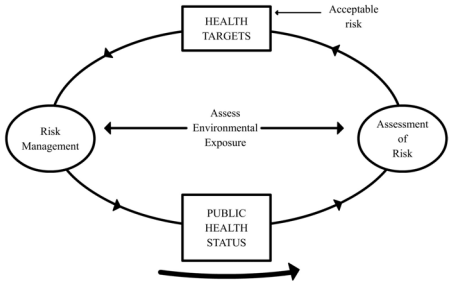

4

Endemic and epidemic infectious intestinal disease and its relationship to drinking water

Pierre Payment and Paul R. Hunter

Guidelines operate from the premise that pathogens do occur in the environment and that there is a susceptible population. This chapter examines this assumption in relation to gastrointestinal pathogens focusing largely on the drinking water environment. It examines the prevalence of diarrhoeal disease in different communities and compares the situation between developing and developed countries.

4.1 INTRODUCTION

It was only in the early part of the twentieth century that waterborne pathogenic micro-organisms and their diseases were finally controlled to an acceptable level in the then rapidly industrialising countries. The control of these diseases was due to

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various factors, not least of which were the introduction of adequate water treatment, including filtration and chlorination. Improved wastewater disposal, pasteurisation of milk, and improved food preparation and storage also contributed to a general enhancement of hygiene. It should be remembered that water is usually only one of several possible routes of transmission of 'waterborne diseases'. While it is assumed that a significant proportion of these gastrointestinal illnesses are waterborne, we have very little data to estimate the proportion of the overall burden of disease that is due to transmission by drinking water. Furthermore, considered as part of a holistic approach, a reduction in water resources contamination would result in measurable reductions in gastrointestinal illnesses associated with other transmission routes.

At the onset of the twenty-first century, what do we know of the health effects of drinking water and their impact on our so-called modern societies? There are many reports on the impact of waterborne diseases in countries worldwide revealing thousands of outbreaks due to bacterial, viral, and parasitic micro-organisms associated with the consumption of untreated or improperly treated drinking water (Ford and Colwell 1996; Hunter 1997; WHO 1993; WHO 1996; see also Chapter 6 of this volume).

The World Health Organization (WHO) estimated in 1996 that every eight seconds a child died from a water-related disease and that each year more that five million people died from illnesses linked to unsafe drinking water or inadequate sanitation (Anon 1996). WHO also suggest that if sustainable safe drinking water and sanitation services were provided to all, each year there would be 200 million fewer diarrhoeal episodes, 2.1 million fewer deaths caused by diarrhoea, 76,000 fewer dracunculiasis cases, 150 million fewer schistosomiasis cases and 75 million fewer trachoma cases.

These statistics serve to shock societies complacent about their water supplies, but do little to give a true estimate of the prevalence of waterborne disease in individual communities. In this chapter, we shall attempt to gain an insight into the prevalence of diarrhoeal disease in different communities and then to estimate the proportion of such disease that may be linked to drinking water.

4.2 AETIOLOGY OF GASTROINTESTINAL ILLNESSES

Many infectious causes of acute gastrointestinal symptoms have been described in the literature (Branski 1984; Bryan 1985; Ellner 1984; Goodman and Segreti 1999; Hunter 1997). These include parasitic agents such as *Cryptosporidium parvum*, *Giardia lamblia*, *Cyclospora* and *Entamoeba histolytica*; bacterial pathogens such as *Salmonella*, *Shigella*, *Campylobacter*, *Vibrio cholera*, enterovirulent *Escherichia coli*, *Aeromonas*, *Yersinia* and *Clostridium perfringens*; and viruses such as the enteroviruses, rotaviruses, parvoviruses,

Norwalk and Hawaii agents, adenoviruses, caliciviruses, and astroviruses. Many of these pathogens have been transmitted by the water route, in addition to person-to-person, animal-to-human, food-borne and aerosol routes.

