but when that meat is minced and made into sausages, the salmonellae are then present in the centre of the sausages and the heat of gentle frying may not penetrate enough to kill the organisms. It is of no avail to wrap sausages in cellophane if the meat they contain is already contaminated with germs.

The same factors affect the wholesomeness of pies. The mincemeat may be infected, and heat penetration, especially if there are cool spots in the oven, may not be enough to sterilize it. In one pie factory there was a magnificent oven which incorporated a cooling chamber to cool the cooked pies rapidly, an excellent hygienic procedure, but after the pies were taken out, agar jelly was injected into them, the 'goodness' of the pie, but the injecting apparatus could not possibly be sterilized, so that the benefit of the expensive oven was largely lost.

One of the main dangers in food shops is where raw and cooked food are handled on the same counter. Salmonellae on the surface of the raw meat may easily be transferred to the cooked meat on hands, knives, weighing machines, slicing machines, or or from the surface of the counter itself. The organisms conveyed to the cooked meat would then be able to multiply readily and as no further cooking is involved, the person who eats it may get a heavy dose of salmonellae. Poultry should not be handled near cooked food, and should certainly not be eviscerated in the same room, for then the danger of cross-contamination is very high. A wooden table can be a dangerous piece of equipment in a food-shop, for it is usually full of cracks and crevices, and salmonellae and other organisms can settle down in these cracks with an ample supply of food from dust and meat particles. Wood should be used only for chopping blocks, and these blocks should be planed down frequently.

There are many hazards between the farm and the dining table. Most of these can be avoided by awareness of the dangers and care in avoiding them.

Toxoplasmosis

Dr H. Williams, M.D. (*Consultant in bacteriology*)

The *toxoplasma* is biologically quite different from any of the other pathogenic organisms being discussed this afternoon. It is a parasitic protozoon, and such organisms necessarily live out their life cycle in very close association with a host. Protozoa are at once biologically more complex than bacteria or viruses; the process of evolution having produced parasites which are very well adapted to the environment of their normal hosts. And the better the adaptation, the less often will they give rise to florid disease in the host. This is the picture we find in toxoplasmosis. Many animals including man are affected but the incidence of disease is relatively low. However, it does occur both in man and animals; the unravelling and recognition of the processes involved has been slow, and probably remains unfinished.

Toxoplasma is a ubiquitous parasite of great versatility. It appears to be of world-wide distribution. Its success as a parasite is in some measure due to its ability to live and multiply within the nucleated cells of so many different species. Birds, as well as man and a great variety of other animals, are all potential hosts for this parasite and all occasionally fall victim to it.

The parasite exists in two forms, proliferative (trophozoite) and cystic. The trophozoite is a small crescent-shaped organism about six microns by two microns, pointed at one end and blunt at the other. It has a highly developed internal structure, and can

bore its way into a suitable host cell where it multiplies repeatedly until the cell is distended with organisms. When the cell ruptures the parasites are set free to repeat the cycle. Thus focal lesions are produced and a parasitaemia ensues. At this stage of generalized infection many organs may be involved, including brain, nerve tissue, lungs, liver, spleen, heart and lymph glands. The process continues until either the host dies or, as is much the more usual outcome, a state of immunity develops, antibodies appear, the parasitaemia lessens, the intracellular trophozoites multiply less frequently and become enclosed in a vacuole-like structure—the beginning of encystment. Such cysts may contain thousands of organisms packed within a resilient cell wall. They occur most abundantly in brain and nerve tissue but are found in lung, heart, liver and spleen, where they can remain for long periods, perhaps indefinitely. At times however, possibly when for some reason or another the host's resistance wanes, the cyst ruptures and parasitaemia by the trophozoite form recurs.

There is great variation in virulence among different strains as judged by their behaviour in experimental animals. The virulent strains multiply rapidly and quickly outstrip the defences of the host. Thus a great variety of clinical syndromes may ensue, varying from a relatively mild, comparatively symptomless state to a fulminating parasitaemia in which encephalitis, hepatitis or myositis are the dominant features. The developing foetus is specially at risk, and congenital toxoplasmosis is now one of the best defined entities in this infection.

Most of the manifestations of toxoplasma infection are treated in hospital, but the family doctor may be concerned with toxoplasmic lymphadenopathy, which is responsible for about six per cent of otherwise undiagnosed glandular enlargement. The range of disability encountered is wide—from a child with enlarged glands feeling generally miserable to one with a febrile illness causing severe systemic upset in which jaundice, pneumonitis or encephalitis may occur. The former is the more common, and if a high or rising dye test titre can be shown, a diagnosis may be made which will reassure many parents and save them much mental anguish—for these children are frequently suspected of having some desperate disease. Uncomplicated toxoplasmic lymphadenopathy is never fatal and no therapy is indicated. Where necessary, treatment by pyrimethamine and sulphonamides is best carried out in hospital where side effects such as anaemia, leucopaenia, granulocytopaenia and thrombocytopaenia can more easily be monitored.

