Memoranda / Mémorandums

Prevention and control of enterohaemorrhagic *Escherichia coli* (EHEC) infections: Memorandum from a WHO meeting*

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Escherichia coli *is a commonly occurring inhabitant of the intestine of humans and other animals, but there are several pathogenic types of* E. coli *which cause a variety of human diseases. One of these pathogenic types,* E. coli *O157:H7, belongs to the group of enterohaemorrhagic* E. coli *(EHEC) which produce potent toxins and cause a particularly severe form of disease, haemorrhagic colitis (HC). About 10% of patients with HC can go on to develop haemolytic uraemic syndrome (HUS), a life-threatening complication of* E. coli *O157:H7 infection that is characterized by acute renal failure, haemolytic anaemia, and thrombocytopenia. These sequelae are particularly serious in young children and older people. On average, 2–7% of patients with HUS die, but in some outbreaks among the elderly the mortality rate has been as high as 50%.*

This Memorandum reviews the growing importance of E. coli *O157:H7 as a foodborne pathogen and reports on the issues of surveillance, outbreak investigation, and control strategies with respect to EHEC infections that were discussed at the WHO Consultation on Prevention and Control of EHEC Infections, held in Geneva on 28 April to 1 May 1997. Recommended measures for prevention and control include the following: use of potable water in food production; presentation of clean animals at slaughter; improved hygiene throughout the slaughter process; appropriate use of food processing measures; thorough cooking of foods; and the education of food handlers, abattoir workers, and farm workers on the principles and application of food hygiene.*

Introduction

In 1982, *Escherichia coli* O157:H7 was recognized as a human pathogen for the first time, and since then has been a steadily increasing cause of foodborne illness worldwide. Although the main reservoir of this pathogen appears to be cattle, the dynamics of *E. coli* O157 in food-producing animals and the environment is not well understood. It is transmitted principally through consumption of contaminated foods, such as raw or undercooked ground meat products and raw milk. Faecal contamination of water and other foods and cross-contamination during food preparation are important routes of infection. Examples of foods implicated in outbreaks of *E. coli* O157 infection include hamburgers, roast beef, raw milk, unpasteurized apple juice, yoghurt, cheese, fermented sausage, cooked maize, mayonnaise-containing dressings, lettuce, and seed sprouts. The pathogen is relatively tolerant to acid and can survive in fermented foods and fresh vegetable produce. Waterborne transmission has also been reported, both from contaminated drinking-water and from recreational waters. Person-to-person contact is an important mode of transmission, particularly in institutional settings, such as day care

* This article is based on: *Prevention and Control of EHEC Infections. Report of a WHO Consultation, Geneva, 28 April to 1 May 1997* (unpublished document WHO/FSF/FOS/97.6, available upon request from Director, Programme of Food Safety and Food Aid, World Health Organization, 1211 Geneva 27, Switzerland).

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Reprint No. **5856**

centres, nursing homes and hospitals. Direct contact with farm animals and birds carrying the organism is also a recognized source of infection. The role of asymptomatic food handlers in outbreaks is unclear but it may be important in view of the low infectious dose. The range of foods reported as vehicles of transmission and the numerous transmission routes create a major challenge in terms of designing prevention and control strategies.

More recently, there have been unprecedented, large outbreaks of *E. coli* O157:H7 infection in Japan and Scotland, and outbreaks due to other enterohaemorrhagic *E. coli* (EHEC) in Australia and Europe. There have also been a significant number of outbreaks in the USA linked to the consumption of contaminated vegetable products, such as lettuce and alfalfa sprouts. The largest ever recall of food on record occurred in the USA in 1997, when about 10 000 tonnes of raw frozen hamburgers were recalled because of suspected contamination by *E. coli* O157.

In view of the magnitude and severity of recent outbreaks of foodborne diseases caused by *E. coli* O157:H7, there is an urgent need for all sectors in the food chain to work together to reduce or eliminate the health impact of this hazard. Achieving a significant reduction in the incidence of foodborne disease caused by this pathogen will require the co-operative efforts of public health and environmental health agencies, farmers, animal producers, food processors and caterers, together with research scientists.

Global overview of EHEC infections

During the consultation, participants presented overviews of current national situations with respect to EHEC infections as outlined below.

African Region

Bloody diarrhoea is a major cause of morbidity and mortality among children in African countries, yet the proportion caused by *E. coli* O157:H7 and other EHEC is largely unknown. In South Africa, for example, infections caused by EHEC are not notifiable and there is very limited information on *E. coli* O157 infection in animals. Since 1988 three cases of *E. coli* O157 colitis have been identified in Pretoria, one of which was associated with eating a hamburger from a fast-food outlet. Many cases of haemorrhagic colitis caused by nonmotile *E. coli* O157 from Swaziland and the adjacent South African provinces of Mpumalanga and KwaZulu-Natal were identified in 1992. Isolates of *E. coli* O157 were obtained from patients, water, cattle faeces and one sample of cooked maize. An undocumented number of cases of haemolytic uraemic syndrome (HUS) occurred during this outbreak.