However, acute infection is not the only cause of acute diarrhoeal disease. Milk or soy protein intolerance, food abuses or diet changes, side-effects of prescription drugs (especially antibiotics) as well as fungal, algal or shellfish toxins may all cause diarrhoea. A number of chemicals such as monosodium glutamate, organic mercury, antimony, and copper (Branski 1984; Ellner 1984) can also induce gastrointestinal symptoms.

Hodges *et al*. (1956) presented data on the surveillance of infectious diseases in Cleveland (US) and offered a table of circumstances explaining the gastrointestinal symptoms observed. From their data, 116 out of 362 cases were due to acute infectious diseases, 63 were due to dietary indiscretion, 59 to coughing/gagging, 45 to medication, 18 to emotional causes and 61 were of unknown origin.

4.3 INCIDENCE OF GASTROINTESTINAL ILLNESS IN INDUSTRIALISED COUNTRIES

It is generally very difficult to derive a good estimate of the incidence of endemic acute gastrointestinal disease in a community. Only a proportion of people infected develop symptoms, and only a proportion of these will seek medical attention. Even if patients with diarrhoea present to their doctor, the doctor may not report the illness or even take samples. Even if samples are taken, subsequent laboratory analysis may not detect a pathogen because the specific pathogen was not screened for or because the laboratory tests were not sufficiently sensitive. Even when the laboratory correctly identifies a pathogen, this may not be reported to appropriate surveillance systems. In many communities, it is still not clear what proportion of acute episodes reach appropriate surveillance systems (see Chapter 6). The consequence is that existing surveillance systems are likely to dramatically underestimate the real burden of acute gastrointestinal disease. It is only through appropriately designed epidemiological studies that the real incidence of acute diarrhoeal disease in a population can be estimated. There are very few such studies reported in the literature.

Few studies have investigated the incidence of gastrointestinal disease at the community level. Three such studies have described the health status of individuals in the US over a long period of time, the Cleveland study (Dingle *et al*. 1953; Hodges *et al*. 1956) the Tecumseh study (Monto and Koopman 1980,

Monto *et al*. 1983) and the Virus Watch Program (Fox *et al*. 1966). These studies have provided information on the illness rates in the northern part of the US. All these studies have reported gastrointestinal illness rates in the range of 0.5–2 episodes/year/person and incidence of 5–100 episodes/1000/ week according to seasons and age. The number of episodes of gastrointestinal illnesses is similar in all these studies despite the fact that more than 40 years have elapsed between some of them.

In the Cleveland study (Hodges *et al*. 1956) the mean incidence of gastrointestinal illness was 1.6 episode/person/year with a maximum of 2.6 observed in children aged four and an incidence of 0.9 in adults. A seasonal pattern was observed, with the lowest incidence in July and the highest in November in 1948/49/50. The Tecumseh study (Monto and Koopman 1980) reported a maximum incidence in children and a mean incidence of 1.2. However, their definitions of gastrointestinal illness were stricter than those of the earlier Cleveland study. Mean rates of enteric illness syndromes were 0.35 episodes/person/year for vomiting, 0.40 for diarrhoea, 0.23 for both at the same time and 0.22 for nausea and/or upset stomach for a mean total of 1.20 (std. dev: 1.5). They also report variation in the seasonal incidence of gastrointestinal illness according to age, with adults (over 20 years old) being least susceptible, and children under five years old being the most susceptible. Peaks of up to 90 episodes/1000/week were observed in children in November, while values as low as five episodes/1000 persons/week were reported in July.

Studies in the UK have suggested a lower level of diarrhoeal disease than those in the US. Feldman and Banatvala (1994) added questions about diarrhoeal disease to the monthly OPCS (Office of Population and Census Survey) Omnibus survey. This is a government survey that interviews about 2000 adults each month on a range of issues. Some 8143 adults were asked whether they had had diarrhoea in the previous month. From the responses, the authors calculated an annual attack rate of 0.95 episodes per person per year. In a study of two general practice populations in South Wales, another group conducted a postal questionnaire survey (Palmer *et al*. 1996). This group estimated an attack rate of 0.89 episodes per person per year.

