References


*Yersinia enterocolitica* epidemiology and antibiotic susceptibility

*Yersinia enterocolitica* was recognized as a distinct species and named by Frederiksen in 1964. It is possible that the organism was recognized as a distinct entity and human pathogen at least 40 years ago (Schleifstein & Coleman, 1939), although the organism they described was pathogenic for small laboratory animals which *Y. enterocolitica* is not. *Y. enterocolitica* has now been classified as a member of the *Enterobacteriaceae*. Probably the greatest interest in the species has been in Scandinavia where infection with the organism is common, 200 probable cases being recognized by Winblad and his
colleagues in Malmö in the period 1964–68. Not only was the organism isolated from cases but a number of patients developed agglutinating antibodies, some being recognized because of the cross-reaction between serotype 9 and Brucellae (Ahvonen, Jansson & Aho, 1969)—brucellosis being virtually non-existent in Sweden and Finland. Y. enterocolitica is a Gram-negative rod which will grow on ordinary culture media at 37°C, but will only grow well on media containing bile salts if the cultures are incubated at 22–29°C at which temperature colonies are visible after 24 h incubation. The organism is motile at these low temperatures, but not at 36°C. Y. enterocolitica is commonly isolated from the stools of cases, but may be isolated from blood of septicaemic cases and from abscesses. Both serological and biotyping schemes have been developed (Winblad, 1967; Wauters, Le Minor & Chalon, 1971; Wauters, Le Minor, Chalon & Lassen, 1972; Knapp & Thal, 1973; Nilén, 1969). Serotypes are recognized by their ‘O’ antigens and types 3 and 9 are common in Europe, but in the U.S.A. multiple serotypes occur (Morris & Feeley, 1976). Humans commonly develop antibodies in the course of infection and these are recognized by agglutination tests.

The world-wide distribution of published cases of infection is interesting. Winblad (1977) listed these as:

- >1000: Sweden, Finland and Hungary
- 500–1000: Belgium and Czechoslovakia
- 100–500 cases: Japan, Canada and Rumania
- 50–100 cases: U.S.A., Norway, Denmark and France
- 10–50 cases: Australia, Switzerland, South Africa, Zaire, West Germany and Holland
- <10 cases: Poland, Spain, United Kingdom, Greece and U.S.S.R.

Infection has also been reported from New Zealand. Although the frequency with which an organism is recognized may often be influenced by the activity of interested laboratory workers, the rarity of isolation of Y. enterocolitica in Britain is not due to inability to grow the organism or for want of looking as surveys have been carried out by several laboratories with little or no success (Fallon, 1978). The reason for its rarity is unknown. The organism is commonly associated with abdominal disease, appendicitis (real or suspected) mesenteric adenitis and terminal ileitis. Hence, Niléhn & Sjöström (1967) found that eight of 10 patients with terminal ileitis yielded the organism from stools as did 5–6% of cases of suspected appendicitis and 3–8% of appendectomy cases, but not 974 controls with no abdominal disease.

In two series of Y. enterocolitica enteritis reported from Japan (Zen-Yoji, Maruyama, Sakai, Kimura, Mizuno & Momose, 1973) and the U.S.A. (Gutman, Quan, Ottesen, Noce & Katz, 1973) cases developed fever, diarrhoea and abdominal pain. Headache and vomiting were not common. Food poisoning outbreaks may occur and have been reported from a number of countries. Hence in New Zealand in 1975 two outbreaks associated with rice occurred at the same establishment. The incubation period was 16 to 42 h indicating an infective rather than a toxic process. Symptoms varied but the more severe cases complained of vomiting, diarrhoea, abdominal pain, fever and headache. Another outbreak occurred in the U.S.A. in 1976 where the vector appeared to be contaminated chocolate milk (Black et al., 1978). Again the symptoms were of abdominal pain and fever resulting in 36 children being admitted to hospital. No less than 16 of the 36 children hospitalized in the course of the outbreak underwent appendicectomy and 10 of the 16 were noted, at operation, to have enlarged mesenteric lymph nodes. It is possible that a food handler may have been responsible for this outbreak as may have been the case in an outbreak in Czechoslovakia (Olsovsky, Olsaková, Chobot & Sviridov, 1975). Food or water-borne community outbreaks were reported from Japan in 1973 involving hundreds of children (Asakawa, et al., 1973).

Arthritis may develop in some cases (Ahvonen, Sievers & Aho, 1969). Winblad (1975) reported 74 cases occurring after enteritis. All had agglutinin titres of ≥320. The illness is not a septic arthritis although Y. enterocolitica may give rise to a septicaemic illness (Rabson, Hallett & Koornhof, 1975; Chessum, Frengley, Flock & Mair, 1971) as well as intra-abdominal sepsis (Rabson, Koornhof, Notman & Maxwell, 1972). Another post-infectious sequel of Y. enterocolitica infection is erythema nodosum (Hannuksela & Ahvonen, 1969). The eruption lasts for 9 to 27 days. Although infection seems, from the epidemiology of both food poisoning and nosocomial infections (Toivanen, Toivanen, Olkkonen & Aantaa, 1973) to be transmitted from human to human, infection with Y. enterocolitica is by
no means confined to man. The organism has been isolated from the alimentary tract of pigs, chinchillas, dogs and hares (Becht, 1962; Dickinson & Moquot, 1961). The possibility of yet another animal to man infection therefore exists although how important this is is unknown.