Reports of EHEC as a cause of diarrhoea in other African countries are sporadic. In a study of childhood diarrhoea in Nigeria, samples of EHEC were isolated from 5.1% of children with diarrhoea (*10*). EHEC was suspected to be the cause of bloody diarrhoea and deaths in refugees in Angola (*3*) and in Malawi (*11*). *E. coli* O157:H7 has also been isolated in Kenya as a cause of severe childhood diarrhoea (*12*). In Egypt, haemorrhagic colitis and child mortalities have been linked to eating hamburgers, *koshari* and dairy products, and *E. coli* O157:H7 has been reported in beef, chicken, lamb, and unpasteurized milk (*1*). Since 1996, an increasing number of cases of acute bloody diarrhoea reported in the Central African Republic have been associated with *E. coli* O157:H7 (*8*); *kanda*, a meat pie that is prepared from smoked zebu meat and cooked marrow squash, was identified as the main food vehicle.

Region of the Americas

In the USA, laboratory-based surveillance for *E. coli* O157:H7 infections was first implemented in late 1992, and the results obtained up to mid-1995 showed that the number of states reporting isolates increased from two to 40. During this period 2946 cases were reported, equivalent to an annual average incidence of 0.74 cases per 100 000 population. Annual, state-specific incidences ranged from 0.03 to 4.99 cases per 100 000 population. Since 1982, more than 100 outbreaks of *E. coli* O157 infection have been reported. Of those outbreaks for which the mode of transmission was identified, 52% were linked to foods derived from cattle, 16% to spread of infection from person-to-person, 14% to fruits and vegetables, 12% to water, and 5% to miscellaneous foods. Recently, fruit and vegetables have increasingly been implicated as vehicles of infection. Since 1995, there have been five outbreaks in North America associated with lettuce, and one with commercial, unpasteurized apple juice.

Infection with verotoxin-producing *E. coli* (VTEC) continues to be a significant public health problem in Canada. In 1991, the reported annual incidence of infection reached a maximum of 5.3 per 100 000 inhabitants and by 1993 had decreased to 3.0 per 100 000. More recently, the reported incidence has again increased, prompting renewed concern over the health impact of this organism. The majority of cases in Canada are believed to be sporadic and in 1995, 16 outbreaks of *E. coli* O157:H7 infection were reported in this manner; nine of these were family outbreaks (19 cases phage-typed), two were restaurant outbreaks (10 cases), three were institutional outbreaks (21 cases), one was a day care outbreak (9 cases), and one was a waterborne outbreak (index case only phage-typed). Preliminary data indicate that 18 outbreaks were reported in 1996; twelve were family outbreaks (28 cases phage-typed), four were community outbreaks (28 cases), and one was a day care outbreak (25 cases). Most VTEC infections reported in Canada are caused by *E. coli* O157:H7.

In South America, HUS has for many years been the most common cause of acute renal failure in childhood and infancy in Argentina, with an estimated annual incidence of 7.8 per 100000 among under-5-year-olds. Over 5500 cases of HUS were reported in Argentina from 1965 to 1993. Children affected are usually aged under 5 years, mostly 6–36 months. Both sexes are equally affected and cases tend to come from middle-income socioeconomic groups, who are well nourished and living in good sanitary domestic conditions. The illness is distributed throughout Argentina, but cases are reported more frequently in southern provinces during warmer months (from October to May). VTEC O157:H7, producing verocytotoxin 2 (VT2), is the most frequently isolated serotype of VTEC from diarrhoea-positive (D+) HUS cases, with bloody and nonbloody diarrhoea. Until now, no foodborne outbreaks have been reported. HUS constitutes an important clinical problem in other South American countries, where it has been reported in Chile and Uruguay (*5*).

Western Pacific Region

In 1996, Japan reported 9451 cases of EHEC infections, 1808 of which were hospitalized and 12 died; three-quarters of all these cases occurred during six major outbreaks. In the largest outbreak, in Sakai City, 5727 people (0.5% of the city's population) were affected, and white radish sprouts served at school lunch were the most likely food vehicle. In outbreaks reported in other areas *E. coli* O157 was also isolated from the salad and seafood sauce that were served at school lunches. In 1997, *E. coli* O157 was detected in wild venison and white radish sprouts associated with sporadic infections.

In other parts of Asia, EHEC infections have been reported. In Malaysia, *E. coli* O157:H7 has been isolated from the stools of patients with diarrhoeal illness (*13*). In a study at a Bangkok hospital in Thailand, EHEC was identified in 7% of children with bloody diarrhoea in whom other enteric pathogens were not identified (*4*). In the Republic of Korea, EHEC was isolated from 1.3% of children with nonbloody diarrhoea. An investigation into the etiology of childhood diarrhoea in China isolated EHEC from 6.8% of children with diarrhoea (*9*); the rarity of *E. coli* O157:H7 identified in this study led the authors to conclude that EHEC may be caused by serotypes other than O157:H7 in China.

There have been two documented outbreaks of infection with EHEC in Australia. The first, in South Australia in 1995, was of serotype O111:H$^-$ and involved 22 cases of paediatric HUS, four cases of thrombotic thrombocytopaenic purpura (TTP), and reports of approximately 200 cases of haemorrhagic colitis (HC) and diarrhoea. The source of the outbreak was an unpasteurized semi-dry, fermented sausage. The second, in Queensland in 1996, involved serotype O157:H7 and involved six cases of diarrhoea, several of which were bloody; an infected food-handler is thought to have been the source. In 1995–96, sporadic cases of HUS occurred throughout Australia in children under 15 years of age at an annual incidence of around 0.93 per 100000, including outbreak-associated cases. This rose to 2.79 per 100000 among children aged under 5 years, and 95% of such cases demonstrated a diarrhoeal prodrome with the following VTEC serogroups being isolated: O111, O157, O113, and O130.

