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The dangers of enterohaemorrhagic Escherichia coli*: an emergent pathogen.*

Review

Aldo Pacheco-Ferreira, Juremí de Oliveira-Carvalho, Carlos A. Silva-Miranda, Ana M. Ugarte.

Fundação Oswaldo Cruz, Escola Nacional de Saúde Pública, Departamento de Saneamento e Saúde Ambiental, Rio de Janeiro, Brasil.

SUMMARY.

Enterohaemorrhagic *Escherichia coli* O157:H7 is an emerging pathogen, being actually an important cause of food-borne illness. Is responsible for serious outbreaks and sporadic cases of haemorrhagic colitis (HC) and haemolytic uraemic syndrome (HUS).

The major challenge of induced diarrhoeal disease is in children under the age of 10 and elderly people, especially the ones that live in less-developed countries of the world, in which bacterial diarrhoeal diseases remain a significant public health problem. In incidence data, the reported rates in developed countries are 5-8 cases/100,000 population per year, with regional variations. Rarely reported in patients in less developed countries.

The epidemiology of the microorganism is revised in several countries being correlated serotypes of *E. coli* O157: H7 to the lethal indexes. ***(Rev Biomed 2002; 13:124-129)***

Key words: *Escherichia coli* O157:H7, epidemiology, haemorrhagic colitis, haemolytic uraemic syndrome.

RESUMEN.

Los peligros de *Escherichia coli* enterohemorrágica: Un patógeno emergente.

El patógeno emergente enterohemorrágico *Escherichia coli* 0157:H7 es actualmente una importante causa de enfermedad por la vía alimentaria, siendo responsable de varios brotes de diarreas y con la capacidad de producir brotes epidémicos. Algunos serotipos son capaces de producir enteritis hemorrágica, que puede complicarse con el síndrome hemolítico urémico.

La mayor incidencia de enfermedad diarreica inducida por este patógeno está en niños menores de 10 años y en adultos mayores y ancianos que viven en los países subdesarrollados del mundo, en donde las enfermedades diarreicas bacterianas

Corresponding address: Aldo Pacheco Ferreira, Fundação Oswaldo Cruz, Escola Nacional de Saúde Pública, Departamento de Saneamento e Saúde Ambiental, Avenida Leopoldo Bulhões, 1480 – Manguinhos – Rio de Janeiro - Brasil, CEP: 21041-210 E-mail: aldo@ensp.fiocruz.br
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siguen siendo un problema significativo de salud pública. En los datos de incidencia, las proporciones informadas en los países desarrollados son 5-8 casos/100,000 habitantes por año, con variaciones regionales. En los pacientes de países subdesarrollados estos reportes son escasos y no refleja la información real.

Se revisa la epidemiologia del microorganismo en varios países correlacionandose serotipos de *E. coli* O157:H7 a los índices letales.

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Palabras clave: *Escherichia coli* O157:H7, epidemiología, colitis hemorrágica, síndrome hemolítico urémica.

INTRODUCTION.

The aim of this study was to use published data to assess the importance of the *Escherichia coli* O157:H7 as a bacterium capable of colonizing or infecting human beings. This should make it possible to develop appropriate measures for preventing cross contamination in daily feeding. Surprisingly, the emergent infectious diseases placed health systems in the developed and in development countries face to face with a series of uncertainties and risks of great magnitude. This Gram-negative bacterial rod occurs as a Vero cytotoxin-producing species (VTEC), mostly of serogroup O157, and has been observed as the cause of outbreaks of haemorrhagic colitis since the early 1980s, often with significant mortality. A not infrequent complication is the haemolytic uraemic syndrome (HUS). VTEC strains are often carried by cattle, with and without disease, and outbreaks in humans have been mostly epidemiologically linked to food products of bovine and other origins, although the microorganism has not always been isolated at source. Contaminated food and water are probably the main vehicles of VTEC transmission, and therefore safe water and hygiene handling of foodstuffs are of great importance for prevention.

