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CHAPTER 4

Parasites, Bacteria and Viruses

THE WORMS

PLATYHELMINTHS
Flat worms which may affect man’s health are the trematodes or ‘flukes’ and the cestodes or ‘tape-worms’.

THE TREMATODES
There are two groups of trematodes —
(a) Those which are hermaphrodites (i.e. male and female sex organs are present in the same worm)
   e.g. *Paragonimus westermanni* — the lung fluke
   *Clonorchis sinensis* — the Chinese liver fluke
   *Fasciola hepatica* — the liver fluke

![Diagram of the life cycle of trematodes](image)

**Figure 10**
A GENERAL LIFE-CYCLE FOR TREMATODES
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(b) Those which are non-hermaphrodite (i.e. worms which are either male or female) — e.g. Schistosomes — the blood fluke.

Distinguishing features in the trematode life cycle include the following:

(i) They have both vertebrate and invertebrate hosts participating in their life cycle.

(ii) They have a free living stage in their life cycle.

(iii) They reproduce both sexually and asexually at different stages of their life cycle. The host in which sexual reproduction of a parasite occurs is the definitive host; asexual reproduction occurs in the intermediate host.

(iv) In the case of *Clonorchis senensis* the eggs are ingested by the snail, in the case of all the other trematodes mentioned the miracidia actively penetrate the snail's foot or head.

(v) The cerceria of the schistosomes actively penetrate the vertebrate host; other cerceria encyst as metacerceria and are ingested by the definitive vertebrate host.

(vi) The trematodes are selective in their choice of hosts.

Table XIX
MORE IMPORTANT FEATURES OF MEDICALLY IMPORTANT TREMATODES

| ORGANISM                | ADULT WORM                      | SNAIL SPECIES | METACERCERIA ENCYST ON | TARGET ORGAN       |
|-------------------------|---------------------------------|---------------|------------------------|--------------------|
| NON-HERMAPHRODITE       |                                 |               |                        |                    |
| *S. mansoni*            | man, baboon                     | Biomphalaria  | —                      | bowel              |
| *S. haematobium*        | man                             | Bulinus       | —                      | bladder            |
| *S. japonicum*          | man, domestic animals           | Oncomyelania  | —                      | abdominal           |
| HERMAPHRODITE           |                                 |               |                        |                    |
| *Clonorchis senensis*   | dog, cat                        | Parafossarula | gills of fish          | biliary system     |
| *Opisthorchis felineus* | cat                             | Bithynia      | muscles of fish        | biliary system     |
| *Paragonimus westermani*| rats, carnivores                | Melania       | fresh water            | lung               |
| *Fasciola hepatica*     | sheep, herbivores               | Lymnaeae      | grass                  | liver              |

Pathology

Disease can be due to:

(i) The presence of the worm — the worm may cause obstruction, e.g. of the bile duct. The adult worm during its migration through the body of the host may get lost and cause local lesions in the brain.

(ii) The eggs — the immune response of the host is more marked towards the eggs than towards the adult worm. Death of the eggs releases antigen and the host responds with granuloma formation. Fibrosis can result in stricture formation and loss of functional parenchymatous tissue.

Diagnosis

A definitive diagnosis is possible if ova are observed in urine, faeces or sputum. Each trematode produces a characteristic ovum. As eggs are produced by mature worms there is a time lapse between exposure, infection
and the production of eggs, e.g. in the case of *Schistosoma mansoni* this delay is 6-8 weeks; in the case of *Schistosoma haematobium* this delay is 13 weeks. Complement fixation tests are also used.

**Control and prevention**

These worms have a complex life cycle. They require the presence of —

(i) a vertebrate host;

(ii) an invertebrate snail host;

(iii) the correct environment — water for the eggs to hatch, grass on which the metacerceria may encyst, etc.

Approach to prevention may be as follows:

(i) Treatment of the disease in the vertebrate host and prevent reinfection of this host.

(ii) Kill snail hosts and break the life cycle required for the propagation of these parasites.

(iii) Separate the vertebrate host and his excreta from snails. Each of these approaches enjoys a measure of success.

**Bilharzia**

Bilharzia or schistosomiasis is an important disease in Southern Africa. Infection by both *Schistosoma haematobium* and *Schistosoma mansoni* may occur simultaneously in the same individual. *Schistosoma haematobium* is found throughout Africa, the distribution of *Schistosoma mansoni* is more patchy.

The presence of bilharzia in an area depends on the presence of snails and water. Snails die in rivers in which the temperature is between 0-5°C for five days. Snails are therefore not found in rivers above 4 000 feet. In South Africa bathing is safe in rivers that flow west into the Atlantic Ocean and in those rivers flowing into the Indian Ocean between Cape Point and Plettenberg Bay.

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**Figure 11**

*THE CESTODES*

SCOLEX (Head)  ADULT WORM SHOWING PROGLOTTIDS
THE CESTODES

The cestodes or tape worms have a body consisting of segments or proglottids. Each proglottid develops from a growth zone near the ‘head’ or scolex of the worm. As the proglottid matures it passes through a male and then a female phase. By the time the proglottid has been displaced to the distal end of the worm it consists of a “bag of eggs”. The proglottid is distended by eggs contained in its uterine branches. This mature proglottid is expelled in the faeces of the host or it may crawl out of the host’s anus.

Cestodes have no free living stage. The adult worm lives in the small intestine of the definitive host. The larval stage migrates and forms cysts in the muscle or parenchymal tissue of the intermediate host.

Figure 12
THE CESTODE LIFE CYCLE

Basic Life Cycle:

The larvae migrate systemically and encyst in viscera or muscle

Cysts are ingested by eating undercooked infected meat

INTERMEDIATE HOST
e.g. pigs, cattle, rarely man

DEFINITIVE HOST
e.g. MAN

LARVAE

The eggs are eaten by the intermediate host

ADULT WORM
(in the host’s intestine)

The eggs produced are excreted with the host’s intestinal contents

EGGS

Pathology

The disease can be due to —

(a) The presence of the worm — the adult worm is found in the intestine of the host. Its eggs are not trapped in the host’s tissues but are freely excreted along with the faecal mass. Side effects caused by the worm can occur as a result of competition for nutrients, e.g. vitamin B12. Absorption of metabolites provided by the worm can lead to psychological effects in the host. The observation of a proglottid in the host’s stool may also lead to psychological symptoms. Certain ‘workers’ attempted to introduce larval tapeworm tablets as a novel means of slimming. This slimming technique came to an inglorious end when tablets left lying in the sunlight started to move.
Table XX
LISTING THE MORE IMPORTANT FEATURES OF MEDICALLY IMPORTANT CEStODES

| ORGANISM               | DEFINITIVE HOST | INTERMEDIATE HOST                       | CYST       |
|------------------------|-----------------|-----------------------------------------|------------|
| Taenia solium          | man             | pig, occasionally man cattle            | cysticercus|
| Taenia saginata        | man             | cattle                                   | cysticercus|
| Taenia multiceps       | dog, cat        | herbivorous animal, occasionally man    | coenurus   |
| Echinococcus granulosus| canines, e.g. jackal | herbivorous animal, occasionally man | hydatid    |

In the above cases when the adult worm is found in man it is well tolerated.

WORM INFESTATIONS PREDOMINATING IN CHILDREN

| Organism                  | Hosts                                      | Cyst            |
|---------------------------|--------------------------------------------|-----------------|
| Dibothriocephalus latus   | carnivor e.g. jackal, man                  | pleurocercoid   |
| Dipyllidium canicum       | dog                                        | cysticercoid    |
| Hymenolepis nana          | birds, rodents                             | cysticercoid    |
|                           | dog flea                                   |                 |
|                           | nil or insects                              |                 |


(b) The presence of the larval cyst — the cysts can lead to serious complications. If man ingests cestode eggs, the eggs can hatch in his intestine. The larvae migrate to various viscera and cysts are formed. These cysts, depending on their anatomical site, can cause various effects. If a cyst is present in the brain it may block drainage of the cerebro-spinal fluid causing raised intracranial pressure; it may on death of the larvae calcify and cause epilepsy. Removal of the cysts from brain, liver, etc., is a dangerous procedure as rupture of a viable cyst releases one or more larvae capable of developing into egg producing adults in the central nervous system or abdominal cavity.

Diagnosis
In general tapeworm ova can be differentiated from other ova by the presence of hooklets. Identification of the type of cestode by examination of the ovum is only possible in certain cases.

Other methods of diagnosing cestodes includes examination of any proglottids passed in the faeces. Cysts squashed between two glass slides can be identified by the number and type of scolices present.

Prevention and control
Treatment of *Taenia saginata* or *Taenia solium* in man results in death of the adult worm. The worm releases its hold on the intestine and is passed out of the intestine by peristalsis. *Taenia solium* may respond to certain therapy by releasing its ova into the lumen of the intestine. Those eggs which are transported by retrograde peristalsis to the stomach hatch in the host's intestine, and release their larvae. Migration of these larvae causes cysticercosis. In cases of cestode infestation a constipated bowel should be evacuated prior to treatment.

Prevention of disease is by adequate control and condemnation of infected meat. Treatment of the cyst, other than surgical excision, is contraindicated as the host's immune response to the dead larva is exaggerated. Treatment of a cerebral cyst can precipitate epilepsy.

Certain of the cestodes are acquired by children during their contact with infected pets.

THE NEMATODES
The nematodes are also called “round worms”. Between the egg and adult stages their life cycle involves a number of different larval stages. Transmission varies:

(a) Certain eggs are transmitted directly from one host to the next by the faecal-oral route, e.g. the pinworm.

(b) Other eggs require a stage of maturation in soil. They hatch to form larvae which actively penetrate the skin of the new host, e.g. hookworms.

(c) Certain nematodes, the filaria, are transmitted by arthropods, e.g. *Loa loa*. 
**Nematodes transmitted by the faecal-oral route**

*Trichuris trichura*: The Whip worm  
*Enterobius vermicularis*: The Pinworm  

Both these round worms are confined to the intestine. The adults are frequently found in the caecum. The female pinworm migrates out of the anus and deposits her eggs in the peri-anal region — this results in pruritis ani. Children are frequently infested by this worm. When one member of a family becomes infested it is necessary to treat the whole family — including father. The eggs shed from the child’s anal area are small light-weight eggs which float and land on many objects in the environment.

Trichuris infestation is usually asymptomatic — only heavy infestations are accompanied by symptoms. Man is the definitive host in the case of both trichuris and enterobius.

The definitive host for *Ascaris lumbricoides* is man; for *Toxocara canis*, the dog and for *Toxocara cati*, the cat. The larvae of these worms undergo a systemic migration prior to settling in the intestinal lumen of their natural host. When man ingests the eggs of toxocara the larvae fail to migrate back to the intestine and become lodged in the visera. *Toxocara canis* and *Toxocara cati*, the dog and cat ascarids, cause viseral larva migrans in man.

**Nematodes requiring ingestion of eggs or larvae in animal tissue for transmission**

*Capillaria hepatica* and *Trichinella spiralis* are transmitted by the consumption of infected animal tissue.

Inadequately cooked pork is a vehicle for the transmission of *Trichinella spiralis*. The larvae are released from their cysts on exposure to the digestive juices of the host’s intestine. The adults mate in the upper gastrointestinal tract and produce larvae which penetrate the intestine and migrate to the host’s skeletal muscle. Cold storage at $-18^\circ\text{C}$ for at least two weeks is required to kill the larvae in pork.
Both *Trichinella spiralis* and *Capillaria hepatica* are not natural parasites of man. They are classified amongst the zoonoses.

*Capillaria hepatica* is a nematode of rodents. Children are occasionally infected. Infection results from the ingestion of eggs found in rat faeces. These eggs hatch, the larvae migrate to the liver and the adults lay their eggs in the liver. The infected child will thus never excrete the ova of this worm in the faeces. If the child ingests eggs found in rat liver, not faeces, then the ingested eggs will be excreted in that child's faeces. In this case the child is the paratenic host or the carrier. These eggs are non-invasive as the egg requires exposure to digestive enzymes plus a time lapse before the larvae can be released. The carrier therefore excretes eggs in his faeces. Only after the eggs have been passed through the gastro-intestinal tract are they infective on subsequent ingestion.

**Figure 14**

*A TYPICAL LIFE CYCLE OF NEMATODES CAPABLE OF PERCUTANEOUS INVASION*

**THE ENVIRONMENT — SOIL**

**THE HOST — MAN**

- **FILARIFORM LARVAL**
  - This actively penetrates skin or mucous membranes. The larva undergoes systemic spread eventually reaching the lung. It is coughed up and swallowed.

- **RHABDITIFORM LARVA**

- **FREE LIVING CYCLE**

- **EGGS**
  - Eggs are produced and shed in the faeces
  - **ADULT WORM**

- **RHABDITIFORM LARVAE**

- **AUTOINFECTION BY STRONGYLOIDES**
  - **EGGS**

**Nematodes transmitted by active percutaneous larval penetration**

*Strongyloides stercoralis, Ancylostoma duodenale* and *Necator americanus* all fall into this group.

Hookworms are recognised as an important cause of anaemia in the tropics. They require a maturation phase in soil during which they undergo a free living larval stage. The definitive host is man.

Strongyloides may cut short its life cycle. Instead of the larvae developing in the soil they may become invasive while still in the host's intestine. Strongyloides can thus auto-infect the host — as strongyloides is capable of multiplication within the same host, suppression of the host immune response is dangerous. Immunosuppression can permit excessive multiplication of this worm in the host. Of all the worms already mentioned, strongyloides is the only one capable of multiplying within the
Man meets Microbes

host — this means that infection by strongyloides has graver implications from the point of view of worm load.

*Ancylostoma braziliensis*, the dog hookworm, causes sandworm in man. The larva attempts to penetrate the skin of the wrong host but finds itself incapable of penetrating the dermis. The larva therefore migrates through the skin leaving in its wake an allergic erythematous streak. Sandworm is also called cutaneous larva migrans.

**Nematodes injected percutaneously into vertebrate hosts**

The filarial worms are mainly found in tropical and sub-tropical areas.

*Wucheria bancrofti* is spread by mosquitoes and causes lymphadenitis and elephantiasis in man.

*Loa-loa* is spread by chrysops, a fly, and this worm causes calabar swellings. Loaiasis manifests itself by migratory sub-cutaneous oedema and erythrema.

*Onchocerca volvulus* is spread by simulium — the black fly. The species of fly which carries oncocercus is called *Simulium damnosum*. Onchocerciasis is a disease which manifests itself as subcutaneous nodules, caused by the adults, and retinal damage culminating in blindness caused by the microfilaria. River blindness is the name given by local people to this disease.

*Acanthocheilonema perstans* is spread by culicoides, the biting midge. This worm has no clear association with disease but may cause eosinophilia.

Female filarial worms are either viviparous, laying embryonated eggs, or ovoviviparous discharging their larvae directly into the host's blood stream. The larvae are called microfilariae. The microfilaria, except for those of onchocercus, circulate in the blood and are picked up by a biting arthropod. The larvae develop further in the arthropod host and when mature are injected by the arthropod through the skin of a new vertebrate host. Man can act as the definitive host for all the filaria mentioned. The adult worms settle in the peritoneal cavity in the case of *Acanthocheilonema*

**Figure 15**

A GENERAL VIEW OF A FILARIAL LIFE CYCLE

- Larvae injected into man
- Growth and maturation of larvae
- Microfilaria ingested by arthropod
- Larvae injected into arthropod
- Adult worm
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*perstans*, in the lymphatics or lymph nodes in the case of *Wuchereria bancrofti* and are found subcutaneously in both onercerciasis and loaiasis. The microfilaria are found in the blood, except in the case of onchocerciasis where they are found in the skin.

The host’s response plays an important role in the disease caused by the filarial worms and their larvae, the microfilaria. Allergy is a major factor in the pathogenesis of river blindness, elephantiasis and calabar swellings. Eosinophilia is often associated with systemic nematode invasion.

**Diagnosis of nematode worms**

(i) The eggs — in many cases microscopic examination of the faeces will lead to the demonstration of ova in individuals infected with nematode worms. Many nematodes produce distinct ova, e.g. ascaris, trichuris, enterobius.

(ii) The larvae — hookworms and strongyloides cannot be distinguished from one another on the appearance of their ova — examination of the larvae will, however, enable one to distinguish between these worms. The hookworms are distinguished by morphological differences between their larvae, while strongyloides is identified by the presence of larvae in a fresh stool.

Microfilaria can be identified according to —

(a) the arrangement of their nuclei; and

(b) the presence or absence of a sheath.

If present the shape of the sheath is also important. The intermediate host and the diurnal variation of the parasitaemia all help to confirm the diagnosis. *Wuchereria bancrofti* is present in the blood at night, *Loa loa* during the day.

**Pathology**

**A. The Adult Worms**

Adults may lead to problems by —

(i) their physical presence — ascaris can cause intestinal obstruction, intestinal perforation and obstruction of the biliary duct.

(ii) their mode of attachment to the host and their nutrition, e.g. hookworms attach to villi in the intestine and blood flows into the intestinal lumen of the worm, much of which is secreted undigested by the worm. Hookworms move from one villus to another leaving a path of oozing villi behind them.

**B. The Larvae**

Those larvae which migrate through various of the host’s organs prior to settling may present the following problems —

(a) They may lose their way and be trapped in a site deleterious to the host.

(b) During their migration they can damage tissue and evoke various host responses, e.g. dyspnoea, cough, eosinophilia.
(c) The host may respond to the presence of the adult worm or the larvae with a hypersensitivity type of reaction. Infection with certain of the nematodes can lead to allergic responses.

**Prevention and control**

Therapy is available which will kill the adult worms. If multiple worm infestation has occurred in a single individual's intestinal tract, it is advisable to treat the ascaris infection first. Ascaris is an irritable worm. Although it is unlikely to have caused the patient's symptoms it can cause serious consequences should it be irritated by treatment used to kill the other worms. An irritable ascarid is an active worm and likely to cause acute obstruction of the intestine or the bile duct.

Nematode infections that can be prevented by adequate hygiene are spread by the faecal-oral route. Hands are a major source of spread. Larvae which actively penetrate the skin usually do so at the level of the feet or ankles. They are incapable of penetrating leather, therefore boots will decrease the incidence of hookworm in endemic areas. Adequate sanitation is of course the better mode of preventing spread.

Filaria can be avoided by protecting the individual against mosquitoes, flies and midges. DDT and other insecticides are of value.

**Dracunculus medinensis**

The 'Guinea Worm' is of great medical interest. The female is a long worm found in skin blisters in the infected host. Treatment is removal of the worm using a matchstick. Each time the matchstick is turned, a few more millimetres of the worm are extracted from the skin. Medical associations sport dracunculus wound around a stick on their badges.

Man, the definitive host, sheds the larvae when the skin blister contacts water and bursts. Infected crustaceans, e.g. cyclops are in turn ingested by man.

Acquisition of this infestation is prevented by adequate boiling of water. Spread is intercepted by preventing those infected by dracunculus from allowing their blisters to burst in, and hence contaminate, the local wells.

**THE HIGHER PROTISTS**

There are two groups of higher protists that require consideration from a medical viewpoint. These are: (A) The Protozoa; (B) The Fungi.