European Region

In Denmark, the annual incidence of VTEC from 1986 to 1996 was 0.1 per 100000. During this period, different serotypes of VTEC were isolated from a total of 60 sporadic human cases. The predominant disease-causing VTEC serotypes were O26:H11, O157:H$^-$, O157:H7 and O26:H$^-$. VTEC O157:H7 have been isolated from cattle herds and cattle at slaughter. *E. coli* O157 has been isolated from minced meat in Denmark, and minced meat other than beef may play a role as a source of infection from possible cross-contamination at the retail level. However, the presence of pathogenic VTEC in cattle and foods has not resulted in any reported outbreaks. At present it is unclear why only a few sporadic VTEC cases are diagnosed each year in Denmark, suggesting that the number of VTEC-associated cases may be underestimated.

Data from Germany indicate that EHEC infections, including *E. coli* O157, occur in all parts of the country. During 1994 and 1995, EHEC was isolated in 2–3% of hospitalized children with diarrhoea, with *E. coli* O157 being the most frequently isolated serotype (94 out of 118 cases, i.e. 79.7%) in children with HUS. Data for 1996 suggest that the proportion of non-O157 VTEC implicated in HUS cases may be increasing, because O157 was isolated in only about two-thirds of HUS cases from which a VTEC could be isolated. The following non-O157 *E. coli* serogroups were associated with HUS: O15, O26, O103, O111, O118, and O145. In an outbreak of HUS in Bavaria between December 1995 and March 1996, 20 of the 32 children with HUS had stool cultures that were positive for EHEC; *E. coli* O157 was detected in samples from 17 of the 20, at least 12 of which fermented sorbitol. In one case *E. coli* O103 and in two cases *E. coli* O55 were identified.

In Germany, farm animals, especially ruminants, constitute the major natural reservoir for VTEC. Repeated examination of cattle and sheep has revealed that nearly all individual animals could excrete VTEC at one or more periods during their life. A large variety of VTEC serotypes has been isolated from animals. Sporadic isolates of VTEC belonging to the classical EHEC types, such as O157:H7, O26:H11, and O22:H8, have been made. Only 1–2% of the animal VTEC isolates possess the *eae* gene and about 60% express the enterohaemolytic phenotype.

The incidence of HUS in the Netherlands amounts to about 30 cases per year, mainly among under-5-year-olds. Studies on sporadic cases of HUS revealed *E. coli* O157 to be the predominant causative agent. The relative importance of EHEC as a causative agent of human diarrhoeal illness in the Netherlands is unknown. Since 1992 various studies have been conducted on the occurrence of *E. coli* O157 in raw meat products and in faecal samples from different categories of cattle. Between 1992 and 1995 a total of 2330 samples of meat products were examined and *E. coli* O157 was isolated from only two samples of minced meat (beef/pork). In 1996 the pathogen was reported in a sample of fermented sausage and a sample of sausage batter. In 1995, *E. coli* O157 was detected in 30 (11.1%) of 270 faecal samples from dairy cows; nine of the 30 isolates were positive for the VT2 and the *eae* gene.

Since 1988 up to three cases of EHEC have been reported in Sweden annually, including those people who contracted the infection abroad. This situation changed between July 1995 and early 1996, when an outbreak occurred with 99 confirmed cases, 24 of which developed HUS. The total number of cases in 1995 and 1996 were 114 and 118, respectively, with the principal serotype reported being *E. coli* O157. The National Veterinary Institute and the National Board of Agriculture are carrying out a survey of the prevalence of EHEC in the faeces of cattle at the 16 main abattoirs which produce 90% of all domestic beef. Up to April 1997 a total of 2195 samples had been analysed and 25 (1.1%) found to be positive for VT-producing (VT1 and/or VT2) *E. coli* O157, which were positive for *eae*A genes.

In 1996 the reported rate of infection with EHEC in England and Wales was 1.29 cases per 100000 population, which compares with 0.49 per 100000 population in 1990. The increase in the number of cases reported during the 1980s may be attributed, in part, to increased surveillance as more laboratories began to screen diarrhoeal stool specimens for *E. coli* O157. However, the continued rise in isolates during the 1990s probably reflects a real increase in the incidence of the pathogen. Recent studies on the incidence of VTEC O157 in animals at slaughter and in retail foods have revealed the presence of VTEC O157 in cattle (15.6%) and sheep (2.2%), but not in pigs or poultry. Also *E. coli* O157 was found in 9% of lamb products, particularly lamb-burgers, and in 1.5% of beef products.

