

IMMUNOLOGY AND MEDICAL MICROBIOLOGY

Study of the general characteristics of disease caused by bacteria, viruses, fungi and protozoa

G. Prasad, Minakshi and Swati Dahiya

Department of Animal Biotechnology

College of Veterinary Sciences

CCS Haryana Agricultural University

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BACTERIAL DISEASES

Tetanus

Tetanus (Greek *tetanus*, means to stretch) is a serious and often fatal disease caused by the neurotoxin tetanospasmin which is produced by an anaerobic Gram-positive spore forming bacterium *Clostridium tetani*. Infection usually originates from a contaminated wound. Endospores of *C. tetani* are commonly found in hospital environment, soil and dust, and in the faeces of many farm animals. Common symptoms are muscle spasms in the jaw (hence the common name 'lockjaw'), followed by difficulty in swallowing and general muscle stiffness in other parts of the body. Infection can be prevented by proper immunization, as well as by post-exposure prophylaxis. Tetanus was first documented by Hippocrates, and records dating back to the 5th century BC are available. However, the etiology of the disease was not discovered until 1884 by physician Arthur Nicolaier. Passive tetanus immunization was first implemented during World War I. Bacilli of *C. tetani* can be found in soil (especially agricultural soil), and the intestines and feces of horses, sheep, cattle, rats, dogs, cats, guinea pigs, and chickens.

Symptoms

On the basis of clinical profile four different forms of tetanus have been observed. I. Generalized (most common), II. Neonatal (a common cause of infant mortality in underdeveloped countries), III. local (uncommon) and IV. cephalic (rare). Generalized tetanus accounts for 80% of tetanus cases. The incubation period for tetanus is 3 days to as long as 15 weeks. The first sign of tetanus is a mild jaw muscle spasm called 'lockjaw' (trismus), followed by stiffness of the neck and back, difficulty in swallowing, and muscle rigidity in the abdomen. These muscle contractions are due to a neurotoxin tetanospasmin produced by *C. tetani*. The toxin selectively cleaves the synaptic vesicle membrane protein synaptobrevin. This prevents exocytosis and inhibits the release of gamma aminobutyric acid and glycine, the neurotransmitters that serve to inhibit muscle contraction.

Typical signs of tetanus include an increase in body temperature by 2 to 4°C, diaphoresis (excessive sweating), and elevated blood pressure. Death usually results from spasms of the diaphragm and intercostal respiratory muscles. *C. tetani* also produces a second toxin called 'tetanolysin' is a hemolysin that causes tissue destruction.

Treatment

The wound must be cleaned, dead and infected tissue should be removed surgically. Metronidazole will help decrease the amount of bacteria however; it has no effect on the bacterial toxin. Human anti-tetanospasmin immunoglobulin (or tetanus immune globulin) is a crucial part of treatment. All tetanus victims should be vaccinated against tetanus or offered a booster vaccine if they have been previously vaccinated. In addition to the measures given above, 5000 units of tetanus immunoglobulin IV or IM, metronidazole 500mg IV for 10 days, diazepam 5 to 20mg tds PO and tetanus vaccination should be given.

Diagnosis

Bacteriological confirmation of the clinical diagnosis is usually difficult because very few *C. tetani* are present in the wound. A search should be made for 'drumstick' bacilli in films and an attempt should be made to isolate the organism by culture and by injection of material from the wound into mice or guinea-pigs. Molecular diagnostic methods such as PCR should be used.

Prevention and Control

Tetanus can be prevented by vaccination. One tetanus booster presently used is called DPT (a protection from diphtheria, pertussis and tetanus). An initial dose is administered a few months after birth, a second dose 4-6 months later and finally a reinforcing dose 6-12 months after the second injection. A final booster is given between the ages of 4-6 years. A booster vaccine is recommended every ten years. Worldwide, there are approximately one million cases of tetanus each year. Tetanus, particularly the neonatal form, remains a significant public health problem in non-industrialized countries, causing an estimated 300,000 to 500,000 deaths each year.

Control measures for tetanus are very difficult because of the wide dissemination of the bacterium in the soil and the long survival of its endospores. The mortality rate in generalized tetanus ranges from 30 to 90% because tetanus treatment is not very effective. Therefore prevention is all the more important and depends on active immunization with toxoid, proper care of wounds contaminated with soil, prophylactic use of antitoxin, and administration of penicillin.

Diphtheria

Diphtheria is an upper respiratory tract disease characterized by mild fever, sore throat and the formation of a pseudomembrane on the tonsil (s), pharynx, and/or nose. A local lesion develops in the upper respiratory tract and involves necrotic injury to epithelial cells. As a result of this injury, blood plasma leaks into the area and a fibrin network forms which is interlaced with rapidly-growing *C. diphtheriae* cells. This membranous network covers over the site of the local lesion and is called the 'pseudomembrane'. A milder form of diphtheria may be confined to the skin.

The causative agent of diphtheria is *Corynebacterium diphtheriae*, an aerobic Gram-positive bacterium. Diphtheria used to be quite common fifty years ago. However, it has been eradicated in developed countries by effective use of DPT (diphtheria-tetanus-pertussis) vaccine.

Diphtheria continues to be an important human disease, with fatality rates ranging from 5 to 20%. Outbreaks, though very rare, still occur worldwide, even in developed countries. After the breakup of the former Soviet Union in the late 1980s, vaccination rates in its constituent countries fell so low that there was an explosion of diphtheria cases in these countries. In 1991 there were 2,000 cases of diphtheria in the USSR. By 1998, according to Red Cross estimates, there were as many as 200,000 cases in the Commonwealth of Independent States, with 5,000 deaths. There was such a great increase that diphtheria was cited in the Guinness Book of World Records as 'most resurgent disease'. Such statistics show that constant monitoring and

surveillance must be maintained even on largely eradicated diseases, especially since many of these diseases show growing resistance to drugs that have been used to fight them for decades.

Signs and symptoms (Respiratory form)

The sick persons experience fatigue, fever, a mild sore throat and problems in swallowing. Infected children have symptoms that include chills, nausea, vomiting and a high fever, although some do not show symptoms until the infection has progressed further. About in 10% of cases, patients experience neck swelling. These cases are associated with a higher risk of death. In addition to symptoms at the site of infection (sore throat), the patient may experience more generalized symptoms, such as listlessness, pallor, and fast heart rate. These symptoms are caused by the toxin released by the bacterium. Low blood pressure may develop in these patients. Longer-term effects of the diphtheria toxin include cardiomyopathy and peripheral neuropathy (sensory type).

Cutaneous form

The cutaneous form of diphtheria is often a secondary infection of a preexisting skin disease. Signs of cutaneous diphtheria infection develop on an average of 7 days after the appearance of the primary skin disease.

Diphtheria is a highly contagious disease spread by inhaling the secretions of those infected or direct physical contact with infected persons. The onset of disease is usually gradual. The respiratory form of diphtheria has an incubation period of 2-5 days.

Diagnosis

The diagnosis of diphtheria is based on both clinical symptoms and laboratory findings. Clinical criteria include upper respiratory tract illness with sore throat, mild fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose. Laboratory criteria include isolation of *Corynebacterium diphtheriae* from a clinical specimen, or histopathologic diagnosis of diphtheria.

Treatment

The disease is manageable, but in more severe cases lymph nodes in the neck may swell, and breathing and swallowing will be more difficult. People in this stage should seek immediate medical attention, as obstruction in the throat may require intubation or tracheotomy. In addition, an increase in heart rate may cause cardiac arrest. Diphtheria can also cause paralysis in the eye, neck, throat, or respiratory muscles. Patients with severe cases must be put in a hospital intensive care unit (ICU) and be given diphtheria anti-toxin. Since antitoxin does not neutralize toxin that is already bound to tissues, delaying its administration is associated with an increase in mortality risk. Therefore, the decision to administer diphtheria antitoxin is based on clinical diagnosis, and should not await laboratory confirmation.

Antibiotics have not been demonstrated to affect healing of local infection in diphtheria patients treated with antitoxin. Antibiotics are used in patients or carriers to eradicate *C. diphtheriae* and prevent its transmission to others. The CDC recommends either:

1. Erythromycin (orally or by injection) for 14 days (40 mg/kg per day with a maximum of 2 g/d), or
2. Procaine penicillin G given intramuscularly for 14 days (300,000 U/d for patients weighing <10 kg and 600,000 U/d for those weighing >10 kg).

Patients with allergies to penicillin G or erythromycin can use rifampin or clindamycin.

Prevention

An effective DPT (Diphtheria-Tetanus-Pertussis) in the form of a combination vaccine is available. DPT vaccine is given to all children. Boosters of the vaccine are recommended for adults because the benefits of the vaccine decrease with age; they are particularly recommended for those traveling to areas where the disease has not been eradicated yet.

Cholera

Cholera is a dreaded disease of human being characterised by severe infection of the small intestine leading to diarrhea. The diarrhea is characterised by passage of thin 'rice-water' stools containing desquamated epithelial cells and flakes of mucus. Dehydration and toxemia are prominent features that may lead to death within a few hours of the onset of symptoms. In the history of cholera, seven pandemics (pandemic refers to an increase in disease occurrence within a large population over a very wide region involving continents) have been reported in various parts of the world especially in Asia including India, the Middle East and Africa. The rice water stools contain high concentrations of sodium, potassium and bicarbonate ions.

Cholera is caused by short and curved comma-shaped gram-negative *Vibrio cholerae* bacterium of the genus *Vibrio* of the family *Vibrionaceae*. Although there are many serogroups, only O1 and O139 have exhibited the ability to cause epidemics. *V. cholerae* O1 is divided into two serotypes, Inaba and Ogawa, and two biotypes, classic and El Tor.

Toxins

Bacteria adhere to the intestinal mucosa of small intestine, where they are not invasive but secrete 'choleragen', the cholera toxin. The toxin is protein in nature and composed of two functional units, an enzymatic A subunit and an intestinal receptor-binding B subunit. The A subunit is again composed of two distinct parts A1 and A2 while B subunit is made up of five components (B1-B5). The A subunit enters the intestinal epithelial cells and activates the enzyme adenylate cyclase (cAMP) activity in the gut leading to an accumulation of cyclic adenosine monophosphate which causes the intestinal wall to secrete chloride and water into the lumen. The patient loses massive quantities of fluid and electrolytes, which is associated with abdominal muscle cramps, vomiting, fever and watery diarrhoea.

V. cholerae produces various enzymes including a neuraminidase (‘receptor destroying enzyme’ or RDE) which breaks down the mucoprotein receptors. It has been suggested that motility and their neuraminidase enables *V. cholerae* to gain access to the intestinal mucosal surface and initiate infection. It is now known that the cholera toxin gene is carried by the CTX filamentous bacteriophage. The phage binds to the pilus used to colonize the host’s gut, enters the bacterium, and incorporates its genes into the bacterial chromosome.

The organisms are often excreted by the patients for a few days during convalescence stage. In contact healthy individuals may become infected and excrete the organisms for some days without developing disease symptoms. Once the bacteria enters the body, the incubation period is from 24 to 72 hours. Outside the infected individual's body, the organisms survive usually for a short period but it sometimes is able to survive for 1-3 weeks in water. Human faeces are the only source of *V. cholerae*. The common routes of the spread of cholera are contaminated water, food, flies and by direct contact. In endemic areas there may be widespread contamination of the environment.

Diagnosis

Laboratory diagnosis is done by culture of the bacterium from faeces and subsequent identification by agglutination reaction with *V. cholerae* antiserum. Numerous vibrios lying with their long axes parallel ‘like fish in a stream’ can be seen in films of mucus from a ‘rice-water’ stool. *V. cholerae* can grow in strongly alkaline media which suppress the growth of many other bacteria. Preliminary incubation of faeces for 5-6 hours in alkaline peptone water and use of special selective media (such as thiosulphate-citrate-bilesalt-sucrose or TCBS medium) facilitates isolation.

Treatment

Oral rehydration therapy with sodium chloride and glucose is done to stimulate water uptake by the intestine. The antibiotics of choice are tetracycline, trimethopim-sulfamethoxazole, or ciprofloxacin.

Control

The most reliable control methods are based on proper sanitation, especially of water supplies.