(A) THE PROTOZOA

The most important 'medical' protozoa are found in the groupings sarcocystigophora and sporozoa. Protozoa are single celled creatures often characterized by a particular mode of transport, e.g. the flagellates have flagellae, the amoebae move by amoeboid movement. Reproduction in this group can be either sexual or asexual. Asexual reproduction can be characterized as simple binary fission — one becomes two — or multiple fission (schigony) where one becomes more than two.
THE SARCOMASTIGOPHORA
Reproduction in this group is basically asexual by binary fission. Two groups are identified: (a) The Flagellates; (b) The Amoebae.

(a) The flagellates
Gut and genito-urinary flagellates are spread by direct or indirect contact. *Trichomonas vaginalis* is an important genito-urinary flagellate. It is transmitted venereally. In the female it usually leads to pruritis and a frothy discharge. Trichomonas prefers a less acid pH than that normally found in the vagina. Alteration of hormone balance may thus be associated with an altered vaginal pH and trichomonas proliferation. The presence of this pear-shaped organism on a vaginal smear is diagnostic.

*Giardia lamblia* is a pathogenic gut parasite. It is diagnosed by the presence of cysts or the vegetative form in the faeces. The portal of entry is the mouth.

Blood flagellates, e.g. trypanosomes, and tissue flagellates, e.g. leishmania both require arthropod vectors. Blood and tissue flagellates go through a variety of morphological forms. They are named according to their flagellum, e.g. the amastigote form is rounded and has no flagellum visible, while the tryptomastigote form has a flagellum running the whole length of the body and protruding at the distal end. Figure 16 shows the various morphological forms assumed by trypanosomes.

![Trypomastigote - Amastigote - Epimastigote - Promastigote](image)

**FIG. 16**

In all cases a local lesion or chancre occurs at the site of the bite of the insect vector. The trypanosomes and *Leishmania donovani* do not remain localized but spread systemically. These diseases are responsible for a proportion of the morbidity and mortality associated with tropical diseases. *Trypanosoma gambiense* is responsible for a devastating disease. Sleeping sickness was recognised by the slave traders — any African who had posterior cervical lymphadenopathy was rejected as a potential slave. An early sign of sleeping sickness is lymphadenopathy, end stage sleeping sickness is manifest as emaciation, a stuporised state and later coma and death.

Trypanosomes are of interest to immunologists as they are thought capable of changing their surface antigens. In this way they continually evade the host's defences.
Control of these diseases can be achieved if the vector and/or host are separated from man. The habits of both the vector and reservoir hosts have been studied. In the past large areas were depleted of game in an effort to control trypanosomiasis. Today more conservative methods are applied, e.g. bush clearing, the sterilization of male tse-tse flies and the use of insecticides. Men who during their work or pleasure are exposed to these diseases are advised to take adequate precautions. Drug therapy is available but is itself toxic.

| ORGANISM | VECTOR | RESERVOIR HOST | DISEASE IN MAN | MODE OF TRANSMISSION |
|----------|--------|----------------|----------------|----------------------|
| T. Brucei gambiense | Glossina (tse-tse fly) | man | Sleeping sickness | bite |
| T. brucei rhodesiense | Glossina (tse-tse fly) | wild and domestic animals | Rhodesian trypanosomiasis | bite |
| T. cruzi | Triatoma (bug) | dog, cat, monkey | Chagas disease | scratching/infected faeces into skin lesion |

| ORGANISM | VECTOR | RESERVOIR HOST | DISEASE IN MAN | MODE OF TRANSMISSION |
|----------|--------|----------------|----------------|----------------------|
| L. donovani | Phlebotomus (sand-fly) | dog, fox, rodent | Kala-azar (Visceral Leishmaniasis) | bite |
| L. tropica | Phlebotomus (sand-fly) | dog, rodent | Cutaneous Leishmaniasis | bite |
| L. braziliensis | Phlebotomus (sand-fly) | dog | Espundia (Mucocutaneous Leishmaniasis) | bite |

(b) The amoebae

Amoebae form a group of organisms some of which are parasites, others of which are free living. The different types of amoebae are identified by features characteristic of both the trophozoite and cyst forms.

Entamoeba histolytica is the invasive pathogenic amoebae responsible for amoebic dysentery and liver disease in man. It is diagnosed in the trophozoite stage by its cartwheel nucleus, the presence of ingested erythrocytes and the explosive movement of its pseudopodia. The cyst form has four nuclei and spiky chromidial bars. Entamoeba coli may be present as a commensal in the intestinal tract and must be distinguished from this pathogenic amoeba.

The factors which precipitate invasion by Entamoeba histolytica are unknown. Factors postulated to precipitate invasion include dietary changes, a mucosal lesion and subjection of the host to stress factors.

Transmission of the organism is from man to man. Faecal oral spread of cysts occurs by food contamination, e.g. the lettuce fertilized by human excreta. Trophozoites quickly succumb to environmental conditions. The
cyst forms are the resistant forms. The cyst is viable after being at a temperature of 20°C for 30 days; it also resists the effects of certain disinfectants, e.g. chlorine and formalin. Storage followed by inadequate washing of infected vegetables is a common source of transmission, provided the vegetables are eaten raw.

Control of amoebiasis is by adequate sanitation and good personal hygiene. Treatment is with metranidazole. This drug is also used in the treatment of Pneumocystis carinii infections.

The Sporozoa

Important pathogens in this sub-phylum include —

Pneumocystis
Toxoplasma
Plasmodium

Pneumocystis carinii is an important pathogen in patients with depressed immunity. In hosts with defective immunity, pneumocystis causes an interstitial pneumonia.

Toxoplasma gondii can be transmitted transplacentally causing congenital abnormalities in the foetus. Like rubella, primary toxoplasmosis contracted during pregnancy leads to serious foetal damage.

Toxoplasmosis may be contracted by ingestion of oocysts excreted in cat faeces. Another route of transmission is the ingestion of toxoplasmic cysts in undercooked meat, e.g. mutton. Pregnant women with negative serological tests for toxoplasma should avoid contact with cats and the eating of undercooked meat.

Toxoplasmosis is a mild, usually sub-clinical disease in the adult. Relapse of chronic toxoplasmosis can occur in patients on immunosuppression.
The plasmodia form an important group of sporozoa. These are the agents responsible for malaria. Different species of plasmodia cause different types of malaria.

Table XXII

| ORGANISM       | TYPE OF DISEASE       | RELAPSES | PARASITAEMIA |
|----------------|-----------------------|----------|--------------|
| *Plasmodium vivax* | Benign tertian malaria | +        | +            |
| *Plasmodium falciparum* | Malignant tertian malaria | -        | +++          |
| *Plasmodium malariae* | Quartian malaria | ++        | +            |
| *Plasmodium ovale* | Ovale malaria | +        | +            |

The life cycle of the malaria parasite is complex. *Plasmodium falciparum* differs from the other forms of malaria in not causing relapses, i.e. in any one malarial infection with falciparum the organisms are only capable of one hepatic phase of development.

The female anopheles mosquito requires a blood meal for the normal maturation of her eggs. On biting an infected host (man) she may ingest macro (female) and micro (male) gametocytes. These gametes fuse and the sexual cycle involving a number of different morphological forms follows. The infective product of sexual reproduction is the sporozoite. Sporozoites
Parasites, Bacteria and Viruses

present in the salivary glands of the female mosquito are transferred to a new host (man) when the mosquito takes her next blood meal.

Two different species of anopheles transmit plasmodia — their distribution and incidence determine whether an area will have endemic malaria or outbreaks of epidemic malaria. *Anopheles funestus* breeds in permanent shaded water and thus is always present and is associated with endemic malaria. *Anopheles gambiae* breeds in shallow open pools, e.g. cattle hoof marks filled with rain water. *Anopheles gambiae* multiply profusely during a heavy rainy season following a drought. Epidemics of malaria are thus most likely to occur during the rains following prolonged drought. Malarial outbreaks are related to the habits of the definitive host and not the organism itself.

The type of organism, i.e. the type of plasmodium, does determine the clinical disease in man. *Plasmodium falciparum* gives rise to malignant tertian malaria. This species frequently causes cerebral malaria. It causes non-relapsing malaria. *Plasmodium ovale* and *Plasmodium vivax* both produce a relatively benign disease which tends to relapse for up to 3 years after the initial infection. *Plasmodium malariae* causes benign quartian malaria which can relapse for up to 20 years after the initial attack.

Relapses are due to the ability of certain species to re-infect the host’s liver during a parasitaemia. *Plasmodium falciparum*, having once passed through its hepatic phase, enters the blood and the products of schizogony are incapable of re-infecting the liver.

Acute malaria is clinically characterized by fever, rigors and sweating. Jaundice may develop. The severity of the clinical symptoms are directly related to the degree of parasitaemia. The schizogony phase of plasmodial development is directly related to lysis of the parasitized red blood cells. Anaemia is a feature of malaria.

Diagnosis of malaria depends on the examination of blood films. Species identification is possible on the morphological characteristics of the plasmodia in the blood film. The percentage of erythrocytes which are parasitized is an index of the severity of the clinical disease.

Early and adequate treatment of malaria can be life saving. Different drugs act on different stages of the organism’s development. The hepatic forms of the organism are more difficult to treat and eliminate than those in the blood. Clinical cure is possible in the presence of hepatic parasites — the clinical symptoms are related to the multiplication of the parasites in erythrocytes. Radical cure implies the death of all the plasmodia in that host.

Prophylaxis against malaria is practised for both personal and public health reasons. The individual taking anti-malarials prophylactically does so before, during and after being in a malarial area. The drugs do not prevent the organism infecting the host, they suppress the clinical symptoms of the disease. Suppressive prophylaxis should thus be taken for a
month after leaving the malarial area. Causal prophalaxis involves the use of more toxic anti-malarials. These latter drugs are capable of interfering with the hepatic phase of the organism's development. A good method of preventing malaria is not to be bitten by the mosquito — mosquito nets, sun-downers behind mesh screens and the wearing of long sleeves are all thus of value in preventing malaria.

Public health authorities in malaria endemic areas exert some control over this disease by attempting to control the mosquitoes. House spraying, and netting are measures employed against the adults; larvae are killed by spreading layers of oil over water used by mosquitoes for breeding. Receptive areas are those areas with mosquitoes but no malaria. A single individual with malaria entering this area could infect the mosquito population.

(B) THE FUNGI
Fungi are higher protists with relatively rigid cell walls. They are found in two forms —
(a) as unicellular organisms — yeasts.
(b) as multicellular filaments — moulds.

Aggregates of hyphae are called mycelia or moulds.

From the medical viewpoint, fungi can interact with man in a variety of ways —
(a) They can cause food poisoning, e.g. mushrooms.
(b) They may be aetiologically implicated in certain carcinomas, e.g. primary hepatoma is linked to aflatoxin on circumstantial evidence.
(c) Hypersensitivity to various fungi is well recognised, e.g. asthma due to aspergillus; allergic alveolitis is associated with mouldy hay and/or sugar cane.
(d) They can cause infections.

Fungal infections are divided into two groups —
(i) superficial;
(ii) deep.

(i) SUPERFICIAL FUNGAL INFECTIONS
The single most important fungal infection is ringworm. Ringworm is a fungal infection of keratin-containing structures — skin, hair and nails. The dermatophytes are the fungi causing ringworm. There are three important genera — Microsporum, Epidermophyton, and Trichophyton.

These fungi may be divided into —
(i) Anthropophilic fungi — those infecting man.
(ii) Zoophilic fungi — ringworm usually associated with animal infections.
(iii) Geophilic fungi — soil fungi.
Infection of man by a zoophilic or geophilic fungus results in a more marked inflammatory reaction than infection by an anthrophilic fungus.

Hair infection may lead to weakening of the hair shaft and the hair may break off close to the scalp. Certain types of ringworm can therefore cause baldness. Infected nails become brittle and lustreless. A variety of skin lesions develop.

Although localized skin ringworm is amenable to topical therapy, hair, nail or extensive skin involvement require systemic therapy. Therapy is long-term.

Ringworm of different anatomical areas has acquired a variety of different names — Tinea pedis — 'Athletes' foot'.
Tinea capitis — ringworm of the scalp.
Tinea corporis — body ringworm, etc.

Ringworm is the only fungal disease readily transmitted from man to man.

(ii) THE DEEP MYCOSES

Many of the fungi capable of causing a deep fungal infection are found in the environment. Certain fungi cause primary infection, others are responsible for secondary or opportunistic infections.

A large number of fungi breach the skin barrier of the host, and often they are introduced into a traumatized area of skin. Lesions caused by this group of fungi usually have a primary skin or subcutaneous lesion. Clinically, ulcers or sinuses are invariably present. Blastomycosis, sporotrichosis, chromomycosis, phycomycosis and mycetoma are all examples of this type of infection.

Mycetoma is a subcutaneous mycosis caused by two different groups of organisms — one group of organisms causing this disease are true fungi, the other group are members of the actinomycetes. Actinomycetes respond to antibiotic and not to antifungal therapy.

A second group of fungi are inhaled and may cause primary lung pathology. Fungal infection of the lung may range from a diffuse infiltration to a single tumour-like mass. Cryptococcosis can present in the lung as a mass or in the brain as a cause of raised intra-cranial pressure. Both histoplasmosis and coccidiomycosis give rise to a benign 'flue-like' illness. Dissemination of histoplasmosis to the reticulo-endothelial system is rare but fatal. When coccidiomycosis disseminates to skin, bones, the central nervous system and other organs, it is fatal. All the deep mycoses mentioned are associated with environmental contact with the organism — many of these fungi are found in soil, wood or plant matter. These infections are exogenous infections.

Endogenous infections may be caused by Actinomycetes israelii or Candida albicans. Actinomycetes israelii is a normal inhabitant of the mouth.
The organism is not contagious and disease results from endogenous infe-
tection of traumatised mucous membrane. Actinomycotic lesions are found
mainly in one of three sites — cervico-facial, abdominal or thoracic. Treat-
ment is with penicillin. Actinomycosis is not caused by a true fungus.

*Candida albicans* is a true fungus found as a commensal in the mouth
and intestinal tract. Endogenous infection is especially common in the very
young, the very old, the diabetic, in people on antibiotics — especially
those on broad spectrum antibiotics which interfere with the normal flora,
and in macerated areas, e.g. in areas traumatised due to prolonged skin
wetness. *Candida* can infect nails, the skin and mucous membranes of the
mouth and genitalia. It can also spread systemically. The classical candida
lesion on mucous membranes is the white patch; on skin a variety of dif-
ferent ‘patches’ are found. *Candida* is a fungus capable of causing disease
in apparently healthy people as well as in certain individuals with a defect
in their host defences. Other fungal diseases found in individuals with de-
fective host defences are aspergillosis and phycomycosis. Spread of can-
dida in hospitals is rarely due to cross-infection. Aspergillosis and phyco-
mycosis are exogenous infections and their spread in hospitals may be as
a result of environmental contamination or by cross-infection.

*Aspergillus fumigatus* can be a secondary invader in lungs with impaired
defences due to damage by tuberculosis, asbestosis or sarcoidosis. This
fungus can exist as a saphrophyte in old tuberculous cavities. It may,
however, produce an allergic alveolitis or become invasive. The incidence
of metastasis of aspergillus to the brain and other organs is highest in
individuals suffering from haematological disorders.

Phycomycosis is caused by fungi which live saprophytically on decaying
vegetable matter. Diabetics and leukaemics are especially prone to infec-
tions of the sinuses with this organism. The fungus invades locally, spread-
ing to the brain. Unless early and adequate treatment is started, this
condition is rapidly fatal.

Table XXIII

| FUNGI FOUND IN THE SOIL           | PRIMARY CLINICAL LESION                  |
|----------------------------------|----------------------------------------|
| *Aspergillus*                    | Lung lesion, allergic, disseminated     |
| *Cryptococcus*                   | Pulmonary lesion, meningitis           |
| *Blastomycetes*                  | Skin lesion                            |
| *Histoplasma*                    | Skin or pulmonary lesions              |
| *Coccidiodes*                    | Respiratory infection                  |
| *Paracoccidiodes*                | Muco-cutaneous                         |
| *Geophilic ringworm*             | Skin                                   |

| FUNGI FOUND ASSOCIATED WITH WOOD/PLANT MATTER |
|-----------------------------------------------|
| *Phialophora* (causes Chromomycosis)          |
| *Sporotrich*                                  |

The host’s response to fungal infections is usually determined by the
efficiency of his cell mediated immunity.
Granulomatous lesions form the common type of histological picture. The fungi can appear as yeasts or mycelia. Certain fungi are dimorphic, i.e., they are yeast-like at 37.5°C (body temperature) and therefore yeast-like in tissue sections; at room temperature they, however, revert to their filamentous form.

Diagnosis of fungal infections are made by —

(i) direct examination of tissue sections, scrapings or excreta;
(ii) culture.

Treatment of fungal infections is occasionally surgical but usually involves the use of anti-fungal agents. The standard anti-fungal agents for topical use include desquamating agents. Those for systemic use include griseofulvin and amphotericin B. The anti-mitotic agent, 5-fluoro cytosine, and iodides have been used in the successful treatment of certain fungal conditions. Fungi and man have in common a eukaryotic cell type. Anti-fungal agents are thus more toxic to the host than anti-bacterial agents. Clinical cure often precedes mycological cure and therefore treatment must not be discontinued as soon as the patient feels better.

Fungi are widely distributed in nature. Environmental fungi assume new importance in medicine in an age where immunosuppression is widely used. The incidence of serious fungal infections is increasing in direct proportion to the increase in the use of immunosuppressives.

**BACTERIA**

A large number of bacteria do not cause disease. Some live in dead organic matter and are called saprophytes. Saprophytes are important in industrial and agricultural microbiology. Saprophytes are responsible for the ripening of cheese, the fermentation of carbohydrate leading to alcohol production and the acidification of milk. In nature bacteria are involved in carbon, nitrogen and sulphur cycles. Decomposition of organic matter is thus associated with the action of bacteria. Those bacteria which do cause disease fall into two groups:

**A. THE PATHOGENS**

These are capable of causing disease because they are endowed with special properties. Pathogens may be arbitrarily placed in one of two groups depending on their clinical presentation —

(a) Those which give rise to specific syndromes, e.g. typhoid, tetanus.
(b) Those which, in common with other organisms, cause a syndrome dependent on the organ of the host which is involved, e.g. meningitis, gastro-enteritis.

**B. THE OPPORTUNISTS**

These organisms may be saprophytes, which on being removed from their normal environment and introduced into certain susceptible hosts, cause disease. The disease pattern in such cases is less related to the organism's ability to cause disease than the inability of the host to defend himself.
Opportunistic pathogens may also be grouped as commensals. Commensals are organisms usually found in certain sites of the body. They do no harm in their natural habitat, e.g. *Streptococcus viridans* in the throat, *Staphylococcus epidermidis* on the skin. If either of these organisms is introduced into an unusual anatomical site, e.g. a heart valve, they become opportunistic pathogens and cause disease.