Laboratory reports of VTEC in Scotland have risen from a total of three in 1984 to 506 in 1996, with the annual rates of infection having increased from 2.24 per 100000 in 1992 to 9.85 per 100000 in 1996. Within these totals there is considerable geographical variation, with the rates in different health boards varying from 2.3 to 33.0 per 100000 in 1996. This latter value includes cases in the largest outbreak reported in the United Kingdom (496 cases, of which 272 were confirmed by laboratory diagnosis), which resulted in 19 deaths. The incidence of VTEC in Scotland is considerably higher than that reported elsewhere in the United Kingdom; also, the variation between Scotland and other parts of the United Kingdom, or indeed the variation within Scotland, has not been explained.

Data reported at a recent international conference on VTEC infections (*2*) in the Czech Republic, Finland, Italy, and Belgium suggest that EHEC infections in these countries are not common. Also, the incidence of HUS in Austria during 1995 was reported to be 0.37 cases per 100000 people aged 0–14 years; in Belgium the annual incidence was 4.2 cases per 100000 children under 5 years of age (0.4 cases per 100000 residents); and in Italy the incidence was 0.2 cases per 100000 population.

Surveillance of EHEC infections

Surveillance is defined as the systematic collection, analysis, interpretation, and dissemination of health data for the purposes of disease prevention and control. The need and ability to conduct surveillance for EHEC infections and their sequelae vary across countries depending upon the specific patterns of clinical disease, the relative importance of specific EHEC strains, and the resources available. The objectives of surveillance for EHEC infections in humans are identification of outbreaks, determination of disease trends, estimation of the burden of illness, and compilation of other data with which to base decisions for resource allocation. When establishing surveillance for EHEC infections, emphasis should be placed on timely collection, analysis, and transmission of data to those who can undertake appropriate responses at local, regional, and national levels. Suitable incentives must exist to encourage supply of the needed data in a timely manner. One of the most important of these is the timely feedback of surveillance information in a useful format. Surveillance systems for EHEC should not be developed *de novo* but rather within the framework of surveillance systems for other diseases transmitted through food, water, and contact with animals.

A variety of approaches has been used to carry out surveillance for EHEC infections. The principal methods for surveillance include hospital-based systems for identification of HUS cases and laboratory-based systems for the identification of infected individuals. Laboratory-based systems can be supplemented by active, sentinel-site surveillance in some circumstances; for example, in regions where culture for *E. coli* O157 is not routine. The development of outbreak surveillance systems is of great value in view of the magnitude of past outbreaks, the serious nature of the disease, and the valuable lessons to be learned from outbreak investigations.

For surveillance and reporting purposes, a case of EHEC infection may be defined as diarrhoea with laboratory evidence of EHEC infection; or bloody diarrhoea or HUS linked to a laboratory-confirmed case. Case reports based on individual cases should be made and include, as a minimum, the following: the patient's age, sex, date of onset of the illness, place of residence, and basis of diagnosis. Depending on the availability of resources, countries should consider collecting additional data on risk factors deemed appropriate to their setting; examples may include recent travel, restaurant exposure, and animal contact. To detect outbreaks, local health authorities should review case reports on at least a weekly basis. An EHEC outbreak should be suspected whenever there is an unusual increase in the number of patients with bloody diarrhoea or HUS.

HUS is a serious illness whose diagnosis does not depend on stool culture, and its incidence may be used as a robust and consistent marker for EHEC infections over time. Thus, in addition to surveillance for EHEC infections, *per se*, countries should consider establishing an independent surveillance system for HUS cases and attempt to define their etiology. This will have the added benefit of providing an efficient means of identifying non-O157 strains that are of public health importance. Countries whose resources prohibit the establishment of surveillance for EHEC infections should none the less consider establishing surveillance for HUS.

Laboratory confirmation of EHEC infection may be defined as isolation from stools of *E. coli* O157 or other VTEC previously shown to cause human disease (e.g. O111, O26); or evidence of an acute serological response to one of these known pathogens. Laboratory confirmation of EHEC infection should be sought for all patients with HUS, visible bloody stools, or a history of bloody diarrhoea. Where resources permit, laboratory confirmation should be sought for patients with nonbloody diarrhoea and asymptomatic individuals epidemiologically linked to a culture-confirmed case. For surveillance, isolation of *E. coli* O157 should be attempted using readily available methods (e.g. cefixime/tellurite/sorbitol, MacConkey agar, and testing of nonfermenting sorbitol colonies with O157 antiserum). Efforts should also be made to isolate non-O157 EHEC.

The above definition of laboratory confirmation is for surveillance purposes only. The range of VTEC strains implicated in human disease continues to expand, and attempts to identify them should be encouraged. Similarly, ancillary tests such as detection of free verocytotoxins in enriched stool cultures or specialized tests for the identification of verocytotoxin or *eae* genes (e.g. PCR, gene probes, etc.) may be indicated in some outbreaks and in some clinical situations (e.g. when EHEC infection is suspected on clinical grounds). If these tests are used, an effort should still be made to isolate the organism. The identification of verocytotoxin alone does not constitute laboratory confirmation of EHEC infection.

Outbreak identification

Aggregation of data at regional, national, and international levels is essential to identify widespread outbreaks, especially those in which the number of cases per unit area is small. Countries should have the ability to aggregate surveillance data at various levels (region, state, country) and to share these data across jurisdictions in a timely manner. Efforts should be made to improve the capacity to undertake this sharing of data electronically and to link laboratory and epidemiological data.

