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Escherichia coli – an overview

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INTRODUCTION

The isolation and description of *Bacillus coli commune* by Escherich a hundred years ago marked the start of a series of scientific investigations which have led to some of the most important discoveries in microbial pathogenicity and genetics that have been made since that time. It is not difficult to find the reasons why so much effort has been concentrated on this organism. *Escherichia coli* is present in the gut of all warm-blooded animals generally forming the predominant aerobic flora; it is of medical and veterinary importance being responsible for a variety of infections in the human and animal populations and it has provided a useful tool for geneticists.

Much of the early work was concerned with the differentiation of *E. coli* from organisms then recognized to act as pathogens in the bowel and it was not until strains could be defined and characterized that work on the epidemiology and pathogenicity of *E. coli* could proceed. A major advance was made with Kauffman's studies in the 1940s on serotyping and since that time some of the properties associated with pathogenicity have been defined. There is now a considerable body of knowledge of the epidemiology of this organism and of its role as a pathogen.

CHARACTERIZATION OF *ESCHERICHIA COLI*

Escherichia coli is the only member of the genus *Escherichia* and its biochemical properties are now well defined. Subdivision of the species for epidemiological purposes or to assess pathogenicity is performed by means of a serological typing system involving O, K and H antigens. This typing system is complex; a large number of antigens are involved and cross-reactions between antisera and heterologous organisms regularly occur. For these reasons full *E. coli* serotyping is performed in only a small number of laboratories. The typing system, although laborious and time consuming, gives a high level of discrimination and shows good reproducibility. Typability is good with European strains from human infection but falls with strains from other sources. Recently a fimbrial typing system has also been introduced. Because the serological typing scheme for *E. coli* is so laborious other typing methods have been attempted. These include phage, colicin and chemo-typing. None have been widely used.

Serotyping is most commonly performed in a attempt to assess pathogenicity in infants with diarrhoeal disease, although it may also be used to assess pathogenicity in other sites, to distinguish between re-infection and recrudescence of infection, particularly in the urinary tract, and for epidemiological studies.

E. coli may also be characterized by a number of properties including production of enterotoxins and haemolysin and by ability to adhere and invade. Such characteristics have been particularly studied in relationship to the pathogenesis of infection in man and animals.

DISTRIBUTION AND METHODS OF SPREAD

Environment

The distribution of *E. coli* in the environment is determined by its presence in the bowel of man and animals, whilst its isolation from water supplies is used as an indicator of recent faecal pollution and of the likelihood of contamination by bowel pathogens. The methods for the detection of *E. coli* are well-established and standardized as are those for the differentiation of *E. coli* from other coliforms which may be present, but which are of less significance.

Faecal pollution of natural waters used for recreational purposes has become of increased importance and the consequences of the discharge of untreated sewage into river estuaries and the sea have been extensively studied. However local conditions at different times considerably affect the results, and there is not a great deal of evidence of disease arising from recreation and water sports except where there is gross fouling. Less direct routes by which pathogens may be transmitted from contaminated water include the eating of contaminated shellfish and use of such water in vegetable growing.

The situation in soil is very similar to that with water in that the density of *E. coli* present is directly related to levels of faecal contamination.

Colonization of human infants and young animals

Under natural conditions many animals are very rapidly colonized by *E. coli*, large numbers being present in the caecum after the end of the first day of life. However they are not essential to the normal development of the gut and laboratory animals kept under defined conditions may appear normal in the absence of a coliform population. Some normal human beings have no readily detectable *E. coli* in the faeces. Human infants acquire their coliforms predominantly from the mother but in maternity units some strains spread and colonize a number of babies.

Colonization of adults

The human faecal coliform flora is heterogeneous and there may be variations with time and also with site in the intestine.

Many authors have recognized the presence of dominant strains in the bowel and there has been a widely held view that such dominant strains may persist for long periods. The persistance of strains in the bowel is however also related to the frequency and numbers of *E. coli* ingested in food. The organism is commonly found in food prepared in hospitals, canteens and schools and is also frequent in retail processed food. In all these situations the numbers present may be sufficient to colonize the bowel and it appears probable that the serotypes of *E. coli* present in the human bowel reflect not only the ability of individual strains to colonize but also the coliform population of the diet.

A number of properties may be important in the ability of *E. coli* strains to establish in the bowel. The possibility that multiply antibiotic-resistant strains may be less able to establish than sensitive strains requires further investigation. There is considerable evidence that colicin production and sensitivity are factors but that they are not of overwhelming significance. Competition for available nutrients, fatty acid production and differences in growth rate may all play a part. Adhesion is likely to be of importance particularly when there is a rapid transit time.

