is a typical of Staphycoccal infe	pus	edema	focal suppuratio	impetigo
Streptococcal sore throat is commonl	sore throat	Strep.throat	infection	disease
named the strains Staphylo	Jenner	Behring	Rosenbach	Klebs
Typical Staphylococci are seen in the	pus	blood	stool	urine
is the selective medium used for	PLET	blood agar	Mac-conkey	PDA
In cultures Bacillus were arranged en	chain	Bamboo-stick	cluster	thread-like
The of Corynebacterium was	exotoxin	antitoxin	size	shape
type of complications are mc	fever	headache	paralytic	nausea
Food poisoningby Clostridium perfri	fish	egg	soup	meat
Pneumococci were first noticed by	Nagler	Robert Hooke	Pasteur and Ster	Kleb and Loeffler
The toxin produced by virulent strain	exotoxin	endotoxin	antitoxin	toxin
The drug of choice for treating gas ga	Penicillin	streptomycin	metranidazole	Amoxycillin
The irregularly stained boat or leaf sh	citron bodies	pleomorphs	irregular bodies	boat bodies
The arrangement of diphtheria bacilli	V shaped	L shaped	Chinese	Bamboo- stick
The causative agent of gas gangrene i	streptococcus	micrococcus	Clostridium perf	Corynebacterium
Clostridium species can grow well in	PLET	Robertson's cc	PDA	Mac-conkey
_____ dyes are used to stain Pneumo	Acidic dyes	Basic dyes	Neutral dyes	Aniline dyes
The most important antigen of Pneun	Type specific (	Type specific	Type specific an	Type specific antibod
When sputum is not available	blood	serum	serum coated lar	egg
is an antigeniccomponent of	lipopolysaccha	teichoic acid	lactate	iron
Staphylococcus cause_____	Tumour	Boils	Lesion	Fever
Staphylococcus were first observe	Vonreckling l	Ogsten	Passet	Pasteur
Staphylococcus citreus produce__	Red	Blue	Brown	Yellow
Non virulent Staphylococcus is fo	Water	Hospital	. Skin	Hair
Mannitol is fermented by _____	Virulant	Avirulant	Commensal	Normal flora
Oil paint appearance is seen in___	Nutrient broth	Nutrient agar	Blood agar	Blood broth
In intoxication the disease is cause	Toxoid	Tetroid	.Enzyme	Toxin

Alpha haemolysis means _____	Complete	Irregular	. Partial	Nolysis
Beeta haemolysis means _____	Complete	Irregular	Partial	Nolysis
Selective media for Staphylococcu	Manittol salt a	Mac conkey a	Blood agar	LJ agar
Streptococcus shows _____	Alpha	Beta	Gamma	delta
Pneumococcus habitate in the ___	Liver	Urinary tr	Respiratory tra	Bone marrow