The Centers for Disease Control (CDC, USA) defines emergent diseases as those infectious diseases whose incidence increased in the last two decades or they tend to increase in the future (1). In the sense of specifying that definition better, different circumstances are mentioned that can characterize the emergence of new health problems, specially, possible connections among genetic engineering/new pathogenic agents and biological weapons, the global traffic of microorganisms and the exchange of diseases between the old and the new world.

E. coli O157:H7 is so-named because it expresses the 157th somatic (O) antigen identified and the 7th flagellar (H) antigen. The recognition of enterohaemorrhagic *E. coli* as a distinct class of pathogenic *E. coli* resulted from two key epidemiologic observations. The first was reported by Riley *et al.* (2), who investigated two outbreaks of a distinctive gastrointestinal illness characterized by severe crampy abdominal pain, watery diarrhoea followed by grossly bloody diarrhoea and little fever. This illness, designated HC was associated with the ingestion of undercooked hamburgers at a fast-food restaurant chain (3). Stool cultures from these patients yielded a previously rarely isolated *E. coli* serotype, O157:H7. Karmali *et al.* (4) reported the second key observation evidencing the association of sporadic cases of HUS with faecal cytotoxin and cytotoxin-producing *E. coli* in stools. HUS is defined by the triad of acute renal failure, thrombocytopenia and microangiopathic haemolytic anaemia, already known to be preceded typically by a bloody diarrhoeal illness indistinguishable from HC. Patients with this illness have kidney failure and usually require dialysis, some have neurologic impairment, such as seizures or blindness, although most of them survive but some have residual high blood pressure and kidney impairment.

Thus, two key clinical microbiological observations, one based on a rare *E. coli* serotype and the other based on production of a specific cytotoxin, led to the recognition of a novel and increasingly important class of enteric pathogens

causing intestinal and renal disease. The number of reported outbreaks and sporadic cases of *E. coli* O157:H7 infection has steadily increased, reflecting not only the proliferation of the organism as a human pathogen, but also the heightened clinical and laboratory awareness of the organism and its manifestations. One study estimated that *E. coli* O157:H7 was associated with 0.6-2.4% of all cases of diarrhoea in an area of Washington state and 15-36% of all cases of bloody diarrhoea or HC, rivalling *Campylobacter*, *Salmonella* and *Shigella* infections (5).

VIRULENCE FACTORS AND PATHOGENESIS.

The major virulence characteristic of E. coli O157:H7 is its ability to produce one or more verocytotoxins. The verocytoxins (vacuolisation of Vero cells induced by toxin) have two variants: verocytoxin 1 and verocytoxin 2.

The Shiga toxins family contains two major, immunologically non-cross-reactive groups. The first of these, Shiga toxin 1 (Stx-1), is identical to Shiga toxin (Stx) produced by *Shigella dysenterie* type 1. The second, Shiga toxin 2 (Stx-2), is a more divergent molecule, with only 56% amino acid homology with Shiga toxin 1. They are called verocytotoxins because of their cytotoxic effect on Vero cells. Isolates of *E. coli* O157:H7 that produce Stx-1 only is uncommon, and strains are more likely to produce either Stx-2 alone or both toxins (6). Production of Stx is now recognized as an important feature of all *E. coli* strains implicated in HUS.

Most *E. coli* produce both toxins, some Stx-2 alone and few Stx-1 alone. The way Stx might mediate HUS is not clear, but it is believed to be through haematogenous spread and direct damage of the target organs causing endothelial cell damage, particularly in the glomerular endothelium in the kidneys. Two pieces of evidence support this hypothesis: first, the natural receptor for the toxin (a cell surface glycolipid named Gb3) is abundant in the enterocytes, erythrocytes, and renal tubular cells, which would explain the preferential damage of these organs; and second, Stx inhibits protein synthesis causing cell rounding and death. A problem with this hypothesis is that even though Stx activity is readily detected in the stool of affected individuals, it has not been shown in their circulatory system. It might be, though, that the toxin does appear in blood but at levels too low to be detected by current assays.