Some serotypes appear to be more likely to persist than others and have been regarded as 'strong'. Whether this is due to the serotype or to a related property is not known. An important aspect to be considered is how well animal strains are able to implant in the human bowel as this has implications as regards the importance to man of antibiotic usage in animals.

Serotype distribution

There is a shortage of information about *E. coli* serotype distribution. Evidence exists for geographical variation in the normal human faecal flora even over quite short distances and also for variation in the serotypes that act as pathogens. Although some serotypes are found in both the animal and human populations the overall distribution of types is different. There is little information about serotype distribution in animals and this might be valuable if it could be related to that of the human population.

Antibiotic usage in animals and its consequences

There has been a great deal of discussion about the importance to man of the use of antibiotics in animals and, although there is insufficient evidence to come to a conclusion about the significance of antibiotic-resistant coliforms reaching the human population, it is perhaps worth considering some of the factors involved.

There is no doubt that the coliform population of animals may be highly antibiotic-resistant. Many animal pathogens are known to reach man and interest has centred mainly on the salmonellas which have caused major outbreaks in the human population. However, in developed countries normally commensal organisms such as *E. coli* are responsible for the majority of infections. There is good evidence that animal strains of *E. coli* do reach the human population by the same route as salmonellas. That is, they are brought into the kitchen on raw meat and are either not destroyed by cooking or cross-contaminate to cooked food. Coliforms may also be transferred between domestic animals and their handlers. In the case of pets it is known that some dogs may have an antibiotic-resistant coliform flora but there is little evidence that this is important to man. Although there is some evidence that animal strains may survive less well in the human gut than human strains, many will persist for several days and some for many weeks after ingestion.

If the survival of antibiotic-resistant organisms following ingestion by man is considered there is again a shortage of information. Much of the work has involved short term studies and we know little about the long term persistance of antibiotic-resistant coliforms in the bowel of man particularly following cessation of antibiotic administration. Antibiotic-resistant animal coliforms which reach the human population may be directly important as pathogens themselves or they may transfer antibiotic resistance to other pathogenic bacteria.

The most common human disease caused by *E. coli* is urinary tract infection and a consideration of the likelihood of animal strains causing such infection in man involves not only the likelihood of their reaching the urethra and bladder but also whether they possess the properties which are associated with the ability to cause urinary tract infection. There is little information on this point.

Transfer of antibiotic resistance may occur as was demonstrated by Williams Smith but the transfer was small and it is known that the large number of bacteroides present in the gut does mechanically inhibit transfer.

We have therefore no real means of assessing the importance of animal strains of *E. coli* for man and unfortunately there appear to be no simple ways of making this assessment.

ESCHERICHIA COLI AND HUMAN DISEASE

Escherichia coli is responsible in British hospitals for more hospital-acquired and community-acquired infections than any other single bacterial species. In a wider context it is responsible for a great deal of infant morbidity and mortality due to its action as a pathogen in the bowel. Its role in causing a variety of human infections will now be briefly considered.

Urinary tract infection

In domiciliary practice urinary tract infections are commonly seen in young women. *E. coli* is frequently isolated and the condition generally responds rapidly to antibiotic therapy, although it is liable to recur and may be distressing and disabling. Urinary tract infection in otherwise healthy young women is unlikely to have important sequelae but in pregnancy bacteriuria is not only more common but may be associated with pyelonephritis, prematurity and foetal loss, although the results obtained by different workers studying this condition have varied.

In the newborn the symptoms of urinary tract infection are apathy, failure to feed and slow weight gain and such infections, and indeed all urinary tract infections occurring before school-age, are liable to result in chronic renal damage.

Urinary tract infections in hospitals generally follow catheterization although spontaneous infections also occur. In domiciliary practice *E. coli* is responsible for the vast majority of urinary tract infections whereas in hospitals, particularly following surgery, other organisms may be involved.

Although there is no doubt that host factors are of importance in the development of urinary tract infection it appears highly probable that the characteristics of the invading organism are also of significance. Some workers have, however, considered that the strains causing urinary tract infection merely reflect those commonly present in the bowel. As the bowel is generally recognized to be the source of strains causing urinary tract infection, comparison of faecal and urinary isolates has been used to demonstrate whether selection has occurred.

Comparison of a heterogeneous faecal coliform population with homogeneous urinary isolates adds to the complexity. The characteristics which have been considered may be of significance include serotype, K antigen content, motility, fimbriation, adhesion, invasion, haemolysin and colicin production, serum sensitivity and dulcitol fermentation.