Typhoid

Typhoid is one of the common bacterial diseases in countries where there is no proper chlorination of water supplies and poor hygiene habits and public sanitation conditions. It is also known as enteric fever. The disease is caused by Gram negative bacterium *Salmonella typhi*. It is transmitted by ingestion of food and water contaminated by faeces of *S. typhi* infected person. Following infection, the bacteria multiply in digestive tract and invade the blood stream of the infected person and thus cause bacteraemia. The causative bacteria enter digestive tract from the blood stream again and are excreted through faeces. Thus the typhoid infected persons become source of infection to healthy individuals in the locality.

The flying insects feeding on faeces having *S. typhi* bacteria may occasionally contaminate food being prepared for consumption. A person may become an asymptomatic carrier of typhoid fever, experiencing no symptoms, but capable of infecting others. According to the Centers for Disease Control (CDC, Atlanta) approximately 5% of people who contract typhoid continue to carry the disease after they recover.

Symptoms

Typhoid is characterised by a high fever from 39 °C to 40 °C (103 °F to 104 °F) that rises slowly, chills, bradycardia (slow heart rate), weakness, diarrhea, headaches, myalgia (muscle pain), not to be confused with the more severe muscle pain in Dengue fever, known as 'Breakbone fever'. Lack of appetite, constipation, stomach pains in some cases, a rash of flat, rose-colored spots called 'rose spots' extreme symptoms such as intestinal perforation or hemorrhage, delusions and confusion are also seen.

Diagnosis

Diagnosis is made by blood, bone marrow or stool cultures and with the Widal test (demonstration of salmonella antibodies against antigens O-somatic and H – flagellar). In epidemics, and in under developed countries, after excluding malaria, dysentery or pneumonia, a therapeutic trial with chloramphenicol is generally undertaken while awaiting the results of Widal test and blood cultures.

Treatment

Typhoid fever can be fatal. Antibiotics, such as ampicillin, amoxycillin, chloramphenicol, trimethoprim-sulfamethoxazole, and ciprofloxacin, are commonly used to treat typhoid fever in developed countries. Prompt treatment of the disease with antibiotics reduces the case-fatality rate to approximately 1%. Usage of Ofloxacin along with *Lactobacillus acidophilus* is also recommended. The untreated typhoid fever persists for three weeks to a month. Death occurs in 10% to 30% of untreated cases.

Prevention

Vaccines for typhoid fever are available. 'Typhim Vi' is an intramuscular killed-bacteria vaccine and Vivotif is an oral live bacterial vaccine. Both vaccines protect against typhoid fever. Neither vaccine is 100% effective against typhoid fever. Public education campaigns encouraging people to wash their hands after toilet use and before handling food are an important component in controlling spread of the disease.

Tuberculosis

Tuberculosis (commonly abbreviated as TB) is an infection caused by the bacterium *Mycobacterium tuberculosis*, which most commonly affects the lungs (pulmonary TB) but can also affect the central nervous system (meningitis), alimentary system (Miliary tuberculosis), lymphatic system, genitourinary system, joints and bones. People from Asian and African descent may have lymph node TB more often than Caucasians. The causative agent of TB was identified by Robert Koch in late 19th century. It is estimated that there are 1 billion (20% of the human population) infected individuals worldwide, with 10 million new cases of the disease and

nearly 3 million deaths per year. TB is one of the top four infectious killer diseases in the world. The World Health Organization declared TB a global health emergency in 1993.

There are a rising number of people in the developed world who contract tuberculosis because they have compromised immune systems, typically as a result of immunosuppressive drugs or HIV/AIDS. These people are at particular risk of tuberculosis infection and active tuberculosis disease. Most of those infected (90%) have asymptomatic latent TB infection (LTBI). There is a 10% lifetime chance that LTBI will progress to TB disease which, if left untreated, will kill more than 50% of its victims. Multiple drug resistant strains of TB (MDR-TB) and extreme drug-resistance in tuberculosis (XDR-TB) are emerging.

Etiology

The cause of tuberculosis, *Mycobacterium tuberculosis* (MTB), is a slow-growing aerobic bacterium that divides every 16 to 20 hours. MTB is not classified as either Gram-positive or Gram-negative because it does not have the chemical characteristics of either. It is a small rod-like bacillus which can withstand weak disinfectants and can survive in a dry state for weeks but can spontaneously grow within a host. Microscopically, MTB is identified by its staining characteristics i.e. it retains certain stains after being treated with acidic solution, and is thus classified as an "acid-fast bacillus" or AFB. In the most common staining technique, the Ziehl-Neelsen stain, AFB are stained a bright red which stands out clearly against a blue background. Acid-fast bacilli can also be visualized by fluorescent microscopy, and by auramine-rhodamine stain.

Transmission

TB is spread by aerosol droplets expelled by people with active TB disease (not latent TB infection) of the lungs when they cough, sneeze, speak, or spit. Each aerosol droplet is 5 µm in diameter which contains 1 to 3 TB bacilli. Close contact people are at highest risk of becoming infected with an infection rate of 22%. A person with untreated, active tuberculosis can infect an estimated 20 other people per year. Others at risk include immunocompromised patients (eg. HIV/AIDS), residents and employees of high-risk congregate settings, health care workers who serve high-risk clients, medically underserved, low-income populations, children exposed to adults in high-risk categories, and people who inject illicit drugs.

Symptoms

TB most commonly affects the lungs (75% or more), where it is called pulmonary TB. Symptoms may include a productive, prolonged cough of more than three weeks duration, chest pain, and hemoptysis. Systemic symptoms include fever, chills, appetite loss, weight loss, night sweats, and easy fatigability. Extrapulmonary sites include the pleura, central nervous system (meningitis), genitor-urinary system, lymphatic system (scrofula of the neck), and bones and joints (Pott's disease of the spine). An especially serious form is the disseminated, or miliary TB, so named because the lesions so-formed resemble millet seeds on x-ray. These are more common in immunosuppressed persons and in young children. Pulmonary TB may co-exist with extrapulmonary TB. Only 10 percent of TB infection progress to active TB disease, the remaining 90 percent have latent TB infection (LTBI) and have no symptoms.

Drug resistance

Recently, new multi-drug-resistant strains of TB (MDR-TB) have developed and are spreading. Drug-resistant TB is transmitted in the same way as regular TB. Primary resistance develops in persons initially infected with resistant organisms. Secondary resistance (acquired resistance) may develop during TB therapy due to inadequate treatment regimen, i.e. not taking the prescribed regimen appropriately or using low quality medication. MDR-TB is an important public health issue in many developing countries, as treatment of drug-resistant TB is longer and requires the use of more expensive drugs. MDR-TB is defined as resistance to the two most effective first line TB drugs - Rifampicin and Isoniazid (INH).

Diagnosis

The medical evaluation for TB includes a complete medical history, physical examination, the Mantoux or tuberculin skin test, serological test, chest X-ray, microbiologic smears, isolation of acid-fast bacterium, cultures, commercially available DNA probes and the BACTEC NAP test. The most effective screening device is the skin test for tuberculin hypersensitivity. When extracts of the tubercle bacillus, called purified protein derivative (PPD), are injected into the skin, persons with cell-mediated immunity against the pathogen will develop a local delayed-type hypersensitivity reaction. Positive skin tests develop early in the course of the disease, long before symptoms are apparent. A positive response indicates only that the person has been exposed to the pathogen and does not necessarily suggest the presence of active tuberculosis. The measurement of a positive skin test depends upon the person's risk factors for progression of TB infection to TB disease. Bacteriophage-based assays are among a few new testing procedures that offer the hope of cheap, fast and accurate TB testing for the impoverished countries that need it most. Phage based assay uses mycobacteriophages (a virus that infects mycobacteria). Two main phage-based approaches are used to detect *M. tuberculosis* (i) amplification of phages after their infection of *M. tuberculosis*, followed by detection of progeny phages using helper cells (plaque formation); and (ii) detection of light produced by luciferase reporter phages (LRP) by live *M. tuberculosis*. Phage tests are based on the ability of viable *M. Tuberculosis* to support the replication of an infecting mycobacteriophage. Plaques of lysed cells in a lawn culture of mycobacteria are counted. The recombinant phage (phage which incorporated the gene for luciferase) can express the luciferase gene when infecting a mycobacterium. In the presence of luciferin substrate, infected bacteria emit light that can be detected with a luminometer or by photosensitive film in a Polaroid film box called the "Bronx Box".

Treatment

For all practical purposes, only patients with tuberculosis of the lungs can spread TB to other people. People with LTBI and are not capable of passing the infection to other people but their treatment is also important to prevent them from progressing to active TB disease later in life (approximately 10% lifetime risk). The distinction is important because treatment options are different for the two groups. Both chemotherapy and chemoprophylaxis are carried out by administering isoniazid, plus rifampicin, ethambutol, and pyrazinamide. These drugs are administered simultaneously for 12-24 months as a way of decreasing the possibility that the patient develops drug resistance.

WHO formulated the Directly Observed Treatment Short Course (DOTS) strategy to improve TB care and control. Directly observed treatment (DOT) is one of the most important elements of the DOTS strategy.

DOT means that a supervisor watches the patient swallowing the anti-TB drug tablets. This ensures that a TB patient takes the right drugs, in the right doses, at the right intervals. Over the years, the definition of a DOT provider/supervisor has been relaxed in order to make the treatment more accessible to the patient. A local health worker or even a trained community member may now be DOT provider.

Prevention and control

Prevention and control of TB requires rapid specific therapy to interrupt infectious spread. The efforts include these priority strategies:

Identifying and treating all people who have TB. Finding and evaluating persons who have been in contact with TB patients to determine whether they have TB infection or disease, and treating them appropriately. Testing high-risk groups for TB infection to identify candidates for treatment of latent infection and to ensure the completion of treatment.

Retreatment of patients who have MDR-TB should be carried out in programmes with comprehensive microbiological, pharmacokinetic, psychosocial, and nutritional support systems.

Vaccines

Many countries other than the United States have immunization programs against tuberculosis, especially for infants. In tropical areas where the incidence of atypical mycobacteria is high, exposure to nontuberculous mycobacteria gives some protection against TB. The vaccine is a nonvirulent variant of *Mycobacterium bovis* called BCG (bacillus of Calmette and Guérin) that stimulates at least partial immunity against tuberculosis by inducing the proliferation of sensitized lymphocytes. The protective efficacy of BCG for preventing serious forms of TB (e.g. meningitis) in children is high (greater than 80%). However, the protective efficacy for preventing pulmonary TB in adolescents and adults is variable, from 0 to 80%.

The first recombinant tuberculosis vaccine entered clinical trials in the United States in 2004 sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). A 2005 study showed that a DNA TB vaccine given with conventional chemotherapy could accelerate the disappearance of bacteria as well as protecting against re-infection in mice; it may take four to five years to be available for use in humans if licensing agencies approve.

Plague

Plague is a scourge of mankind. It was also known as 'Black Death'. It is infectious disease caused by a rod-shaped Gram negative bacterium called *Yersinia pestis*. Rats are the main reservoir of *Y. pestis* for infection in human beings. Plague is transmitted from animal to animal by *Xenopsylla cheopis*, a rat flea. *X. cheopis* can survive for 6 to 12 months off a host in dung, an abandoned rodent's nest, textile bales, and on rodents, such as rats, field mice, squirrels, etc.

Sylvatic plague

Black rats (*Rattus rattus*) were more common in ancient times which have now been replaced by brown much bigger and aggressive rats (*Norvegicus rattus*). Plague organism multiplies in the gut of flea (*X. cheopis*). The flea regurgitates *Y. pestis* infected material as it feeds on the rodents. This is how rodents contract a form of the fatal disease called murine or 'Sylvatic Plague'. *Y. pestis* grows in rats in large amount that they block the biliary duct resulting into

unusual increase in size of rats. Such rats exhibit staggering as if intoxicated. The infected fleas then leave their dying hosts and find another host which is often another rat, but if no rat is available the flea will bite man.