There is still a great deal to learn about toxoplasmosis, and epidemiology would be greatly assisted if practitioners keep the disease in mind and seek laboratory confirmation. They would thereby make a useful contribution towards the elucidation of this interesting and sometimes baffling disease. The parasite was probably first seen by Laveran, at the beginning of the century. The description he gave, however, was insufficient to be certain that he was indeed seeing toxoplasma. In 1908, Nicolle and Manceaux observed within the mononuclear cells of the spleen and liver of a North African rodent—the gondii—a parasite very closely resembling *Leishmania*, but with differences enough to make them suggest that it was not *Leishmania*, and they proposed the name *Toxoplasma gondii*. The following year, Splendore observed a similar organism which he called *Toxoplasma cuniculi* during an outbreak among rabbits in Brazil. Up to this point the parasite was primarily of interest to biologists and those concerned with disease in animals.

In 1923 a Czech ophthalmologist named Janku described a parasite in the retina of a baby; however, this paper was not well known until a German translation was made in 1959. The first real impact on human medicine was made in 1937 when Wolf and Cowan showed that toxoplasma was associated with a congenital granulomatous encephalitis. Soon thereafter the generalized and fatal form of the disease was noted by Pinkerton and Weinman in Peru. In 1950, Gard and Magnusson described the glandular

form of the disease and, during the ensuing years, various disease syndromes have been associated with this parasite, some of which are still the subject of dispute.

If a virulent toxoplasma strain is inoculated intraperitoneally into mice, within three to five days, depending on the age and size of the animals, they sicken, lie huddled together, and die. None survive the inoculation of virulent strains. At the stage of early sickening, there is a copious peritoneal exudate which is very rich in toxoplasma. If the strain is less virulent the mouse survives, perhaps indefinitely, and apparently without disease. However, if such an animal is killed and a search made throughout different tissues (especially brain) evidence should be found of the other form of the parasite—the cyst, in which large numbers of toxoplasma are packed close together within a cyst wall.

Isolation of the parasite from human material involves inoculating the suitably prepared suspect specimen into mice, the chorioallantoic membrane of eggs or tissue cultures. Sometimes it is possible to see the parasites in tissue sections, but they are sparse and difficult to find. Failing the isolation of the parasites for diagnosis, one falls back on immunological phenomena—the search for antibodies, or hypersensitivity to products of the parasite.

Various tests can be done on serum to detect antibodies to toxoplasma. The dye test is the most widely employed. This test depends on the fact that antibody in the presence of a labile substance found in fresh normal serum alters the parasites in such a way that they will not take up a methylene-blue stain. Complement fixation can be carried out using infected peritoneal exudate of mice or cotton rats as antigen and gives results similar to the dye test. The haemagglutination test also gives results similar to these two tests. Fluorescence inhibition is newer, and appears to be a sensitive test for toxoplasma antibodies, as is the direct agglutination test, where a peritoneal exudate of infected cotton rats must be used as antigen. The precipitin and skin tests are somewhat insensitive; the latter has been used mainly for epidemiological surveys, rather than individual diagnosis. All of these tests have some drawbacks. How does man become infected? It is easy to understand how meat eaters may be infected but less easy to understand the heavy infection of herbivores. The outcome of congential infection with toxoplasma may vary—the end result depending on the stage of development of the foetus at which invasion by the parasite took place. If late on in pregnancy there is systemic involvement, and the results of this in the newborn are rash, and hepatic and splenic enlargement. If, however, invasion occurs early in pregnancy the CNS takes the brunt of the attack and the child may be born with internal hydrocephalus, choroidoretinitis, convulsions and cerebral calcifications—the so-called Sabin's tetrad, though not all these signs may be present.

In postnatal infection lymphadenopathy is the commonest effect, but occasionally the generalized form occurs, when encephalitis, pneumonitis, myocarditis, or hepatitis may ensue.

Some epidemiological observations may help to show the widespread nature of infection with this parasite. In general, the hotter and wetter areas of the world are most infected.

The numbers are rather small but probably even within this area (North of Scotland) considerable differences in incidence occur, as confirmed by serum tests. Toxoplasma is a ubiquitous parasite, sheep are often affected and it is undoubtedly a cause of abortion in ewes. In some areas of the world, e.g. in New Zealand and Australia this is economically a serious disease. In this country outbreaks of abortion in sheep do occur.

Carnivores are specially at risk since they are liable to ingest the cysts present in the flesh they feed on. This can be shown in mink, many of which have high titres, and toxoplasma can readily be recovered from the brains of these animals.