Also in the UK, a study was carried out to establish the incidence and aetiology of infectious intestinal disease in the community and presenting to general practitioners in comparison with incidence and aetiology of cases reaching the national laboratory surveillance scheme (Wheeler *et al*. 1999). An incidence of 0.194 episodes/person/year was observed in the community-based study. Based on 8770 cases presenting to their general practitioner the incidence was only 0.033 episodes/person/year. One case was reported to national surveillance for every 1.4 laboratory identifications, 6.2 stools sent for laboratory investigation, 23 cases presenting to general practice, and 136

community cases. The ratio of cases in the community to cases reaching national surveillance was lower for bacterial pathogens (*Salmonella* 3.2:1, *Campylobacter* 7.6:1) than for viruses (rotavirus 35:1, small round structured viruses 1562:1). There were many cases for which no organism was identified. The authors concluded that infectious intestinal disease occurs in one in five people each year, of whom one in six presents to a general practitioner. The proportion of cases not recorded by national laboratory surveillance is large and varies widely by micro-organism. The attack rate of only 0.194 episodes per person per year is well under usually reported values. The large discrepancy between this and earlier studies probably reflects the case definition and the different study design, a prospective longitudinal study. Instead of asking whether respondents had had diarrhoea in the previous month, the study asked participants to send in postcards on a weekly basis for six months declaring the absence of symptoms (those with symptoms sent a stool sample). Interestingly, at the start of the prospective community study, participants were asked whether they had had diarrhoea in the past month. Based on this figure the estimated attack rate would be 0.55 episodes per person per year, with the difference thought to be due to 'telescoping' of recent events.

In many developed countries, food-borne infections are under surveillance and data on the occurrence of cases can be found in reports produced by various agencies. While they provide an interesting list of the micro-organisms implicated, the reported cases are often only the tip of the iceberg as very few individuals are severely affected. Reports to physicians and samples sent to laboratories for analysis do not reflect the true level of food-borne disease. The United States have increased their level of surveillance through a network called 'FoodNet' (www.cdc.gov/ncidod/dbmd/foodnet) (CDC 1997, 1998, 1999). Their data provides information on several pathogens by age, sex, site and pathogen on an ongoing basis. Cases reported through active surveillance represent a fraction of the number of cases in the community. To better estimate the number of cases of food-borne disease in the community, FoodNet conducted surveys of laboratories, physicians, and the general population in the FoodNet sites. Of the 10,000 residents covered by the FoodNet survey, 11% reported a diarrhoeal illness during the previous month or 1.4 episodes of diarrhoea per person per year. Of those who were ill, only 8% sought medical care. Of those seeking medical care, 20% reported submitting a stool specimen for culture. Through active surveillance and additional studies, FoodNet is providing better estimates of the burden of food-borne illness and is tracking trends in these diseases over time. In 1997, surveillance of the seven pathogens studied showed that 50 cases of these infections were diagnosed per 100,000 population, representing a total of 130,000 culture-confirmed cases in the entire US population. Additional

FoodNet surveys showed that these cases represent a fraction of the burden of food-borne illness. Based on these surveys, at least 60 more of these infections may have occurred for each one that was diagnosed, suggesting that approximately eight million cases of these bacterial infections occurred in 1997 in the US. However, the only community-based study carried out as part of the FoodNet programme was a retrospective study which has been shown in the UK to overestimate the incidence of diarrhoeal disease by about a factor of three (Wheeler *et al*. 1999).

Even taking into consideration differences in methodology between some of the US and UK studies, it would appear that the incidence of acute diarrhoeal disease in the US is about twice that in the UK. It is not clear to the authors of this chapter why this should be, although the more extreme differences of the US climate and a higher level of convenience food consumption may be factors.