Bubonic plague

Incubation period of plague in human beings is generally 1-6 days. After an infected flea bite, the lymph nodes in the armpit and groin region are characterized by profuse swelling (up to 10 cm in diameter) and tenderness. The very painful swollen lymph nodes are called buboes (from the Greek *bubo*, meaning groin). The 'buboes' may suppurate, i.e., break and discharge particularly fetid pus. It has been observed that some times the flea bite site becomes infected and suppurates. Subsequently, the site becomes gangrenous and necrotic. The human plague is characterized by staggering gait, rapid pulse, mental confusion, restlessness, and nausea, prostration, delirium, aching of the extremities and back, and a high fever (at least 40° C = 104° F). Subsequently, the disease may follow two course, either fever breaks or it continues. If the fever breaks, there is usually remission and the immune system has gained the upper hand over the pathogen and the patient has chances to recover. But if the fever doesn't break, the infection spreads to the blood, causing septicemia and death. This is often the course of 'bubonic plague'. In bubonic form of plague, there is bleeding, multiple system failure, and death within 3-7 days. The mortality rate for untreated bubonic plague is about 50-75%.

Septicemic plague

In some cases *Y. pestis* can enter directly to the blood stream and causes septicaemia. This type of plague is called 'septicemic plague'. It can occur before the formation of buboes and may result in death before diagnosis could be made. In septicemic form of plague, blood vessels break and leak under the skin causing a dark rash as the blood dries (hence the name 'Black Death' which was given in the 1500s). In septicemic plague, there is bleeding, multiple system failure, and death within 2-5 days. The mortality rate is 100% for untreated septicemic plague.

Pneumonic plague

Y. pestis enters the lungs, whereupon the victims initially cough up a blood-spotted mucus and then graduate to coughing bloody froth. The sputum teems with *Y. pestis* and the patient is highly infectious. Human-to-human transmission of pneumonic plague occurs by droplet infection and rat fleas are not involved. This form of plague spreads very rapidly in human population. Similar to septicemic plague mortality rate is 100%, if untreated, and death can occur in a matter of hours.

Plague is typically a very severe disease with a high mortality, e.g. recovery from pneumonic plague is unusual. A mild ambulatory form of plague is also recognized. Plague occurs in epidemic and sporadic forms. Epidemics are preceded by an outbreak among rodents in one of the permanent endemic centres notably in India and also in parts of Asia, Africa and America. From time to time the disease has appeared in most countries. In England the 'Black Death' of the fourteenth century was a pandemic of pneumonic plague. In countries where plague is endemic in wild rodents other than rats sporadic cases of infection in hunters and other workers in rural areas occur as a result of handling infected animals.

Diagnosis

Characteristic organisms are found in fluid aspirated from the buboes or in sputum from cases of pneumonic plague. They are identified by their cultural and biochemical properties, agglutination with specific antiserum, susceptibility to a specific phage, and inoculation of rats or guinea-pigs. Blood culture is of value in the early septicaemic stages.

Treatment

Streptomycin, gentamycin, and tetracycline are drugs of choice for all three varieties of plague. Medication must be given within the first 18 hours of infection to be completely effective.

Prevention

This depends on measures which reduce contact between rats and man, e.g. improvements in housing, domestic hygiene and refuse disposal; reduction of the rat population by poisons; preventing rats entering and leaving ships by rat-guards placed on hawsers and by fumigation; control of fleas with insecticides when epidemics threaten. Masks and protective clothing should be used when caring for cases of pneumonic plague. Killed or living attenuated vaccines can be used for active immunization.

Syphilis

Venereal syphilis is a contagious sexually transmitted disease caused by the spirochete *Treponema pallidum* subsp. *Pallidum* (*T. pallidum*). The spirochetes are extremely slender and have small, sharp, regular spirals with a wavelength of about 1 μm . Congenital syphilis is the disease acquired *in utero* from the mother. The spirochaete is very susceptible to drying and light and soon dies when outside the body. It is rare for infection to be conveyed by contaminated articles.

Syphilis was first recognized in Europe near the end of the fifteenth century. According to one hypothesis, Christopher Columbus and his crew acquired the disease in the West Indies and brought it back to Spain after returning from their historic voyage. Its venereal transmission was not definitely shown until the eighteenth century. The term venereal is derived from the name Venus, the Roman goddess of love.

The causative agent, *T. pallidum*, enters the body through mucous membrane or minor abrasions of the skin. After migrating to regional lymph nodes, it rapidly spreads throughout the body. Three stages of syphilis occur in untreated adults. The primary lesion, a small, painless, reddened indurated ulcer known as the *primary chancre* ('hard chancre') containing spirochetes, appears 9-90 days after infection. It is usually on the genitalia but may occur in the mouth, in the rectum or on a finger. Serological tests are positive in about 80% of the individuals during this stage. In about 1/3 of the cases, the disease does not progress further and the chancre disappears. In the remaining cases the spirochetes enter the bloodstream and are distributed throughout the body.

The secondary stage begins in 2-12 weeks and takes the form of rashes, lesions of the mucous membranes, loss of hair patches, malaise, fever and painless enlargement of the lymph nodes. By this time 100% of the individuals are serologically positive.

The tertiary stage is often delayed for several years. During this period the disease is not normally infectious except for congenital syphilis. It is characterized by chronic inflammatory degenerative lesions (gummas) which involve the cardiovascular system, nervous system, skin, internal organs and bones. Late manifestations of syphilis are degeneration of the spinal cord and brain (general paralysis).

Diagnosis

A clinical history, thorough physical examination, and dark-field and immunofluorescence examination of lesion fluids for presence of typical motile or fluorescent spirochetes helps in diagnosis of syphilis. Confirmation is done by demonstrating the spirochetes in the early stages of the disease and by serological tests for syphilis (STS) in later stages. In wet preparations examined under dark-field illumination it shows a rapid corkscrew motion and periodic angular bending of the body. Its progression is relatively slow. It cannot be gram-stained but will take Giemsa stain and can be demonstrated in tissue sections by silver impregnation methods. Non-pathogenic spirochetes are sometimes present, but are usually thicker and more irregular than *T. pallidum* or show a different type of motility.

T. pallidum cannot be cultured on artificial media. Under experimental conditions it can infect apes and rabbits. Serial propagation in the testis of the rabbit is used to prepare suspensions of the organism.

Humans respond to *T. pallidum* with the formation of antitreponemal antibody and a complement-fixing 'reagin' therefore, serological tests are very informative. Serological tests for nontreponemal antigens include VDRL (venereal disease research laboratory) test; RPR (rapid plasma reagin) card test; the Kahn test, complement fixation or the Wassermann test.

Wassermann reaction depends on the similarity between a normal tissue lipid (a hapten) and a lipid present in *T. pallidum*. The lipid can be obtained by ethanol extraction of bovine heart muscle and is available in a purified form known as *cardiolipin*. In practice, the 'antigen' used in this test consists of cardiolipin together with suitable proportions of lecithin and cholesterol. The WR, probably the best known serological test of all time, is now obsolete because flocculation (precipitation) reactions such as VDRL tests have proved to be simpler, quicker, cheaper and slightly more sensitive. VDRL test is usually performed on a slide using colloidal suspension of cardiolipin antigen. A positive serum causes aggregation of the particles and flocculation. By adding carbon particles to the system the result can be read by naked eye. The VDRL test is of value as a rapid screening test for examining large numbers of sera and is the preferred flocculation test in most laboratories.

So-called 'biological false positive reactions' may occur in malaria, leprosy, infectious mononucleosis, pregnancy and the acute stages of various infectious diseases. In most cases the positive reaction is a temporary phenomenon. Persistent false positive reactions are not common but are often associated with serious conditions such as systemic lupus erythematosus and other autoimmune diseases.

Serological tests for treponemal antibodies include FTA-ABS, fluorescent treponemal antibody-absorption test; TPI, *T. pallidum* immobilization; *T. pallidum* complement fixation; TPHA, *T. pallidum* haemagglutination assay. In TPHA, the patient's serum is allowed to react with a suspension of formalinized tanned sheep and red cells coated with antigens obtained from *T. pallidum*. Syphilitic antibodies cause agglutination of the red cells. The TPHA test is easily performed and is the most suitable specific test for examining large numbers of sera in a general diagnostic laboratory. False positive reactions are occasionally encountered.

Treatment

In early stages of infection long acting benzyl penicillin G or aqueous procaine penicillin is used for treatment of syphilis. Later stages of disease are more difficult to treat with drugs and require much larger doses over a longer period.

Prevention and Control

This depends on prompt and adequate treatment of all new cases of syphilis, follow-up on sources of infection and contact so they can be treated, public education, sexual hygiene and prophylaxis (condoms) to prevent exposure.

VIRAL DISEASES

Rabies

Rabies is a Latin word meaning *rage*. It is a viral disease of animals and human beings. Rabies virus has very vast host range and can infect several species of warm-blooded animals including humans. Rabies chiefly affects dogs, wolves, foxes and vampire bats, but may occur in many other wild and domestic animals. In some parts of the world various species of bats suffer from latent rabies infection and are an important reservoir of the virus. Dogs are the most important source of human infection. In un-immunized humans; rabies is fatal once full-blown symptoms have developed. However, prompt post-exposure vaccination usually prevents symptoms from developing. The rabid dogs exhibit foaming at the mouth, however cats, ferrets, raccoons, jackals, skunks, foxes, coyotes and bats can also become rabid. Rabies may also be present in a so-called "paralytic" form, rendering the infected animal unnaturally quiet and withdrawn. In India, rabies is endemic and causes more than 30,000 deaths annually. Several domestic and wild animals may serve as reservoirs of rabies virus. However, in Asia, parts of Latin America and large parts of Africa, dogs are the main host.

Rabies is caused by a bullet-shaped RNA virus measuring 75x180 nm. The virion is enveloped and has helical symmetry. Rabies virus belongs to genus *Lyssavirus* of family *Rhabdoviridae*. The virus can be easily isolated by intra-cerebral inoculation of mice. It can also be grown in chick embryos and various animal and human origin cell cultures. Since rabies virus is present in the saliva of symptomatic rabid animals, it is transmitted by a bite. By causing the infected animal to be exceptionally aggressive, the virus ensures its transmission to the next host. Transmission from person to person is extremely rare, though it can happen through transplant surgery or even more rarely through bites or kisses.

After a typical human infection by animal bite, the virus directly or indirectly enters the peripheral nervous system. It then travels along the nerves towards the central nervous system. During this phase, the virus cannot be easily detected within the host, and vaccination may still confer cell-mediated immunity to pre-empt symptomatic rabies. Once the virus reaches the brain, it rapidly causes encephalitis and symptoms appear. It may also inflame the spinal cord.

Symptoms

The period between infection and the first flu-like symptoms is normally 3–12 weeks, but can be as long as two years. Soon after, the symptoms expand to cerebral dysfunction leading to anxiety, insomnia, confusion, agitation, abnormal behavior, hallucinations, progressing to delirium. The production of large quantities of saliva and tears coupled with an inability to speak or swallow are typical during the later stages of the disease. This can result in "hydrophobia". Death almost invariably results 2–10 days after the first symptoms. Some persons who are known to have survived the disease were all left with severe brain damage.

Diagnosis

Because brain tissue is required for the diagnosis of rabies, it is recommended that rabid animals should not to be shot in the head. Diagnosis in dogs and man can be confirmed in life by isolating the virus from saliva. After death characteristic eosinophilic inclusions (Negri bodies) can be found inside nerve cells particularly in the hippocampus. The rabies antigen in Negri bodies and in the salivary glands can be specifically identified within a few hours by staining with a fluorescent antibody. The virus can also be isolated from brain tissue and salivary glands. If the dog is alive when first seen it should be kept in captivity for ten days. If it survives it has no rabies, if it dies the brain is examined for Negri bodies.

Prevention and Control

A number of preventive measures including, killing of stray dogs, dog licensing, muzzling and large-scale vaccination of cats, dogs and ferrets etc have helped certain countries in the control and eradication of rabies. Oral vaccines can be safely distributed in baits. This approach has been successfully used for vaccination against rabies in rural areas of some European countries. Australia is one of the few parts of the world where rabies has never been introduced. Many territories, such as the United Kingdom, Ireland, Hawaii, and Guam, are free of rabies

Rabies can be prevented by effective vaccination, both in humans and animals. Virtually every infection with rabies was historically a death sentence, until Louis Pasteur developed the first rabies vaccination in 1886. The human diploid cell rabies vaccine (HDCV) was started in 1967. Human diploid cell rabies vaccines are made using the attenuated Pitman-Moore L503 strain of the virus. Newer and less expensive purified chick embryo cell vaccine and purified Vero cell rabies vaccine are now available. The purified Vero cell rabies vaccine uses the attenuated Wistar strain of the rabies virus. Post-exposure prophylaxis treatment after exposure (known as post-exposure prophylaxis or "PEP") is highly successful in preventing the disease if administered promptly, within 14 days after infection. Rabies immunoglobulin and the first dose of rabies vaccine should be given as soon as possible after exposure, with additional doses on days 3, 7, 14, and 28 after the first. The vaccinations are relatively painless and are given in one's arm, in contrast to previous treatments which were given through a large needle inserted into the

abdomen. In case of animal bites it is also helpful to remove, by thorough washing, as much infectious material as soon as possible. Rabies virus reaches brain by nerves. Therefore, the time required to infect the brain is dependent on distance of site of the bite from the brain. If the bite is on the foot, the time required to infect the brain would be more compared to bite on the face. Therefore, if the victim is bitten in the face, for example, the time between initial infection and infection of the brain is very short and PEP may not be successful.