Unit IV

Vibrio cholerae shows res	negative	positive	neutral	no reaction
CLED stands for _____agar .	cystine lactos	crystalviolet	citrate lactose e	cultural lactose elec
Strains of V.cholerae O1 is subdiv	V.cholerae O	Hikojima	panama	Ogawa
Widal test is performed for the ser	*V.cholerae O.*	*Salmonella*	*Klebsiella*	*Pseudomonas*
E.coli is an _____ in humans	Pathogen	predator	Parasite	commensal
E.coli exhibits IMViC_____	.++--	--++	.+-+-	++++
The K antigen in *E.coli* is compos	Protein	lipid		carbohydrate
._____is known as travelers c	EPEC	ETEC	EHEC	EAEC
EHEC is also known as_____	EPEC	EAEC	VTEC	EXEC
SIDS is seen in case of _____	*E.coli*	*Klebsiella*	*Proteus*	*Pseudomonas*
Klebsiella is_____	Non motile a	motile and ca	Non motile and	motile and non caps
Klebsiella exhibits_____ col	Dry	mucoid	Pale	diffuse
K. pneumoniae is also known as _	Jansen's bacil	Koch's bacill	Friedlander's b	Escherich's bacilli
Klebsiella exhibits IMViC_____	++--	--++	+++	----
The tribe proteae are_____	Fermentors	. non ferment	Late fermentor	early fermentors
The proteae is classified into_____	One	two	three	Four
Proteus exhibits _____ m	Swarming	no	Fish in stream	Darting
The predominant aerobic bacterial	Non sporing b	non acid fast	viruses	Gram negative baci
The clinical picture of dysentery is	*Mycobacteria*	*Pseudomona*	*Klebsiella*	*Shigella*
Shigella is _____	Flagellated.	sporing	capsulated	Non motile
The selective medium used for *Shi*	Deoxycholate	EMB	MSA	Martin Thayer
The *Shigella* culture filtrates dem	Hypersensitiv	Lytic	Chemotoxicity	Neurotoxicity
The minimum infective dose for o	10-50 bacilli	10-100 bacill	100-1000 bacil	1-10 bacilli
Bacillary dysentery has an incubat	6 hours	1 day	1-7 days	more than 7 days
The main features of bacillary dys	Rice watery d	presence of p	Abdominal dis	Loose scanty feces
The infection with *Salmonella* is	Malaise	gastric ulcer	Septicemia	Enteric fever
Salmonella is known as_____	Eberth gaffky	Shiga	Friedlander's	Escherich
Salmonella typhi is the causative a	Typhoid feve	paratyphoid f	Enteric fever	Malaise
The incubation period of *Salmone*	6 hours	1 day	1-7 days	7-14 days
The infective dose for *Salmonella*	1-10 bacilli	100000 bacil	100000000 bac	10000 bacilli
Vibrio is _____rods.	Helical	Elongated	Twisted	Curved
Vibrio cholerae was first isolated	Pasteur	Koch	Paccini	Boyd
Vibrio is_____	Motile	Non motile	Slime	Capsulated.
Vibrio cholerae are_____rods	Gram positive	Non motile	Spore forming.	curved, Cylindrical.
._____Is used as transp	Alcohol medi	Acid	sea water	V R Medium
Vibrio colonies may be easily ider	Biochemical t	String test	Cultural charac	Coombs test
Heiberg classified Vibrios into___	2	4	6	8
The route of infection with Vibrio	Oral	respiratory tr	Ingestion	inhalation

Pseudomonas is motile by_____	polar	bipolar	peritrichous	Atrichous
*Vibrio is motile by*_____ *fl*	Atrichous	peritrichous	polar	Lopotrichous.
Glycocalyx is composed of _____	Protein	lipid	Polysaccharide	carbohydrate
*Pseudomonas produces*_____	Ruby	lucosin	Pyocynanin	Verdin
Pyocyanin is a _____ co	Blue	green	. Red	yellow
Pyocynanin is soluble in_____	Acid	Base	chloroform , W	ether
Fluorescin is_____ colored p	Greenish yell	Green	red	blue
Pyorubin is_____colored pi	yellow	Green	red	blue
Pyomelanin is_____ colored p	brown	red	Green	yellow
Pseudomonas aeruginosa produc	Pyocyanin	melanin	rubin	verdin
The term 'blue pus' is associated v	*Proteus*	*Pseudomona*	*E.coli*	*Vibrio*
._____is used as selective me	Citrimide aga	EMB	DCA	MSA
enteric fever is caused by _____	Salmonella ty	S. paratyphi l	S. enterica	Proteus
EHEC strains are able to secrete _	verotoxin	exotoxin	endotoxin	exfoliate toxin
._____isolated influenza baci	Andrews and	Koch	Boyd	Pasteur
The accessory factors required by	X and Y	X and V	X and Z	Y and Z
_____ enzyme aids the invas	pectinase	elastase	protease	amylase
._____is the drug of choice	Chloramipher	Bacitracin	ceftazidime, C	Streptomycin
selective media for Pseudomonas a	Mac conkey a	blood agar	PLET	Dettol agar
. *T. pallidum* causes_____	Syphilis	typhoid	Tuberculosis	pertusis
T. pallidum are highly sensitive to	Acid	Antiseptics	drying	antibiotic
Pseudomonas mainly causes____	Primary infec	secondary in	re- infection	nosocomial infectio
Unit V				
The common post operator conseq	Fever	gangrene	cold	sore
Semelweiss was able to control __	puerperal sep	meningitis	cholera	diarrhoea
Lister overcome surgical infection	acid	base	charcoal	phenol
The concept of asepsis _____ t	reduce	elevate	. increase	improve
The incidence of hospital infectior	10-20%	12-20%	2-12%	10-15%
In hospital environment the norm	Drug resistan	common	Nosocomial	saprophyte
Hospital acquired infection is also	Nominal	Neutral	Normal	Nosocomial
Hospital acquired infection are typ	Exogenous	Endogenous	Epigenous	Eugenous
. _____ is diagnostic inte	Primary infec	re infection	post infection	Iatragenic infection
The opportunity of a microorganis	Diet	immune	Invasive	Infection
The hospital environment is heavil	Commensals	Contaminant	Pathogen	Normal flora
The blister caused in bed return p	Bed sore	Bedbug	Bedding	Bed wet
The slightest lapse in asepsis in h	Invention	Infection	Interaction	Innovatoin
_____ is the important cause	E.coli	Treponema	HIV	Streptococcus pyog
Staphylococcus of drug resistant b	80/81	60/61	10/10/	44/10
The drug resistance is _____	Phage	Plasmid	Phasmid	cosmid
. _____ can grow	E.coli	Klebsiella	Pseudomonas	Proteus
_____ spores can surviv	Tetanus	E.coli	Klebsiella	Bacillus
HIV is transmitted through _____	Sputum	Urine	Blood	Stool
Viral infection are transmitted thro	Pus	Blood	CSF	Swab
_____ the pathogen cause	Candida	E.coli	Klebsiella	Cryptococcus