**CLASSIFICATION**

| Table XXIV |
| --- |

**BACTERIA OF MEDICAL IMPORTANCE**

**A LIGHT MICROSCOPIC CLASSIFICATION**

| GENUS | SPECIES | IMPORTANT CAUSES OF |
| --- | --- | --- |
| **GRAM-POSITIVE COCCI** | | |
| **STREPTOCoccus** | *Streptococcus pyogenes* | Throat and skin infection (N.B. delayed sequelae) |
| | *Streptococcus pneumoniae* | Pneumonia, meningitis |
| | *Streptococcus mutans* | Dental caries |
| | *Streptococcus faecalis* | Opportunists — urinary tract infection, bacterial endocarditis |
| | *Streptococcus viridans* | Endocarditis |

Standard culture media — Blood agar, Nutrient agar.

Selective media — MacConkey, aesculin bile.

| **STAPHYLOCOCCI** | *Staphylococcus aureus* | Localized suppuration, food poisoning, septicemia |
| (Staphylococcus pyogenes) | *Staphylococcus epidermidis* | Opportunists — bacterial endocarditis |

Standard culture media — Blood agar.

Selective media — Chapman’s agar (high salt content).

| **GRAM-NEGATIVE COCCI** | | |
| **NEISSERIA** | *Neisseria gonorrhoeae* | Gonorrhoea |
| (diplococci) | *Neisseria meningitidis* | Meningitis |

Standard culture media — Chocolate agar (5-10% CO₂).

Selective media — Thayer-Martin (above plus antibiotics).

| **GRAM-POSITIVE BACILLI** | | |
| **LACTOBACCILLUS** | *Lactobacillus acidophilus* | Responsible for acid pH in mature vagina |

Selective media — Tomato agar.

| **CORYNEBACILLUS** | *Corynebacterium diphtheriae* | Diphtheria |

Standard media — Blood Agar.

Selective media — Hoyles plate (Potassium tellurite), Loefflers slope.

| **BACILLUS** | *Bacillus anthracis* | Anthrax |
| **CLOSTRIDIUM** | *Clostridium tetani* | Tetanus |
| | *Clostridium botulinum* | Botulism |
| | *Clostridium perfringens* | Gas gangrene |
| | *Clostridium novyi* | |
| | *Clostridium septicum* | |

Selective culture media — Willis and Hobbs plate.
| GENUS       | SPECIES                        | IMPORTANT CAUSES OF                                      |
|------------|--------------------------------|----------------------------------------------------------|
| **BRUCELLA**| *Brucella abortus*              | Brucellosis                                              |
|            | *Brucella melitensis*           |                                                          |
|            | *Brucella suis*                 |                                                          |
|            | Selective media — Castenedas medium |                                                          |
| **HAEMOPHILUS** | *Haemophilus influenzae*      | Meningitis, respiratory tract infections                  |
|            | *Haemophilus aegypticus*        | Conjunctivitis                                            |
|            | Selective media — BHB (Bacitracin in haemolysed blood) | Whooping cough |
| **BORDATELLA** | *Bordetella pertussis*      | Whooping cough                                            |
| **YERSINIA** | *Yersinia pestis*               | Plague — bubonic, pneumonic, septicaemic                  |
|            | *Yersinia enterocolitica*       | Arthritis, mesenteric adenitis, gastro-enteritis          |
| **PASTURELLA** | *Pasteurella multocida*     | Abscess (zoanosis)                                       |
| **BACTEROIDES** | *Bacteroides fragilis*    | Abscess (anaerobic conditions)                           |
| **B. THE ENTEROBACTERIACEAE** |                              |                                                          |
| **SALMONELLA** | *Salmonella typhi*             | Typhoid                                                  |
|            | *Salmonella species*            | Gastro-enteritis                                         |
| **SHIGELLA** | *Shigella dysenteriae*          | Bacillary dysentery                                       |
|            | *Shigella sonnei*               |                                                          |
|            | *Shigella flexneri*             |                                                          |
|            | *Shigella boydii*               |                                                          |
|            | Selective media — S.S. medium (Shigella — Salmonella medium) | Opportunist — urinary tract infection, neonatal meningitis, infant diarrhoea |
| **ESCHERICHIA** | *Escherichia coli*           | Opporunists — urinary tract infection                    |
| **KLEBSIELLA** | *Klebsiella pneumoniae*        | Pneumonia, opportunist — urinary tract infection          |
| **PROTEUS** | *Proteus morgani*               | Urinary tract infection                                   |
|            | *Proteus rettgeri*              | Opportunists                                             |
|            | *Proteus vulgaris*              |                                                          |
|            | *Proteus mirabilis*             |                                                          |
| **ENTEROBACTER, CITROBACTER, ERWINIA, PROVIDENTIA** | All may cause opportunistic infection. |                                                          |
| **C. VIBRIO** |                              |                                                          |
| **VIBRIO** | *Vibrio cholerae*               | Cholera                                                  |
|            | *Vibrio parahaemolyticus*       | Food poisoning/gastro-enteritis                          |
|            | Selective media — T.C.B.S. (sucrose bile salt media; alkaline with an indicator) | |
| **D. PSEUDOMONAS** | *Pseudomonas aeruginosa* | Opportunists — wound and burns infected, septicaemia |}

**FILAMENTOUS BACTERIA**

| Anaerobic Actinomyces (gram positive) | *Actinomyces israelii* | Actinomycosis |
| Aerobic Nocardia | *Nocardia asteroides* | Nocardiosis, Actinomyctoma |
GENUS SPECIES IMPORTANT CAUSES OF

**STRICT ANAEROBES**

**GRAM-NEGATIVE BACILLI** — Bacteroides  
  e.g. *Bacteroides fragilis, Bacteroides melaninogenicus*  
  — Fusobacterium  
  e.g. *Fusobacterium nucleatum*

**GRAM-POSITIVE BACILLI** — Clostridia

**GRAM-POSITIVE COCCI** — Peptococci  
  — Peptostreptococci

See page 86

Abscess, ulceration

Abscess

GROUPING BASED ON THE ZIEHL-NEELSEN STAIN AND MORPHOLOGY — ACID-FAST BACILLI

**GENUS** SPECIES IMPORTANT CAUSE OF

**MYCOBACTERIUM**  
  *M. tuberculosis* Human tuberculosis  
  *M. bovis* Cattle tuberculosis (Intestinal tuberculosis in man)  
  *M. leprae* Leprosy

Mycobacteria not causing tuberculosis previously called atypical mycobacteria — opportunistic infections, saprophytes.

Selective media — Lowenstein Jensen.  
Mycobacterium leprae does not grow on artificial culture media.

**NOCARDIA**  
  *Nocardia asteroides* Mycetoma, Nocardiosis

A modified stain is required to demonstrate acid fastness in this aerobic actinomycete.

GROUPING BASED ON MORPHOLOGY AND DARK FIELD MICROSCOPY — SPIROCHAETES/SPIRAL ORGANISMS

**GENUS** SPECIES IMPORTANT CAUSE OF

**TREPONEMA**  
  *Treponema pallidum* Syphilis

**BORRELLIA**  
  *Borreliia recurrentis* Relapsing fever  
  *Borreliia duttoni* Relapsing fever  
  *Borreliia vincenti* Vincent’s angina (when with a fusiform bacterium)

**LEPTOSPIRA**  
  *L. icterohaemorrhagica* Leptospirosis

Culture — highly selective, Treponemes fail to grow in artificial culture media.

The preceding organisms may be further grouped according to —

(i) optimal growth temperature — see Table XXV. Organisms grow best at certain temperatures. Three groups of organisms have been identified on the basis of their ability to grow at certain temperatures.

(ii) oxygen requirements — see Table XXVI. Hydrogen acceptors are substances capable of accepting a hydrogen ion during oxidation-reduction reactions. Oxidation-reduction reactions are energy yielding.
Parasites, Bacteria and Viruses

Table XXV
GROUPING OF ORGANISMS ON THE BASIS OF TEMPERATURE

| BACTERIAL GROUP | TEMPERATURE RANGE FOR OPTIMAL GROWTH |
|-----------------|--------------------------------------|
| PSYCHROPHILIC   | 15 to 20°C                            |
| MESOPHILIC      | 30 to 37°C                            |
| THERMOPHILIC    | 50 to 60°C                            |

Bacteria pathogenic to man are usually mesophilic.

Table XXVI
ORGANISMS AS GROUPED ON THE BASIS OF THEIR RESPONSE TO OXYGEN

| BACTERIAL GROUP       | RELATIONSHIP TO OXYGEN                                                                 |
|-----------------------|---------------------------------------------------------------------------------------|
| OBLIGATE AEROBE       | This group specifically requires oxygen as the hydrogen acceptor. These bacteria obtain energy from respiration. |
| FACULTATIVE          | These organisms may live in the presence or absence of oxygen. They are capable of respiration and fermentation depending on the environment. |
| OBLIGATE ANAEROBE     | Oxygen is toxic to these bacteria. It is never used as a hydrogen acceptor by this group. These bacteria use fermentation to obtain their energy. |

Bacteria pathogenic to man may fall into any one of these groups.

COCCI
Cocci are —
(i) spherical
(ii) non-motile
(iii) non-sporing
(iv) organisms which multiply by binary fission
(v) lower protists and bacteria.

STREPTOCOCCI
Streptococci are —
(1) Cocci in chains
(2) Gram-positive
(3) Capable of causing haemolysis — streptococci secrete enzymes, streptolysin O and S. Both these streptolysins are capable of causing damage to the cell membrane of erythrocytes. Haemolysis is tested by culturing the organisms on a blood agar plate. The resulting haemolysis may be classified as one of the following types —
   a haemolysis — incomplete haemolysis resulting in a greenish zone around the colony.
   β haemolysis — complete haemolysis resulting in a colourless zone around the colony.
   γ haemolysis — here no haemolysis is visible (haemolysis may be detected underneath the colony).
Groups according to Lancefield’s grouping — this classification of streptococci is based on the specific antigenic structure of the grouped carbohydrate. Each different type is designated with a letter from the alphabet, e.g. A, B, etc.

**Figure 19**

THE STRUCTURE OF A STREPTOCOCCUS

![Diagram of the structure of a streptococcus](image)

*Streptococcus pyogenes* — Beta-Haemolytic Streptococcus Group A Gram-positive cocci in chains.

**Source:** Patient or carrier. *Streptococcus pyogenes* may be carried by 5-10% of people. The highest carrier rate is in children. The organism may be carried on the skin or in the nose or throat.

**Spread:** Spread occurs by droplet spray, e.g. coughing, sneezing, or by direct contact. Transfer of the organism may be direct or by contamination of fomites such as clothing, bedding, books. The throat provides the best source of pathogenic bacteria; the nose is a better organ for the dissemination of bacteria.

Streptococci succumb to direct sunlight but can survive for weeks in dusty crevices. The main route of spread is that of close person-to-person contact permitting the spread of moist secretions.

**Virulence:** *Streptococcus pyogenes* causes disease in the host by its ability to —

(i) Resist phagocytosis. Incorporated into the bacterial cell wall is a protein layer — type M protein is resistant to phagocytosis.

(ii) Secrete a number of enzymes and toxins. Examples of these include — hyaluronidase which breaks down the ground substance of the host; streptodornase (DNAse) which depolymerises DNA and streptolysin which is toxic to host cells. A toxin which deserves
special mention is erythrogenic toxin. Infection of \textit{Streptococcus pyogenes} by a specific bacteriophage (bacterial virus) confers on this bacterium the ability to produce erythrogenic toxin. This toxin is responsible for the characteristic erythematosus rash of scarlet fever.

Host: Overcrowding increases close contact and this is a major factor in the spread and incidence of streptococcal disease.

The immune response of the host to the organism can lead to delayed sequelae becoming apparent in the host some weeks after the initial infection. A decrease in the host's immunity may alter the local manifestations of the disease, e.g. a viral infection of the respiratory system may be complicated by streptococcal pneumonia.

Disease pattern: This is determined by the portal of entry of the organism. Entry by the respiratory tract is associated with a sore throat, direct contact or spread by way of a skin defect is associated with erysipelas, impetigo or another skin infection.

In a certain group of hosts, selected on the basis of their immune systems, delayed sequelae may follow \textit{Streptococcus pyogenes} infection. These immunological complications follow some 2-4 weeks after the initial acute infection. In these individuals a sore throat may be the introduction to rheumatic fever. Many different types of \textit{Streptococcus pyogenes} are capable of causing rheumatic fever in susceptible hosts. Contact with the organism is inevitable owing to it being widespread. A patient who has suffered one attack of rheumatic fever is therefore at risk of further attacks. With each attack of rheumatic fever the heart valves may be damaged. The patient is thus likely to suffer, at some stage of his life, haemodynamic difficulties and infection of the damaged valves (sub-acute bacterial endocarditis). The aim is thus prevention of rheumatic fever. After one attack of rheumatic fever an individual is labelled as being at risk of future attacks. These individuals must be protected against \textit{Streptococcus pyogenes} infections. This can be achieved by the daily administration of a low dose of penicillin.

Attacks of acute glomerulonephritis may follow either skin or throat infections by \textit{Streptococcus pyogenes}. The number of \textit{Streptococcus pyogenes} capable of inducing renal sequelae is limited. After one attack of acute glomerulonephritis the patient is therefore not subject to years of antibiotic therapy. Eradication of the nephritogenic strain of \textit{Streptococcus pyogenes} from the family unit is advocated. This is achieved by antibiotic therapy.

Drug of Choice: \textit{Streptococcus pyogenes} is exquisitely sensitive to penicillin. The drug of choice in the treatment and prophylaxis of diseases caused by this organism is therefore clear cut.

\textit{Streptococcus agalactiae} — Beta Haemolytic Streptococcus Group B. \textit{Streptococcus agalactiae} is found as a normal commensal in the genital tract of some 50\% of females tested. This organism does the host (mother)
Man meets Microbes

no harm but certain members of this group of organisms are capable of causing meningitis and septicaemia in the newborn. The organism is spread by aspiration as the baby passes through the birth canal. Premature infants and those subject to instrument delivery or prolonged labour are particularly susceptible to infection by *Streptococcus agalactiae*. *Streptococcus agalactiae* septicaemia has a 50% mortality rate.

Babies born after prolonged labour or following premature rupture of membranes are frequently given prophylactic antibiotics. In mothers who have already lost one baby due to infection with this organism, caesarian section is often considered for the delivery of the next child.

*Streptococcus faecalis* — Enterococci

The haemolysis of these streptococci is variable.

Source: *Streptococcus faecalis* is a natural inhabitant of the intestinal tract.

Spread: Usually by direct contact.

Virulence: They cause opportunistic infections, i.e. these organisms only cause disease when introduced into an unusual anatomical site. Transfer of the organism from the bowel to the bladder results in a urinary tract infection; transfer from the bowel to the blood stream in the presence of a deformed or damaged heart valve can lead to bacterial endocarditis.

Enterococci are responsible for a large number of endogenous infections.

Treatment: Ampicillin is the drug of choice.

*Streptococcus viridans*

This group of organisms gives rise to alpha haemolysis.

Source: These are oral commensals. They help to make up the salivary complement of bacteria. Saliva contains of the order of $10^9$ organisms per millilitre.

Spread: They may spread by direct contact. Infections are, however, usually endogenous.

Virulence: These organisms are not primarily pathogens. They take advantage of a host's impaired immune response. They cause endogenous infections, e.g. bacteria are shed into the blood stream each time dental manipulations are performed. Sub-acute bacterial endocarditis, i.e. infection of a damaged or defective heart valve is most commonly caused by a member of the *Streptococcus viridans* group of organisms.

Of this group of organisms, *Streptococcus mutans* is the main culprit in the pathogenesis of dental caries and periodontal disease. This organism plays a role in the development of dental caries by causing a change in the environment of the tooth. Dental plaques are composed of bacteria and their products — *Streptococcus mutans* plays an important role in the formation of the plaque.
The Prevention of Endocarditis

Bacterial endocarditis caused in the presence of bacteraemia following dental manipulation can be prevented in known rheumatic fever cases. Prophylactic antibiotics can be administered just prior to the visit to the dentist. High doses of penicillin are given prior to dental manipulation in these patients. This leads to high antibiotic blood levels which kill the organism without giving it an opportunity to establish itself on the distorted valve. Therapy for the prevention of sub-acute bacterial endocarditis caused by *Streptococcus viridans* is penicillin given in high doses for a limited period.

**Treatment:** *Streptococcus viridans* is sensitive to penicillin. It is, however, much less sensitive than *Streptococcus pyogenes*. Prophylaxis against rheumatic fever and sub-acute bacterial endocarditis differs — the type of antibiotic used in the same, the dose vastly different.

*Streptococcus pneumoniae* — Pneumococci

This is the second alpha haemolytic streptococcus of importance to man.

**Source:** Some 30% of healthy people carry pneumococci in their throats. The organism is relatively resistant to drying and spread can therefore be in secretions — nasal or oral. Fomites and dust may harbour viable pneumococci.

**Disease Pattern:** There are basically two groups of pneumococci —

(a) Those that are essentially commensals causing disease only if aided by some decrease in the host's resistance, e.g. a preceding viral infection, smoking or atmospheric pollution. These factors stimulate excess secretion in the respiratory tract and hence interfere with surface phagocytosis of the organism. Depression of the cough reflex, e.g. in anaesthetised or intoxicated individuals, may result in aspiration of respiratory secretions. These secretions may contain pneumococci.

This group of pneumococci takes advantage of any breach in the host's defences. They cause endogenous infections especially at the extremes of life.

(b) Those pneumococci which are overtly pathogenic causing disease in primarily healthy individuals. These are exogenous infections.

The types of disease caused by pneumococci are referable to both upper and lower respiratory tracts, e.g. otitis media, sinusitis, pneumonia. Meningitis caused by pneumococci is frequently associated with a fractured base of skull. This may possibly represent spread of commensal nasopharyngeal pneumococci to the meninges.

**Virulence:** The organism depends for its virulence on its capsule. Pneumococci are lanceolate diplococci surrounded by a capsule. The mechanism whereby the capsule protects the organism against phagocytosis is disputed. The lipid-containing membrane of the
Man meets Microbes

pseudopodia may be electrically repelled by the charge on the hydrated capsule. This charge could conceivably be neutralized by opsonin or specific antibody.

There are over 80 different antigen capsular types amongst the pneumococci.

Treatment: Pneumococci are sensitive to penicillin.

Prevention: Theoretically protection against this organism could be achieved by immunization. The host produces antibodies against the capsule. Unfortunately the number of different capsular types possessed by this group of organisms makes it difficult to produce a comprehensive vaccine.

STAPHYLOCOCCI

These gram positive cocci are characteristically found in clusters.

*Staphylococcus aureus*

Source: Staphylococci are found in the environment. They do not necessarily multiply in the environment but may remain dormant for several months. They do multiply in moist nutrient material, e.g. milk, meat. Staphylococci are killed by moist heat; exposure to 65°C kills these organisms in 30 minutes.

Spread of staphylococci is by contact — direct or indirect, and by dust or droplet spray. Nasal, throat and skin carriage occurs.

Virulence: The infective dose of staphylococci is of the order of one million organisms. If the host’s defences are compromised due to the presence of a foreign body, the infective dose drops to approximately one hundred organisms. *Staphylococcus aureus* is quick to take advantage of impaired host resistance. Hospital patients especially at risk of staphylococcal infections are the neonate, the post-operative patient, the diabetic and any individual who is elderly or debilitated.

*Staphylococcus aureus* depends for its virulence on the following factors:

(a) Certain antiphagocytic properties are demonstrated by these organisms. A limited number of staphylococci have the ability to resist digestion once inside the phagocyte.