Although most cases of yersinia infection do well, the fact that occasionally septicaemia, intra-abdominal sepsis or terminal ileitis may occur points to the need for antibiotic therapy in some cases. *Y. enterocolitica* is sensitive to a wide range of antibiotics. Hence, Niléhn (1967) found all of 28 strains to be sensitive (on disc testing) to streptomycin, tetracycline, chloramphenicol, colistin and sulphonamide, but resistant to benzyl penicillin and erythromycin. Most strains were also resistant to ampicillin. The 36 strains isolated from patients in the food poisoning outbreak in the U.S.A. (Black et al., 1978) had a similar sensitivity pattern and in addition were sensitive to cotrimoxazole and gentamicin. Similar patterns have been reported by other workers, the sensitivity to ampicillin varying from strain to strain.

Severe clinical manifestations occur in children and may lead to laparotomy and appendicectomy before the results of culture could be available. Nevertheless, in enteritis and ileitis the organism should be sought as a history of preceding diarrhoea and abdominal pain in patients with arthritis or erythema nodosum. In this way more cases of yersinia infection may be revealed than occur points to the need for antibiotic therapy in some cases. *Y. enterocolitica* is sensitive to ampicillin with special reference to bacterial diagnosis and occurrence in human acute enteric disease. *Acta Pathologica et Microbiologica Scandinavica* 69: 83–91 (1967).


Leading articles

Treating toxoplasmosis

Toxoplasmosis occurs all over the world and is the commonest protozoal infection in England, where 30% of adults have serum antibodies to the parasite (Beattie, 1957). Recently-acquired infection is diagnosed serologically by a significant rise in titre in the Sabin–Feldman dye test, or by the detection of specific IgM using immunofluorescence. While most infections are subclinical some become manifest as painless enlargement of lymph nodes or as 'glandular fever' syndromes. Illness of this nature may be prolonged but are nearly always self-limiting.

Much more serious disease may result when the organism attacks either an immunodeficient individual or the unborn baby. CNS toxoplasmosis may arise in patients suffering from lymphoreticular malignancy or connective tissue disorders, particularly if they have received corticosteroids or cytotoxics. In such patients meningo-encephalitis or focal neurological signs may be wrongly attributed to the primary disease (Townsend et al., 1978): the heart, skeletal muscles and lungs may also be involved. Rarely, toxoplasmosis can also cause severe systemic disease in previously healthy subjects.

Maternal toxoplasmosis is not often diagnosed during pregnancy but can lead to transplacental infection and, less frequently, to congenital disease in the foetus. The overall likelihood of foetal death or severe congenital abnormality is low but is greatest when a woman becomes infected between the second and sixth month of pregnancy (Desmonts & Couvreur, 1974). Choroido-retinitis presenting later in life usually has its origins in undetected congenital infection.

For many years pyrimethamine and sulphonamides (usually triple sulphonamides, sulphadimidine or sulphadiazine) have been widely used for the treatment of toxoplasmosis. These agents act synergistically against experimental toxoplasmosis in mice, and also in infected tissue culture systems (Eyles & Coleman, 1953; Nguyen, Stadtsbaeder & Horvat, 1977). Although active against trophozoites they have no effect on tissue cysts (Summers, 1953). A once-daily regime of pyrimethamine-sulphonamide combinations has been employed successfully in all forms of toxoplasmosis including CNS infection and disease in the compromised host (Townsend et al., 1975, Ruskin & Remington, 1975). When used for choroido-retinitis systemic corticosteroids are usually added, especially if vision is threatened (O’Connor, 1974). The main disadvantage of this antimicrobial combination is the inhibitory effect of pyrimethamine on human folate metabolism with the subsequent risk of bone marrow depression: and since patients usually have to be treated for at least four weeks a close watch must be kept on the peripheral blood count. In the event of leucopenia (<1000 neutrophils/mm3) or a fall in platelets (<100,000/mm3) the drugs must be stopped and intra-muscular folinic acid substituted. Because of this antifolate activity pyrimethamine-sulphonamide combinations are also potentially teratogenic. Nevertheless their use in maternal toxoplasmosis reduces the risk of transplacental infection (Kräubig, 1966).

The macrolide antibiotic spiramycin is a less toxic alternative agent which has been widely used in continental Europe for some twenty years. It is active against experimental toxoplasmosis, reaches high levels in many