The view that certain 'O' types are particularly associated with urinary tract infection has had support for many years. Generally, although the O types causing infection are also regularly found in faeces, a small number of types cause most infections. These O types include O 2, O 4, O 6, O 18 and O 75. Whether these O types are more liable to cause infection due to some property directly associated with the O antigen itself or whether it is because other properties are linked to that O type is not clear. This is a general problem in considering the relationship of *E. coli* serotype to pathogenicity.

K antigens may be involved in the development of urinary tract infection in a number of ways. Capsulate strains have been found to be more common in urinary than in faecal isolates and in addition strains associated with disease of the upper urinary tract may produce larger amounts of K antigen than strains from infections limited to the bladder. As well as the amount of K antigen the type may also be important. K 1 and K 2 are common amongst pyelonephritic strains.

Haemolysin production is one of the properties first associated with pathogenicity in the urinary tract. A number of workers have found urinary strains to be more commonly haemolytic than faecal strains; the haemolysins enable the organism to obtain iron from red blood cells, although they may also be associated with a cytotoxic action seen in tissue cultures.

E. coli which gain access to the urinary tract are liable to be washed out and fail to establish themselves unless they are able to adhere to the urinary epithelium and much interest has recently been focussed on the ability of *E. coli* in the urinary tract and bowel to adhere to host cells. Adhesion involves an interaction between the invading organism and host receptors and study of this phenomenon may throw light not only on bacterial virulence factors but also on host susceptibility to infection.

Cell surface structures that mediate adhesion are termed adhesins and the best studied of these are the fimbrial adhesins. Their presence is often demonstrated by red cell agglutination which may be sensitive to the presence of small amounts of mannose (MSHA) or resistant to it (MRHA).

MRHA is important in urinary tract infection as many strains with this property bind to the widely distributed P blood group antigen. P fimbriate *E. coli* are particularly found in infections of the upper urinary tract. Other MRHA bind to different receptors but the importance of these adhesins in urinary tract infection has not been fully assessed. Strains with MSHA bind to mucus and their role in urinary tract infection is ill-understood. Their elimination may, in fact, be assisted by mucus binding. Adhesion in the urinary tract has also been studied by examining the ability of *E. coli* to bind to cells including urinary epithelial cells. Urinary *E. coli* adhere more commonly than faecal strains. The relationship between adhesion and haemagglutination is complex depending on the presence of similar receptors in the erythrocytes and epithelial cells. Following adhesion, invasion of cells by some urinary *E. coli* has been reported by one group of workers. The development of knowledge of the adhesive properties of *E. coli* and particularly the ability to define the P receptor has advanced understanding of bacterial pathogenicity and has led to a great upsurge of interest in bacterial adherence in a number of bacterial species.

Serum sensitivity studies show no difference between faecal and urinary strains nor does colicin production appear to be important, but there have been reports that dulcitol fermentation may be of significance perhaps because the gene is situated near that of a virulence determinant and their expression linked.

The association of serotype and enteropathogenicity and also enterotoxin production and invasiveness is well established, as is that of serotype and antibiotic resistance. In the case of urinary strains the association between the serotypes common in urinary tract infection and haemolysin production is also well known. There have been, in addition, some reports of the association of these serotypes with the K1 antigen, high K antigen production and adhesion to urinary epithelial cells in strains from this source. The relationship of these properties to the ability to cause urinary tract infection is not clear cut. No single property is consistantly found and, although the properties of the group may vary, individual strains may be indistinguishable from faecal strains. This possibly reflects the importance of host factors. Certain individuals may be so predisposed to infection of the urinary tract that strains with few virulence factors may be able to establish themselves. In individuals less predisposed to infection it may be that rather than a single attribute some association of properties is required, strains able to cause infection possessing differing numbers and types of uropathic attributes.

Diseases of the gastro-intestinal tract

It is in the study of *E. coli* gastro-enteritis, particularly in infants but also in adults, that major advances have been made in our understanding of bacterial pathogenicity in the gut. But there are some other diseases of the gut in which a study of the coliform flora is also of interest.

The aetiology of acute appendicitis is probably multi-factorial and it appears unlikely that bacteria play more than a contributory role. There have been a number of reports that the *E. coli* flora of the inflamed appendix differs from that of the normal bowel and it has been suggested that the strains present resemble those from urinary tract infection. They are commonly haemolytic, belong to a small number of serotypes, adhere to HeLa cells and are serum resistant. Whether these *E. coli* strains have any involvement in the pathogenesis of the condition, or whether the differences occur because conditions in the inflamed appendix predispose to the selective overgrowth of previously minority populations with these properties, is not known.