A peculiar aspect of *E. coli* O157:H7 is that a single strain can produce a wide spectrum of clinical manifestations. The incidence of HUS and thrombotic thrombocytopenic purpura can be fatal and may be resulted from vascular ischemia secondary to thrombus formation, localised in the kidney in HUS and disseminated in thrombotic thrombocytopenic purpura. However, HC is the most common manifestation of *E. coli* O157:H7 infections, and is characterised by abdominal cramps, which are sufficiently severe to be compared with the pains of childbirth or appendicitis. Depending on the population, 2-7% of HC sufferers go on to develop HUS and the mortality rate is 5-10% and a third of survivors have a persistent disability (5).

EPIDEMIOLOGIC INCIDENCE.

Human contamination with *E. coli* O157:H7 has been reported from over 30 countries on six continents (Table 1). Annual occurrence rates of 8 per 100.000 inhabitants or greater, have been registered in areas from USA, Japan, Scotland, Canada and United Kingdom (7-11).

In some countries of South America blunt some regions with high rates, especially Argentina and Uruguay, where the HUS is endemic (12), has an incidence 5-10 times higher than in USA, and also many patients with HUS presented infection due to *E. coli* O157:H7. In Brazil, the investigations have been initialised in 1998 and the available data from some regions show that in research in bovine meat, especially in Rio de Janeiro and São Paulo, the presence of *E. coli* O157:H7 was identified in 43% of samples.

With improved emphasis on cost containment in the clinical microbiology laboratory, there is no

economic pressure for regularly testing stool samples for *E. coli* O157:H7. Individual cases of HC or HUS should be considered as markers signalling promising widespread infection. *E. coli* O157:H7 is perhaps the most dangerous enteric pathogens that clinical microbiologists are likely to encounter. The level of biohazard is high due to the extremely low dose required for infection (10 microorganisms). They can be found on a small number of cattle farms and can live in the intestines of healthy cattle. Meat can become contaminated during slaughter and the microorganisms can be mixed into beef when it is ground. This way, *E. coli* O157:H7 present on the cow's udders or on equipment may get into raw milk. Eating meat, especially ground beef, which has not been cooked sufficiently to destroy any contaminant, particularly *E. coli* O157:H7 would be able to cause infection.

Learning more about the ecology of this organism in cattle may help in devising methods to decrease prevalence of this and other human pathogens in food animals. Decreasing the incidence of these infections would decrease the incidence of HUS, which is the major cause of acute kidney failure in children in reported cases.

Table 1
Outbreaks associated with *E. coli* O157:H7 in food products.

Type of food product		Country
Meat	Ground beef	USA, Brazil, Argentina, Uruguay
	Hamburguer	USA, Canada, England, Japan
	Roast Beef	USA
	Cooked beef products	Scotland
	Fermented sausage	USA
	Turkey roll	England
General foods	Apple cider	USA
	Mayonnaise	USA
	Vegetables	USA, England, Japan
Lacteous	Raw milk	USA, Canada, England, Scotland
	Pasteurised milk	Scotland
	Yoghurt	England
	Cheese	Scotland

DIAGNOSIS AND DETECTION.

The identification of *E. coli* O157:H7 infection should be considered in any person who reports acute bloody diarrhoea, has visibly bloody stools or has postdiarrhoeal HUS. In Figure 1 the current mode of infection with *E. coli* O157:H7 is demonstrated.

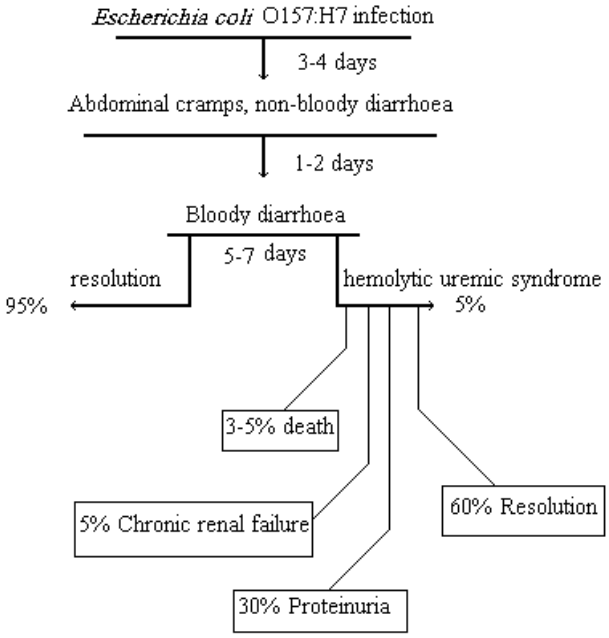

Figure 1.- Current mode of infection with *E. coli* O157:H7.