(b) The secretion of toxins and enzymes. These toxins include enzymes which may damage cell membrane, e.g. leucocidins and haemolysins. Enterotoxin is a potent exotoxin. Enterotoxin is secreted by staphylococci which have undergone lysogenic conversion by a temperate phage, i.e. the bacterium is infected by a non-lytic bacterial virus.

Disease pattern: The diseases caused by *Staphylococcus aureus* fall into three distinct groups —
(i) Local suppuration — the pus can be found superficially, e.g. as a pustule; or subcutaneously as an abscess or carbuncle or even within organs, e.g. osteomyelitis. Infection of wounds by staphylococci can lead to wound breakdown and failure of healing. Deep infections with staphylococci which may assure importance are pneumonia, a perinephric abscess and septicaemia.

(ii) Food poisoning — this is an intoxication and not an infection. The food, often meat, is contaminated — usually at some stage of processing. The staphylococci can be introduced on the fingers of the housewife or other foodhandler. Foodhandlers should not be carriers of staphylococci. The organism multiplies in the food, producing its toxin. Ideal conditions for multiplication are warmth and moisture. If the meat is heated, in other words if the meat is subject to temperatures of over 65°C for over half an hour, the organisms will be killed but the enterotoxin will not be inactivated. Enterotoxin is heat stable, its action will be unaffected even after temperatures reaching 100°C have been maintained for three minutes. Persons subsequently eating the meat ingest toxin and not viable organisms. Enterotoxin causes vomiting, and sometimes diarrhoea, 2-8 hours after its ingestion.

(iii) Staphylococcal enterocolitis — this infection may be fatal. It is a result of interference with the normal microbial flora. The normal microbial flora may be depleted due to the administration of a broad spectrum antibiotic. Staphylococcus aureus, if resistant to this antibiotic, proliferates and causes disease.

**Staphylococci in the Hospital**

Staphylococci are important in the hospital situation where they are associated with antibiotic resistance. These organisms are capable of incorporating pieces of genetic material called plasmids. The plasmid may confer certain new properties on the organism, e.g. the ability to resist antibiotics. Immunity to antibiotics may be conferred on the organism by giving it the ability to produce enzymes capable of breaking down the antibiotic, e.g. penicillinase may be introduced. Organisms containing plasmids which confer resistance to certain antibiotics will thus be favoured in hospital situations where frequent exposure to those antibiotics is possible. The organism resistant to the antibiotic has an advantage over the organism which is sensitive. In an antibiotic environment selective pressure is then placed on the microbial population. Hospital environments select strains of staphylococci for hospital or antibiotic. Community staphylococci are frequently successfully treated with penicillin, hospital acquired staphylococci are usually resistant to this antibiotic. Hospital staphylococci constitute an antibiotic resistant population.

**Staphylococcus epidermidis**

Source: This organism is a normal skin commensal.

Spread: *Staphylococcus epidermidis* is only pathogenic if transferred to
Man meets Microbes

an area of the body which is normally sterile. It causes endogenous infections.

Disease Pattern: Infection of damaged heart valves leads to sub-acute bacterial endocarditis. *Staphylococcus epidermidis* may have a rôle in the pathogenesis of acne.

Treatment: This organism is often more resistant to antimicrobial therapy than is *Staphylococcus pyogenes*.

**NEISSERIA**

Some characteristics of this group —

(i) They are Gram-negative cocci.

(ii) The pathogens present as kidney bean-shaped diplococci.

(iii) Their natural host is man.

(iv) They are very sensitive to environmental conditions.

*Neisseria meningitidis*

Source: Five to thirty per cent of the population carries *Neisseria meningitidis* in their throats. During epidemics this carrier rate reaches 80% and over. The only natural host for the organism is man.

Spread: Spread of *N. meningitidis* is person to person. The main danger of acquiring the organism is from carriers rather than cases. As the organism is very sensitive to sunlight and drying, spread requires close contact. Overcrowding leads to a three-fold increase in the carrier rate.

Virulence: *N. meningitidis* usually causes disease in a host who has some defect in his immunity — this defect is often of a transient nature, e.g. following a viral infection. Neisseria resist phagocytosis due to the presence of a capsule. They are Gram-negative organisms and therefore have endotoxin or lipopolysaccharide incorporated in their cell walls. Endotoxin is released on lysis of the bacteria.

Disease Pattern: Meningococcal meningitis is a well recognised entity. Meningitis due to this organism peaks around late winter and early spring. The seasonal fluctuation of meningococcal meningitis is well recognised. Meningococcaemia or meningococcal septicaemia is a condition which may be fulminating. The overall mortality rate for meningococcal disease is 5-10%.

Treatment: Meningococci are becoming increasingly resistant to sulphonamides. Today the treatment of choice for meningococcal meningitis is no longer sulphonamides but penicillin.

**Prevention and Prophylaxis**

*Neisseria meningitidis* has a polysaccharide capsule which is antigenic. The antigenic constituents determine if the organism is Type A, B or C, or one of those less frequently encountered in the clinical situation. Vaccines containing extracts from *N. meningitidis* types A and C are available for persons at risk.
Individuals who have been in contact with a case of meningococcal meningitis may elect to be placed on prophylactic antimicrobial therapy. Rifampicin and minocycline are used. Certain authorities advocate careful observation in the absence of prophylaxis, others feel that prophylaxis will decrease further spread of the organism.

*Neisseria gonorrhoeae*

Source: The genital tract of man.

Spread: Venereal. These organisms are extremely sensitive to ultraviolet light, to dessication and also to disinfectants. Toilet seats are an unlikely mode of spread. Spread is by direct intimate person-to-person contact.

Virulence: Gonococci colonize a new host by attaching to the superficial cells of mucous membranes. Stratified squamous epithelium is relatively resistant to penetration by gonococci. The gonococci attach to the cells of the mucous membrane by means of pili. Pili are protuberances extending from the cytoplasmic membrane of the organism. For gonococci to be infective they require the presence of these thin needle-like pili. Gonococci left on a shaded cool wooden toilet seat for a few hours remain viable but are not infective as they have lost their pili. Gonococci once attached to the host’s cells via the pili are rendered relatively resistant to phagocytosis.

Disease Pattern: Gonorrhoea usually symptomatic in males is often asymptomatic in females. It is a medical and social problem. In certain countries gonorrhoea is second only to the common cold in incidence. Systemic spread of the organism can result in gonococcal septicaemia — this may be acute or chronic. Gonococcal arthritis, salpingitis, proctitis and asymptomatic pharyngitis are but a few of the conditions attributed to this organism.

An infant passing through an infected birth canal can acquire a gonococcal infection of the eye. Ophthalmia neonatorum can lead to blindness. Treatment: Penicillin is the drug of choice. Some strains of gonococci have recently been reported as having developed resistance to this organism.

At birth silver nitrate or penicillin drops are routinely instilled into the eyes of the newborn. This is a precaution against an asymptomatic mother infecting her baby.

**BACILLI**

Bacilli are —

(i) rod-shaped organisms;

(ii) classified as bacteria amongst the lower protists;

(iii) capable of being classified into broad groups on the basis of their morphology and staining reactions using either the Gram or the
Ziehl-Neelsen stain. They may be further classified on the basis of
their ability to excrete certain potent exotoxins or on their charac­
teristic metabolic profile.

(vi) They multiply by binary fission.

GRAM-POSITIVE BACILLI

Certain Gram-positive bacilli are capable of producing spores. A major
division in this group is thus into spore forming organisms and non­
sporing organisms. Certain vegetative cells may under adverse environ­
mental conditions undergo a physical change and develop spores. Sporu­
lation results in the production of the spore form of the organism which
is resistant to heat, cold, dessication and disinfectants. The spore is essen­
tially a resting stage. It is a resistant but non-reproductive form of the
organism. When conditions become favourable, e.g. adequate moisture
becomes available, the spore may germinate and revert to the vegetative
form. The vegetative form of the bacillus is capable of multiplication or
binary fission.

Spore forms are resistant to temperature and disinfectants and therefore
constitute a problem in the hospital environment. Minimal requirements
for sterility are determined by the resistance of spores to heat. Tempera­
ture and exposure time are determined by the ability of the spore to resist
defeat. Spores of *Bacillus stearothermophilus* are used as a biological steri­
licity control. The spores of this non-pathogenic organism are placed in a
packet and introduced into the autoclave in the centre of the pack to be
sterilized. After autoclaving an attempt is made to culture the organism.
If the spores fail to germinate under favourable conditions then the spores
are dead and it may be assumed that the pack is sterile. This biological
control, in conjunction with steritape, is routinely used in hospitals. Both
saprophytes and pathogens are found amongst Gram-positive bacilli.

Spore forming Gram-positive bacilli

This group of organisms is further divided into aerobic and anaerobic
groups.

Aerobic spore forming Gram-positive bacilli

*Bacillus stearothermophilus*

A saprophyte used as the biological control for sterility testing of auto­
claved material.

*Bacillus anthracis*

*Bacillus anthracis* causes anthrax. Anthrax is a zoonosis, i.e. it is a disease
spread from animals to man.

Source: Certain population groups are at risk of exposure to anthrax.

*Bacillus anthracis* may cause a fatal disease in sheep, cattle and
horses. People at risk are those working with animal hides, the
wool sorters and those working with animal carcasses.

Spread: The organism may be inhaled, ingested or may be spread to a
new host by contact with a skin lesion. *B. anthracis* is usually spread in the spore form.

Virulence: The spore germinates at its site of entry. *B. anthracis* is pathogenic due to —

(a) The presence of a capsule. This capsule is composed of polypeptide units. Most organisms with capsules have polysaccharide capsules. Notable exceptions are *Yersinia pestis* and *B. anthracis* with their polypeptide capsule. On culture these colonies are said to have a 'Medusa head' appearance.

(b) Its ability to produce toxins. Three heat sensitive substances are produced. These substances are called fractions 1, 2 and 3. Fraction 1, the oedema factor and fraction 3, the lethal factor are required together with fraction 2 for efficient pathogenicity. Fraction 2, the protective factor, is antigenic and it is against this fraction that the host produces antibody.

Disease Pattern: The clinical picture of anthrax is largely determined by its portal of entry. Entry of the organism into a skin lesion results in formation of a malignant pustule; inhalation results in haemorrhagic mediastinitis and ingestion of poorly cooked meat results in intestinal anthrax.

Treatment: Penicillin is the drug of choice. Anthrax may be fatal.

Prevention and Control: Anthrax is primarily a disease of animals and the control of this problem rests essentially at this level. Cattle and sheep should be immunized against the disease. The live vaccine is too toxic for use in man. Men at risk of exposure to anthrax are protected by a fraction 2 antigen vaccine. Frequent boosters are required. Men working with animals in an anthrax endemic area are obliged to wear protective clothing.

Animals dying of suspected anthrax are incinerated or buried in deep lime (anaerobic conditions inhibit spore formation). Post mortems are not performed, but a splenic aspirate may be performed. These precautions decrease the probability of spore formation. Anthrax spores are known to have survived for over 100 years.

*Bacillus cereus*

Source: The organism is thought to grow on rice and other cereals.

Virulence: A toxin is produced.

Disease Pattern: The toxin produced induces vomiting. The gastroenteritis caused by *Bacillus cereus* is characterised by the onset of symptoms within two hours after ingestion of the infected food.

Anaerobic spore forming Gram-positive bacilli

The important pathogens in this group are the clostridia.

Source: Clostridia are found in soil. They are also normal inhabitants
of the gastrointestinal tract of both man and animals. Exposure to
clostridia is inevitable. Infection may be endogenous or exogenous.

Virulence: Clostridia cause disease by secretion of exotoxins. It is the
vegetative cell which produces and releases the toxin. The spores
only germinate in the absence of oxygen — germination of clostridia requires anaerobic conditions. Clostridia only cause disease
under conditions where germination is possible, e.g. in bottled
food, in deep wounds.

Disease Pattern: Four important diseases are attributed to the clostri-
dial organisms —

- Cl. botulinum — Botulism (food poisoning)
- Cl. tetani — Tetanus
- Cl. perfringens
- Cl. septicum
- Cl. novyi (oedematiens)
- Cl. perfringens — Food poisoning

In each the exotoxin secreted is responsible for the disease. The organism
is non-invasive except in gas gangrene where limited invasiveness is dis-
played.

Treatment: Definitive treatment in diseases caused by the secretion of
exotoxin may be by the administration of antitoxin. Antitoxin con-
sists of specific antibody, produced occasionally in man but more
frequently in animals, against the exotoxin. Administration of these
antibodies leads to neutralization of the toxin provided the toxin
has not become attached to cells. Once toxin has become attached
to cells the antitoxin has no effect and the toxin continues to exert
its deleterious effects. If antitoxin is to be administered it must be
given early.

Prevention: Depending on the number of toxins produced and the num-
ber of antigenic types of toxin, prophylaxis may be possible by
immunization using a specific toxoid. Toxoid is a biologically in-
active but antigenically unchanged toxin.

Laboratory Diagnosis: The gram stain is of value in identifying Gram-
positive bacilli. Spores may also often be seen. Species differentia-
tion is, however, more difficult, e.g. both Cl. tetani (pathogen) and
Cl. tetanomorphum (saprophyte) have terminal bulging spores and
are classically referred to as having a tennis racket shape. The defi-
nitive laboratory identification of Gram-positive bacili often in-
volves the use of —

(a) immunological techniques, e.g. the diagnosis of clostridia causing
gas gangrene by neutralization tests

(b) laboratory animals, e.g. in the identification of botulism or tetanus.

Clostridium botulinum
(Clostridial food poisoning.)
Parasites, Bacteria and Viruses

Source: Spores of *Clostridium botulinum* are widely distributed in soil and may contaminate fruit, vegetables, fish and other food products.

Spread: The spores are highly resistant to heat, withstanding temperatures of over 100°C for three hours or more. Adequate cooking of contaminated food will kill all the vegetative forms but will not destroy the clostridial spores. Bottling introduces an anaerobic environment and the spores are given the opportunity to germinate. The vegetative bacteria so produced multiply and produce toxin. The toxin is heat labile and can be destroyed if exposed to 100°C for 10 minutes. Often bottled, canned and vacuum packed foods are eaten without heating.

Virulence: Botulism is due to toxin production. Botulinum toxin is one of the most potent biological toxins known to man — 1µg or less may kill an adult man. Different types of toxin A-E are recognised. Types A and B are predominantly associated with canned or bottled foods, type E with fish.

Disease Pattern: Botulism is an intoxication. The toxin, if ingested, is absorbed through the mucous membrane of the gastro-intestinal tract. The toxin is not inactivated by the proteolytic enzymes of the gastro-intestinal tract — in fact it may be activated by these enzymes. It may also be absorbed directly through the skin. The toxin once absorbed is thought to attach to the gangliosides of the presynaptic membrane of cholinergic nerves. The toxin-ganglioside complex so formed is thought to block the release of acetylcholine — the neurotransmitter. Clinically, paralysis supervenes in 18-24 hours after ingestion of the toxin. Only type E causes nausea and vomiting.

Prevention and Control: Food contaminated by *Clostridium botulinum* may appear perfectly good, alternately food that appears “off” need not be contaminated by *Clostridium botulinum*. Although a blown can is not diagnostic of botulism, it may be infected. All blown cans should therefore be discarded as a safety precaution. The canning industry is aware of the dangers of botulism and uses high temperatures (120°C) in the preparation of their products. Nitrates used to preserve meats inhibit the growth of *Clostridium botulinum*. (Nitrates converted to nitrites and nitrosamines bear a postulated aetiological association with gastric cancer.) The main danger of botulism today lies in home preserves. These should be boiled for at least 15 minutes immediately prior to use.

Botulism is fatal in over 30% of cases. In each case type specific antitoxin, if given early enough, could be life saving.

*Clostridium tetani*

Source: The organism is found in soil and may also be found occasionally in the gastro-intestinal tract of man.
Spread: The organism is spread in the spore form. If introduced into puncture wounds the spore form can germinate and toxin production can start. The spore germinates under anaerobic conditions — deep penetrating wounds, especially those containing foreign material, e.g. soil or bacteria, are especially conducive to the germination of Cl. tetani.

Virulence: Cl. tetani produces a potent exotoxin, tetanospasmin.

Disease Pattern: Tetanospasmin spreads by the blood stream, plus possibly along nerve axons, to the anterior horn cells of the spinal cord. Spasms and convulsions result.

The spores may remain dormant for long periods and the patient may only present with overt tetanus long after the wound (e.g. caused by a rose thorn) has been forgotten. This condition is termed occult tetanus.

Tetanospasmin differs from botulinum toxin in that:
(i) Tetanospasmin has only one antigenic type — a single toxoid is therefore protective.
(ii) It is more heat sensitive — tetanus toxin is inactivated at 65°C for 5 minutes; it is inactivated by proteolytic enzymes.
(iii) Tetanus is an infection; botulism an intoxication.
(iv) Tetanus leads to convulsions; botulism to paralysis.

Prevention and Control: Cl. tetani are widespread. Prevention against tetanus is possible by immunization. Protective antibodies are produced against the toxoid. The antibodies neutralize the toxin in the event of infection. Once an individual has had tetanus he still requires a course of immunization. The quantity of the toxin released in natural infection is insufficient to adequately prime the immune system.

Tetanus Neonatorum — this occurs in infants in areas where tribal customs require treatment of the umbilical cord with cowdung. Infection of the cord with Clostridium tetani leads to tetanus in the infant. Prophylaxis is best achieved by immunization of the mother. A booster should be given during pregnancy so that the high level of maternal antibodies can filter across the placenta and protect the baby. Health education should be practised but not relied upon in this situation.

Lockjaw is the layman's term for localized tetanus of the jaw.

Clostridium perfringens — gastroenteritis.

Source: Cl. perfringens may be found in soil, faeces and contaminated foods, e.g. meat.

Spread: The spores survive normal cooking and germinate as the temperature drops. In the centre of, for example, a piece of meat, anaerobic conditions prevail and allow the spores to germinate. The organism multiples prolifically. Long slow cooling plus storage in
warm areas allow sufficient multiplication of the organism to cause disease. A large number of organisms must be ingested before gastroenteritis develops. Cooked meat and poultry are the prime vehicles for the spread of Cl. perfringens gastroenteritis.

Virulence: *Clostridium perfringens* produces an enterotoxin when the organism sporulates in the gastro-intestinal tract of the host. Lecithinases are also produced — these are postulated to lead to the production of irritant products. *Cl. perfringens* does not cause an intoxication, it causes an infection. It therefore does not cause true food poisoning but gastroenteritis.

Disease Pattern: After an incubation period of 18 hours the organism, if ingested in sufficient quantities, will have produced sufficient toxin to cause the host to develop profuse diarrhoea.

**The Gas Gangrene Clostridia**

A number of different species of clostridia are capable of causing gas gangrene. Of those capable of causing gas gangrene *Clostridium perfringes* is the most commonly encountered culprit.

Source: These clostridia are frequently encountered in the intestinal tract of man. Nine out of every ten men excrete clostridial spores in their faeces.