Because the identification of EHEC strain by serotype alone may not be a sufficiently specific epidemiological marker for the identification of some outbreaks, countries should establish and maintain national reference laboratories for subtyping of EHEC. To facilitate the identification of multinational outbreaks, efforts should be made to standardize subtyping methods so that data may be exchanged between countries.

When an outbreak of EHEC infection is detected, local, provincial (or national) health authorities should be notified immediately. Initial outbreak reports should specify the serotype, the number of patients, their ages, the dates of onset of illness, the towns or areas affected, and the basis of the diagnosis. Local health authorities should be encouraged to directly notify officials in adjacent localities. Reports of outbreaks should be shared with neighbouring countries and countries whose residents may have consumed the suspect product.

In view of the severity of EHEC-associated illness, there is a special urgency to provide accurate and timely surveillance information so that data may be linked to an appropriate response. Thus, data should be disseminated to all levels of government, industry, and the general public in a readily usable format, subject to restrictions related to accuracy and patient and proprietary confidentiality.

Experience with recent outbreaks shows that media attention will be swift, dramatic and intense because of the serious nature of EHEC infection and the age groups affected. Accurate and consistent information from the outbreak team should be channelled to the media via regular press briefings by a designated officer. It is advisable for public health authorities to have a robust media-handling strategy as part of their major outbreak plans for the containment of foodborne infections. Public health authorities must be prepared in advance to deal with large numbers of enquiries from the media, and persons designated to deal with the media must have received adequate training. It is also advisable for agencies dealing with an outbreak to speak always from the same brief. Experience has demonstrated the advantages of pre-empting the demobilizing effects of news coverage of outbreaks by running regular food safety campaigns and for producing accurate, consistent, and user-friendly press releases. Alternative and supplementary approaches to conveying preventive health information could be considered, such as buying advertising space in newspapers for food safety information/bulletins, buying radio or television time for food safety information advertising, or providing a free telephone help line where members of the public can obtain accurate information during the outbreak.

Outbreak investigation

The objectives of outbreak investigations are as follows: to identify how EHEC transmission is occurring and take timely corrective action; to enlarge knowledge about EHEC, the diseases they cause, and their epidemiology; and to use such knowledge for the further prevention of EHEC transmission. Successful outbreak investigations often depend on effective communication between agencies involved with public health, food, and agriculture. Coordination between agencies is critical to ensure efficient management of outbreaks and the dissemination of accurate information to the public.

The conceptual framework used to investigate an EHEC outbreak does not differ substantially from that used to investigate outbreaks caused by other enteric pathogens. Nevertheless, EHEC have distinctive features that may complicate the investigation, including a propensity to affect children, high morbidity and case fatality rates, and a low infective dose.

Outbreaks may be recognized from data in the surveillance system or by an unusual cluster of clinical disease (bloody diarrhoea or HUS) not yet registered by a surveillance system. An outbreak is defined either as two or more linked cases of the same illness, or as an unexplained increase in the number of cases above the background level. It is important to verify that an outbreak is occurring and this will include ascertaining the details of the clinical illness in the index cases and the details of any microbiological or laboratory testing if performed. Laboratory confirmation of initial cases is essential.

The case definition used during an EHEC outbreak may differ from that used in EHEC surveillance. An agreed case definition should be used throughout the investigation. Potential choices of case definitions that were proposed during the WHO Consultation include those outlined below.

- *Confirmed symptomatic case* (gastrointestinal illness in a person with microbiological confirmation of EHEC infection).
- *Confirmed asymptomatic case* (an asymptomatic person in an outbreak setting with microbiological confirmation of EHEC infection).
- *Probable case* (bloody diarrhoea and/or HUS in a person without microbiological confirmation of EHEC infection).
- *Possible case* (nonbloody diarrhoea in a person in an outbreak setting without microbiological confirmation).

Control measures

Once a food, beverage or facility has been demonstrated to be associated with EHEC transmission, control measures must be taken in a timely manner. These may include removal of a commercially available product from distribution, collection of the already purchased product, closure of a facility, or modification of a process. Dissemination of this information to the appropriate public audience is a key component in eliminating EHEC transmission. Before recall of an implicated food or beverage can take place, records of distribution and sale need to be sought.

Where an outbreak has been attributed to person-to-person transmission, control measures include the following: strict hand washing and good hygienic practices among residents and those caring for ill persons; infection control precautions for hospitalized or institutionalized persons; and medical clearance of patients before returning to schools or employment.

An important control measure in the management of an outbreak is continuous communication between the investigation team and the public, professional groups, authorities and business. The objectives of informing professional groups are to assure accurate case-finding and a smooth implementation of control measures. The objectives of informing the public should be to give accurate information on signs and symptoms of EHEC infection; on what steps need to be taken for those that have been exposed; to provide information on implicated products and how they should be handled; and to provide advice on personal hygiene to reduce person-to-person spread. Information should be regularly exchanged between the outbreak team and the producer of the food implicated in an outbreak. The objectives are to keep the business abreast of the findings of the outbreak investigation and to prepare the business for the possible implementation of control measures. For producers of related products, the objective of communication is to increase awareness about food safety issues with the type of product or process causing the outbreak.

Recommendations from the Consultation with respect to investigation of EHEC outbreaks include those shown below.