4.3.1 Waterborne disease

While the most often reported disease associated with drinking water remains gastroenteritis, this is probably due to the very apparent nature of the symptoms and the fact that the attack rates for these infections can reach over 50% of the exposed population. Even infectious disease specialists often forget that enteric micro-organisms are associated with a wide range of symptoms and diseases. Protozoan parasites such as amoebae can cause severe liver or brain infections and contact-lens wearers are warned of the dangers of eye infections. Bacteria can cause pneumonia (*Legionella*) and some are suggesting the possibility that *Helicobacter pylori*, which has been associated with gastric ulcers, could be transmitted by the water route (Hulten *et al*. 1998).

In all industrialised countries, a steady decline in gastrointestinal disease was evidenced by the virtual elimination of cholera and the reduction of waterborne outbreaks to very low levels. Most bacterial waterborne pathogens have been eliminated by the simple use of chlorine disinfection. However, we are finding strains of *Vibrio cholerae* that are more resistant to disinfection, *Legionella* has been found in water heaters and the *Mycobacterium avium* complex (MAC) is now on the list of potential pathogens.

The micro-organisms implicated in waterborne diseases have been well described (Hunter 1997; Hurst *et al*. 1997; Murray *et al*. 1995). Waterborne diseases are usually described in terms of outbreak reporting in the various countries. Two countries, the US (Craun 1992) and the UK (Hunter 1997) have produced most of the available data (see Chapter 6). In other countries, data gathering is often very poorly performed because of lack of resources to identify the water-related events as well as the lack of centralised official data-gathering authorities. Several methods for the detection and investigation of waterborne

outbreaks have been described, but are still not widely used (Craun 1990) as resources and funds are critically lacking even in industrialised countries. An enormous effort is needed to educate populations on the importance of water in the dissemination of disease. All levels of society, from consumer to politicians, must be educated about the benefits of improving water quality (Ford and Colwell 1996) as a major step in improving quality of life and health.

Since the 1950s, with the development of methods to detect and identify viruses, many outbreaks of waterborne gastrointestinal illness that would have been simply classified as of non-bacterial origin have been attributed to enteric viruses. Hepatitis A and E, Norwalk, small round structured viruses (SRSV), astroviruses, caliciviruses and many others are now well-known names in the water industry.

Parasites are being identified as pathogens of importance even in industrialised countries. Numerous waterborne outbreaks of giardiasis have been reported in the US (Craun 1986). During the last twenty years there have also been a number of outbreaks of cryptosporidiosis in the UK (Badenoch 1990a,b). The continued problem with parasitic infection in drinking water is largely related to parasites' resistance to the water disinfection process. Dozens of outbreaks of cryptosporidiosis have now been reported worldwide, but most are small compared to the explosive outbreak experienced in Milwaukee (US) in the spring of 1993 (Edwards 1993; Mackenzie *et al*. 1994). Following what appears to be a combination of storm-washed faecal contamination from a compromised catchment and failure in treatment, water that met US microbiological water quality guidelines caused gastrointestinal illnesses in an estimated 400,000+ people, or one-third of the population of this city, over a period of one month. Most of these illnesses were cryptosporidiosis but many were probably of viral origin. The most surprising aspect of this event is that cryptosporidiosis was probably occurring even before it was detected following a report from an inquisitive pharmacist (Morris *et al*. 1998). This fact suggests that unless an effort is made to identify waterborne diseases they will remain undetected, buried in the endemic level of illness in the population.

Enteric viruses are also excreted through faeces into the environment by infected individuals with or without clinical illness. There are over 100 types of enteric virus, including enterovirus (poliovirus, coxsackievirus, echovirus, hepatitis A), reovirus, rotavirus, adenoviruses, coronavirus, calicivirus, astrovirus, Norwalk-like agents, and so on. While viruses are excreted in large numbers in the faeces of infected individuals, the low incidence of infection in a population, the dilution factor after their release in the water, and difficulty in detection accounts for low numbers in contaminated surface waters (Bitton 1980; Bitton et al. 1985; Rao and Melnick 1986). Reported numbers range from absence of enteric virus in uncontaminated

waters to several thousand or millions of viruses per litre of untreated wastewater (Bitton 1980; Bitton et al. 1985, Rao and Melnick 1986). Cultivable enteric viruses are however quite prevalent and can serve as an indicator of the overall viral population (Payment 1993a).