Spread: Like tetanus, the spore once introduced into a wound requires anaerobic conditions for germination. People at risk of developing gas gangrene are —

(i) those with extensive contaminated raw areas, e.g. motor vehicle accidents, war wounds, septic abortions;

(ii) those with vascular disease, e.g. mesenteric thrombosis leading to gas gangrene of the intestine, peripheral vascular disease with contamination of the amputation stump by faecal clostridia. The diabetic is particularly at risk. Infection by these clostridia is often endogenous.

Virulence: The clostridia of gas gangrene secrete a variety of enzymes and toxins. These enzymes and toxins lead to tissue death and necrosis. Death of adjacent tissue facilitates further spread. The clostridia responsible for gas gangrene are the following —

*Cl. perfringens*, *Cl. novyi* and *Cl. septicum*

Disease Pattern: There are three forms of clostridial infection — clostridial wound contamination, clostridial cellulitis and clostridial myositis. Clostridial wound contamination is common — more than 80% of wounds are contaminated by clostridia. Provided the wound is superficial and contains no necrotic or foreign material, this presents no problem. The second stage is that of anaerobic cellulitis where a superficial infection with clostridia has occurred. This should be treated but is not life threatening. Clostridial myo-
Man meets Microbes

sitis, the last of the trio, is better known as gas gangrene. As the toxins produced by the organism destroy the adjacent muscle cells, spread into these anaerobic areas occurs. Clostridial metabolism leads to the production of gas, e.g. CO₂ and H₂. This is released into the tissues and is responsible for the crepitations felt on palpation. Other organisms, e.g. E. coli, klebsiella, bacteroides and peptostreptococci also produce gas and must not be confused with clostridia.

Prevention and Treatment: Prevention of gas gangrene involves removal of clostridia. This can be achieved by adequate debridement of the wound. Hyperbaric oxygen is now being successfully used in the treatment of gas gangrene. Oxygen is toxic to the organism and also prevents germination of spores. Adjuncts to therapy are antibiotics and polyvalent antitoxin. Amputation is all too frequently the last resort used in an attempt to save the patient’s life.

Non-sporing Gram-positive bacilli

Propionibacteria

These organisms are skin commensals. Propionibacterium acnes may have a role in acne. They are postulated to release lipases which convert skin lipids to free fatty acids. These free fatty acids may cause tissue irritation resulting in inflammation and acne.

Corynebacteria

Corynebacteria are aerobic non-sporing Gram-positive bacilli. They form a group of organisms which includes saprophytes and pathogens. The saprophytes, collectively called “diphtheroids”, are commensals of respiratory mucosa and conjunctiva. They must be distinguished from the pathogen C. diphtheriae.

Corynebacterium diphtheriae

Source: Corynebacterium diphtheriae occurs in the respiratory tract and skin of both patients and carriers.

Spread: This is by direct contact, or by droplet infection. The portal of entry could be the throat, nasal mucosa, larynx or rarely a skin wound.

Virulence: The organism multiplies producing a toxin. The toxin induces local epithelial cell death and a superficial inflammatory reaction results. These combine to give the classical clinical picture of a pseudomembrane. The organism does not invade.

Not all C. diphtheriae organisms are capable of producing toxin. As diphtheria is a disease caused by a toxin it is important to know whether the organism is toxigenic or not. The ability of the organism to produce toxin depends on:

(i) Infection of the organism by a specific β phage. This is a bacteriophage (viral) infection of a bacterium.
(ii) A low iron content in the bacterial cell facilitates toxin production.

A diphtheria organism which has not been infected by the β phage is harmless until such time as it becomes infected. Once lysogeny by the β phage has occurred the diphtheria organism becomes potentially lethal.

Disease Pattern: The pseudomembrane of diphtheria may be found in the nose, covering the larynx or in the throat. The throat is the most common site. Depending on the site of the membrane the child may complain of a nasal discharge, or a sore throat or may even die of asphyxia. The organism produces toxin as it multiplies. Locally, toxin causes production of the pseudomembrane, absorbed toxin causes the more serious manifestations of diphtheria. The absorbed toxin attaches to cells, notably those of the adrenal, the nervous system and the kidney. Diphtheria toxin has two fractions — fragment B which attaches to the cytoplasmic membrane, and fragment A which diffuses into the cell's cytoplasm. Fragment A acts on the machinery involved in protein synthesis at the level of the ribosomes. It interferes with protein synthesis by preventing elongation of the polypeptide chain.

Prevention and Control: It is public health practice to immunize the population against diphtheria. An individual who has been immunized and is exposed to a toxigenic strain of *C. diphtheriae* may become a carrier but he will not develop clinical disease. He will, however, pose a threat to any individual in the community who has not been protected against diphtheria. Patients who have recovered from diphtheria are therefore subjected to repeated throat swabs. Ideally three consecutive negative throat swabs are required at 24-48 hour intervals prior to discharge of a diphtheria case.

Control of diphtheria in a community is based on immunization and on the control of carriers. Swabbing diphtheria contacts and Schick testing of high risk individuals and contacts is routinely performed in certain areas.

Treatment: The early administration of antitoxin is essential. The diagnosis of diphtheria is thus a clinical one. The laboratory can confirm the clinical diagnosis. The antibiotic of choice is penicillin.

Laboratory Findings: The laboratory used a special stain when trying to morphologically identify a member of the genus Corynebacterium. Both Ponders' stain and Albert's stain are of value. *Corynebacteria diphtheriae* have metachromatic granules and classically lie in the form of Chinese letters. Differentiation of this organism from the diphtheroids is based on their sugar reactions. Once the organism has been identified as *C. diphtheriae* it is necessary to perform immunodiffusion tests to show whether the strain isolated produces toxin or not.

Certain characteristics shared by Gram-positive bacilli

(1) Penicillin is the antibiotic of choice.
Exotoxin production is a major mechanism of disease induction.

Specific therapy must be instituted early. Once the exotoxin has attached to its target cell, no therapy is available to reverse its action. Neutralization of the effects of exotoxin must be achieved prior to the attachment of the toxin to the cell.

It is therefore contra-indicated to wait for laboratory confirmation of a clinical diagnosis of tetanus, gas gangrene or diphtheria. Specific therapy is an attempt to neutralize the toxin with specific antitoxin. A complication attributable to the use of horse antiserum (antitoxin) is serum sickness. The incidence of severe side effects increases with subsequent exposures to horse serum. It is therefore necessary to ensure that any individual who has had horse serum once, be protected as far as possible, from requiring horse serum a second time. This is achieved by immunizing the patient against diphtheria and tetanus. Repeated intra-venous exposure to foreign protein can be fatal.

The extent of the clinical disease will determine the use of antibiotics and supportive therapy.

The disease produced by secretion of a specific exotoxin is often characteristic of the organism producing the toxin, i.e. the disease is organism specific.

Exotoxins are potent toxins. Public health measures may be employed to control the spread of organisms capable of secreting these toxins.

Control of these diseases is often based on immunization. Immunization is based on exposure of the individual’s immune system to a specific toxoid. The treated toxin or toxoid is harmless. The toxoid primes the individual’s immune system which is then enabled to recognise the toxin and react protectively on future exposure. An immunization programme involves repeated exposure to the toxoid during primary immunization in order to speed up and improve both the quantitative and the qualitative immune response of the host. Routine immunization against tetanus and diphtheria is practised in many countries. Individuals exposed to an occupational risk of anthrax or botulism are immunized against these diseases.

**Gram-negative Bacilli**

All Gram-negative bacilli have lipopolysaccharide in their cell walls. The polysaccharide portion is antigenic, the lipid portion, termed Lipid A, is toxic. Endotoxic shock is associated with Gram-negative septicaemia. The organisms lyse in the blood stream and release their lipopolysaccharide (endotoxin).

Endotoxin has the following effects:

(i) It causes the release of endogenous pyrogens from members of the white cell series. The result is pyrexia.
(ii) The combined effects of endotoxin and infection lead to changes in the leucocyte count.

(iii) Release of kinins, histamine, serotonin and the activation of complement contribute to an imbalance between the blood volume and the vasculature capacity. This results in a drop in blood pressure.

(iv) Endotoxin activates both blood coagulation and fibrinolysis (clot lysis). This may lead to disseminated intravascular coagulation with haemorrhage.

(v) Irreversible shock may lead to the death of the patient.

The response of the individual to endotoxin may be modified by his immune response. Many Gram-negative bacilli are normal inhabitants of man's intestinal tract. Man's exposure to the lipopolysaccharide in his intestine may exaggerate his response on subsequent exposure to endotoxin in his blood stream.

Salmonella

There are two important groups of salmonellae — those which cause typhoid fever and those which cause gastroenteritis. The salmonellae causing typhoid in man are human pathogens, those causing gastroenteritis in man are animal pathogens.

Salmonella typhi

Source: Man is the animal that contaminates water and food supplies with *Salmonella typhi*. Both patients and carriers excrete the typhoid organism in their faeces or urine. Faecal shedders are ten times more important as culprits in the spread of *Salmonella typhi* than are carriers excreting the organism in their urine.

Spread: *Salmonella typhi* can be spread by food but is more usually spread by water. Water borne typhoid is usually as a result of contamination of the water supply by man.

Virulence: *Salmonella typhi* and hence typhoid are world wide. The organism only causes disease in man. The organism is resistant to digestion by macrophages. It resides in the macrophage which protects it against the host's circulating antibody and also makes it difficult for antimicrobial agents to reach the organism. *S. typhi* has endotoxin within its cell wall.

Disease Pattern: After man has ingested the contaminated water or food the organism passes into the intestine and invades the bowel wall. The infective dose of *S. typhi* is 100 000 organisms. During the 7-14 day incubation period the organisms penetrate the bowel wall and spread by the blood stream to the liver, spleen and other reticulo-endothelial tissue. Clinical symptoms coincide with the second bacteraemic phase when the organism reaches the skin, the central nervous system and the gastro-intestinal tract. The skin rash — rose spots, the headache, and the bloated constipated feeling associated with typhoid occur at this stage.
Man meets Microbes

Depending on the stage of the disease the organism may be isolated from one or more of the following sites — blood, stool and/or urine. Serological tests, for antibodies against the organism, become positive during the second week of illness. The typhoid patient develops high levels of antibodies against the organism but the organism lies protected inside macrophages.

Treatment: Typhoid may be treated with ampicillin, co-trimoxazole or chloramphenicol. In view of the mortality associated with typhoid, e.g. due to haemorrhage, perforation or shock, the use of chloramphenicol is justified in spite of the hazard of bone marrow depression.

Prevention and Control: Typhoid is not a contagious disease. It is not spread directly from person to person. It requires a period in either water or food in order to multiply and reach an adequate number to constitute an infective dose. In areas of poor hygiene, typhoid outbreaks are usually water borne; food borne typhoid is associated with better socio-economic conditions.

Adequate sanitation, regular water analysis for faecal contamination and follow-up of both cases and carriers are important principles in typhoid control. Routine checks on food handlers are also carried out. Typhoid carriers discovered amongst food handlers must not be permitted to continue working with food until they are declared free of the organism.

Vaccination is also practised against typhoid but is not entirely effective.

Typhoid or enteric fever is caused not only by *Salmonella typhi* but to a lesser extent by *Salmonella paratyphi* A and B.

**Salmonella gastroenteritis**

Source: Salmonella producing gastroenteritis in man are primary animal pathogens. They may be transmitted from animals to man in animal products, e.g. meat, eggs, etc. There are a multitude of different salmonella capable of causing gastroenteritis in man — many are named according to the geographical area in which they were first identified, e.g. *Salmonella johannesburg*, *Salmonella london*. As a group the organisms responsible for gastroenteritis are referred to as *Salmonella species*.

Spread: The organisms are frequently ingested in pork, less frequently in beef. Processed meat is a greater hazard than fresh meat. Raw milk is a danger — it can act as a vehicle of spread not only of brucellosis and tuberculosis but also of salmonella gastroenteritis. Egg products — particularly custards, cakes and egg nogs — can lead to outbreaks of salmonellosis. Salmonella gastroenteritis has occurred in hospitals due to the preparation of egg nogs with contaminated eggs.
Virulence: The organisms are less well adapted to man than *Salmonella typhi*. Their infective dose is $10^9$ organisms. The organisms illicit an inflammation response in the lamina propria of the terminal ileum.

Disease Pattern: Symptoms develop 8-24 hours after ingestion of contaminated food and constitutional symptoms are prominent. The patient complains of headache and fever. Diarrhoea may be mild or fulminant. Unlike food poisoning caused by staphylococci, nausea and vomiting are not prominent.

Treatment: This is supportive. Fluids and electrolyte solutions should replace those lost. Antibiotics are not indicated as they prolong the carrier state.

Prevention and Control: Prevention of salmonellosis starts at the level of animal husbandry. Animals transported to the abattoir should be subject to minimal stress.

Spread of salmonellae is exaggerated if fearful animals are cooped up in trucks. The separation of the gastrointestinal tract and its contents from muscles and other organs during slaughter is important. The housewife and foodhandler can minimize the opportunity for multiplication of any organism which has contaminated the food by deep freezing and adequate thawing prior to use. Adequate cooking is a simple way of killing these organisms and preventing disease.

**Shigella**

Source: These Gram-negative bacilli are spread from patients by direct contact or by flies, fomites and food.

Spread: An individual suffering from bacillary dysentery after passing a dysenteric stool may contaminate his hands, the doorknob and the tap before washing his hands. A healthy individual may handle the tap and suck his now contaminated finger. The infective dose of shigella is $10^4$ organisms. They do not require a period of multiplication before infecting a new host. They are susceptible to drying and heat but will survive for many weeks on moist toilet seats.

Virulence: Shigella are postulated to cause disease by their ability to invade the superficial epithelial cells and also by their ability to cause the release of prostaglandins from the cells of the small intestine. Prostaglandins are thought to stimulate adenyl cyclase, an enzyme which stimulates the release of fluid and electrolytes into the lumen of the small bowel.

Disease Pattern: The clinical picture will be determined by the strain of shigella involved and also by the area of bowel involved. There are four strains of shigella responsible for bacillary dysentery in man. These are *Shigella dysenteriae*, *Shigella sonnei*, *Shigella flexneri* and *Shigella boydii*. If the predominant lesion is in the small intestine
the dysentry will simulate diarrhoea; if the predominant lesion is in the large bowel a frank dysentry will result. Dysentry differs from diarrhoea in that blood, mucus and cells are present in the stool.

Treatment: Antibiotic therapy is not contra-indicated as is the case in salmonellosis.

Prevention and Control: Control of shigellosis or bacillary dysentry is at the level of personal hygiene. In adults outbreaks are usually self limiting. Children often require treatment.

Vibrio
There are two vibrios of importance to man. *V. cholerae*, the organism responsible for cholera, that devastating disease with the rice water stool, and *V. parahaemolyticus*, an organism causing gastroenteritis.

*Vibrio cholerae*
Source: Man is the source of *V. cholerae*. Carriers contaminate water supplies.

Spread: Cholera is usually spread by water. Occasionally in certain arid regions cholera has been shown to be spread by direct contact.

Virulence: Both the classical and El tor biotypes give rise to fulminating diarrhoea. The organism in both cases is non-invasive and causes disease by secretion of enterotoxin.

Disease Pattern: Ingestion by a healthy person of $10^8$ or $10^9$ organisms leads to clinically overt disease. The organisms are sensitive to acid and many demise in the stomach. Those which survive and reach the small intestine multiply in the lumen of the intestine. Adherence to the epithelial cells of the small intestine is required before the organisms can start to secrete their enterotoxin. Enterotoxin, an exotoxin, stimulates the production of adenyl cyclase which in turn leads to the secretion of fluid and electrolytes into the bowel lumen. Absorption, which remains normal, is masked by the excess outpouring of fluid. Enterotoxin is therefore responsible for a fulminating diarrhoea. Patients dying of cholera do so due to an excessive loss of fluid and electrolytes.

Management: Dehydration and shock must be prevented. This is achieved by the restoration of fluids and electrolytes by either the oral or intravenous routes. Special "metabolic beds" with a cavity in the buttock region are available. The watery stool flows directly from the patient into a calibrated bucket. Exact fluid loss is noted and the patient is not persistently disturbed. The collecting bucket should contain a known volume of disinfectant to destroy the bacilli excreted in the stool.

Tetracyclines may be used to eradicate the organisms present in the patient's bowel.
Prevention and Control: Cholera is often quoted as the disease best demonstrating the iceberg phenomenon. For every one clinical case of cholera there are nine sub-clinical infections.

Health education and the correct handling of sewage is necessary in cholera endemic areas. *V. cholerae* can survive for 24 hours in sewage; it is sensitive to disinfectants, including chlorine.

Cholera immunization is no longer required by International Health Authorities for travellers. This ruling is based on the observation that the value of immunization is limited — it is of limited value to the individual and of no value to the general public. Immunization against cholera will prevent some individuals who come in contact with the organism from developing the disease, but it will not stop them from becoming carriers and spreading the organism. The taking of prophylactic antibiotics by travellers is frowned upon as this leads to alteration of the normal microbial flora in the intestinal tract and also selects for antibiotic resistant strains of bacteria.

Cholera control depends on good sanitation, an adequate surveillance in cholera receptive areas and on the early diagnosis of cases and carriers. Early diagnosis and adequate treatment can reduce the mortality rate to zero. Early identification of carriers and constant checks on water supplies can prevent epidemics.

*Vibrio parahaemolyticus*

Source: This organism is found in the sea and contaminates sea food. In Japan *V. parahaemolyticus* is responsible for 80% of infective gastroenteritis. In other countries microbiologists seldom incriminate this organism as a contaminant of food. This is probably not because the organisms are not present but rather because it is missed on routine testing. The organisms require a selective culture medium with a high salt content.

Spread: The organism is spread by the ingestion of fresh sea food.

Virulence: The pathogenesis of the organism has not been well worked out. Enterotoxin is not thought to play a role.

Disease Pattern: Gastroenteritis develops 12-15 hours after the ingestion of fish. The patient usually has diarrhoea but may occasionally pass a blood stained stool. *V. parahaemolyticus* causes an infection, not an intoxication.

Treatment: The illness is usually self limiting, recovery occurring in one to two days.

*Escherichia*

*Escherichia coli*

Source: *E. coli* is a normal inhabitant of the bowel.

Spread: *E. coli* may cause disease by being removed from its normal
anatomical site and being introduced into a normally sterile area, e.g. meninges, bladder, blood. In these cases *E. coli* is behaving as an opportunistic pathogen. *E. coli* can under certain circumstances behave as a true pathogen and cause disease in its normal anatomical site. These *E. coli* strains are not commensals of that individual's bowel and are possibly derived from an infected water source.

**Virulence:** Certain strains of *E. coli* are capable of causing disease by secretion of an enterotoxin. These strains are infected by an extraneous piece of nuclear material termed a plasmid. The plasmid confers the ability to produce enterotoxin on the infected bacterium. Another strain of *E. coli* is capable of invading the superficial cells lining the gastro-intestinal tract. All *E. coli* are Gram-negative and therefore capable of releasing endotoxin on lysis.

**Disease Pattern:** Certain strains of *E. coli* are capable of producing diarrhoea — diarrhoea in infants is thought to often be due to enteropathogenic *E. coli*. Invasive *E. coli* can cause a dysentry-like picture. Any strain of *E. coli* introduced into a normally sterile site can cause opportunistic infection, e.g. urinary tract infection, neonatal meningitis, septicaemia.