Currently pre-exposure immunization is carried out in domesticated animals. In many jurisdictions, domestic dogs, cats, and ferrets are required to be vaccinated. A new, orally active, genetically recombined virus vaccine for raccoon rabies waits licensing by the U.S. Department of Agriculture. A pre-exposure vaccination is also available for humans, most commonly given to veterinarians and those traveling to parts of the world where the disease is endemic. However, should a vaccinated person be bitten by any animal possibly having rabies, they must have subsequent post-exposure treatment. Persons bitten by rapid animals should be given human anti-rabies immunoglobulin (or horse anti-rabies serum), injected partly into the wound and partly intramuscularly, and a course of rabies vaccine. Failure to do so could be fatal.

Hepatitis

Hepatitis is a gastroenterological disease, characterized by inflammation of the liver. It is caused by virus.

Signs and symptoms

Hepatitis is characterised by fatigue, malaise, joint aches, abdominal pain, vomiting 2-3 times per day for the first 5 days, loss of appetite, dark urine, fever, hepatomegaly (enlarged liver) and jaundice (icterus). Some chronic forms of hepatitis show very few of these signs and only present when the longstanding inflammation has led to the replacement of liver cells by connective tissue; the result is cirrhosis. Certain liver function tests can also indicate hepatitis.

Types of hepatitis

Most cases of acute hepatitis are caused by viruses classified as: hepatitis A, hepatitis B, hepatitis C, D-agent (requires presence of the hepatitis B virus to produce disease), hepatitis E, hepatitis F (discredited as many scientists have questioned the existence of such virus), hepatitis G. In addition to the hepatitis viruses, some other viruses such as cytomegalovirus, Epstein-Barr virus, yellow fever, etc. can also cause hepatitis.

Hepatitis A

Hepatitis A or infectious jaundice is an enterovirus transmitted by the oro-fecal route, transmitted to humans through methods such as contaminated food. It causes an acute form of hepatitis and does not have a chronic stage. The patient's immune system makes antibodies against hepatitis A that confer immunity against future infection. People with hepatitis A are advised to rest, stay hydrated and avoid alcohol. A vaccine is available that will prevent infection from hepatitis A for life. It can be spread through personal contact, consumption of raw sea food or drinking contaminated water. Hepatitis A is primarily spread in so-called "third world countries", and can also be more often found in southern Europe than in northern and western

Europe. Strict personal hygiene and the avoidance of raw and unpeeled foods can help in preventing the infection. Infected persons already begin excreting the hepatitis A virus with their stool two weeks after the appearance of the first symptoms. The time between the infection and the start of the illness can run from 15 to 45 days.

Hepatitis B

Hepatitis B causes both acute and chronic hepatitis in some patients who are unable to eliminate the virus. Methods of transmission include blood (blood transfusion), tattoos (both amateur and professionally done), horizontally (sexually or through contact with blood or bodily fluids), or vertically (from mother to her unborn child). Blood contact can occur by sharing syringes in intravenous drug users, shaving accessories such as razor blades, or touching wounds of infected persons. Needle-exchange programmes have been created in many countries as a form of prevention. In the United States, 95% of patients clear their infection and develop antibodies against hepatitis B virus. 5% of patients are unable to clear the infection and develop chronic infection; only these people are at risk of long term complications of hepatitis B.

Patients with chronic hepatitis B have antibodies against hepatitis B, but these antibodies are not enough to clear the infection that establishes itself in the affected liver cells. The continued production of virus combined with antibodies is a likely cause of immune complex disease seen in these patients. A vaccine is available that will prevent infection from hepatitis B for life. Hepatitis B infections result in 500,000 to 1,200,000 deaths per year worldwide due to the complications of chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Hepatitis B is endemic in a number of (mainly South-East Asian) countries including India, making cirrhosis and hepatocellular carcinoma big killers. There are three, FDA-approved treatment options available for persons with a chronic hepatitis B infection: alpha-interferon, adefovir and lamivudine. About 45% of persons on treatment achieve a sustained response.

Hepatitis C

Hepatitis C (originally called "non-A non-B hepatitis" or NANB) can be transmitted through contact with blood (including through sexual contact). It may lead to a chronic form of hepatitis, culminating in cirrhosis. It can remain asymptomatic for 10-20 years. No vaccine is available for hepatitis C. Patients with hepatitis C are prone to severe hepatitis if they contract either hepatitis A or B, so all hepatitis C patients should be immunized against hepatitis A and hepatitis B if they are not already immune. However, hepatitis C itself is a very lethal virus and can cause cirrhosis of the liver. The virus, if detected early on can be treated by a combination of interferon and the antiviral drug ribavirin. There are variations in the response to this treatment regimen based on the genotype or strain of the infecting virus.

Hepatitis D

Hepatitis D is an RNA passenger virus that cannot proliferate without the presence of hepatitis B virus, because its genome lacks certain essential genes.

Hepatitis E

It produces symptoms similar to hepatitis A, although it can take a fulminant course in some patients, particularly pregnant women; it is more prevalent in the Indian subcontinent.

Hepatitis G

Hepatitis G another kind of hepatitis, has been identified.

Other viruses which can cause infectious hepatitis include mumps, rubella, cytomegalovirus, Epstein-Barr virus and other herpes viruses.

Polio

Polio is also known as polio poliomyelitis or infantile paralysis. It is caused by a RNA virus called poliovirus. It belongs to *Enterovirus* genus of the family *Picornaviridae*. The poliovirus has three different strains and is extremely infectious. The virus enters the body orally through contaminated food and water and infects susceptible cells of the intestinal mucosa. It may enter the blood stream and eventually into the central nervous system causing muscle weakness and often paralysis. An ancient disease, it was first recognized as a medical entity by Jakob Heine in 1840. Polio is a communicable disease which is categorized as a disease of civilization. The virus invades the nervous system, and the onset of paralysis can occur in a matter of hours. While polio can strike a person at any age, over fifty percent of the cases occur in children between the ages of three and five. The incubation period of polio, from the time of first exposure to first symptoms, ranges from three to thirty five days, thus polio can spread widely before a polio outbreak is apparent. Most people infected with the poliovirus have no symptoms or outward signs of the illness and are thus never aware they have been infected. After initial infection with poliovirus, virus particles are excreted in the faeces for several weeks and are highly transmissible to others in the community. Initial infection is of cells lining the small intestine. Immunization interrupts the process here. After multiplication there, viraemia occurs, with distribution of virus to other parts of the body.

Symptoms

Polio is characterized by fatigue, fever, vomiting, headache and pain in the neck and extremities. Around 1% of unimmunized people develop paralytic complications, in some cases bulbar paralysis. Flu-like symptoms are typical of viraemia from any cause. The virus has an affinity for the cell bodies of motor neurons, which carry commands to the muscles. Non-paralytic polio may result in fever, vomiting, abdominal pain, lethargy, and irritability, and some muscles tender to the touch. In some cases there may be no significant symptoms whatsoever.

Spinal polio

The virus affects the anterior horn cells in the spinal column which control movement of the trunk and limb muscles including the intercostal muscles. An affected limb becomes floppy and poorly controlled the condition of acute flaccid paralysis (AFP). This presentation can lead to permanent paralysis of the body yet it only occurs in around 1% of cases. The classic later appearance (as seen in ancient Egyptian illustrations) is of muscle wasting in a leg. Destroyed motor neurons do not regenerate and the affected motor units of muscles will not be able to contract. However, some sprouting from nearby surviving neurons may reinnervate the denervated muscle. This additional load on surviving motor neurons may precipitate the later developing symptoms of post-polio syndrome.

Prevention

The first effective polio vaccine was developed by Jonas Salk at the University of Pittsburgh, although it was the oral vaccine developed by Albert Sabin eight years later that was used for modern mass inoculation. The Salk vaccine is based on formalin-inactivated poliovirus. The Sabin vaccine is a live-attenuated vaccine, produced by the passage of the virus through non-human cells at a subphysiological temperature. Through mass immunization, the disease was wiped out in the Americas, although it recently has re-appeared in Haiti, where political strife and poverty have interfered with vaccination efforts.

Control

In 1988, the World Health Organization passed a resolution to eradicate polio by 2000, a measure which was inspired by Rotary International's 1985 pledge to raise \$120 million toward immunising all of the world's children against the disease. The next plan called for a stop of spreading the virus by 2005. Most remaining polio infections are located in two areas: the Indian sub-continent and Nigeria. Eradication efforts in the Indian sub-continent have met with a large measure of success. The Indian Government started the Pulse Polio Campaign to get rid of polio. Most families allowed their children to take the vaccine. Some Muslim families refused due to false rumors that the vaccine causes impotence or infertility or both. A few hundred cases of polio especially from UP have been reported in 2005-2006. In India a few cases of polio have been recorded from some states.

AIDS

Acquired immunodeficiency syndrome (AIDS) is the most severe manifestation of infection with human immunodeficiency virus (HIV). The AIDS cases were for the first time noticed on June 5, 1981, when the US Centers for Disease Control (CDC) and Prevention reported a cluster of *Pneumocystis carinii* pneumonia (now classified as *Pneumocystis jiroveci* pneumonia) in five homosexual men in Los Angeles, California. Originally these cases were dubbed as Gay-Related Immune Deficiency (GRID). The health authorities soon realized that nearly half of the people identified with the immunodeficiency syndrome were not homosexual males. Subsequently, the CDC introduced the term AIDS in 1982 to describe the newly identified syndrome.

AIDS is the occurrence of life-threatening opportunistic infections and malignant tumours associated with severe defects of cell-mediated immunity occurring without obvious cause in previously healthy individuals. The patients develop infections such as *Pneumocystis carinii* pneumonia, generalized cytomegalovirus infection, progressive herpes and mucocutaneous candidiasis and tumours, particularly a tumour of the skin and viscera known as Kaposi's sarcoma and various types of lymphomas. The patients lose weight, hence AIDS is also called as 'slim disease' in some countries and the outcome is usually fatal. AIDS was first recognized in the USA in early 1980s. Subsequently the number of AIDS cases increased rapidly through out the world and the disease has been reported in most countries. HIV is transmitted mainly through homosexual and heterosexual intercourse. In central Africa, AIDS is almost entirely a heterosexual disease affecting men and women in equal numbers. In addition, intravenous drug abusers, haemophiliacs and other recipients of blood products and multiple transfusions are also at high risk.

According to the WHO estimate AIDS has killed more than 25 million people since it was first recognized in 1981, making it one of the most destructive epidemics in recorded history. Despite recent, improved access to antiretroviral treatment and care in many regions of the world, the AIDS epidemic claimed an estimated 2.8 million lives in 2005 of which more than half a million (5,70,000) were children. Globally, around 46 million people are currently infected with HIV.

Sub-Saharan Africa remains by far the worst affected region, with an estimated 21.6 to 27.4 million people currently living with HIV. South and South East Asia are second worst affected with 15% AIDS patients. Two-thirds of HIV/AIDS infections in Asia occur in India, with an estimated 5.7 million infections (estimated 3.4 - 9.4 million) (0.9% of population), surpassing South Africa's estimated 5.5 million (4.9-6.1 million) (11.9% of population) infections, making it the country with the highest number of HIV infections in the world.