• Creation of effective lines of communication among the different national agencies involved in public health, food, and agriculture. Ideally, these should already be in place before an outbreak occurs.

• Coordination between representatives of the relevant agencies should be a very high priority during the outbreak. Ideally one person should be in charge of the outbreak investigation and facilitate coordination between agencies.

• Notification of neighbouring health jurisdictions and regional or national health authorities to determine whether other cases have been or are occurring. Preferably the same case definition should be used in the other locations. Depending on the nature and extent of the outbreak, national authorities may consider notifying other countries.

• In-depth investigation of EHEC outbreaks should aspire, not only to stop the actual outbreak, but also to determine the point or process where EHEC contamination has occurred, so that changes can be introduced to prevent reoccurrence.

• There is a clear need to train individuals to conduct epidemiological investigations.

• Effective press management is crucial at all stages of the outbreak investigation. Information from the outbreak team should be channelled to the media via a designated officer by means of regular press briefings. The information should be accurate and consistent.

• Strong epidemiological evidence identifying a food or beverage vehicle is sufficient grounds to initiate a trace-back effort and recall a product. Ideally, the epidemiological data should be reviewed by an independent panel.

• An environmental investigation of the implicated facility, source, or process is an integral part of the epidemiological investigation. It is of great importance for this part of the outbreak investigation to involve persons with the technical knowledge (e.g. food, sanitation, animal health, water) relevant to the item that has been implicated in disease transmission.

• The effectiveness of any control measures undertaken will need to be monitored. Even with a marked decrease in cases with the outbreak strain, the continued presence of the organism at a lower frequency can imply continuing transmission. This would prompt a further reassessment of all control measures.

Prevention and control of EHEC infections

In general, the prevention of foodborne diseases must be based on good hygienic practices and control of the contamination of foods by biological and chemical hazards. This can be achieved most effectively through the application of food safety assurance programmes, based on the principles of the Hazard Analysis and Critical Control Point (HACCP) system. Such a system should be applied by primary producers, manufacturers, retailers, and food service establishments. Guidelines can be found in the Codex Code of Practice on General Requirements of Food Hygiene (*7*).

Specific controls for EHEC contamination throughout the food chain can best be identified by conducting a systematic risk assessment exercise as discussed in the Joint FAO/WHO Expert Consultation on the Application of Risk Analysis to Food Standards Issues (*17*). Risk management then weighs policy alternatives in the light of the assessment and selects appropriate control options (*6*).

EHEC is assumed to be present in animal and human faeces; therefore, appropriate animal husbandry practices should be adopted to minimize the spread of contaminated material to animals or on ground used for crops. If faecal contamination or EHEC is present in any raw material, the organisms must be eliminated at some point in the production process or by the consumer prior to consumption.

The recommendations shown below are based upon current, albeit limited, knowledge and understanding of EHEC and experience gained through the investigation of EHEC infections and outbreaks. They are presented in the order of the food chain, from animal and plant production through to the point of consumption, followed by general issues, and are not prioritized.

Recommendations

Animal and plant production

- Because of the low infectious dose of the *E. coli* O157 group of organisms, all producers should recognize the importance of hygiene and good manufacturing practice. Particular attention should be paid to maintaining the cleanliness of animals and prevention of spread of faecal material, which is the primary source of contamination. At the point of slaughter, animals should be clean and free of visible contamination.

- Animal slurry and human faecal waste (night soil) should not be used on or near crops intended for human consumption, unless it has been adequately treated.

- Animal and human (faecal) waste must be disposed of in a manner that does not contaminate the water supply. Both run-off water and proximity of animals to wells have been shown to contaminate water supplies.

- Crops used for raising seeds that are going to be used as sprouts should not be fertilized with animal slurry or human faecal waste, even if some form of treatment has been applied.

- Crops for food should be irrigated with water that is not faecally contaminated.

Transportation

- Animals for slaughter should be transported in a manner that maintains cleanliness, minimizes contamination from other animals, and limits undue stress.

- Transport vehicles should be cleaned and dried before any further use.

- Water should be decontaminated before coming into contact with fruits and vegetables for cooling and rehydrating purposes during packing, transportation, and processing.

- Fruits and vegetables should be transported in such a way to minimize damage and to prevent entry of EHEC and other pathogens into these products.

Harvesting of animals and plant produce

- Any water used for washing and/or processing of animals, fruits, and vegetables should be of potable quality.

- Holding of animals prior to slaughter should be done in such a manner that they are kept clean.

- All abattoirs/establishments where animals are slaughtered should have in place a system of good hygienic practice and an effective HACCP plan covering all stages in the production process, from the time animals arrive until the carcasses or meat products leave the establishment.

- In handling carcasses, particular care should be taken during the dehiding stage, removal of hoofs, evisceration, and cutting to minimize cross-contamination. In addition, care should be taken to minimize spillage of intestinal tract contents.

- Good abattoir practices should include the minimal use of water, especially where this contributes to the spread of faecal material.

- Special care should be paid to fruit and other produce to prevent its accidental contact with soil or animal faeces (e.g. fallen apples), since these have been implicated in the transmission of EHEC infections.

Processing of animal products and plant produce

- Food producers who purchase meat from abattoirs, or those who have their own slaughtering facilities, should undertake regular hygiene inspections of the slaughter premises. In addition, food producers should establish raw material specifications, since these have been shown to improve the quality of meat, reducing the risk of EHEC being present on raw material.