The Lubbock health effect study has also provided a very comprehensive data set on the prevalence of antibodies to several enteric viruses in an North American population (Camaan *et al*. 1985). Data on the seroprevalence of several enteric viruses in the Montreal area were obtained during an epidemiological survey on water-related illnesses (Payment 1993a,b). The seroprevalence of antibodies to several enteric viruses including hepatitis A virus (Payment 1991) and Norwalk virus (Payment *et al*. 1994) were reported (Table 4.1). Results indicated that the rates of hepatitis A viral infections are slightly lower than those reported for other countries. The data indicate that the hepatitis A virus is an infection progressively acquired in life and that in the Montreal area relatively few children have antibodies to this virus. This observation is in contrast with many countries where, due to a low level of hygiene, these infections are acquired early in life (Brüssow *et al*. 1990; Brüssow *et al*. 1988; Morag *et al*. 1984; Nikolaev 1966; Papaevangelou 1980).

Table 4.1. Seroprevalence (expressed as a percentage) to selected enteric pathogens in a French-Canadian population (Payment 1991; Payment *et al*. 1994; unpublished data for *Cryptosporidium*)

	Age groups (years)				
Micro-organism	9–19	20–39	40–49	50–59	60+
Hepatitis A	1	10	49	60	82
Cryptosporidium	21	55	59	52	20
Norwalk virus	36	67	80	70	64
Echovirus 9	40	69	70	51	60
Coxsackievirus B-2	51	60	67	66	60
Coxsackievirus B-3	51	64	63	55	60
Coxsackievirus B-4	44	80	77	74	80
Coxsackievirus B-5	58	74	61	62	20
Echovirus 11	78	84	91	83	80
Echovirus 30	96	98	92	96	100
Rotavirus	100	100	100	100	100

4.4 ENDEMIC WATERBORNE DISEASE IN INDUSTRIALISED COUNTRIES

While many micro-organisms have been implicated in outbreaks of various diseases, there is little epidemiological data on the endemic level of waterborne diseases. Those studies that have attempted to define the burden of waterborne disease have generally concentrated on gastrointestinal illness.

Batik *et al*. (1979) using hepatitis A virus cases as an indicator could not establish a correlation with water quality or find a correlation between current indicators and the risk of waterborne outbreaks (Batik *et al*. 1983).

In France, Collin *et al*. (1981) prospectively studied gastrointestinal illnesses associated with the consumption of tap water using reports from physicians, pharmacists and teachers. Their results were based on more than 200 distribution systems or treated or untreated water and they reported five epidemics (more than 1000 cases) associated with poor quality water. This study is typical of most studies which rely on the detection of epidemics to assess the level of water quality: they do not address the endemic level of gastrointestinal illnesses which may be due to low-level contamination of the water. The same group, in a prospective follow-up study on 48 villages for 64 weeks, evaluated untreated groundwater and found a relationship between faecal streptococci and acute gastrointestinal disease (Ferley *et al*. 1986; Zmirou *et al*. 1987). Faecal coliforms did not appear to be independently related to acute disease. Total coliforms and total bacteria showed no correlation with disease.

In a more recent study carried out in France, Zmirou *et al*. (1995) investigated the effect of chlorination alone on water that did not otherwise satisfy microbiological criteria. They prospectively followed up some 2033 schoolchildren aged between 7 and 11 years from 24 villages. In 13 villages the water had no treatment as it met current microbiological criteria in its raw state. In the other 11 villages, the raw water had evidence of faecal pollution and was chlorinated before it met current standards. The gastrointestinal morbidity of the children was recorded daily under the supervision of the schoolteachers. The crude incidence of diarrhoea was 1.4 times more frequent in the children from villages whose water supplies had evidence of faecal pollution, even after chlorination. These results strongly suggest that there are some pathogens in faecally polluted drinking water which are not adequately treated by chlorination alone.