*E. coli* and water — *E. coli* constitute a group of organisms regularly found in faeces. The presence of *E. coli* in a river, dam or stream is therefore an index of faecal contamination of that water. Tests are regularly performed to detect the presence of *E. coli* in water used for human consumption. Water containing *E. coli* is condemned, not because of this organism *per se* but because faecal contamination of the water has occurred. The faecally polluted water is suspect — it may be a source of cholera or typhoid.

**OPPORTUNISTIC GRAM-NEGATIVE BACILLI**

A large number of Gram-negative bacilli are capable of causing disease in hosts with an impaired resistance. This impaired resistance may be:

(i) At the level of a superficial barrier, e.g. in burns the organism bypasses the skin barrier; organism may be introduced into the bladder on a contaminated catheter or by trauma of the urethra.

(ii) It may be related to defects in non-specific immunity, e.g. a congenital defect of leucocytes, a rubeola induced defect in polymorph chemotaxis.

(iii) It may be at the level of specific immunity, e.g. Hodgkin's disease, cancer, iatrogenic depression of immunity due to steroid therapy.

Only three members of these Gram-negative organisms classified as potential pathogens are to be discussed. All these organisms can present problems in the hospital environment. The three groups to be discussed are:

Klebsiella
Proteus
Pseudomonas
Klebsiella
Source: Klebsiella are found in the environment. They are normally found in soil and must be differentiated in water testing so as to avoid misidentification as *E. coli*.

Virulence: These organisms resist phagocytosis due to the presence of a large capsule.

Disease Pattern: *Klebsiella pneumoniae* is the most pathogenic of the species and may act as a primary invader causing Klebsiella or Friedlander's pneumonia. This may be fatal. Diabetic and alcoholic patients are particularly at risk.

Infections with klebsiella organisms are on the increase in the hospital situation. This increase runs hand in hand with the increase in immunosuppression used in transplantation and the increase of cancer chemotherapy. The persistent and often indiscriminate use of antibiotics exag­gerates the problem of nosocomial klebsiella infections.

Klebsiella organisms can act as opportunistic invaders in urinary tract infections in bronchopneumonia, in osteomyelitis, etc.

Other members of the *Enterobacteriaceae* family (serratia and entero­bacter) are also increasingly listed as hospital acquired infections. They are more resistant than klebsiella to antibiotic therapy.

Proteus
There are four species in this group. All are motile but two are so actively motile that if grown on one side of a solid medium they will spread over the whole surface of the medium. This is termed swarming.

Source: Proteus organisms are widespread in the environment. They are found in soil and in sewage.

Disease Pattern: One member of this group of opportunists is suspected, but not proven, of causing diarrhoea. All the members of this group are well recognised as urinary tract pathogens. Once these opportunists have gained entrance to the bladder they split urea and make the urine alkali. The ammonia so produced may inactivate complement, thus compromising the host's defences.

Urinary tract infections due to proteus are common in both the hospital and the community. Proteus bacteraemia and wound sepsis are a hospital problem.

Pseudomonas
Source: The green film found in many hospital and household drains may be nothing less than a pseudomonas culture. Pseudomonas species has included amongst its members an organism, *Pseudomonas aeruginosa*, which is easily recognised by its green pigment. Pseudomonas is an organism found in water. It proliferates freely in drains and sinks.
Disease Pattern: Pseudomonas prefers hosts with some defect in their immune system. The immunosuppressed host provides the organism with a new play-ground. It frequently causes systemic disease in these patients. Localized infections, e.g. of the eye due to the use of contaminated eyedrops, or of bedsores due to washing with utensils from contaminated sinks, do occur.

The patient with burns is at particular risk — local infection followed by septicaemia and death is a sadly familiar sequence. In the paraplegic patient pseudomonas is a formidable cause of urinary tract infection.

Pseudomonas does not exclusively cause infection in hospitals. It does, however, produce about 200 hospital infections to every one community infection. Pseudomonas, an organism which multiplies in damp areas, is a most important cause of nosocomial infections.

**THE SMALL GRAM-NEGATIVE BACILLI**

The small Gram-negative bacilli have been grouped together as *Parvobacteriaceae* or *Brucellaceae*. Among this group of bacteroides, an anaerobic organism which is the predominant bacterium of the normal intestinal flora. Of the group of small Gram-negative organisms only four members will be considered:

- **Haemophilus**
- **Bordetella**
- **Brucella**
- **Yersinia**

These organisms have specific cultural requirements.

These organisms usually cause disease in animals but may be transmitted to man, i.e. they may be classified as zoonoses.

**Haemophilus**

These are pleomorphic Gram-negative coccobacilli. They depend on one or two factors for their normal growth. The X factor (haemin, found in red blood cells) and the V factor (a coenzyme NAD or NADP) are necessary for normal metabolism. The V factor can be produced by certain organisms amongst which are staphylococci. Identification of *Haemophilus influenzae* can be definitely made by culturing the organism on a blood agar plate and seeing if the colonies are larger and more numerous in the vicinity of a staphylococcal streak culture. This phenomenon is termed satellitism.

**Figure 20**

**SATELLITISM**

*E. coli* does not show satellitism

*H. influenzae* showing satellitism
**Haemophilus aegypticus**, also called Koch-Weeks bacillus, is an important cause of conjunctivitis. This form of conjunctivitis is highly communicable, especially amongst small children.

**Haemophilus ducreyi** is spread venereally. It is the causative organism of chancroid or soft sore. Chancroid presents as an ulcer on the genitalia and has associated tender draining lymph nodes. Treatment for this venereal disease is sulphonamides.

**Haemophilus influenzae**

Source and spread: Varieties of non-encapsulated *H. influenzae* are found in the throat and nasopharynx of 60-80% of children. Spread of *H. influenzae* is person-to-person by droplets. The patient with haemophilus meningitis is a far less important source of infection than the carrier.

Virulence: These organisms only cause disease in the face of a decreased host resistance. The types of *H. influenzae* causing severe disease are encapsulated. Their capsules protect them against phagocytosis.

Disease Pattern: *H. influenzae* is an important pathogen in children. It is the commonest cause of acute bacterial meningitis in early childhood. Late neurological and intellectual impairment following influenza meningitis are well recognised. The peak incidence occurs between 2 months and 3 years of age. *H. influenzae* can cause fatal acute epiglottitis in the 2 to 7 year age group. Acute oedema of the epiglottis can block the respiratory passages resulting in asphyxia. Tracheostomy may be life saving.

In the adult, *H. influenzae* is thought to play a role in exacerbations of chronic bronchitis.

*Haemophilus influenzae* and *Streptococcus pneumoniae* have certain similar characteristics.

(i) There are high carrier rates in the upper respiratory tract of the relatively non-pathogenic forms, while there is a low carrier rate of the virulent variety.

(ii) Immunity depends on the production of antibodies to capsular antigen.

(iii) Their pathogenicity depends on their ability to resist phagocytosis. This ability is related to the presence of their capsules. There is antigenic cross-reactivity of the capsular polysaccharide amongst certain types of *H. influenzae* and pneumococci.

(iv) Diseases caused by these organisms may involve either the respiratory system or the meninges.

(v) Both are spread by droplet infection.

(vi) Both groups contain members which are primary pathogens and virulent; other members are opportunists.
Bordetella
Source and Spread: Bordetella is an organism causing disease in man. It is spread from man to man by droplets. These organisms are very fastidious — special collection and culture techniques are necessary if the organism is to be isolated.

Virulence: During the incubation period of 1-2 weeks the organism multiplies. It does not cause disease by invasion but by the secretion of toxins.

Disease Pattern: *Bordetella pertussis* and *Bordetella parapertussis* are responsible for respiratory infection during childhood. *Bordetella pertussis* is responsible for the more severe disease. The clinical picture of bordetella infection is characterized by a paroxysm of coughing followed by a long inspiration. The disease is called whooping cough. All that whoops is not whooping cough — certain viruses, e.g. the adenovirus, can give a similar picture.

Whooping cough is characterized by three phases:
the catarrhal phase
the whooping or paroxysmal phase
the convalescent phase.

Each phase lasts about two weeks. The patient is infectious during the first two to three weeks. During the whooping phase bronchioli can be blocked by mucus plugs and areas of atelectasis can occur. Collapsed areas of lung are susceptible to secondary infection. If sufficient atelectasis occurs, hypoxia can become a problem. Vomiting and convulsions are a feature of whooping cough.

Treatment: Antibiotics, unless administered during the incubation period, do not alter the course of the pertussis infection. Penicillin is, however, usually given to whooping cough patients — this will have no effect on bordetella, it is administered as prophylaxis against secondary infection. Deaths associated with whooping cough are usually attributed to secondary infection.

Prevention and Control: The mother is incapable of transplacentally transferring protective antibody against whooping cough. Infants less than 6 months of age are therefore particularly at risk. Immunization against whooping cough is usually started when the infant is 3 months of age. The triple vaccine against whooping cough, tetanus and diphtheria is routinely given to infants. Whooping cough vaccine is not 100 per cent protective.

Brucella
There are a number of brucella species — the most important pathogen in man is *Brucella melitensis*.

Source: Brucella is a disease of animals which can be spread to man. The
species of brucella is determined by the animal infected, e.g. *Brucella suis* infects pigs, *Brucella melitensis* sheep and goats, *Brucella abortus* cattle and *Brucella canis* dogs.

Spread: Brucella is spread by direct contact with abraded epidermal areas and mucous membranes including the conjunctiva. Aerosol spread is suspected.

Virulence: The organism is resistant to digestion by phagocytes. It is an intracellular pathogen.

Disease Pattern: Brucellosis is a diagnostic challenge. The onset is insidious and the presentation often that of a pyrexia of unknown origin. Chronic cases of brucellosis are often mis-diagnosed as psychiatric problems. Arthritis is a feature of the disease.

Prevention and Control: As brucellosis can often be acquired from unpasteurized milk or infected animal carcasses, vets, farmers and abattoir workers are the population at risk. Immunization for at risk workers is available, but the vaccine has side effects. Control of herds can be achieved by immunization of the herds with a live attenuated vaccine. Milk should be pasteurized. In certain countries brucellosis is a notifiable disease.

**Yersinia**

*Yersinia pestis* is a small Gram-negative bacillus which exhibits bipolar staining. It is the causative organism of plague. Plague is a zoonosis.

Spread: *Yersinia pestis* is spread to man in one of two ways:

(a) The bite of a flea inoculating the bacillus.

(b) More rarely, and only during epidemics, by droplet inhalation from a human with pneumonic plague.

Virulence: The infective dose of *Yersinia pestis* is one. *Yersinia pestis* has some ability to resist phagocytosis. It secretes a variety of virulence factors. Pesticin and fraction 1 (only produced at 37°C) provide a lethal combination.

Disease Pattern: Man rarely, if ever, recovers from pneumonic or septicaemic plague. He may, however, resist death in the case of bubonic plague. Should the local lymph node fail to localize the infection, blood spread will rapidly convert bubonic plague into the more sinister septicaemic plague.

In any isolated population, bubonic plague precedes pneumonic plague. Failure to localize the organism in the draining lymph node leads to systemic spread. Infection of the lungs is followed by respiratory spread of the organism. The organism spread by the flea is less virulent than the organism spread by droplet infection. The organism spread from man to man has fraction 1 as one of its virulent factors.
Treatment: Tetracyclines are used in the treatment of plague. The early diagnosis and treatment of plague can be life-saving.

Prevention and Control: Plague outbreaks can be predicted by observing the rodent population. When an increase in the rodent population is followed by a high death rate amongst rodents, then plague should be suspected. Plague is spread by fleas from the wild rodent population to the semi-domestic rodents, from the semi-domestic rodents to the domestic rodents, and from the domestic rodents to man.

**Figure 21**
THE SPREAD OF *YERSINIA PESTIS* FROM WILD RODENTS TO MAN

Wild rodent — (gerbils) *Talera brandsii*
  ↓ flea
  ↓ Semi-domestic rodents (multimammate mouse) *Mastomys natalensis*
    ↓ flea
    ↓ Domestic rat — *Rattus rattus*
      ↓ flea
      ↓ Man
      ↓ flea or droplet infection
      ↓ Man

As each population dies the number becomes depleted so that the fleas, e.g. *Xenopsylla cheopis* leave their dying host and seek new healthy companions. They carry *Yersinia pestis* from one population to the next leaving disaster in their wake. *Yersinia pestis* kills rodents, man and also the fleas.

Man is at risk of exposure to plague if:

(a) he goes into the forests and contacts wild rodents;
(b) if he is exposed to infected rats and fleas in his home and city.

Control depends on the separation of man from domestic rodents. Houses and other buildings are ratproofed. Rat poisons and traps are used on the outskirts of cities to catch rats in order to test them and their fleas bacteriologically and serologically for the presence of *Yersinia pestis*. This continual surveillance system gives early warning of a plague epidemic.

Persons who have been in contact with suspected plague are immediately treated with tetracyclines. Suspected plague is treated first and the diagnosis confirmed later.

Vaccination against plague involves the use of dead organisms.

*Yersinia enterocolitica*
Man may present with a variety of symptoms, e.g. mesenteric adenitis, regional ileitis and arthritis.
MYCOBACTERIA
This group of organisms consists of those organisms capable of resisting decolourization by acid and alcohol. This differentiation depends on the of the Ziehl-Neelsen stain.

Three broad groups can be differentiated:

(a) Those which cause tuberculosis —
M. tuberculosis — human tuberculosis
M. bovis — cattle tuberculosis
M. avium — bird tuberculosis

(b) Those which cause leprosy —
M. leprae

(c) A group of atypical mycobacteria (Mott bacilli). This group of organism have pathogens and saprophytes amongst their members. Pathogens cause diseases of the lung, skin or lymph nodes. They do not cause disease in laboratory animals, e.g. guinea pigs, rabbits.

The atypical mycobacteria have been classed into 2 groups:
(i) The rapid growers — visible colonies are cultured in 4-7 days.
(ii) The slow growers — 3 to 6 weeks are necessary before colonies become visible to the naked eye. These colonies will fall into one of the following groups according to their pigment production:
(a) The non-chromogenic group — this group fails to produce pigment.
(b) The scotochromogenic group — this group produces pigment.
(c) The photochromogenic group — this group only produces pigment if exposed to light.

The mycobacteria form a group of organisms capable of resisting digestion by phagocytes. These organisms survive and multiply in cells of the reticulo-endothelial system. Bacteria which are found surviving inside cells are associated with chronic disease. Extracellular bacteria are usually associated with a more acute type of illness. Specific host defences are adapted to cope differently with different types of infection — cell mediated immunity is more important in intracellular infections, humoral immunity in extracellular infections.

| Specific host defence | INTRACELLULAR ORGANISM | EXTRACELLULAR ORGANISM |
|-----------------------|-------------------------|------------------------|
| Disease               | Cell mediated immunity  | Humoral immunity       |
|                       | Chronic                 | Acute                  |

*Mycobacterium tuberculosis*
World figures show that approximately three million people die of tuberculosis every year. This is a chronic devastating disease.
Spread: *Mycobacterium tuberculosis* is spread by droplet infection.

Disease Pattern: There are two risks associated with the acquisition of tuberculosis. There is the risk associated with exposure to the organism — this risk is especially high in medical personnel coming into contact with undiagnosed tuberculosis. The risk of developing disease is especially high in those groups who have a defect in cell mediated immunity, e.g. those who are on steroids, have leukemia or are malnourished.

As *M. tuberculosis* is usually inhaled, the primary lesion is commonly in lung parenchyma with spread to, and enlargement of, the hilar lymph nodes. *M. bovis* may be spread to man in unpasteurized milk. Ingestion of infected milk leads to infection of the intestine with spread to, and enlargement of, the mesenteric lymph nodes. Tuberculosis is usually held in check by the host’s defences — when these fail, generalized spread of the organism can occur, resulting in miliary tuberculosis.

Diagnosis: The diagnosis of tuberculosis is essential from both the public health and personal points of view. An individual with pulmonary tuberculosis spreads the disease. Treatment of the individual rapidly renders him non-infectious. Population surveys to find undiagnosed cases of tuberculosis are carried out. The techniques commonly used are:

(a) X-ray screening — this is the least effective means of diagnosis.
(b) Skin testing.
(c) Sputum testing

Skin Testing: This is based on the interpretation of the host’s response to an extract of *M. tuberculosis*. Purified protein derivative (PPD) is an antigenic extract of the human tuberculosis organism. The response to the intradermal inoculation of PPD into the forearm of an individual is recorded 48-72 hours after injection.

If the individual has been previously exposed to, and reacted against, the bacterium, his immune system recognises the antigen and the skin reflects this recognition. The PPD administered stimulates the memory cells of the host’s cell mediated immune system and lymphocytes arrive at the site of the foreign antigen in 2-3 days. An area of reddening and induration indicates previous exposure and adequate resistance against the organism. An area of dermal necrosis implies active tuberculosis. False positive and false negative results do occur.

Sputum Testing: The bacteriological method of diagnosis is the most satisfactory. Staining of the sputum with the Ziehl-Neelsen stain may reveal the presence of acid-fast bacilli. To determine whether these acid-fast bacilli are *M. tuberculosis* or not, it is necessary to culture the organism and do biochemical tests. A positive slide indicates many mycobacteria are being shed — positive microscopy requires a concentration of about 10 000 organisms per millilitre.
of sputum. Once a patient has been diagnosed as having tuberculosis, microscopy is a valuable tool in following the patient's progress.

A provisional identification, i.e. the observation of acid-fast bacilli, becomes available within hours after sending in the specimen. A definitive identification of *M. tuberculosis* takes 6-8 weeks. This delay is due to the slow multiplication of these bacilli.

Immunization: In populations or groups at risk it is advisable to immunize against tuberculosis. Medical personnel in a country where tuberculosis is prevalent should all be skin tested (e.g. the Heaf or Mantoux test). If negative, these individuals should be protected against tuberculosis by immunization.

BCG (Bacillus Calmette Guerin) is the name of the preparation used to immunize against tuberculosis. It consists of a viable, attenuated strain of *M. bovis*. Due to the cross reactivity between *M. tuberculosis* and *M. bovis*, BCG gives some protection against human tuberculosis.

Treatment: Today tuberculosis is a treatable condition. Drug therapy is based on three principles:

(a) It must be uninterrupted.
(b) Multiple drugs are used simultaneously — three drugs are often combined.
(c) Prolonged therapy is essential.

Tuberculosis is treated by continuous, prolonged combined drug therapy.

*M. leprae*

Leprosy is a chronic disease caused by an organism which has not yet been successfully cultured in artificial media. The organism has been cultivated in the footpads of mice and in the nine banded armadillo.

Source and Spread: *M. tuberculosis* takes 20 hours to multiply, *M. leprae* is thought to take longer. Leprosy is only communicable after prolonged close contact. The nasal mucosa and skin are thought to be the main source of spread.

Disease Pattern: Leprosy is a disease characterized by differences in the host's immune response. On the one hand, if the host lacks an adequate cell mediated immune response the organism multiplies prolifically — this is clinically diagnosed as lepromatous leprosy. These patients are infectious. On the other hand, the host may exhibit an exaggerated immune response to the bacillus. The organisms are rapidly killed. The exaggerated response leads to tissue destruction in the host. The tissues most severely affected are the nerves. Tuberculoid leprosy is characterised by anaesthesia, contractures and deformity. This patient is not infectious.
SPIROCHAETES — THE SPIRAL ORGANISMS

These large spiral organisms may be pathogenic or saphrophytic. The family containing pathogenic members includes those organisms causing syphilis and relapsing fever.