• Experts agreed that it is practically impossible to produce raw milk without faecal contamination, and felt strongly that to prevent EHEC transmission from milk it should be pasteurized or treated using procedures able to deliver an equal level of safety.

• Post-pasteurization contamination in the plant or after packaging must be avoided by adherence to a comprehensive HACCP plan.

• For raw, ready-to-drink fruit or vegetable juices where the safety of the product cannot be assured, a processing step that can remove or destroy EHEC, such as pasteurization, should be applied.

• Irradiation should be considered as a decontamination step for some products, especially if there is no other practical control or prevention step available, or if they are ready-to-eat foods for highly susceptible individuals.

• Manufacturers of fermented foods (such as cereal products, salami, mettwurst, yoghurt or cheese made from unpasteurized milk) which use raw materials that may harbour EHEC should assure their absence in a serving portion (i.e. demonstrate that their process is sufficient to remove or destroy the organisms in a serving portion).

• Producers of sprouts from seeds (manufacturers, retailers, food service establishments, and those doing so at home) should use potable water.

Food retail and food services

• The objective here should be to reduce the risk of direct and indirect cross-contamination between raw and ready-to-eat foods; this can be achieved through time and spatial physical separation, together with safe food hygiene practices. Decisions about the degree of separation and handling practices should be made within the framework of an HACCP approach. In practice, consideration will need to be given as to how the separation will be achieved in storage, production, sale, and display; for example, it may involve separate refrigeration, work areas, equipment, utensils, and staff.

• Food handlers, including home caterers, should be trained in the principles of food hygiene and the application of HACCP, with particular attention to the special precautions for preparing and serving food to vulnerable groups, in accordance with WHO recommendations (*14*).

Non-foodborne transmission of EHEC

• Regulatory authorities should be made aware that EHEC infections have been attributed to drinking untreated well-water, and swimming/playing in (untreated) water contaminated by a variety of sources; and they should take appropriate action.

• Both adults and children having contact with animals on farms and at other sites should be made aware of the extremely low infective dose of *E. coli* O157, and possibly other EHEC, and the potential for transmission from such contact. Measures to implement and enhance strict hygienic practices in these settings should be encouraged. Visitors to farms, who may be unaware of the highly infectious nature of EHEC in these settings, must also be instructed to maintain good handwashing and other hygienic practices. This is of particular importance for children, as several outbreaks have occurred among school-children after visiting farms.

• Staff in laboratories working with EHEC organisms should be made aware of the due care required because of the low infectious dose and the severity of disease caused by these organisms.

Consumer education

The reported low infectious dose of some EHEC strains, such as O157:H7, necessitates fundamental change in the way meat and other foods likely to be contaminated are handled by the consumer.

• Existing education programmes should be reviewed to ensure that they adequately address the low infectious dose of EHEC, the understanding of severe, long-term effects of infection, and the need for thorough cooking of food.

• Food hygiene training should be carried out wherever possible within the primary and secondary school curriculum through the use of well-designed educational material, such as those provided by WHO (*15*).

• An education strategy on food safety for the consumer, conducted by a variety of organizations (e.g. government, the food industry, consumer associations, trade associations, and consumer groups) should provide consistent, clearly understood messages, soundly based on scientific principles. Messages could be tested by focus groups. Conflicting messages must be avoided.

• Educational programmes should use all means of disseminating information, including the media (newspapers, TV, radio) leaflets, lectures/lessons, training courses, labelling, and in-store posters/ leaflets.

• The concept of risk communication involving all interested parties, including consumers, should be adopted to reduce EHEC infections.

Enacting regulatory changes

• Where regulatory change affecting food supply is considered by governments, risk assessments and cost-benefit analyses should be conducted first. These analyses should be transparent, available to all interested parties, and clearly document food safety, consumer risk, and economic trade-offs.

• In order to enhance the success of trace-back of contaminated foods, sufficient information should be recorded or documented at each stage of movement along the food chain, to identify the origin and destination of the product.

Role of international organizations

• EHEC outbreaks are rare and not all countries have sufficient experience or capacity to investigate them adequately. Countries may be reluctant to accept direct assistance from other countries. WHO should therefore strengthen its capacity to provide support rapidly to countries for outbreak investigations and in applying prevention and control strategies when EHEC outbreaks are suspected.

• International organizations should coordinate international exchange of food safety information specifically on EHEC to eliminate duplication of country efforts.

• WHO, in collaboration with countries, should act internationally as a collection point and clearing house for EHEC data. National authorities can also disseminate information on EHEC.

• The Joint FAO/WHO Food Standards Programme (Codex Alimentarius) should support and develop the principles of risk analysis in developing countries, through coordination of international experts and those in developing countries, to collect relevant data, educate and train expert teams in risk assessment to prioritize risk management options and develop risk communication approaches.

• Codex Alimentarius should promote the application of the HACCP system and encourage both developed and developing countries to design and implement HACCP plans for specific food commodities, from production to marketing of locally produced foods and food products.

• WHO should recommend that countries entering into specific control programmes, such as herd-control systems, should make available to the organization information on the success of such systems.