Stitch abscesses is _____ infe	Brain	Wound	. CSF	Pus
Streptococcus wound infection m	Month	Year	Week	Day
Clostridial wound infection manif	Month	Year	Week	Day
Pseudomonas cause infection in__	Burns	Wound	Brain	Blood
Neonatal tetanus have occurred du	Blood	Body	Umblical cord	Brain
Cathetrization cause _____	UTI	RTI	CTI	systemic
About _____ of patient UTI cc	10 percent	2percent	5percent	7percent
E.coli and Proteus cause_____ i	Mixed	single	. combined	complicated
_____ catheter are used in p	French	Glass	Indwelling	Rubber
Pulmonary ventilation may lead to	Pneumonia	. Bleeding	Abscesses	Fever
Multiplication of bacteria in blood	Bacteria	Bacteremia	Viremia	Septicemia
Multiplication of virus in blood ca	Bacteria	Bacteremia	Viremia	Septicemia
viral infection are transmitted thro	. Fungemia	Bacteremia	Viremia	Septicemia
The liberation of toxin in blood is	Fungemia	Bacteremia	Viremia	Toximia
Pus filled cavity called as_____	Abscesses	Lesion	Necrosis	Fever
Programmed cell death is called as	Abscesses	. Lesion	Necrosis	Fever
Stool sample must be transported	1 hour	2 hours	3 hours	4 hours
Fever inducing agent is called as_	Pyrogen	Pyogen	Phelm	Parotid
Phlebitis sets in with consequent _	Bacteria	Bacteremia	Viremia	Septicemia
Staphylococcus epidermidis bacte	Skin	Catheter	Heart valve	Inhaler
Many hospital infection occur as_	Epidemic	Endemic	Pandemic	Randamic
When out break occurs the source	Cultured	Eliminated	Elevated	Intricate
An important contribution of micr	Immunization	Innovation	Infection	Intricate
At sixth week _____ vaccina	OPV	BCG	DPT	TT
At tenth week _____ vaccina	OPV	BCG	DPT	TT
At ninth month _____ vacci	OPV	BCG	DPT	measles
At 5-6 years _____ vaccinati	DT	BCG	DPT	TT
At 10 years _____ vaccinatic	DT	BCG	DPT	TT
At 16 years _____ vaccinatic	DT	TT	DPT	BCG
Pregnant women should be given a	DT	BCG	DPT	TT
OPV –O is given at _____ to c	At birth	Week	Month	Year
Booster dose help _____cells to	. B	T	Memmory	Plasma
Fever of unknown origin is called_	Pyrexia	Pyrogen	Pyogen	Phylogenic
Ulcer on finger is called as_____	Boils	Tuleremia	Wound	Abscesses
Di dot is a test used for_____	HIV	Rabies	Meningitis	Carditis
Inflammation of meninges is calle	Meningia	Meningitis	Peritonitis	Carditis
Arthritis is a _____ disorder	Immune	Auto immun	Mental	Blood
Allergic manifestation is called as_	Hypersensitiv	Hyposensitiv	. sensitivity	Histeria
Topical ointments are used for ___	Bacteria	Bacteremia	Viremia	Septicemia