The organisms are coiled and move by twisting without the aid of flagellae. These spiral organisms stain poorly and are therefore usually examined under dark field microscopy or using immunofluorescence. These organisms are difficult to propagate in the laboratory as they require specially enriched media. *Treponema pallidum*, the organism causing syphilis, fails to grow on artificial culture media. The spirochaetes are sensitive to penicillin.

*Treponema pallidum*

Source: *Treponema pallidum* is an organism adapted to man and spread by man.

Spread: This spirochaete is a delicate organism. It is sensitive to drying and is killed by temperatures of 42°C and over. An organism so sensitive to environmental conditions requires a special mode of transmission. *T. pallidum* is transmitted by direct contact. The organism penetrates intact mucosa or skin abrasions. Syphilis is a venereal disease.

Virulence: *Treponema pallidum* appears to resist phagocytosis but is susceptible to immune lysis. Complement plus specific antibody can react with these organisms and cause their death.

Disease Pattern: Once the organism reaches its new host it multiplies at its site of entry. The multiplication time is relatively long and the incubation period varies between 2-9 weeks. Syphilis presents clinically as a disease with three stages:

Primary syphilis — A local lesion appears at the site of inoculation. This is often described as a punched out ulcer. The primary chancre is painless and infectious. The draining lymph nodes are enlarged, hard and painless. The chancre is often on the genitalia and the nodes in the groin.

Secondary syphilis — here systemic spread of the organism has led to multiple infectious foci, e.g. skin rashes, mucous patches. The nursing staff should handle these patients with gloved hands as tiny abrasions on the attendant’s hands can become infected from the syphilitic patient’s skin rash.

Tertiary syphilis — this can occur 20 years after the initial infection. Here the host’s defences respond to the organism with localized granuloma formation. Cell mediated immunity is expressed destructively and the patient responds to his chronic infection with a delayed hypersensitivity response. The presence of destructive lesions in different anatomical sites can lead to the destruction of
various cells, e.g. brain cells, leading to general paralysis of the insane; elastic tissue in the aortic arch, leading to dilatation and rupture of the aorta.

*Treponema pallidum* can spread across the placenta. Children are born mentally defective, blind and deaf, thanks to a promiscuous parent. Congenital syphilis is a preventable condition if pregnant females are screened, diagnosed and treated early.

**Treatment:** Penicillin is the drug of choice.

**Borrelia**

These organisms cause relapsing fever.

**Source and Spread:** *Borrelia duttoni* is transmitted by the bite of a tick. *Borrelia recurrentis* is transmitted by a body louse. The organisms are released from the louse's coelomic cavity when the host crushes the louse. In so doing the host introduces the organisms into the skin defect created by the louse's bite.

**Virulence:** The host's defences against relapsing fever are impaired due to two mechanisms employed by the organism —

(i) The organism breaches the host's superficial defences — the intact skin barrier is breached by the bite of the arthropod.

(ii) The organism evades the host's specific humoral defences by changing its superficial antigenic structure. The host's defences therefore remain one step behind that of the organism's ingenuity.

This phenomenon accounts for the relapses classical of this condition.

**Disease Pattern:** The organism causes fever in man. The attacks of pyrexia may recur up to ten times.

**Leptospirosis**

**Source:** These spiral organisms cause disease in animals. Accidental transmission to man may occur — usually by contact with contaminated animal products or excreta.

**Spread:** The organism is spread from the contaminated source, e.g. a sewer, the dock area where rat urine contaminates the water, by direct contact with abraded or scratched skin.

**Disease Pattern:** The organism multiplies in the blood causing a leptospiraemia. It is later isolated from urine — leptospiruria.

Specific antibody assists the phagocytosis of these organisms. On reaching the kidney the organisms are protected against the body's defences in the renal medulla. At this stage the disease is very difficult to treat.

Depending on the species of the organism involved, the disease can vary from mild conjunctivitis to fulminating jaundice.

People at risk are those in contact with rats and contaminated water.
ACTINOMYCETES

Actinomycetes are filamentous branching organisms. The branching mycelium is subject to fragmentation. Certain of the members of this group are saprophytes, others are pathogenic to man.

A. MICROAEROPHILIC TO ANAEROBIC ACTINOMYCETES

These are non acid-fast organisms characterized by branching filaments.

Actinomyces israelii

Source: This organism is a commensal in the mouth. Human infections by Actinomyces israelii are endogenous and often preceded by trauma to the oral mucosa.

Disease Pattern: The classical lesion in actinomycosis is that of a mass. These woody masses may break down and form abscesses. Pus may be discharged by sinus formation. The pus contains 'sulphur granules'. These granules are clusters of the organism.

There are three typical clinical sites in which actinomycosis is found: 60% of cases occur in the cervico-facial region, 22% are found in the abdomen and the remainder are found in the thorax.

Treatment: Penicillin is the drug of choice. Surgical drainage is an adjunct to antibiotic therapy.

B. AEROBIC ACTINOMYCETES

(i) Norcardia asteroides

Source: Norcardia is present in soil.

Disease Pattern: The primary lesion is in the lungs. A chronic suppurative pulmonary lesion is usually associated with spread of the organism to the central nervous system and the intestinal tract. Sinuses may form but no granules are found in the exuded pus. Norcardiosis frequently complicates leukaemia, Hodgkin's disease or any condition associated with impaired immunity.

Treatment: Treatment in the early stages with sulphonamides or ampicillin may be curative.

(ii) Norcardia madurae

Source: The organisms are commonly found in soil or on vegetable matter.

Disease Pattern: Infection is often preceded by trauma leading to inoculation of the organism. Mycetoma, often a localized lesion, starts as a papule which may become a fixed nodule or break down to form an abscess with discharging sinuses. Granules consisting of micro-colonies of norcardia are found in the discharged fluid.

Treatment: Antibiotics are useful, e.g. sulphonamides are frequently used.
Actinomycetoma must be distinguished from maduramycetoma. Clinically the lesions are similar but maduramycetoma is caused by a true fungus and treatment is with antifungal agents.

MYCOPLASMA
Mycoplasmas are simple unicellular organisms which differ from the eubacteria in lacking a cell wall. Bacteria which normally have cell walls may, on occasion, lose these cell walls — these bacteria are termed L forms or protoplasts. Protoplasts and mycoplasma have certain features in common.

(i) These organisms are resistant to penicillin. Penicillin acts on cell wall synthesis.

(ii) These organisms are susceptible to lysis due to changes in osmotic pressure.

Protoplasts are derived from bacteria — these cell wall defective mutants can occur spontaneously or be induced by chemicals. They may revert back to their bacterial form. Mycoplasmas are not derived from bacteria but form a special group of small prokaryotic organisms.

Source: Many species of mycoplasma are included amongst the normal flora and the genito-urinary tract of the oropharynx.

Disease Pattern: Disease attributed to mycoplasma organisms involve mucous membranes. The organism attaches to the cells of the mucous membrane by a plate-like appendage. Mycoplasmas are known to cause primary atypical pneumonia; they are suspected of playing a role in many diseases of the genito-urinary tract, e.g. non-gonococcal urethritis, infertility, cervicitis, etc.

Mycoplasma pneumoniae
Spread: The organism is spread by droplet inhalation.

Disease Pattern: Mycoplasma pneumoniae is the pathogen responsible for primary atypical pneumonia. This respiratory disease is characterized by more severe X-ray findings than are suggested on physical examination.

Treatment: Tetracycline is the drug of choice.

OBLIGATE INTRACELLULAR PARASITES
There are four groups of intracellular parasites of medical importance.

These are: The Rickettsiae (with the exception of R. quintana)
Coxiella burnetii
The Chlamydiae
The Viruses

The first groups are prokaryotic cells, i.e. they are bacteria-like. The last group forms a group on its own. The above organisms are all located inside their host’s cells. This ‘anatomical’ situation is not by chance — it
is essential for the survival of these organisms that they infect cells. They may depend on the host cell for energy, for the correct osmotic environment or for the necessary mechanical equipment to synthesise proteins. These are obligate intracellular parasites.

**THE RICKETTSIAE**

**Source and Spread:** Lice, fleas and ticks are the common arthropod hosts involved in the transmission of rickettsial diseases. The rickettsiae are intestinal parasites of these blood sucking arthropods. They do not cause disease in their natural arthropod host.

Rickettsiae may be transmitted from arthropod to arthropod by feeding on the same infected vertebrate host or by transovarial transmission, e.g. in ticks.

Rickettsiae are transmitted to man with the assistance of the arthropod host — the organism may be transmitted in the bite of a tick or scratched into the skin defect along with the faeces of the louse. Rickettsiae enter man by way of a skin lesion created by the biting arthropod host.

**Disease Pattern:** The diseases caused by rickettsiae are characterized by an incubation period of 7-10 days. The rickettsiae parasitize endothelial cells. The organisms multiply in the host cell by means of binary fission and appear to have little effect on the host cell. When sufficient multiplication has occurred, the host cell, now packed with rickettsiae, bursts. The released rickettsiae seek new host cells. Entry into the host cell is an active process requiring the use of energy in the form of ATP (adenosine triphosphate). The target cell of the rickettsial infection is the endothelial cell of blood vessels — rickettsia cause vascular infections. The local lesion may be referred to as the typhus node.

The host's response to rickettsial infection is usually associated with fever and a rash. The presence of infected endothelial cells in the central nervous systems vasculature can be associated with delirium. Infected endothelial cells in the pulmonary blood vessels can present as pneumonitis.

Different species of rickettsiae are transmitted by different arthropod hosts and are associated with different clinical diseases.

**Table XXVIII**

| THE ORGANISM     | ARTHROPOD HOST | DISEASE IN MAN                           |
|------------------|----------------|------------------------------------------|
| *R. prowazeki*   | louse          | Epidemic typhus                          |
| *R. mooseri*     | flea           | Murine (Endemic) typhus                  |
| *R. conori*      | tick           | Tick bite fever                          |
| *R. akari*       | mite           | Rickettsial pox                          |
| *R. rickettsiae* | tick           | Rocky mountain spotted fever             |
| *R. tsutsugamushi* | mite         | Scrub typhus                             |
Parasites, Bacteria and Viruses

Treatment: Tetracycline is the drug of choice. Administration of tetracyclines is necessary for a full 48 hours before a clinical response is detected.

Rickettsiae are prokaryotic cells with thick cell walls and contain both DNA and RNA.

COXIELLA BURNETI

Coxiella burneti differs from rickettsiae in that they are stable outside host cells; rickettsiae have unstable leaky cell membranes. These organisms were previously classified amongst the rickettsiae.

Source and Spread: This agent may be spread by ticks, but it is more often spread in dust. Aerosol spread from animal products and contaminated dust are important sources of infection. The fine dust layer covering the hide of a goat, a cow or a sheep may harbour this organism.

Disease Pattern: Coxiella burneti causes Q fever. Q fever has the fever common to the rickettsial diseases; it does not, however, have the characteristic skin rash. Q fever is characterized by respiratory and hepatic symptoms.

Treatment: Tetracycline is the drug of choice. Coxiella are less susceptible to tetracycline than rickettsiae.

CHLAMYDIAE

Chlamydiae contain both DNA and RNA. They have their own 70s ribosomes and do not depend on their host’s cell machinery for protein synthesis. They are energy parasites. Chlamydiae lack the full complement of cytochromes. A defective electron ladder leads to defective ATP production. Chlamydiae depend on the host cell for ATP. Chlamydiae are more dependent than rickettsiae for metabolic aid from their host cell.

The infectious chlamydial particle is termed the ‘elementary body’. Elementary bodies are phagocytosed by the host cell. Once inside the host cell, surrounded by the host cell’s cytoplasmic membrane, the chlamydial organism is reorganised and an ‘initial body’ is formed. Multiplication of the organism by binary fission leads to the formation of ‘inclusion bodies’. These inclusion bodies may be liberated and new cells can become infected. The chlamydial cycle takes 24-48 hours.

There are two groups of chlamydiae —
(a) those which cause psittacosis;
(b) those responsible for the trachoma — lymphogranuloma venereum complex of diseases.

In their natural hosts chlamydiae produce subclinical rather than overt infection.

Psittacosis

Source: This is a disease of birds. The organism may be transferred to man.
Spread: *Chlamydia psittaci* is spread by inhalation of the excreta of infected birds.

Disease Pattern: Psittacosis is associated with headache, fever and a pneumonitis-like picture. Respiratory symptoms are prominent. Organs of the reticulo-endothelial system — the lungs, liver and spleen are all infected. The mortality rate may be as high as 20%.

Treatment: Tetracyclines are used in the treatment of psittacosis. They are unable to prevent the carrier state.

**Trachoma-lymphogranuloma venereum complex**

Source and Spread: These chlamydiae are probably spread from man to man by direct contact, or by indirect contact — eye to finger to eye or genitalia to finger to eye.

Disease Pattern: These chlamydiae are responsible for both ocular and genital infections in man. The eye involvement varies from trachoma, a condition leading to blindness, to inclusion conjunctivitis, a condition producing minimal corneal scarring.

Lymphogranuloma venereum is a venereal disease which in the chronic stages is characterized by excessive fibrosis, scarring, stricture formation and lymphatic obstruction. The lymphadenopathy of early lymphogranuloma venereum, unlike that of syphilis, is painful.

Treatment: Sulphonamides are the drugs of choice in the treatment in the trachoma-lymphogranuloma complex.

**VIRUSES**

These agents differ from the other obligate intracellular parasites in certain important respects:

(i) Viruses contain either DNA or RNA, not both. Exceptions to this rule include variola.

(ii) They do not multiply by binary fission.

(iii) They undergo an 'eclipse' phase during infection of the host cell. During this period the virus is indistinguishable from the constituents of the host cell.

(iv) They are completely dependent on the host cell for the machinery and raw materials necessary for life and replication. Viruses possess the blue print — the host supplies the factory.

The infectious viral particle is termed a virion. A virion consists of a central core of nucleic acid, either DNA or RNA, protected by a protein coat, the capsid. Together the protein coat and the nucleic acid constitute the nucleocapsid. Certain viruses have an outer membrane called the envelope surrounding the nucleocapsid. The envelope is partly derived from the host's cell membrane.

Viruses are spread from patients, carriers and from healthy individuals who are in the incubation stage of the disease. Viruses are spread by droplets, by contact, venereally, by congenital spread and by arthropods.
Viruses may be ingested, inhaled or introduced through a lesion in the skin or mucous membranes. As these organisms require the host cell's machinery for their replication, it is necessary for them to enter the cell and establish themselves in an intracellular environment.

Infection of the host cell by the virion starts with the adsorption phase. Contact between the virus and the host cell leads to adsorption, provided the proteins of the virus have a specific affinity for the receptor site on that host cell. The protein coat of the virus is antigenic and stimulates antibody production in the host. Specific antibody can inhibit adsorption of the virus onto the host cell.

Penetration of the virus into the cytoplasm of the host cell is accompanied by the loss of the viral envelope. The virus then undergoes a process of uncoating at the end of which the nucleic acid of the virus is lying free in the host cell.

The viral nucleic acid now directs cell metabolism to produce viral nucleic acid, enzymes and proteins. During this phase the virus is not detectable within the cell. The 'eclipse' phase ends with the assembly of these constituents into new virus particles. Viral assembly may take place in either the nucleus or the cytoplasm of the host cell. The infected cell may lyse and release the virions or these may bud off from the cell cytoplasmic membrane.

In summary, viruses infect host cells in the following sequence:

(i) Adsorption — the virus attaches to the host cell membrane.
(ii) Pinocytosis — the virus moves from outside (extracellular) to the inside (intracellular) of the host cell.
(iii) Uncoating — the virus loses its covering and lies naked as the nucleic acid.
(iv) Eclipse phase — viral replication takes place. The constituents of the virus are not distinguishable from host cell constituents.
(v) Assembly — the viral constituents are assembled into virus particles.

The virus may effect the host cell in a number of ways —

(a) It may cause histological changes in the cell, e.g. giant cells may be formed as in infections with the respiratory syncitial virus; inclusion bodies may be formed in either the nucleus or the cytoplasm, e.g. herpes or poxviruses. These inclusions may be altered host cells or viral particle aggregates.

(b) It may cause physiological changes in the cell, e.g. rubella leads to decreased cell growth and multiplication; papilloma virus leads to increased cell proliferation.

Viral-host cell interaction may fall into one of three possible patterns:

(1) The lytic cycle. When a virulent virus infects a cell it utilizes that cell as a factory for its (the virus') reproduction. The cell bursts or
Figure 22
INFECTION OF AN ANIMAL CELL BY A VIRUS

Virion → Host Cell

Absorption →

Penetration

Uncoating → Replication

Assembly

Host Cell Lysis → Budding of Virus

Viral Release →

Virion capable of infecting a new Host Cell
lyses when replication of the virus is complete. The released viruses are then capable of infecting new cells and repeating the cycle.

(2) A steady state cycle. The virus and host cell live in equilibrium. The virus does not lyse the cell, instead the cell steadily and slowly releases the new viruses produced within its cytoplasm and/or nucleus.

(3) Lysogeny. Lysogeny is an infection of a cell in which the virus does not propagate except in synchrony with the host’s cell chromosomes. Virions are not produced. Host cells may acquire certain new characteristics as a result of this interaction with the viral nucleic acid. Examples of lysogenic conversion amongst bacteria infected by viruses include the ability bestowed on *C. diphtheriae* to produce diphtheria toxin, and upon *Streptococcus pyogenes* to produce erythrogenic toxin.

The virus may leave the host cell by budding off from the host cell or it may be released by lysis of the host cell. The shed virus then spreads and infects other cells. Spread to other cells may be by direct contact, by spread in natural passages, by blood spread or in lymphocytes. Virus may also be released into the environment and infect others.

When a virus infects a new host it undergoes a period of multiplication. This is the incubation period, which is an asymptomatic period starting with the infection of a host and ending with the appearance of the first symptom. The incubation for many of the common viral infections, e.g. measles, mumps, rubella and chicken-pox, varies between one and two or three weeks. Multiplication at the site of the primary focus can lead to spread of the virus in the host — virus may also be shed into the environment. The spread of the virus, often inside macrophages, into lymphatics and via the thoracic duct into the blood stream, leads to the primary viraemia. The primary viraemia is manifest clinically as the prodromal signs or as the minor illness.

In general there are two different kinds of clinical presentations in viral diseases. The first is characterized by a biphasic illness — the minor illness followed by the major illness. Viruses multiply at the site of introduction, i.e. local multiplication occurs; this is followed by systemic spread. During and after the primary viraemia, macrophages of the reticulo-endothelial system phagocytose the viruses. After the minor illness further viral multiplication occurs followed by a secondary viraemia with spread of the virus to target organs. The major illness is the latter phase of the disease. The individual may acquire life-long immunity after his initial illness. The time delay between the minor and major illness in subsequent infections gives the host the opportunity to produce antibodies or re-stimulate his primed cell mediated immunity. The antibody produced neutralises virus during the second viraemic phase and prevents viral infection of the target organs.