• Following the "WHO 10 Golden Rules" will result in a reduction of foodborne disease in general (*16*); however, it is recommended that these rules be reviewed and, if necessary, revised, in view of more recent information about foodborne EHEC infections. Particular attention should be paid to the low infectious dose, washing of fruits and vegetables, cooking and reheating temperatures, and alternative processing procedures, such as *sous-vide* cooking.

Résumé

Infections à *Escherichia coli* entérohémorragique (ECEH): prévention et lutte

Escherichia coli est un hôte habituel de l'intestin chez l'homme et l'animal, mais il en existe certains types pathogènes à l'origine de diverses maladies humaines. L'un de ces types pathogènes, *E. coli* O157:H7, appartient au groupe des *E. coli* entérohémorragiques (ECEH) qui produisent des toxines puissantes et sont à l'origine d'une maladie particulièrement grave, la rectocolite hémorragique. Chez environ 10% des malades, l'affection peut se compliquer d'un syndrome urémique hémolytique gravissime, caractérisé par une insuffisance rénale aiguë, une anémie hémolytique et une thrombopénie. Ces séquelles sont particulièrement graves chez les jeunes enfants et les personnes âgées. En moyenne, 2–7% des malades atteints de cette complication décèdent, mais lors de certaines flambées la mortalité a atteint 50% chez les personnes âgées.

Le présent Mémorandum montre l'importance croissante de *E. coli* O157:H7 en tant qu'agent pathogène transmis par les aliments. Il traite de la surveillance, de l'investigation des flambées et des stratégies de lutte, questions débattues lors de la Consultation OMS sur la prévention et le contrôle des infections à ECEH. Parmi les mesures de prévention et de lutte recommandées figurent l'utilisation d'eau potable dans la production alimentaire, la propreté des animaux conduits à l'abattoir, l'amélioration de l'hygiène à toutes les étapes de l'abattage, l'utilisation appropriée des

techniques de production alimentaire, la cuisson suffisante des aliments, et l'éducation des manipulateurs de denrées alimentaires, des travailleurs des abattoirs et des travailleurs agricoles sur les principes et la pratique de l'hygiène des denrées alimentaires.

References

1. **Abdul-Raouf UM et al.** Isolation of *Escherichia coli* O157:H7 from some Egyptian foods. *International journal of food microbiology*, 1995, **29**: 423–426.
2. *Third International Symposium and Workshop on Shiga Toxin (Verocytotoxin)-producing* Escherichia coli *Infections, 22–26 June 1997, Baltimore, MD, USA* (in press).
3. **Bernardino L et al.** Haemorrhagic colitis epidemic in Africa. *Lancet*, 1993, **342**: 495–496.
4. **Brown JE et al.** Determination by DNA hybridization of Shiga-like-toxin-producing *Escherichia coli* in children with diarrhoea in Thailand. *Journal of clinical microbiology*, 1989, **27**: 291–294.
5. **Cordovez A et al.** Enterohemorrhagic *Escherichia coli* associated with haemolytic uraemic syndrome in Chilean children. *Journal of clinical microbiology*, 1992, **30**: 2153–2157.
6. *Risk management and food safety: report of a Joint FAO/WHO Consultation, Rome, Italy, 27–31 January 1997.* Rome, Food and Agriculture Organization of the United Nations, 1997 (FAO Food and Nutrition Paper No. 65).
7. *Report of the Twenty-Ninth Session of the Codex Committee on Food Hygiene.* Food and Agriculture Organization of the United Nations Rome, 1997.
8. **Germani Y et al.** Enterohaemorrhagic *Escherichia coli* in Central African Republic. *Lancet*, 1997, **349**: 1670.
9. **Kain KC et al.** Etiology of childhood diarrhea in Beijing, China. *Journal of clinical microbiology*, 1991, **29**: 90–95.
10. **Ogunsanya TI et al.** A study of the aetiological agents of childhood diarrhoea in Lagos, Nigeria. *Journal of medical microbiology*, 1994, **40**: 10–14.
11. **Paquet C et al.** Aetiology of haemorrhagic colitis epidemic in Africa. *Lancet*, 1993, **342**: 175.
12. **Sang WK.** Prevalence of diarrhoeagenic *Escherichia coli* in Kenyan children. *Journal of diarrhoeal disease research*, 1996, **14**: 216–217.
13. **Son R et al.** Isolation of verotoxin-producing *Escherichia coli* associated with diarrhoea in Malaysia containing plasmids showing homology with biotinylated Shiga-like toxin DNA gene probes. *World journal of microbiology and biotechnology*, 1996, **12**: 243–246.
14. **Jacob M.** *Safe food handling: a guide for managers of food service establishments.* Geneva, World Health Organization, 1989.
15. **Williams T, Moon A, Williams M.** *Food, environment and health: a guide for primary school teachers.* Geneva, World Health Organization, 1990.
16. **Käferstein FK.** Pleasures and pitfalls of eating. *World health*, November 1988, 6–7.
17. *Application of risk analysis to food standards issues: Report of a Joint FAO/WHO Expert Consultation, Geneva, 13–17 March 1995.* (Unpublished document WHO/FNU/FOS/95.3, 1995; available upon request from Food Safety, World Health Organization, 1211 Geneva 27, Switzerland).