Etiology

HIV is a retrovirus belonging to the genus *Lentivirus* of the family *Retroviridae*. The members of this family are characterized by the presence of reverse transcriptase enzyme, hence the name 'retrovirus'. Two serotypes (HIV-1 and HIV-2) of the virus have been identified. HIV-1 is more virulent and more easily transmitted. HIV-1 is the source of the majority of HIV infections throughout the world, while HIV-2 is less easily transmitted and is largely confined to West Africa. It is believed that the origin of HIV-1 is the Central common chimpanzee (*Pan troglodytes troglodytes*) found in southern Cameroon where as it is established that HIV-2 originated from the Sooty Mangabey (*Cercocebus atys*), an Old World monkey of Guinea Bissau, Gabon, and Cameroon.

HIV has been isolated from blood, semen, vaginal secretions, breast milk, tears and saliva of AIDS patients. The levels of virus in tears and saliva are very low and infection from these sources is highly unlikely. HIV has been isolated from vaginal secretions from apparently healthy women with antibodies to the virus and male heterosexuals can contract AIDS from such women. Mosquitoes and other blood sucking insects may carry HIV but there is no evidence that they transmit it to man. Virtually all AIDS patients have antibodies against HIV. Possession of HIV antibodies indicates past exposure to the virus. Infection is probably life-long and the patient is likely to remain an excreter of the virus and a danger to others.

The majority of HIV infections are transmitted through unprotected sexual relations between partners, one of whom has HIV. Sexual transmission occurs with the contact between sexual secretions of one partner with the rectal, genital or oral mucous membranes of another. Unprotected receptive sexual acts are riskier than unprotected insertive sexual acts, with the risk for transmitting HIV from an infected partner to an uninfected partner through unprotected insertive anal intercourse greater than the risk for transmission through vaginal intercourse or oral sex. Oral sex is not without its risks as HIV is transmissible through both insertive and receptive oral sex. The risk of HIV transmission from exposure to saliva is considerably smaller than the risk from exposure to semen; contrary to popular belief, one would have to swallow gallons of saliva from a carrier to run a significant risk of becoming infected. The transmission of the virus from the mother to the child can occur *in utero* during the last weeks of pregnancy and at childbirth.

Sexually transmitted diseases (STD) increase the risk of HIV transmission and infection because they cause the disruption of the normal epithelial barrier by genital ulceration and/or microulceration; and by accumulation of pools of HIV-susceptible or HIV-infected cells (lymphocytes and macrophages) in semen and vaginal secretions. Epidemiological studies from sub-Saharan Africa, Europe and North America have suggested that there is approximately a four times greater risk of becoming infected with HIV in the presence of a genital ulcer such as those caused by syphilis. Transmission of HIV depends on the infectiousness of the index case and the susceptibility of the uninfected partner. Infectivity seems to vary during the course of illness and is not constant between individuals. Women are more susceptible to HIV-1 infection due to hormonal changes, vaginal microbial ecology and physiology, and a higher prevalence of sexually transmitted diseases. People who are infected with HIV can still be infected by other, more virulent strains.

HIV primarily infects vital components of the human immune system such as CD⁴⁺ T lymphocytes (helper T cells), macrophages and dendritic cells. It directly and indirectly destroys CD⁴⁺ T cells. CD⁴⁺ T cells are required for the proper functioning of the immune system. When HIV kills CD⁴⁺ T cells so that there are fewer than 200 CD⁴⁺ T cells per microliter of blood, cellular immunity is lost, leading to AIDS.

Symptoms

Most individuals infected with HIV show no symptoms initially. Later many of them develop *persistent generalized lymphadenopathy* or an *AIDS-related* complex of fever, loss of weight, weakness and other symptoms, signs and immunological progress to AIDS. Children born to seropositive women are commonly infected and may develop AIDS. HIV-infected children may be antibody-negative. In addition to its effect on the immune system HIV can cause brain damage. At least 50% of AIDS patients develop encephalopathy with loss of memory, impaired speech and dementia. The incubation period of AIDS is usually very long, e.g. about two years for transfusion-associated AIDS.

In 1990, the WHO classified AIDS infections and conditions together by introducing a staging system for patients infected with HIV-1. This system was updated in September 2005. According to this system there are four stages:

- Stage I:* HIV disease is asymptomatic and not categorized as AIDS.
- Stage II:* Includes minor mucocutaneous manifestations and recurrent upper respiratory tract infections.
- Stage III:* Includes unexplained chronic diarrhea for longer than a month, severe bacterial infections and pulmonary tuberculosis.
- Stage IV:* Includes toxoplasmosis of the brain, candidiasis of the esophagus, trachea, bronchi or lungs and Kaposi's sarcoma; these diseases are indicators of AIDS.

Diagnosis

Since HIV infection does not cause full blown disease rapidly, the infected persons do not know their HIV status until tested by virus tests. Now HIV screening of donor blood and blood products used for medical purposes has been made mandatory. Typical HIV tests, including the HIV enzyme immunoassay and the Western blot assay, detect HIV antibodies in serum, plasma,

oral fluid, dried blood spot or urine of patients. Commercially available tests to detect other HIV antigens, HIV-RNA, and HIV-DNA in order to detect HIV infection prior to the development of detectable antibodies are available. However, for the diagnosis of HIV infection these assays are not specifically approved, but are nonetheless routinely used in developed countries.

Prevention

There is currently no vaccine against HIV or AIDS, the only known methods of prevention are based on avoiding exposure to the virus. During a sexual act, only male or female condoms can reduce the chances of infection with HIV and other STDs and the chances of becoming pregnant. The best evidence to date indicates that condom use reduces the risk of heterosexual HIV transmission by approximately 80%. The effective use of condoms and screening of blood transfusion in North America, Western and Central Europe is credited with contributing to the low rates of AIDS in these regions. The health organizations through out the world endorse the *ABC Approach* to lower the risk of acquiring AIDS during sex:

- A: Abstinence or delay of sexual activity, especially for youth,
- B: Being faithful, especially for those in committed relationships,
- C: Condom use, for those who engage in risky behavior.

Treatment

Not even a single case has been documented in which systemic HIV infection has been cured using anti-retroviral therapy. Treatment for HIV can suppress viral replication to a degree sufficient to apparently stop disease progression. In western countries, most patients survive many years following diagnosis because of the availability of the highly active antiretroviral therapy (HAART). HAART dramatically increases the time from diagnosis to death. Current optimal HAART options consist of combinations (or "cocktails") consisting of at least three drugs belonging to at least two types, or "classes," of anti-retroviral agents. Typical regimens consist of two nucleoside analogue reverse transcriptase inhibitors (NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI). Anti-retroviral treatments, along with medications intended to prevent AIDS-related opportunistic infections, have played a part in delaying complications associated with AIDS, reducing the symptoms of HIV infection, and extending patients' life spans. Over the past decade, the success of these treatments in prolonging and improving the quality of life of people with AIDS has improved dramatically. However, There are several concerns about antiretroviral regimens, as side effects of these antiretrovirals have caused problems such as lipodystrophy, dyslipidaemia, insulin resistance, an increase in cardiovascular risks and birth defects.

Measles

Measles is a RNA viral disease which is also called as 'rubeola'. Measles virus belongs to the *Mobillivirus* genus of family *Paramyxoviridae*. The causative agent of measles was isolated in 1954. Measles is spread through respiration (contact with fluids from an infected person's nose and mouth, either directly or through aerosol transmission), and is highly contagious. Ninety percent of people without immunity and sharing a house with an infected person will catch it.

Symptoms

The incubation period usually lasts for 10-12 days (during which there are no symptoms). Infected people remain contagious from the appearance of the first symptoms until 3-5 days after the rash appears. The classical symptoms of measles include a fever for at least three days' duration, and the three C's – cough, coryza, (runny nose) and conjunctivitis (red eyes). The fever may reach up to 40 degrees Celsius (105 Fahrenheit). Koplik's spots seen inside the mouth are pathognomic (diagnostic) for measles but are not often seen, even in real cases of measles, because they are transient and may disappear within a day of arising. The rash in measles is classically described as a generalised, maculopapular, erythematous rash that begins several days after the fever starts. It starts on the head before spreading to cover most of the body. The measles rash also classically "stains" by changing colour to dark brown from red before disappearing later. The rash can be itchy.

Diagnosis

A detailed history should be taken including course of the disease so far, vaccination, contact, and travel. Clinical diagnosis of measles requires a history of fever of at least three days together with at least one of the three Cs above. Observation of Koplik's spots is also diagnostic of measles. Alternatively, laboratory diagnosis of measles can be done with confirmation of positive measles IgM antibodies or isolation of measles virus RNA from respiratory specimens. Positive contact with other patients known to have measles adds strong epidemiological evidence to the diagnosis.

Treatment

There is no specific treatment for uncomplicated measles. Patients with uncomplicated measles will recover with rest and supportive treatment. Complications with measles are common, ranging from relatively common and less serious diarrhea, to pneumonia and subacute sclerosing encephalitis. Complications are usually more severe amongst adults who catch the virus. The fatality rate from measles for otherwise healthy people in developed countries is low: approximately 1 death per thousand cases. In underdeveloped nations with high rates of malnutrition and poor healthcare, fatality rates of 10 percent are common. In immunocompromised patients, the fatality rate is approximately 30 percent.

Prevention

Airborne precautions should be taken for all suspected cases of measles. In developed countries, most children are immunised against measles at the age of 18 months, generally as part of a MMR vaccine (measles, mumps, and rubella). The vaccination is generally not given earlier than this age because children younger than 18 months usually retain anti-measles immunoglobulins (antibodies) transmitted from the mother during pregnancy. A "booster" vaccine is then given between the ages of four and five. Vaccinations have been high enough to make measles relatively uncommon. In developing countries, measles remains common.

The recent vaccine controversy in the UK regarding a potential link between the combined MMR vaccine (vaccinating children from mumps, measles and rubella) and autism has prompted a resurgence in popularity of the "measles party", where parents deliberately infect the child with measles in order to build up the child's immunity without requiring an injection. This practice

poses many health risks to the child, and has been discouraged by the UK's National Health Service.

Measles is a significant infectious disease because, while the rate of complications is not high, the disease itself is so infectious that the sheer number of people who would suffer complications in an outbreak amongst non-immune people would quickly overwhelm available hospital resources. If vaccination rates fall, the number of non-immune persons in the community rises and the risk of an outbreak of measles consequently rises.

According to the WHO, measles is a leading cause of vaccine-preventable childhood mortality - there were 30 million cases and 875,000 deaths caused by measles every year. The WHO and the United Nations Children's Fund (UNICEF) reports that the global immunization drive has cut measles deaths by nearly half between 1999 and 2004 (from 871,000 in 1999 to an estimated 454,000 in 2004),

Mumps

Mumps or epidemic parotitis is a viral disease of humans. Prior to the introduction of a vaccine, it was a common childhood disease worldwide, and is still a significant threat to health in the third world. Mumps virus is a negative single stranded RNA belonging to the genus *Rubulavirus* of family *Paramyxoviridae*.

Causes and risks

The mumps are caused by a paramyxovirus, and are spread from person to person by saliva droplets or direct contact with articles that have been contaminated with infected saliva. The parotid glands (the salivary glands between the ear and the jaw) are usually involved. Unvaccinated children between the ages of 2 and 12 are most commonly infected, but the infection can occur in other age groups. Orchitis (swelling of the testes occurs in 10–20% of infected males, but sterility only rarely ensues; a viral meningitis occurs in about 5% of those infected. In older people, the central nervous system, the pancreas the prostate, the breasts, and other organs may be involved.

Symptoms

The incubation period is usually 18 to 21 days, but may range from as few as 12 to as many as 35 days. Mumps is generally a mild illness in children in developed countries. After adolescence, mumps tends to affect the ovary, causing oophoritis, and the testes, causing orchitis. The mature testis is particularly susceptible to damage from mumps which can lead to infertility. Painful swelling of the salivary glands (classically the parotid gland) and fever is the most typical presentation. Painful testicular swelling and rash may also occur. While symptoms are generally not severe in children, the symptoms, in teenagers and adults, can be more severe and complications such as infertility or subfertility are relatively common, although still rare in absolute terms. The disease is generally self-limiting, and there is no specific treatment apart from controlling the symptoms with painkillers.

Diagnosis

A physical examination confirms the presence of the swollen glands. Usually the disease is diagnosed on clinical grounds and no confirmatory laboratory testing is needed. If there is uncertainty about the diagnosis, serology or a saliva test for the virus may be carried out.