Determination of the etiological agents of diarrhoea is important in developing rational therapy and in implementing control measures. Taking into account such concepts *E. coli* O157:H7 is arising interest for the clinical methodologies development. Most infections related to *E. coli* O157:H7 have been associated with consumption of undercooked beef, particularly in fast-food restaurants and for swimming in or drinking sewage-contaminated water. This microorganism is blunting as an emerging pathogen of worldwide public health importance, and is also responsible for expressive outbreaks.

The importance of clinical investigations is improved by the fact that few pathogens can routinely cause such striking clinical syndromes in different organ systems as *E. coli* O157:H7 can and screening it will be possible to diagnose them and detect outbreaks. Repeated cases of HUS are relatively uncommon being diagnosed twice in the same patient in 2.6% all cases researched over a period of 20 years (13). The benefit of a prompt and accurate *E. coli* O157:H7 diagnosis can also be quite profitable for the fact of avoiding possible mistakes in patients evaluations such as: ischemic colitis, primary inflammatory bowel disease, intussusception and appendicitis. The need for routinely culture stool samples from patients with bloody diarrhoea in clinical microbiology laboratories or HUS for *E. coli* O157:H7 (14) has emerged and the culture medium most indicated is MacConkey Sorbitol Agar.

Although biochemical characteristics associated with the great majority of *E. coli* O157:H7 serotypes, are not common there is some biochemical data of identification exploited of *E. coli* O157:H7 serotype. It should be noted that O157:H7 strains do not ferment D-sorbitol rapidly, in contrast to about 75 to 94% of other *E. coli* strains (15). Another parameter are data from Abbott *et al.* (16) which emphasise that more than 90% of *E. coli* O157:H7 strains give one of two unique biochemical profile numbers on a MicroScan conventional gram-negative identification panel (Baxter Diagnostics, Inc., California, USA) that were not detected with other D-sorbitol negatives. It is also notable the inability of this pathogen to produce -glucuronidase which hydrolyzes 4-methyl-umbelliferyl-D-glucuronide (MUG), that differs from the majority of other serotypes of *E. coli* (17).

CONCLUSION.

The control of transmissible diseases is based on interventions that, acting one an or more known links of the epidemic chain of transmission, are capable of interrupting them. However, man's interaction with the environment is very complex, involving ignored factors or ones that might have modified it when the action is unchained. In this way, intervention methods tend to be perfect or substituted, in the measure that new knowledge is contributed, by scientific discoveries (therapeutic, epidemic), by the systematic observation of behaviour, or by prevention procedures and established control. The evolution of that knowledge also contributes, for the modification of concepts and ways to organize health services aiming for quality.

HUS in its most common classic form, is due to infection by *E. coli* strains that produce Shiga toxins, mainly the serotype O157:H7. These infections are food-borne with a tendency to occur in outbreaks, affecting mostly young children. Surveillance and contact investigation are important to control outbreaks, as well as early and aggressive treatment of symptomatic subjects to prevent mortality and severe complications, such as chronic renal disease. Antimotility agents and antimicrobials must be avoided. Close contacts, as in the household and day care centers, should be monitored because they are at risk of infection.

E. coli O157:H7 is an emerging pathogen of worldwide public health importance, and it also responsible for expressive outbreaks. This way, it is necessary to improve the control in suspect stools one to the fact that few pathogens can routinely cause such striking clinical syndromes in different organ systems as can *E. coli* O157:H7 can. By monitoring its presence it will be possible to diagnose and detect outbreaks.

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