THE PROBLEMS OF PATHOGENICITY OF *ESCHERICHIA COLI* IN ANIMALS AND MAN*

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ESCHERICHIA COLI is normally pathogenic only in the young animal. Predisposing factors and epidemiological features in the various species show a marked similarity.

Researchers in the animal field, Jensen, Christiansen, Theobald, Smith and Lovell, all working on calf scours were the first to suspect the pathogenicity of *E. coli* (17). Their work was hampered by the confusion and difficulties in serological classification. In 1942–43, Kauffmann, later Kauffmann and Knipschildt and then Vahlne clarified the antigenic nature of *E. coli* (8, 5, 17) recognizing heat-resistant "O" or somatic antigens; more or less thermolabile "K" surface antigens which are further subdivided into "A", "B" and "L"; and, flagellar or "H" antigens. There are 142 known "O" antigens, 86 "K" antigens and 40 "H" antigens.

Since the description by Bray in 1945 of the so-called *Bacterium coli neapolitanum* (0111:B4), attention has been focused on the possible pathogenic role of specific serotypes of *E. coli* (3). At least 16 of the existing 142 "O" serotypes have so far been associated with infantile gastro-enteritis and other diseases in humans. The distribution of almost all pathogenic serotypes seems to be worldwide. Significantly, all "O" antigens of human enteropathogenic serotypes have also been isolated from animals and all but three, 0125, 0126 and 0127, have also been associated with disease in animals. For example, the same "O" antigen might occur in infantile gastro-enteritis, calf scours and bovine mastitis in combination with different "K" or "H" antigens. These strains should not be considered identical. However, the frequent isolation of identical "O" antigens from a variety of pathologic conditions is of a certain interest. *E. coli* bovine mastitis has been detected more frequently in recent years. Other conditions reported are meningitis, arthritis and serositis of sheep and omphalitis, coli granulomatosis and eye lesions in chickens. A secondary *E. coli* infection is usually associated with chronic respiratory disease. Many of the antigenic components of animal pathogenic strains were encountered in man. Three exceptions are strains 0138:B81, 0139:B82 and 0141:B85 or "B?" or "L?". These three serotypes have been isolated only from pigs and constitute the so-called "edema–disease–serotypes" (15).

There are at present about twenty strains associated with calf scours and about twelve strains associated with bovine mastitis. *E. coli* is by far the most frequently incriminated organism responsible for mortality in baby pigs (16). Edema disease of swine is an interesting example of what appears to be a true

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enterotoxemia. In this condition, three serotypes are isolated with a high frequency and in pure culture from the intestine, but not from other organs. Yet the affected animals do not suffer from an acute or severe enteric illness; the symptoms are those of a toxemia, primarily affecting the central nervous system, and rapid death. The condition can be reproduced by intravenous injection of intestinal supernatant. In poultry *E. coli* is such a common postmortem tissue invader that its pathogenic role is hard to assess. The isolation of similar serotypes from cases of omphalitis is probably significant. Are we to conclude that *E. coli* infections are a good example of a zoonosis (animal disease transmissible to man, *i.e.* rabies)? Certainly not. Similar serotypes and antigenic components occur in man and animals, but cross infection has not been established.

The search for a specific toxin was made on the basis of our knowledge of the biochemistry of Gram negative organisms, particularly the *Enterobacteriaceae*. The early workers, Boivin and Mesrobeanu (2), Raistrick and Topley (14), and Morgan and Partridge (13) have all concentrated their investigations on the phospholipid-polysaccharide complex also known as "antigen complet" or "undegraded polysaccharide". Recently Harvey and Carne (7) have prepared "antigen complet" from pathogenic and non-pathogenic serotypes of *E. coli*. Both products were highly toxic to mice and no difference could be found in toxicity when the pathogenic and non-pathogenic strains were compared. The results of our experiments on edema disease of swine indicate that there is no significant difference in the toxicity of "antigen complet" whether derived from pathogenic, "edema disease" serotypes, non-pathogenic *E. coli* or *Salmonella typhimurium*. The toxicity of the phospholipid-polysaccharide extracts again seems to be unrelated to serotype or species pathogenicity.

Miles (12) defined pathogenicity as "an index of behaviour of a microbe in the tissues of a given host in a certain agreed or defined state of health". The extraneous factors contributing to the state of health have been greatly stressed in the past. Some of these factors are weather, climate, feeding, management and hygienic practices and deficiencies. The close association of susceptible individuals, infants or young animals is probably of particular significance. Infants in hospitals or institutions, or young calves in large groups are invariably exposed to *E. coli* infections. Age is probably the most important single factor determining the susceptibility of the host. Calves, lambs, foals, and piglets are born without any antibody protection. It has been demonstrated (6, 10) that survival of newborn calves depends almost entirely on maternal transmission of immunity through colostrum. This transmission must occur within hours following birth if it is to be effective. The protection is specific and limited to the dam's immunologic history.

The significance of selective occurrence of pathogenic serotypes of *E. coli* is not yet clear. As Lovell (11) pointed out, "the dead cells and endotoxins of many of the Salmonella are no more toxic than those of *E. coli*; toxic chemical extracts of *E. coli* show no difference whether they are prepared from virulent or avirulent strains. It is apparently the ability to survive and to multiply in the animal's tissues which constitutes the important attribute of the virulence of a strain." The population that Coliforms or other intestinal bacteria can attain is remarkably high (1). It is possible that very slight differences in capacity to

multiply or survive are the reason for the isolation, often in pure culture, of certain serotypes in disease.

Little is yet known about the competitive growth of enteric bacteria. Dunne *et al.* (4) consider that "the present day concepts of mixed infections, synergisms, animal viruses and phage systems suggest innumerable possibilities for combination of etiological agents as the cause of enteritis of the newborn." This multiplicity of individual factors or their combination might explain the yearly or periodic fluctuation in the incidence of serotypes associated with disease. Such fluctuations have been observed in individual persons (9) and in epidemics attributed to enteropathogenic *E. coli* (11). It is conceivable that lysogenic strains will shift the balance from one serotype to another. In contrast to Salmonellosis, the source of infection for many serotypes of *E. coli* is always present in most environments. A synthesis of the present-day concepts of enteric diseases might lead to a better understanding of their etiology and epidemiology.

There is no doubt that detailed investigations of enteric infections such as the interplay between the host, the bacterium, and perhaps the bacterial virus would add much to our present meagre knowledge of this field.

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