Treatment

There is no specific treatment for mumps. Symptoms may be relieved by the application of intermittent ice or heat to the affected neck area and by acetaminophen (paracetamol) for pain relief (aspirin is discouraged in children with a viral illness because of the risk of Reye's syndrome). Warm salt water gargles, soft foods, and extra fluids may also help relieve symptoms. Patients are advised to avoid fruit juice or any acidic foods, since these stimulate the salivary glands, which can be painful. Death is very unusual. The disease is self-limiting, and general outcome is good, even if other organs are involved. Sterility in men from involvement of the testes is very rare. After the illness, life-long immunity to mumps generally develops.

Prevention

The most common preventative measure against mumps is immunisation with a mumps vaccine. This has been a component of the MMR immunization vaccine which also protects against measles and rubella and is now being supplanted by a combination of the three with varicella vaccine - MMRV - which adds protection against Chickenpox. The WHO recommends the use of mumps vaccines in all countries with well-functioning childhood vaccination programmes. In the United Kingdom it is routinely given to children at age 15 months. The American Academy of Pediatrics recommends the routine administration of MMR vaccine at ages 12-15 months and 4-6 years. The vaccination is repeated in some locations between 4 to 6 years of age, or between 11 and 12 years of age if not previously given. Efficacy of the vaccine depends on the strain of the vaccine, but is usually around 80%. Some anti-vaccine activists protest against the administration of a vaccine against mumps, claiming that the attenuated vaccine strain is harmful, and/or that the wild disease is beneficial. Disagreeing, the WHO, the American Academy of Pediatrics, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention, the American Academy of Family Physicians, the British Medical Association and the Royal Pharmaceutical Society of Great Britain currently recommend routine vaccination of children against mumps.

Common cold

The common cold or acute nasopharyngitis is the most common of all human illnesses. It is a mild viral infectious disease of the upper respiratory system (nose and throat). About 50% of the cases are caused by rhinoviruses (Greek *rhinos*, means nose) which are single stranded RNA viruses in the family *Picornaviridae*. The common cold is caused by several other viruses including coronaviruses, echoviruses, parainfluenza viruses, paramyxoviruses and coxsackieviruses infecting the upper respiratory system. The nasopharynx is the central area infected may be because of the low temperature and presence of high concentration of cells with receptors needed by the virus. The virus enters the cells of the lining of the nasopharynx (the area between the nose and throat) by binding to the adhesion molecule ICAM-1 (intercellular adhesion molecule-1), and rapidly multiplies. The colds are common because of the involvement

of large number of respiratory viruses, different serotypes and antigenic types of the viruses and lack of strong immunity. Infection is most common early in life and generally decreases with increasing age.

Transmission

The source of the common cold viruses may be the infected individuals secreting viruses in droplets from coughs or sneezes, or transmitted from hand to hand via handshakes or objects such as door knobs, other fomites and then introduced to the nasal passages when the hand touches the nose or eyes. The major entry points are the nose and eyes, through the nasolacrimal duct. Sneezes expel a significantly larger concentration of virus "cloud" than coughing. The "cloud" is partly invisible and falls at a rate slow enough to last for hours—with part of the droplet nuclei evaporating and leaving much smaller and invisible "droplet nuclei" in the air. Droplets from turbulent sneezing or coughing or hand contact also can last for hours on surfaces. The mouth is not a major point of entry and transmission does not usually occur with kissing or swallowing. A sufferer is most infectious within the first three days of the illness. Asymptomatic persons can also shed or transmit viruses as common cold viruses have been exhibited in their nasal swabs.

Symptoms

Ninety-five percent of people exposed to a common cold virus become infected, although only 75% show symptoms. The symptoms start 1–2 days after infection. Generally a cold starts with a sore throat, without any respiratory blockage. From then onwards the symptoms are a result of the body's defense mechanisms: sneezes, runny nose, and cough to expel the invader, and inflammation to attract and activate immune cells. The clinical manifestations include nasal stuffiness and/or partial obstruction, sneezing, scratchy throat and watery discharge from nose. General malaise is commonly present. The nasal discharge becomes thicker and yellowish over several days. The complications associated with common cold include bacterial infection of middle ear (in children) and bacterial sinusitis because of weakened immune system. The reason may be the strong blowing of nose drives nasal fluids into the ears or sinuses. After a common cold, a sufferer develops immunity to the particular virus encountered. However, because of the large number and serotypes of different cold viruses, this immunity offers limited protection. A person therefore can be easily infected by another cold virus, starting the process all over again.

Prevention

The best way to avoid a cold is to avoid close contact with existing sufferers, to wash hands thoroughly and regularly, and to avoid touching the face. Anti-bacterial soaps have no effect on the cold virus - it is the mechanical action of hand washing that removes the virus particles. In 2002, the Centers for Disease Control and Prevention recommended alcohol based hand gels as an effective method for reducing infectious viruses on the hands. However, as with standard hand washing, alcohol gels provide no residual protection from re-infection. Tobacco smoking has also been linked with the weakening of the immune system and susceptibility to infection by viruses; non-smokers are known on average to take fewer days off sick than the smoking population. Smokers on average take 25% more sick days a year. Because of the large variety of viruses causing the common cold, vaccination is impractical.

Treatment

There is no cure for the common cold, i.e. there is no treatment that directly fights the virus. These infections soon clear up - as the saying goes – ‘in a week if treated but only seven days if ignored’. Only the body's immune system can effectively destroy the invader. A cold may be composed of several million viral particles, and typically within a few days the body begins mass producing a better tailored antibody that can prevent the virus from infecting cells, as well as white blood cells which destroy the virus through phagocytosis and destroy infected cells to prevent further viral replication. Furthermore the duration of infection is of the order of a few days to one week so at most a "cure" could hope to reduce the duration by only a few days.

A warm and humid environment and drinking lots of fluids, especially hot liquids, alleviate symptoms somewhat. Common home remedies include chamomile, lemon or ginger root tisanes and chicken soup (which probably work by soothing the irritated respiratory passages with their steam), nebulized medicinal mixtures, hot compresses, mustard plasters, hot toddies, licorice. Eating very spicy food can help alleviate congestion, although it may also irritate the already-tender throat. Coffee, or its active component, caffeine, has also been shown to improve mood and mental performance during rhinovirus infection. Antibiotics are ineffective against the common cold and all other viral infections. They are useful in treating any secondary bacterial infections that sometimes occur, but treatment with antibiotics *before* these coinfections develop is counterproductive, as it produces drug resistance, and can even promote infections by killing off normal bodily flora.

Publications in the 1960s and 1970s suggested that large doses of Vitamin C could both prevent and reduce the effects of the common cold. A particularly vociferous proponent of this theory was Nobel Prize winner Linus Pauling, who heavily advocated the intake of large doses of Vitamin C to prevent infection. Regular vitamin C supplementation shortened the duration of colds in children by 14% and in adults by 8%.

FUNGAL DISEASES

Dermatomycosis

The common name of dermatophytosis is "ringworm". The term ‘ringworm’ is a misnomer since it is not caused by a worm. Dermatophytosis is caused by fungal infection of skin, hair and nails of man and animals. These fungi are collectively known as dermatophytes. There are mainly three genera of dermatophytes (*Epidermophyton*, *Trichophyton* and *Microsporum*). Dermatophytosis can be caused by any species of these three genera. The dermatophytes are keratinophilic and they grow on keratin. The keratinophilic fungi, produce extracellular enzymes (keratinases) which are capable of hydrolyzing keratin. The superficial (cutaneous) mycoses are usually confined to the outer layers of skin, hair, and nails, and do not invade living tissues. The literal meaning of dermatophytes is ‘skin plants’. These fungi have different natural sources and modes of transmission. These are mainly three types:

- 1. Anthrophilic:** These are usually associated with humans only and the transmission is from man to man by close contact or through contaminated objects.
- 2. Zoophilic:** These are associated with animals and the transmission to man is by close contact with animals (cats, dogs, cows) or with contaminated products.

3. Geophilic: These are usually found in the soil and transmitted to man and animals by direct exposure.

Dermatophytes occur worldwide, but some species have geographically limited distribution. The dermatophyte infections of different external parts of the human body have been named separately using Latin binomial system classification which sounds like classification of disease causing fungi. However, these are tineas. Tinea means 'ringworm' or 'moth-like'. That is why dermatophytosis is also called ringworms. These include Tinea capitis (infection of the scalp), Tinea favosa, Tinea corporis (small lesions occurring anywhere on the body), Tinea pedis ('athlete's foot', infection of toe webs and soles of feet), Tinea manuum, Tinea imbricate, Tinea cruris ('jock itch', infection of the groin, perineum or perianal area), Tinea barbae (ringworm of the bearded areas of the face and neck-Fig.1A), Tinea nigra, Tinea unguium (infection of nails – Fig. 1B) and Tinea versicolor (blotchy discoloration of skin).



A



B

Fig. 1: Dermatomycosis of Neck (A) and Toe (B)

Etiologic agents

There are mainly three genera of fungi involved in dermatophytosis:

1. Trichophyton

There are 19 species under this genus. These mainly infect skin, hair and nails, however, may cause subcutaneous infections in immunocompromised individuals. Take 2-3 weeks to grow in culture. The conidia are large (macroconidia), smooth, thin-wall, septate (0-10 septa), and pencil-shaped; colonies are a loose aerial mycelium which grow in a variety of colors. Identification requires special biochemical and morphological techniques.

2. Microsporum

Thirteen members of this genus infect skin and hair. These fungi can be easily identified on the scalp because infected hairs emit a bright green color when illuminated with a UV-emitting Wood's light. The loose, cottony mycelia produce macroconidia which are thick-walled, spindle-shaped, multi-cellular, and echinulate (spiny). *Microsporum canis* is one of the most common dermatophyte species infecting humans.

3. Epidermophyton

These infect skin and nails and rarely hair. They form yellow-colored, cottony cultures and are usually readily identified by the thick, bifurcated hyphae with multiple smooth, club-shaped macroconidia.

Pathogenicity

Different species of *Epidermophyton*, *Microsporum* and *Trichophyton* genera differ in their pathogenicity profile *in vivo*. The stratum corneum of the epidermis and the follicular ostium of hairs are invaded by all the species. The reasons for this observed tissue specificity are unknown, but are thought to be related to specific nutritional requirements or the enzyme production of individual fungus. The enzymes synthesized by fungi enhance their survival in tissues by chemically or physically altering the immediate environment by digesting host proteins, thus providing a source of nutrition. Therefore the pathogenic potential of a fungal agent depends on its ability to produce enzymes (i.e. proteinases, elastases and keratinases). In turn variations in enzymatic potential of a fungus may be responsible for differences in the pathogenic effects of various strains. It has been demonstrated that certain strains of *Microsporum* and *Trichophyton* species produce enzymes that are able to digest the keratin and related fibrous proteins found in skin, hair, claws and hoof. The role of enzymes as virulence factors has also been inferred as they are often found in the tissues of infected animals.

Diagnosis

Diagnosis of dermatophyte infection can be done by clinical observation based on the lesions. However, identification of the genera and species of the dermatophytes requires culture and microscopic examination of skin and nail scrapings/hairs under microscope. A few species of the fungi cause a distinct apple green fluorescence in the infected hair shafts when illuminated by UV light. The presence of infective spores on hair shafts may occasionally be visualized microscopically. Recently molecular diagnostic procedures such as PCR have also been employed for identification of fungal species causing dermatophytosis.

Treatment

A combination of topical and systemic treatment of infected individuals as well as painstaking hygiene and decontamination of the environment are required to eradicate these often stubborn pathogens. Skin fungal infections can be treated (more or less successfully) with a variety of drugs including Tolfnatate (Tinactin), Clotrimazole, Miconazole available as topical application, Itraconazole as oral and Terbinafine (oral and topical) for skin and nail infections. For infections involving the scalp and particularly the nails, griseofulvin is commonly used. This antimycotic must be incorporated into the newly produced keratin layer to form a barrier against further invasion by the fungus. This is a very slow process requiring oral administration of the drug for long periods - up to 6 to 9 months for fingernail infections and 12 to 18 months for toenail infections.