In Israel, Fattal *et al*. (1988) addressed the health effects of both drinking water and aerosols. Their studies on kibbutz water quality and morbidity were performed in an area with relatively high endemicity of gastrointestinal disease and did not show a relationship between health effects and total or faecal coliforms. This study was, however, based only on morbidity reported to physicians, data that is considered to represent only 1% of the actual cases in a population. In Windhoek (Namibia), Isaäcson and Sayed (1988) conducted a similar study over several years on thousands of individuals served by recycled waste water as well as normal drinking water. They did not observe an increased risk of reported acute gastrointestinal illness associated with the

consumption of recycled waters. The populations compared had higher incidence rates than those observed in the US and they were subjected to a high endemicity level due to other causes, thus masking low levels of illnesses.

4.4.1 Intervention studies

Two major epidemiological studies have been conducted in Canada to evaluate the level of waterborne disease. The results of these studies suggest that a very high proportion of gastrointestinal illnesses could still be attributable to tap water consumption, even when water met the current water quality guidelines (Payment *et al*. 1991a,b, 1997). The first study was carried out from September 1988 to June 1989. It was a randomised intervention trial carried out on 299 randomly selected eligible households which were supplied with domestic water filters (reverse-osmosis (RO)) which eliminated microbial and most chemical contaminants from their tap water and on 307 randomly selected households which were left with their usual untreated tap water. The gastrointestinal symptomatology was evaluated by means of a family health diary maintained prospectively by all study families. The estimated annual incidence of gastrointestinal illness was 0.76 among tap water drinkers as compared with 0.50 among RO-filtered water drinkers ($p<0.01$). Because participants in the RO-filter group were still exposed to tap water (i.e. about 40% of their water intake was tap water), it was estimated that about 50% of the illnesses were probably tap-water-related and thus preventable. The remaining illnesses were probably attributable to the other possible causes such as endemic infectious illnesses, food-related infections, allergies, etc.

Attempts were also made to determine the aetiology of the observed illnesses. Sera were collected on four occasions from volunteers and they were tested for antibodies to various pathogens. There was no indication, by serology, of water-related infections caused by enteroviruses, hepatitis A virus and rotavirus or Norwalk virus infections (Payment *et al*. 1994).

The second Canadian study (Payment *et al*. 1997) was more complex: its objective was not only to re-evaluate the level of waterborne illness, but also to identify the source of the pathogens responsible for them. It was conducted from September 1993 until December 1994 and compared the levels of gastrointestinal illness in four randomly selected groups of 250 families, who were served water from one of the following sources:

- normal tap water
- tap water with a valve on the cold water line (to examine the effect of home plumbing)

- plant effluent water as it leaves the plant and bottled (not influenced by the distribution system) ('plant')
- plant effluent water further treated and bottled (to remove any contaminants) ('purified')

The treatment plant was selected for the poor raw water quality (i.e. high microbial contamination) and for its treatment performance. Raw water entering the plant was contaminated with parasites, viruses and bacteria at levels typically found in faecally contaminated waters. The end product met or exceeded current Canadian and US regulations for drinking water quality. The distribution system was in compliance for coliforms but residual chlorine was not detectable at all times in all parts of the distribution system.

The rates of highly credible gastrointestinal illnesses (HCGI) were within the expected range for this population at 0.66 episodes/person/year for all subjects and 0.84 for children aged 2 to 12. The rate of illness was highest in autumn/winter and lowest in summer. Overall, there were more illnesses among tap water consumers than among subjects in the 'purified' water group, suggesting a potential adverse effect originating from the plant or the distribution system. Children were consistently more affected than adults and up to 40% of their gastrointestinal illnesses were attributable to water. The rates of gastrointestinal illness among consumers of water obtained directly at the treatment plant were similar to the rate of illness among consumers of purified water. Two periods of increased tap-water-attributable illnesses were observed in November 1993 and in March 1994.