The same problem occurs in relation to ulcerative colitis. This chronic, relapsing inflammatory disease of the large bowel is associated with *E. coli* strains that are haemolytic, belong to a small number of serotypes and adhere to and invade HeLa cells. Such evidence as there is suggests that these changes may follow rather than initiate relapse of the condition. It is also of interest that, whereas the normal faecal coliform flora is highly heterogeneous, the flora in the acutely inflamed appendix and in the diseased colon shows a greater degree of homogeneity.

There have also been reports that *E. coli* with a variety of enteropathogenic properties may be associated with the first attack of the ulcerative colitis before the condition is fully developed clinically.

Wound infections

E. coli is a common cause of wound infection particularly following operations on the bowel when anaerobic organisms may also be present. The most frequent source of the infecting organism is the patient's own bowel. Strains from wound infections resemble in some ways those from the urinary tract in that they tend to belong to a small number of serotypes, produce haemolysin and are serum resistant. Again the coliform flora is homogeneous and it appears that selection from the heterogeneous faecal flora has probably occurred.

Studies of the possibility that particular strains of *E. coli* may cross-infect post-operative wounds have not so far been reported although there have been suggestions that a nosocomial *E. coli* flora exists. The absence of information of this sort is probably related to the complexity of the typing system.

Septicaemia

It might be expected that differences between infecting strains of *E. coli* and those present in the faeces might best be demonstrated by studying strains from septicaemia and meningitis, conditions in which the clinical significance of the isolates cannot be doubted. *E. coli* is a common cause of septicaemia. Host factors are of outstanding importance but strains from septicaemia again demonstrate properties which clearly distinguish them from faecal strains. They commonly belong to a small number of serotypes, are K antigen-rich, serum resistant, haemolysin and colicin producers and ferment dulcitol. Shock and death following septicaemia is associated with certain serotypes (O4, O6 and O8) and with serum resistance.

The source of the invading organism is often the urinary tract so that some of the properties may be related to the source of the strain. However, there are differences notably, as would be expected, in serum resistance but also in colicin production and dulcitol fermentation.

Meningitis

Coliform meningitis is particularly a disease of neonates being responsible for about a third of cases in this age group. Differences between meningitic and faecal strains are again clear. The prevalent O groups are O1, O6, O7, O16, O18 and O83 and all these are associated with the K1 antigen when isolated from meningitis. The relationship between K1 and the disease is particularly clear, 80% of the strains having this antigen. The neonatal faecal carriage rate is much lower.

In adults meningitis is less common and is associated with serotypes O4 and O75 but the K1 antigen, which has the same structure as *Neisseria meningitis* B capsule, is not significant. Capsules not only enable the organism to evade non-specific host defences but may also evade recognition by the host, perhaps because of similarities with host cell-surface structures. K1 is an antigen which is able to do this.

Pneumonia

Although coliform pneumonia appears to have become of increasing importance during recent years this is a condition on which the assessment of the significance of the organism isolated is very difficult unless samples are taken directly by transtracheal aspiration. There appears to be little data on the properties of *E. coli* associated with pneumonia.

E. COLI AND DISEASE IN ANIMALS

In addition to causing disease in farm animals, *E. coli* is also responsible for illness in pets and in wild animals although these are of much less economic importance and are less well studied than in farm animals. In puppies enteric and systemic colibacillosis may occur and *E. coli* also causes urinary tract infection in dogs. It is interesting that although dogs have lived in close contact with man for thousands of years their coliform flora is distinct. Strains causing urinary infection in dogs, as in man, are commonly haemolytic suggesting that this may be an important characteristic. Coliform diseases in wild animals, although known to occur, have been little studied.

CONCLUSION

In considering the general pattern of coliform diseases in man and animals a picture emerges of an organism widely distributed in the gut and causing a variety of infections. The disease-associated strains tend to have particular properties and some of these such as haemolysin production, the presence of a K antigen and possession of one of a small number of 'O' antigens are found in a number of diseases. Others are associated with particular illnesses such as serum resistance with septicaemia and the K1 antigen with meningitis. Strains causing gastroenteritis have quite distinct properties and indeed an absence of the properties associated with other infections.

It is difficult to escape the view that some selection of strains from the mixed faecal flora occurs so that the infecting strains form groups with distinct properties.

The investigation of *E. coli* diseases has increased our knowledge of the importance of toxin production in bowel disease, it has lead to increased information about adhesion and invasion and to the recognition of receptors for adhesion. It has added to our information about evasion of host defences and demonstrated once again the value of the study of animal diseases in elucidating human infection.

Bacillus coli commune has provided a lot of interest in the last 100 years. I expect it will continue to do so.

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