PARASITIC PROTOZOAN DISEASES

Amoebiasis

Amoebiasis (amoebic dysentery) is one of the common diseases of developing countries including India where adequate sanitation and effective personal hygiene is lacking. According to an estimate about 500 million people suffer from amoebiasis and as many as 100,000 die each year. Amoebiasis is very common in India. It is caused by a protozoan parasite called *Entamoeba*. Three species viz. *E. dispar*, *E. coli* and *E. histolytica* have been reported to infect human beings. Of the three species, only *E. histolytica* is pathogenic and causes amoebic dysentery. Amoebiasis is often symptomless, however, it may be sometimes characterised by vague gastrointestinal distress, dysentery accompanied by blood and mucus, appendicitis, and abscesses in the liver and lungs. In asymptomatic infections *E. histolytica* thrives by eating and digesting bacteria and food particles in the gut. It does not usually come in contact with the intestine itself due to the protective layer of mucus that lines the gut. Disease occurs when *E. histolytica* comes in contact with the cells lining the intestine.

Life of cycle of amoebiasis is depicted in the Fig. 2. People get infection by ingestion of mature cysts of the parasite. Subsequent to the infection excystation occurs in the lower region of the small intestine. Eight small trophozoites are produced as a result of rapid division of metacyst. These trophozoites migrate to the large intestine where they can live as commensals in the lumen of the intestine, or invade the host tissue or undergo encystation. If the infective trophozoites invade the intestinal tissues, they multiply rapidly and spread laterally, while feeding on erythrocytes, bacteria and yeasts. The epithelial lining of large intestine is destroyed by invading trophozoites by producing enzymes (cysteine proteinases). The cysteine proteinases have been considered as possible virulence factors of *E. histolytica*. They may play a role in intestinal invasion by degrading extracellular matrix and circumventing the host immune response through cleavage of secretory immunoglobulin A, IgG, and complement factors. At least seven genes have been found to encode cysteine proteinases in *E. histolytica* whereas these are missing in *E. dispar* which is non pathogenic.

Diagnosis

The diagnosis of amoebiasis can be made on the basis of the symptoms followed by laboratory confirmation by detecting trophozoites in fresh warm stools and cysts in ordinary stools by microscopic examination. Microscopy is still the most widespread method of diagnosis around the world. However it is not as sensitive or accurate in diagnosis as the other tests available. Since there are non pathogenic amoeba that can infect human beings, it is important to distinguish the *E. histolytica* cysts from the cysts of nonpathogenic intestinal protozoa such as *Entamoeba coli* and *E. dispar* by its appearance. There are a maximum of four nuclei in the cysts of *E. histolytica* whereas, there may be up to 8 nuclei in the commensal *Entamoeba coli*. In addition, endosome is centrally located in the nucleus in *E. histolytica*, while it is off-center in *E. coli*. However *E. dispar* cannot be distinguished from *E. histolytica* under the microscope. Since *E. dispar* is much more common than *E. histolytica* in most parts of the world this means that there is a lot of incorrect diagnosis of *E. histolytica* infection. According to WHO recommendation the infections diagnosed by microscopy alone should not be treated if they are asymptomatic and there is no other reason to suspect that the infection is actually *E. histolytica*. Some antibody and DNA based tests can also be employed to detect *E. histolytica*.

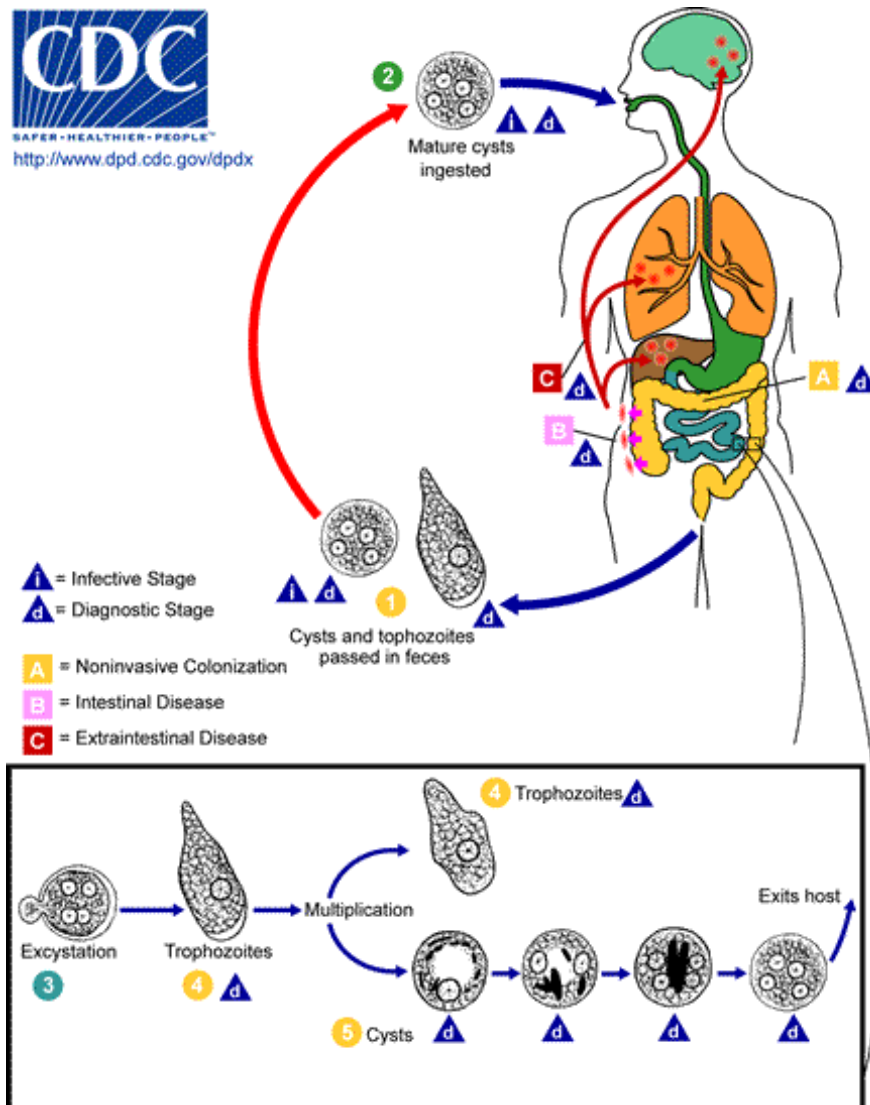


Fig. 2: Life cycle of amoebiasis: Cysts and trophozoites are passed in feces

①. Cysts are typically found in formed stool, whereas trophozoites are typically found in diarrheal stool. Infection by *Entamoeba histolytica* occurs by ingestion of mature cysts ② in fecally contaminated food, water, or hands. Excystation ③ occurs in the small intestine and trophozoites ④ are released, which migrate to the large intestine. The trophozoites multiply by binary fission and produce cysts ⑤, and both stages are passed in the feces ①. Because of the protection conferred by their walls, the cysts can survive days to weeks in the external environment and are responsible for transmission. Trophozoites passed in the stool are rapidly destroyed once outside the body, and if ingested would not survive exposure to the gastric environment. In many cases, the trophozoites remain confined to the intestinal lumen (A: noninvasive infection) of individuals who are asymptomatic carriers, passing cysts in their stool. In some patients the trophozoites invade the intestinal mucosa (B: intestinal disease), or, through the bloodstream, extraintestinal sites such as the liver, brain, and lungs (C: extraintestinal disease), with resultant pathologic manifestations. It has been established that the invasive and noninvasive forms represent two separate species, respectively *E. histolytica* and *E. dispar*. These two species are morphologically indistinguishable unless *E. histolytica* is observed with ingested red blood cells (erythrophagocytosis). Transmission can also occur through exposure to fecal matter during sexual contact (in which case not only cysts, but also trophozoites could prove infective).

Treatment

The treatment of amebiasis is quite complex and depends largely on the location of the infection within host and the host's condition. Iodoquinol or paromomycin are often recommended for the treatment of asymptomatic carriers that are passing cysts because they are most important reservoir of the parasite in the population. In symptomatic intestinal amoebiasis, metronidazole or iodoquinol are the drugs of choice. Prevention and control of amoebiasis is achieved by avoiding water or food that might be contaminated with human faeces in endemic areas such as India. Viable cysts in water can be destroyed by hyperchlorination or iodination.

Malaria

Malaria (Medieval Italian: *mala aria* — "bad air") and formerly called 'ague' or marsh fever in English. The cause of malaria was discovered by Charles Louis Alphonse Laveran, a French army doctor who was awarded the Nobel Prize for Physiology or Medicine in 1907. Sir Ronald Ross was also awarded Nobel Prize in 1902 for demonstrating that certain species of mosquito can transmit malaria to birds and describing the life cycle stages that develop within the mosquito.

It is one of the most important parasitic diseases of human beings. According to WHO estimates, around 350-500 million suffer from malaria and more than 1.3-3 million die annually through out the world. Mainly the tropics, Sub-Saharan Africa and Asia account for 85–90% of these fatalities. In India malaria is endemic and millions of people are affected annually. Children under the age of five and pregnant women are most vulnerable to fatalities of malaria.

Malaria is caused by a protozoan parasite known as *Plasmodium*. There are mainly 4 species of *Plasmodium* including *P. falciparum*, *P. malariae*, *P. vivax*, and *P. ovale* which have been found to cause malaria in human beings. The malarial parasite is transmitted by female *Anopheles* mosquito. The life cycle of malaria starts with feeding of infected female *Anopheles* mosquito on blood of the human host. During the feeding on human blood by bite, the infected female *Anopheles* mosquito injects saliva containing an anticoagulant along with haploid sporozoites. The first target of the mosquito transmitted sporozoites in blood stream is liver where they undergo schizogony (multiple asexual fission) in hepatic cells and produce hundreds of merozoites. Subsequently after release from the hepatic cells, merozoites penetrate the red blood cells (erythrocytes). In the erythrocytes merozoites enlarge and develop in to uninucleate cell termed as trophozoite. The trophozoite nucleus divides asexually to produce a schizont having 6-24 nuclei. The division of schizont leads to formation of numerous mononucleated merozoites. Eventually due to numerous merozoites, the cytoplasmic membrane of erythrocytes ruptures and thus merozoites are released in the blood stream to penetrate other erythrocytes. The erythrocytic stage is cyclic and repeats itself every 48 to 72 hours or longer depending on the species of *Plasmodium* (Fig. 3).

Symptoms

Chills and fever are the hallmarks of malaria that are caused by sudden release of merozoites, toxins, and erythrocyte debris. Some times, merozoites differentiate into microgametocytes and macrogametocytes which do not rupture the erythrocytes. When these are ingested by a

mosquito through blood meal, they develop into male and female gametes, respectively. The infected erythrocytes are lysed in the mosquito's gut and the gametes fuse to form a diploid zygote called the ookinete. The ookinete develops as oocyst in the mosquitoes gut. The oocysts undergo meiosis and form sporozoites that migrate to the salivary glands of the mosquito. The cycle is now complete, and when the mosquito bites another human host, the cycle begins anew.