The second classical viral disease pattern is that of local and systemic clinical symptoms in the absence of systemic viral spread. In the absence
of viraemia, immunity is short lived. This is especially true of viruses subject to frequent antigenic alteration, e.g. influenza.

Host defences against viral infections involve both humoral and cellular immune mechanisms. Antibodies neutralize the virus and prevent attachment of the virus to the host cell. Viruses which are unable to infect cells are incapable of replication. Neutralized virus, while unable to attach to target cells and cause disease, is more easily phagocytosed by cells of the immune system. The cell mediated immune system produces cytotoxic cells capable of killing the virus. These killer cells play an important role in immunity to viral infections. Primed lymphocytes also produce a humoral substance, interferon, which prevents multiplication of the virus. Interferon production interferes with viral protein synthesis. Interferon is produced early in infection — in fact it precedes antibody production.

Viruses can infect any organ system. Many viruses have specific target organs, e.g. the skin in the case of herpes I and III; mucous membranes in the case of herpes II; the respiratory tract in the case of the influenza viruses and the nervous system in the case of rabies and poliomyelitis. The liver bears the brunt of infection in yellow fever and in both serum and infectious hepatitis. During the primary viraemia many viruses are removed by platelets, lymphocytes and monocytes, and killed; those that are not removed and killed reach their target organs. Measles and rubella both start as infections of the respiratory tract. They both spread systemically and present clinically as skin rashes. Occasionally the portal of entry and the target organ are the same, e.g. influenza.

Viruses may give rise to a clinical syndrome which is characteristic of that virus, e.g. smallpox, or they may present clinically as manifestations of organ dysfunction. Many different viruses may thus give a similar clinical picture when the feature of the disease is that of organ dysfunction, e.g. aseptic meningitis. This broad pattern of organism specific disease is also found amongst bacterial infections.

Slow virus infections

Certain viruses or certain altered viruses are capable of causing slow viral infections. Slow viral disease may follow clinical or subclinical infections. They are characterized by long incubation periods, e.g. years. Different slow virus diseases may be accompanied by one or more of the following features: demyelination, immune complex disease or spongiform degeneration. Subacute sclerosing panencephalitis occurs in people who have all had measles. The measles virus or an altered measles virus is believed to cause the disease in certain individuals. Subacute sclerosing panencephalitis occurs years after the acute attack of measles.

Workers feel that certain agents even smaller than viruses may be incriminated in the aetiology of disease at present classified as slow virus diseases. Amongst these is the agent responsible for Kuru. The membrane bound agent responsible for Kuru is not believed to be antigenic. It causes disease by its persistent multiplication in the host cell. After several years the agent is believed to cause degeneration of the infected host cells. Kuru
was first described as a disease confined to females in a certain tribe. The females in this tribe had the custom of eating their deceased grandmother’s brain. The grandmothers had terminated with Kuru — an illness charac­terized by central nervous system degeneration. Infection of the female members of the tribe occurred by ingestion of the infected brain. The males escaped Kuru as they ingested the tastier muscles of grandmother.

**The classification of viruses**

Viruses can be classified into two large groups on the basis of their nucleic acid. Further differentiation on the presence or absence of an envelope is made. Enveloped viruses are sensitive to ether and bile; viruses not enveloped are resistant to these substances. Virions are sensitive to phenols and ultraviolet light; they are stabilized in salt solutions.

**Table XXIX**

A CLASSIFICATION OF VIRUSES

| DNA VIRUSES | DNA viruses with envelopes |
|-------------|---------------------------|
|             | Double stranded enveloped DNA viruses — |
|             | Herpesviruses |
|             | Poxviruses |
| DNA viruses without an envelope | Double stranded naked DNA viruses — |
|             | Papova virus |
|             | Adenovirus |
|             | Single stranded DNA viruses — |
|             | Parvovirus |

| RNA VIRUSES | RNA viruses with envelopes |
|-------------|---------------------------|
|             | Single stranded enveloped RNA viruses — |
|             | Orthomyxoviruses — influenza |
|             | Paramyxoviruses — parainfluenza |
|             | measles |
|             | mumps |
|             | respiratory syncitial |
|             | Togaviruses (formally classified amongst the arboviruses) |
|             | Rhabdovirus |

| RNA viruses without envelopes | Naked single stranded RNA viruses — |
|------------------------------|-------------------------------------|
|                              | Picorna viruses — (a) Rhinovirus |
|                              | (b) Enterovirus — poliovirus |
|                              | — coxsackievirus |
|                              | — echovirus |

| Naked double stranded RNA viruses — |
| Reovirus |

| Other RNA viruses — |
| Coronaviruses |

**UNCLASSIFIED**

The viruses responsible for infective and serum hepatitis have not yet been fully classified.
THE ARBOVIRUSES
This is a group of viruses grouped together on the basis of their mode of transmission. All the above viruses are transmitted by arthropods. Arboviruses are further classified into the following groups —

- alphaviruses
- flaviviruses
- rhabdoviruses
- orbiviruses
- bunyaviruses

\[ \text{Togaviruses} \]

A CONSIDERATION OF CERTAIN MEDICALLY IMPORTANT VIRUSES

THE DNA VIRUSES

The herpes group of viruses
This group of viruses is characterized by latent infection and clinical recurrences. They are also postulated to play a role in certain malignant diseases in man and animals. There are five members of the herpes family known to cause disease in man.

- Herpes type I — *Herpesvirus hominis*/*herpes labialis*
- Herpes type II — *Herpesvirus genitalis*
- Herpes type III — *Herpesvirus varicella*
- Herpes type IV — Ebstein Barr virus
- Herpes type V — Cytomegalovirus

Herpes type I
Primary infection with herpes I leads to gingivo-stomatitis.

Source and Spread: Man is the source of *Herpesvirus hominis*. The virus is secreted in the saliva and may be spread directly or by contamination of fomites with infected saliva.

Pathogenesis: Herpes type I is adapted to the head and neck region. It infects cells and undergoes a lytic cycle leading to rupture of the cell with vesicle formation. The vesicle ulcerates to leave a painful base. The virus spreads in the same individual by continuity and contiguity.

Recrudescence of herpes labialis is common. The precipitating factor may be stress — emotional or physical, sunlight or a feverish illness. No precipitating factor need be apparent.

Clinical Disease: The common manifestation of herpes I is as a vesicle which breaks down to form a white ulcer with a red rim. Lips are most commonly involved — tongue, gums and conjunctiva may also be involved.

Most individuals (50-98%) are infected with herpes by the age of five years. Recurrences occur in less than half this number; recurrence of herpes conjunctivitis can lead to herpes kerato-conjunctivitis and blindness.

A rare but serious complication of herpes type I infection is herpes encephalitis. This condition usually leads to death or mental retardation. Treatment with nucleic acid analogues is of limited value.
Parasites, Bacteria and Viruses

Herpes type II
Source and Spread: Herpes type II or herpes genitalis is spread by direct contact. The virus is spread by venereal contact. The primary lesion is usually on the penis, the vagina or the cervix.

Clinical Disease: The lesion of herpes genitalis is similar to that of herpes type I. A painful herpes ulcer can lead to dysparunia (painful intercourse) for the afflicted partner.

Infection of the baby as it passes down the birth canal can lead to neonatal herpes. Neonatal herpes varies from mild to severe generalized disease. It is best avoided by caesarean section. Herpes type II may or may not be an aetiological factor in cervical cancer. Those women who present with cervical cancer of a particular histological type have a high correlation rate with frequent sexual intercourse, a variety of partners, trichomoniasis, syphilis and herpes II.

The incidence of herpes genitalis is very low below the age of 10 years. The incidence then increases. The prevalence of the disease varies in different population groups; in certain groups it is as high as 80%. Like herpes I, herpes II recurs at intervals.

Herpes type III
Source and Spread: Chicken-pox is a highly infectious condition that spreads by droplets or contact with the skin lesions. It is usually acquired in childhood.

Disease pattern: The skin is the target organ for varicella. Papules, vesicles, and ulcers covered by scabs occur in crops. The trunk is the area mainly involved.

Chicken-pox, a mild disease in children, must be distinguished from smallpox. Both are spread by droplets, both present with papules, vesicles and scab covered ulcers. The lesions in chicken-pox are mainly on the trunk; those of smallpox have a peripheral distribution. The lesions in chicken-pox are found at different stages of development; those of smallpox are all at the same stage. Chicken-pox is caused by a herpes virus, smallpox by a poxvirus.

Herpes zoster
This is a recrudescent herpes. The virus causes painful vesicles and ulcers in the distribution of the nerve roots. Zoster found on the trunk is attributed to varicella, that on the face to herpes type I and that in the genital region to herpes III.

Zoster occurs in adults. The virus is thought to be latent in the dorsal root ganglion of the nerve supplying the dermatome which develops the lesion. Contact spread of zoster is rare.
**Herpes type IV**

Disease Pattern: Infectious mononucleosis or glandular fever is due to an infection by the Ebstein-Barr virus (EB virus), herpes group IV. This disease presents as a sore throat accompanied by generalized enlargement of the reticulo-endothelial system (spleen and lymph nodes particularly), and a lymphocytosis.

Infectious mononucleosis is an interrupted malignancy of the lymph-glands — lymphocytes infected by the EB virus multiply and are capable of forming cell lines. Lymphocytes not infected by this virus behave as normal cells and are incapable of producing cell lines. A characteristic of malignant cells is their ability to form cell lines.

The EB virus may play an aetiological role in the evolution of a tumour of the jaw. Burkitts lymphoma, and also nasopharyngeal carcinoma, are primarily diseases found in African children.

**Herpes type V**

Cytomegalovirus or herpes type V is a virus well adapted to man. Most infections are subclinical. Once infected, man probably carries the latent virus for life.

Cytomegalovirus can cause severe disease in the foetus. A mother who acquires the disease during pregnancy can spread the virus transplacentally to her unborn child. Infection during the third trimester leads to infection of all the foetus’s parenchymal organs except muscle and bone. The disease can lead to death of the infected foetus, those babies that survive have hepatic, haematological and central nervous system defects.

**Immunity and the herpes group of viruses**

Herpes types I, III and V are especially of interest in patients who are subject to immunosuppression. Immunosuppressed patients can develop fatal generalized disease due to recrudescence of latent infections by these viruses.

**The poxviruses**

The target organ in infections with the poxvirus is the skin. Different poxviruses infect man and animals. Variola is the poxvirus responsible for smallpox. In 1967 smallpox was endemic in 30 communities. The WHO undertook an extensive eradication campaign and in 1975 announced the global eradication of this disease. In late 1976 further cases of smallpox were diagnosed in Somalia. This disease can be fatal and travellers require vaccination against smallpox on moving from one country to another. The vaccine used to protect against smallpox consists of a live attenuated vaccinia virus. The vaccinia and variola viruses have antigenic similarities.

**The adenoviruses**

Adenoviruses preferentially infect mucous membrane surfaces. They spread from person to person; the incidence of adenovirus infection increases rapidly in susceptible populations when overcrowding is present.
Adenovirus infection leads to acute upper and lower respiratory tract infection. Infection with one of the adenovirus strains leads to a whooping cough-like syndrome. Adenovirus is also a cause of conjunctivitis.

Adenovirus may persist for years in lymphoid tissue.

**The papovavirus group**

Papovaviruses usually cause disease in animals. One member of the group causes warts in man.

**The parvoviruses**

Members of this group are believed to cause diarrhoea in man.

**THE RNA VIRUSES**

**The picornaviruses**

Amongst this group are two subgroups important to man. These are:

(a) The enteroviruses
(b) The rhinoviruses

The rhinovirus group are the viruses most commonly implicated as the cause of the common cold. Spread is by droplet infection.

**The enteroviruses**

Spread of the enteroviruses is faecal-oral. Good hygiene may therefore play an important role in decreasing their spread. Members of the enterovirus group include —

The poliovirus
The coxsachieviruses

these cause important diseases.

The echovirus is responsible for aseptic meningitis. Echovirus may also cause a rash which may or may not be accompanied by fever. The echovirus has been incriminated as a cause of the common cold.

Enterovirus 70 causes acute haemorrhage conjunctivitis.

Hepatitis A, the virus causing infective hepatitis, is probably a picornavirus.

**The poliovirus**

The poliovirus is spread by the faecal-oral route. Ingestion of the virus leads to multiplication of the virus in the lymphoid tissue of the throat and intestinal tract.

Clinically, most infections with the poliovirus are sub-clinical. Overt infections may present as a minor illness with a sore throat, fever, anorexia and headache. These symptoms last a few days. Abortive polio stops after the minor illness, paralytic polio proceeds to the major illness where muscle pain and paralysis become major symptoms. The poliovirus destroys the motor neurones.

Poliovirus may occasionally be detected in the patient’s stool for up to six months after the onset of clinical symptoms. The most infectious period
is, however, during the minor illness. Virus is also present in the patient's throat during the early stages of the disease. By the time the child presents with paralysis it is difficult to isolate the virus.

Polio can be successfully prevented by adequate immunization. The live attenuated virus used in the polio vaccine can be differentiated from the wild strain in the laboratory.

The coxsackieviruses
Coxsackieviruses are divided into two groups. A number of different clinical syndromes have been attributed to these viruses.

Coxsackie A
This viral infection presents with fever, rash and/or meningoencephalitis. One or more of these symptoms may be present in the patient simultaneously.

Coxsackie B
This virus may present a similar clinical picture to coxsackie A. Coxsackie B is also associated with pleurodynia (severe pleuritic pain) in the adult. It may be the cause of fatal myocarditis in the neonate.

Coxsackie B infections are especially common amongst children. Children are not permitted to visit mothers in maternity hospitals. Coxsackie B is one of the reasons for this restriction. Outbreaks of coxsackie B myocarditis in maternity hospitals have led to the closing of that hospital.

The arenaviruses
Included in the arenavirus group is Lassa fever virus. Lassa fever is an often fatal disease spread by this highly contagious virus. In the absence of extreme precautions in the examination and nursing of these patients, infection of the nursing and medical attendants is a serious hazard. Gloves, masks, complete change of clothing, caps and goggles are recommended in the safe handling of Lassa fever cases.

Slow viruses are also grouped amongst the arenaviruses.

The orthomyxoviruses

Influenzavirus
This virus has three different types — influenzavirus A, B and C. Influenza type A is responsible for epidemics, type B is endemic. All the influenza viruses are subject to frequent antigenic alteration. It is, therefore, possible to have many attacks of influenza in one lifetime. Influenza may herald the start of a terminal illness for the elderly cardiac or respiratory cripple. Every year the employer will lose a substantial number of working hours due to staff illness caused by the influenzavirus. Influenza is thus an economic hazard in the healthy individual. It may sound the death knell for the elderly.

The paramyxoviruses

Parainfluenza
These viruses infect the respiratory tract. There are four different types —
type I causes lower respiratory disease; type II causes upper respiratory disease and type III causes both. Type IV does not cause human disease. Laryngo-tracheo bronchitis and croup are important diseases caused by the parainfluenza viruses.

Respiratory syncitial virus
These paramyxoviruses are responsible for respiratory diseases during childhood.

Rubeolavirus
Measles starts as a catarrhal illness. During this stage the virus is rapidly spread by droplets. In a susceptible population one individual with measles may infect four others. Measles is more infectious than influenza.

Measles is usually diagnosed when the fever, cough and runny nose are improving and the maculopapular rash appears. Secondary bacterial infection of the respiratory tract is a problem. Bacterial complications in measles include broncho-pneumonia, otitis media, chronic sinusitis and blindness. The incidence of bacterial complications of measles increases in direct proportion to the degree of malnutrition, and poor socio-economic circumstances of the victims.

Measles may be complicated by encephalitis in any population group. Measles or an altered measles virus appears responsible for a slow virus disease.

Paramyxovirus parotidis — the mumps virus
Mumps, like measles, is a common contagious disease of childhood. Spread is by droplet infection. The target organs in mumps are the salivary glands, notably the parotid, the pancreas and the gonads. Adult males may become sterile after an attack of mumps orchitis.

Newcastle Disease
This is a disease of fowls caused by a RNA virus. Men working with sick chickens can develop Newcastle conjunctivitis.

The togaviruses
Rubella
The virus responsible for German measles is included in this group. Spread of rubella is by droplets from the respiratory tract. Infection leads to the development of a rash and occipital lymphadenopathy. German measles in the mature individual is a mild disease. Foetal infection with rubella-virus may lead to the congenital rubella syndrome. When expectant mothers are infected during the first or even in the second trimester of pregnancy the virus spreads transplacentally and infects the foetus. The virus infects the cells of the developing foetus and slows down cell multiplication. Infected foetuses may be born with a variety of different clinical symptoms, e.g. blindness, deafness, heart defects, etc.

Many arboviruses are grouped amongst the togaviruses.
Coronaviruses
These viruses cause acute upper respiratory tract infections.

Rhabdoviruses
Marburg and rabies viruses both fall into this category. They are animal viruses which may cause fatal disease in man.

Rabies virus is spread in the saliva of infected animals. Rabies is spread by meercats, dogs and many other wild animals. All these animals are sick and often die. The natural host of rabies may be the bat. Rabies is not known to spread from man to man. It causes spasm of the neck and throat muscles and this has earned it the name of hydrophobia. Rabies effects the nervous system — excitation and paralysis precede death.

Reovirus group
These viruses may cause diarrhoea in man.

Arboviruses
The arboviruses are grouped together on the basis of their mode of transmission. All the arboviruses are transmitted by arthropods. The arthropods commonly incriminated are ticks and mosquitoes. Arboviruses often have a wide range of possible vertebrate hosts. The distribution of arboviruses depends on the presence of the arthropod and the presence of the vertebrate host.

Important diseases amongst this group are yellow fever, dengue, chickungunye, rift valley fever and west nile. Arboviruses are also responsible for a number of different encephalitis syndromes.

Unclassified
Hepatitis B
This virus is responsible for serum hepatitis. Australia antigen, the Dane particle and long incubation hepatitis virus, are all different names for this virus.

The virus is spread in the blood or in blood products, in saliva and in seminal fluid. It may give rise to an acute disease which may result in recovery or lead to chronic liver disease. Sub-clinical disease followed by a carrier state is common in certain population groups, e.g. the rural African.

Rotavirus
This virus is a cause of gastro-enteritis in babies.

TREATMENT
Viral infections are widespread. The treatment of viral infections is for the most part symptomatic. Specific therapy is difficult as the action of the drug must be directed against the viral nucleic acid. Viral and host nucleic acid are structurally composed of very similar building blocks. Any agent used to specifically treat a viral infection will have toxic side
effects. Only individuals with critical viral diseases are thus considered as candidates for specific therapy. Herpes encephalitis, a condition, which when not fatal leaves the victim mentally retarded, is treated with a drug which interferes with nucleic acid metabolism. Hyper-immune gamma globulin is occasionally used but this must be administered early in the diseases before the virus has attached to its target organ.

Non-specific therapy, such as adequate nutrition, treatment of acute respiratory obstruction with tracheostomy or intubation are all important adjuncts in the treatment of viral diseases. Bed rest and anti-pyretics are often the only treatments available. Prevention and treatment of secondary bacterial infections, especially secondary bacterial pneumonias, may be life saving.