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EDITORIAL

EPIDEMIOLOGY OF ESCHERICHIA COLI–AN IMPORTANT BUT NEGLECTED FIELD

Extensive genetic studies on *Escherichia coli*, initially begun as an academic work, have been rewarding and they have opened up a vast vista of knowledge. These studies not only have enabled us to get a glimpse of what may be happening in the field of microbiology but have even given us some insight of the genetic process that may be going on in the living world in general.

E. coli K-12 has been the most extensively studied strain and has often been used by the genetic engineers as a carrier strain for transferring genetic characteristics between species, even though the gene and its product has no relation to *E. coli*. *E. coli* K-12 has been the special favourite for such experiments mainly because it has been so thoroughly dissected that we know most of the details of its genetic structure. Any change that might be introduced into this strain and the consequences that may follow can be more critically analysed than if we used some other strains of *E. coli*. However, in nature, many strains of *E. coli* must be capable of doing what *E. coli* K-12 is able to do, although we may not be able to understand the processes that may be taking place as easily as would be the case with *E. coli* K-12.

The above work suggests that, for better or worse, continuous genetic exchanges are going on inside the intestine affecting the characteristics of most organisms it harbours. Though apparently stable, they will undergo some changes, sooner or later. As an example it may be cited that studies on the molecular comparison of virulence plasmids of *Shigella* and *E. coli* species show that there are many homologous sequences throughout the molecule indicating that they were derived from a common ancestor (1).

We know that the R-factors (resistance) are frequently transmitted from one strain to another and the same must be true with many other factors. A current trend is to construct oral vaccines by-loading *E. coli* K-12 with the genetic characteristics determining limited invasive properties along with the protective antigens of *Shigella* and to use it as a live oral vaccine. Not having the full characteristics of the pathogenic bacteria it can multiply in the host cells only to a limited but sufficient extent to confer significant protection. Some such oral vaccine have been tried on monkeys with promising results and further trials on human volunteers are contemplated (2).

Though existing genetic works on *E. coli* have been enlightening, very little studies have been carried out to develop techniques which can guide us on the epidemiological aspects of *E. coli* infections. This has become all the more important because of our growing understanding of the role of *E. coli* as a major cause of diarrhoea in most countries of the world.

E. coli has long been known as a harmless bacteria, living inside the intestine, and probably playing a useful role in providing a regular supply of vitamins and growth factors for the body. Under special conditions it was known to cause urinary infections and could cause bacteraemia or even septicaemia and meningitis, but only in the infant and, in older subjects, under unusual conditions when there was a breakdown of the defense mechanisms. It is a lactose fermenter, and lactose fermenters inside the intestine were virtually taken for granted as being non-pathogens, not deserving further study.

The role of *E. coli* as a diarrhoea-producing organism became obvious in the late 1940s with the identification of enteropathogenic *E. coli* (EPEC) with nursery infections in children. Later enterotoxigenic *E. coli* (ETEC) became identified and its role as a major cause of diarrhoea, all over the world, is now well-recognised. Generally, the EPEC elaborate a toxin that is apparently identical to *Shigella* toxin (3). Later, the enteroinvasive *E. coli* (EIEC) was added to the list. It is now known that EIECs also share antigenic components and other characteristics with *Shigella*, so much so that an extensive outbreak due to EIEC (0124) in the United States of America was first identified as being caused by *S. dysenteriae* 3. We now know that plasmids obtained from EIECs and *Shigella* share considerable homology (1).

The last to receive recognition is the entero-

haemorrhagic *E. coli* (4). It will be a surprise if many more were not added to the list, sooner or later. Recent publications indicate that EPECs and ETECs could also be present in asymptomatic individuals (5,6,7,8) and the same is the case with EIECs (9). When these strains are isolated from infants with diarrhoea, they are generally present as the predominant *E. coli* population of the gut. However, when isolated from healthy carriers they are present only in small numbers. One may explain travellers' diarrhoea as due to exposure to a new pathogenic agent. But how does one explain the incidence of ETEC, EPEC or EIEC diarrhoeas, especially during certain times of the year, among the local population in many countries (6,9,10,11) ? The answer probably lies in the fact that the low numbers of EPECs, ETECs and EIECs, known to be present in the asymptomatic population, produce the disease when they find a favourable condition to develop as the predominant strain of *E. coli* population in the gut. Of these, the EIECs are probably the least diagnosed because the Sereny test is seldom done in most laboratories. The clinical symptoms of EIECs being similar to those of dysentery, many of them are most likely missed as undiagnosed cases of dysentery. It is likely that there are other *E. coli* infections for which we do not know the identification characteristics and they, therefore, still remain unknown and undiagnosed.

All the major enterobacteria need to be studied for their pathogenic characteristics, epidemiological behaviour and changes of properties. Of these, obviously *E. coli* is most important. But the *E. coli* population of the gut are a changing mixture of a huge number of different strains (12,13,14,15), which cannot be differentiated by looking at the colonies. How then can we follow a strain by picking different colonies from the same plate ? For this we need a marker to identify and trace individual strains as it travels inside the intestine. The question is what tools can we use ? Serotyping can be used to identify different strains. But this is a time-consuming process, and only a few laboratories in the world are equipped to carry out serotyping of all *E. coli* strains. Therefore, it is not very suitable for large scale routine testing of all *E. coli* strains that may be present in any one individual specimen. A simpler tool, other than serotyping, is desirable for screening in large numbers. Unfortunately, no such tool has yet been developed and this makes the study of the dynamics of *E. coli* infection so difficult. Some workers are now interested in evolving a sensitive, specific and practical new diagnostic tool (6). Candidate methods include genetic probes, identification of phage lysotypes, plasmid profile and perhaps simple tests for identification of specific antigens by development of co-agglutination techniques for each individual antigen. The problem has perhaps been avoided by most investigators on account of the task being too difficult for any one individual to attempt. This may be true, but that is why there is the need for an organised serious effort to understand the essential behaviour of our most important and intimate companion which affects our health and causes disease. Preliminary studies in this laboratory appear to indicate that the identification of phage lysotypes may have some promise and studies are being pursued to see how far this can take us. A few recent publications indicate that phage is able to trace a few selected *E. coli* strains, some of clinical importance, by identifying their specific antigens (16,17). More intensive studies of this nature may enable us to identify many more strains of clinical and epidemiological significance.

Already difficult under well-defined laboratory conditions, the test would be much more so in the complex milieu of the intestine. There may be many routes to explore and we must try and find them one by one. A combination of techniques may give better insights to identify minor changes that may be going on in individual strains. Whatever tools or guides we may pick up, it may only lead us to a limited extent. To devise new tools and methods, new studies will have to be executed. The process is bound to be long, tenuous and almost unending and this may need collaborative efforts of scientists from all over the world. To understand how this pathogenic organism behaves in the mini-universe of the intestine and how they influence our health and cause disease is certainly worth the trying effort.

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