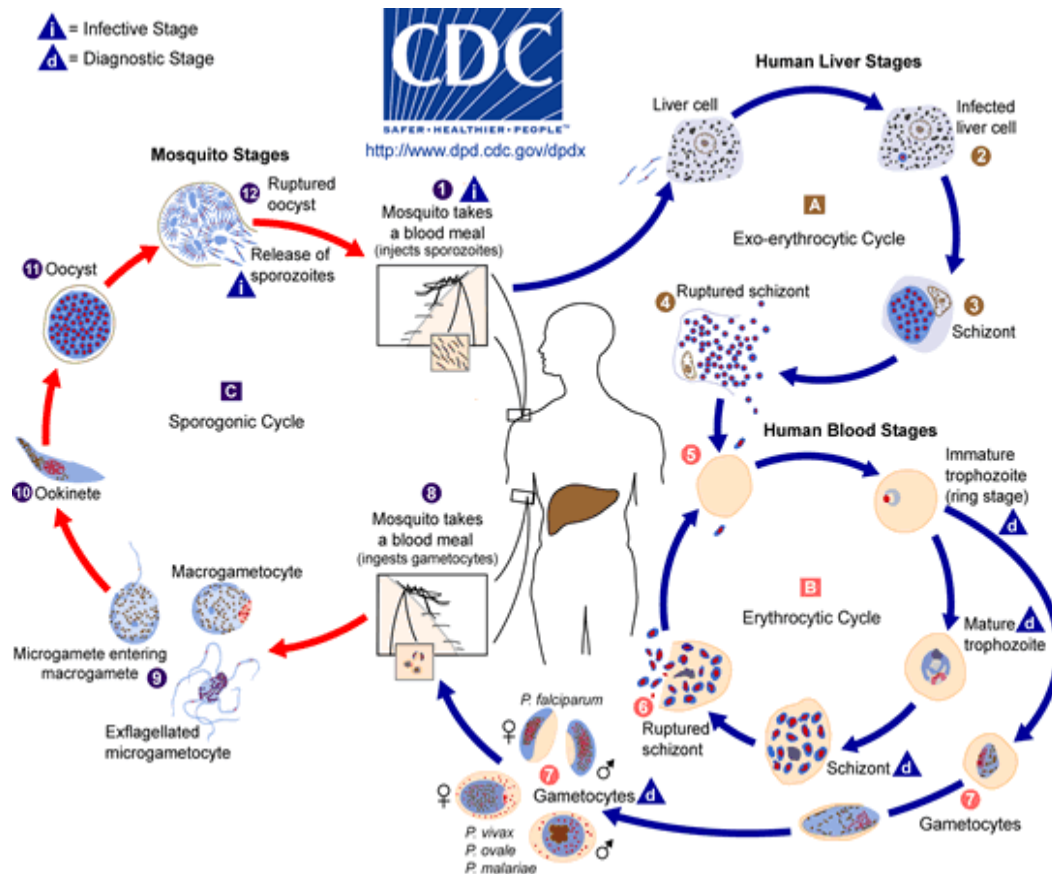


Fig. 3: Life cycle of Malaria: The malaria parasite life cycle involves two hosts. During a blood meal, a malaria-infected female *Anopheles* mosquito inoculates sporozoites into the human host

1. Sporozoites infect liver cells 2 and mature into schizonts 3, which rupture and release merozoites 4. (Of note, in *P. vivax* and *P. ovale* a dormant stage [hypnozoites] can persist in the liver and cause relapses by invading the bloodstream weeks, or even years later.) After this initial replication in the liver (exo-erythrocytic schizogony A), the parasites undergo asexual multiplication in the erythrocytes (erythrocytic schizogony B). Merozoites infect red blood cells 5. The ring stage trophozoites mature into schizonts, which rupture releasing merozoites 6. Some parasites differentiate into sexual erythrocytic stages (gametocytes) 7. Blood stage parasites are responsible for the clinical manifestations of the disease. The gametocytes, male (microgametocytes) and female (macrogametocytes), are ingested by an *Anopheles* mosquito during a blood meal 8. The parasites' multiplication in the mosquito is known as the sporogonic cycle C. While in the mosquito's stomach, the microgametes penetrate the macrogametes generating zygotes 9. The zygotes in turn become motile and elongated (ookinetes) 10 which invade the midgut wall of the mosquito where they develop into oocysts 11. The oocysts grow, rupture, and release sporozoites 12, which make their way to the mosquito's salivary glands. Inoculation of the sporozoites 1 into a new human host perpetuates the malaria life cycle.

Fever, shivering, arthralgia (joint pain), vomiting, anaemia caused by haemolysis, haemoglobinuria and convulsions are common symptoms of malaria. There may be the feeling of tingling in the skin, particularly with malaria caused by *P. falciparum*. Consequences of infection with malaria include coma and death if untreated. Splenomegaly (enlarged spleen), severe headache, cerebral ischemia and hemoglobinuria with renal failure may also occur.

Diagnosis

Microscopic examination of blood films is the gold standard for diagnosis of malaria. Diagnosis of malaria is made by demonstrating the presence of parasites within Wright-or Giemsa-stained erythrocytes. When blood smears are negative, serological testing can establish a diagnosis of malaria in individuals.

Treatment

There are several families of drugs used to treat malaria. Chloroquine was the antimalarial drug of choice for many years in most parts of the world. However, resistance of *Plasmodium falciparum* to chloroquine has spread recently from Asia to Africa, making the drug ineffective against the most dangerous Plasmodium strain in many affected regions of the world. Therefore, recommendations for treatment are region specific. Treatment includes administration of chloroquine, amodiaquine, or mefloquine. These suppressant drugs are effective in eradicating erythrocytic asexual stages. Primaquine has proved satisfactory in eradicating the exoerythrocytic stages. However, because resistance to these drugs is occurring rapidly, more expensive drug combinations are being used. One example is Fansidar, a combination of pyrimethamine and sulfadoxine. It is worth noting that individuals who are travelling to areas where malaria is endemic should receive chemoprophylactic treatment with chloroquine.

Prevention

Efforts to develop a vaccine are under way. Methods used to prevent the spread of disease, or to protect individuals in areas where malaria is endemic, include prophylactic drugs, mosquito eradication, and the prevention of mosquito bites. There is currently no vaccine that will prevent malaria, but this is an active field of research.

Leishmaniasis

Leishmaniasis is a very important human disease which is caused by parasites belonging to the genus *Leishmania*. Leishmaniasis is also known as 'kala azar', 'sandfly disease', 'Dum-Dum fever', 'black fever' and 'espundia'. The disease was named after a Scottish pathologist William Boog Leishman in 1901. It is transmitted by the bite of certain species of sandfly of the genera *Lutzomyia* and *Phlebotomus*.

Most forms of the disease are transmitted from animals through sandfly to humans, however, some forms of the disease may spread between humans. Twenty one of 30 species that infect mammals can cause infection in human beings. These include the *L. donovani* complex with three species (*L. donovani*, *L. infantum*, and *L. chagasi*); the *L. mexicana* complex with 3 main species (*L. mexicana*, *L. amazonensis*, and *L. venezuelensis*); *L. tropica*; *L. major*; *L. aethiopica*; and the subgenus *Viannia* with four main species (*L. (V.) braziliensis*, *L. (V.) guyanensis*, *L. (V.)*

panamensis, and *L. (V.) peruviana*). The different species are morphologically indistinguishable, however they can be differentiated by nucleic acid based methods, isoenzyme analysis, or monoclonal antibodies. Leishmaniasis is widely distributed in the world however, tropical and subtropical regions are more affected. As many as 88 tropical and sub-tropical countries have reported prevalence of Leishmaniasis. According to an estimate more than 90 % of the world's cases of visceral leishmaniasis are in India, Bangladesh, Nepal, Sudan and Brazil.

Symptoms

Leishmaniasis is characterized by skin sores, fever, damage to the spleen (enlargement of spleen) and liver, and anaemia. There are four main forms of leishmaniasis.

1. Visceral leishmaniasis: the most serious form and potentially fatal if untreated.
2. Cutaneous leishmaniasis: the most common form which causes numerous sores on the body, which heal within a few months leaving unpleasant looking scars.
3. Diffuse cutaneous leishmaniasis: this form produces widespread skin lesions which resemble leprosy and is particularly difficult to treat.
4. Mucocutaneous leishmaniasis: commences with skin ulcers which spread causing tissue damage to (particularly) nose and mouth.

Leishmaniasis is transmitted by the bite of female phlebotomine sandflies. The sandflies inject the infective stage, promastigotes, during blood meals. Promastigotes that reach the puncture wound are phagocytized by macrophages and transform into amastigotes. Amastigotes multiply in infected cells and affect different tissues, depending partly on the *Leishmania* species is involved. Sandflies become infected during blood meals on an infected host when they ingest macrophages infected with amastigotes. In the sandfly's midgut, the parasites differentiate into promastigotes, which multiply and migrate to the proboscis (Fig. 4).

Treatment

Several potential vaccines are being developed. Miltefosine has received approval by the Indian and German regulatory authorities and is the first orally administered breakthrough therapy for visceral leishmaniasis. There is problem with toxicity (gastrointestinal and renal) as well as the rapid development of resistance. Because it is available as an oral formulation, the expense and inconvenience of hospitalization is avoided, which makes it an attractive alternative.

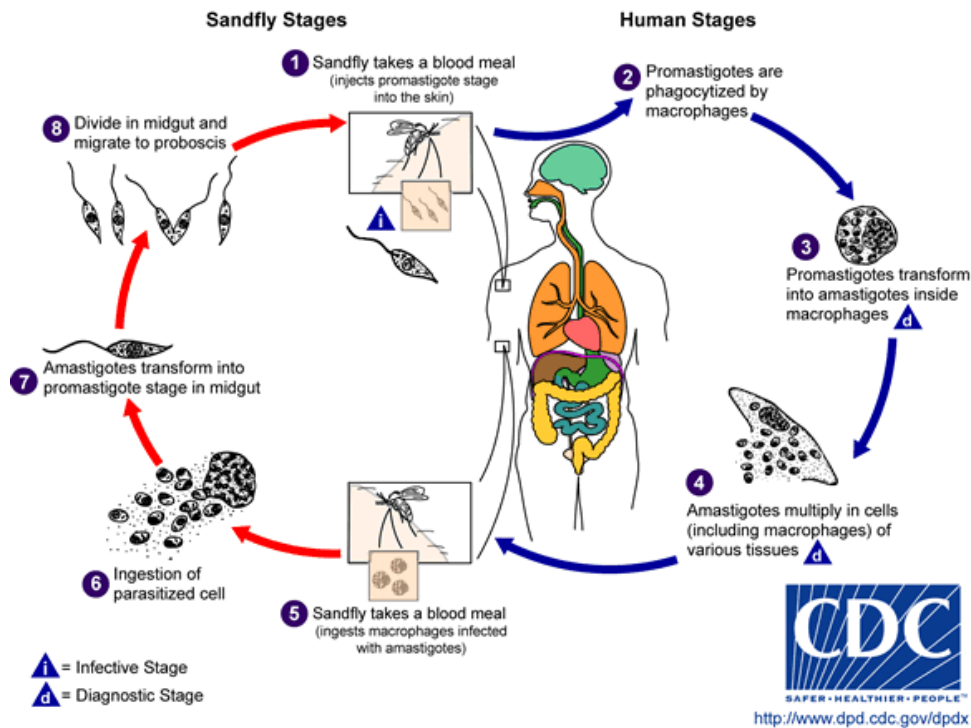


Fig. 4: Life cycle of *Leishmania*: Leishmaniasis is transmitted by the bite of female phlebotomine sandflies. The sandflies inject the infective stage, promastigotes, during blood meals

1. Promastigotes that reach the puncture wound are phagocytized by macrophages 2 and transform into amastigotes 3. Amastigotes multiply in infected cells and affect different tissues, depending in part on the *Leishmania* species 4. This originates the clinical manifestations of leishmaniasis. Sandflies become infected during blood meals on an infected host when they ingest macrophages infected with amastigotes (5, 6). In the sandfly's midgut, the parasites differentiate into promastigotes 7, which multiply and migrate to the proboscis 8.

Suggested Readings

1. Elliott, T., Gill, M., Osman, H. and Worthington, T. (2006). Lecture Notes Medical Microbiology and Infection, 4th Edition, Blackwell Pub, 273p.
2. Greenwood, D., , Slack, Richard C. B. , Peutherer, John F. and Barer, Michael R. (2007). Medical Microbiology: A Guide to Microbial Infections: Pathogenesis, Immunity, Laboratory Diagnosis and Control, Churchill Livingstone; 17Rev Ed edition, 752p.
3. Murray, Patrick R., Pfaller, Michael A., Rosenthal, K.S. (2005). Medical Microbiology. 5th Edition, Elsevier Books, Mosby.
4. Pommerville, Jeffrey C. (2006). Alcamo's Fundamentals of Microbiology, 8th Edition, Jones & Bartlett Pub, 952p.
5. Prescott, Lansing M., Harley, John P. & Klien, Donald A. (2005). Microbiology, 6th Edition, McGraw-Hill Companies Inc. 1221 Avenue of the Americas, New York, 992p.
6. Tortora, J.J., Funke, B.R. & Case, C.L. (1998). Microbiology: In introduction, Addison Wesley Longman, Inc., 2725 Sand Hill Road, Menlo Park, California, 832p.
7. Winn, Washington C., Allen, S., Janda, William M., Koneman, Elmer W., Schreckenberger, Paul C., Procop, G., and Woods, Gail, B. (2005). Koneman's Color Atlas and Textbook of Diagnostic Microbiology, Lippincott Williams & Wilkins, US; 6Rev Ed edition, 1736 p.