Answer

4°C
early
infection
clean catch mid-stream
stool
pathagon
pathogenicity
Specimen
cerebrospinal fluid
serum
room temperature
Cary-Blair medium
alkaline-peptone water
screw-cap container
Antimicrobial drugs
Germicide
6
Isopropyl alcohol
20
37°C
20
Renal failure
Boric acid
3
Arachnoid space
Ventricle
20
Sterile catheter
Conjuctival scrapings
2
Antibacterial
Cotton woll swab
48
6
8
Alkaline peptone water
Phosphate buffered saline
9
Trisodium citrate
2 to 3
Anticoagulant
morning
Acid-fast
Lesions

Saline solution
Sputum
Formalin solution
Ziehl Neelsen
Rectal swabs
Blood
Blood
Thioglycollate semisolid medium
Buffered glycerol water
Para amino benzoic acid
Sodium citrate
Labelled
Refrigerated
Saliva
urine
blood

Suffering
infection
primary
Re-infection
Secondary
Focal
Cross
Nosocomial
Iatrogenic
Inapparent
Inapparent
Latent
Carrier
Healthy carrier
Convalescent
Temporary
Contact
Acute or chronic
Paradoxical
Zoonosis
Biological vector
Vertical
Pathogenicity
Virulence
Epidemiology
Epidemiologist
Disease
Infection

Endemic
Endemic
hyperendemic
Pandemic
index case
outbreak
Pandemic
epizootiology
enzootic
panzotic
zoonoses
zoonoses
incubation
prodromal stage
infectious disease cycle
communicable disease
predormal stage
GTL
Quarentum section
Catridge
QC
Settle plate
Air handling unit
Air pressure
HEPA
Decontaminated
QA
Epidemic
Disinfectants
Phenol
BPL
Quality assurance

streptococcus
alexander ogston
NaCl
crystal violet blood agar
impetigo
slide coagulase test
bacitracin
hide porter's disease
staphylococcus aureus
60C
60

46
Multibaciliry disease
dapsone
BCG
Hansen
Klebs
Quellung
Varied
smooth-rough
Broncho-pneumonia
Park Williams 8 Strain
Bile solubility
2 to 5
Fernandez
active immunization
M'Fadyean's
Penicillin
focal suppuration
sore throat
Rosenbach
pus
PLET
Bamboo-stick
antitoxin
paralytic
meat
Pasteur and Sternberg
exotoxin
metranidazole
pleomorphs
Chinese
Clostridium perfringens
Robertson's cooked meat
Aniline dyes
Type specific capsular polysaccharide
serum coated laryngeal swabs
teichoic acid
Lesion
Vonreckling hausen
Yellow
. Skin
Virulant
Nutrient agar
Toxin

. Partial
Complete
Manittol salt agar
Beta
Bone marrow

positive
cystine lactose electrolyte deficient
Ogawa
Salmonella
Parasite
.++--
Polysaccharide
ETEC
VTEC
E.coli
Non motile and capsulated
mucoid
Friedlander’s bacilli
--++
. non fermentors
three
Swarming
Gram negative bacilli
Shigella
Non motile
Deoxycholate citrate agar
Neurotoxicity
10-100 bacilli
1-7 days
Loose scanty feces
Enteric fever
Eberth gaffky
Typhoid fever
7-14 days
100000000 bacilli
Curved
Koch
Motile
curved, Cylindrical.
V R Medium
String test
6
Oral

polar
polar
Polysaccharide
Pyocynanin
Blue
chloroform , Water
Greenish yellow
red
brown
Pyocyanin
Pseudomonas
Citrimide agar
Salmonella typhii
verotoxin
Andrews and Laidlaw
X and V
elastase
Chloramiphenicol
Dettol agar
Syphilis
drying
nosocomial infection

Fever
puerperal sepsis
phenol
reduce
2-12%
Drug resistant
Nosocomial
Exogenous
Iatragenic infection
immune
Contaminants
Bed sore
Infection
Streptococcus pyogenes.
80/81
Phage
Pseudomonas
Tetanus
Blood
Blood
Candida

Wound
Day
Day
Burns
Umblical cord
UTI
2percent
Mixed
Indwelling
Pneumonia
Bacteremia
Viremia
Viremia
Toximia
Abscesses
Necrosis
2 hours
Pyrogen
Bacteremia
Skin
Endemic
Eliminated
Immunization
BCG
DPT
measles
DT
TT
TT
TT
At birth
Memmory
Pyrexia
Tuleremia
HIV
Meningitis
Auto immune
Hypersensitivity
Bacteria