Subjects in the two bottled water groups (i.e. 'purified' and 'plant') still consumed about one-third of their drinking water as tap water. They were thus exposed to some tap water and its contaminants: as a result the risks due to tap water may be underestimated.

Consumers of water from a continuously running tap had a higher rate of illness than any other group during most of the observation period. This was completely unexpected, since the continuously running tap was thought to minimise the effects of regrowth in home plumbing. Although there are several theories as to the cause of this effect, they remain unsubstantiated.

The data collected during those two epidemiological studies suggest that there are measurable gastrointestinal health effects associated with tap water meeting current standards and that contaminants originating from the water treatment plant or the distribution system could be the source of these illnesses. Short-term turbidity breakthrough from individual filters at the water treatment plant might explain the observed health effects. Potential follow-up research should further examine the relationship of turbidity breakthrough and should

investigate the role of the continuously running tap in the occurrence of gastrointestinal illness.

In the Canadian studies, it was not possible to assign a single cause (or aetiological agent) to the observed effects although the authors suggested three explanations: low level or sporadic breakthrough of pathogens at the water treatment plant, intrusions in the distribution system (repairs, breaks, etc.) and finally bacterial regrowth in the mains or in the household plumbing.

4.4.2 Health significance of bacterial regrowth

Bacterial regrowth is common in water and has been observed even in distilled water. In water distribution systems, the heterotrophic plate count can occasionally be elevated and there have been concerns that this flora could contain opportunistic pathogens. Data from epidemiological studies involving reverse-osmosis units suggested that there was a correlation between gastrointestinal illnesses and heterotrophic plate counts at 35°C (Payment *et al*. 1991b). However, a few outliers in the data set drove the correlation and the study would have to be repeated in order to confirm the relationship. Furthermore, this observation could be limited to certain water purification devices such as those in which a rubber bladder is used to accumulate the purified water.

4.4.3 Health significance of turbidity

The Milwaukee outbreak with an estimated 400,000+ cases of gastrointestinal illness occurring in the spring of 1993 is a good illustration of turbidity-related health effects (Mackenzie *et al*. 1994). The outbreak occurred at the beginning of April and was linked to inadequate water treatment as well as to a decrease in river water quality. Turbidity data from the water treatment plant revealed that one of the two water treatment plants was distributing finished water with a turbidity of more than 1.5 NTU. The lag between the turbidity increases and reported illness was seven days in children and eight days in adults. This lag time may reflect the incubation period of *Cryptosporidium* which was identified as the aetiological agent in many of the cases of gastroenteritis. Subsequent to the investigation of the main Milwaukee outbreak, Morris *et al*. (1996) carried out an analysis of hospital records and water turbidity readings over a period of 16 months before the recognised outbreak. They found that attendance of children with gastrointestinal illness at hospital emergency departments showed a strong correlation with rises and falls in turbidity, but did not describe any specific time-lag relationships.

Beaudeau *et al*. (1999) reported data from Le Havre (France) which operates two water treatment plants and distributes water to 200,000 people. The karstic resources used are subject to episodic microbiological quality degradations. One plant only chlorinates, whereas the second plant normally uses slow sand filtration before chlorination but can also implement coagulation-settling when turbidity of the raw water exceeds 3 NTU. During the study period there were several occasions when the chlorine residual was not maintained and there were also significant variations in turbidity. Despite these occurrences the treated water still met all microbiological criteria for potable water in France and the study was undertaken to determine if public health was adequately protected. An ecological time series study was carried out on data collected between April 1993 and September 1996. Records of sales of prescribed and off-the-shelf gastroenteritis medication were provided by the pharmacists participating in the epidemiological surveillance network of Le Havre. Sales data, residual chlorine and turbidity measurements were analysed. Interruption of chlorination of the unfiltered water resulted in a significant increase of medication sales three to eight days later. Raw water turbidity increases resulted in increases of medication sales during the following three weeks. The data analysed suggest that about 10% of the annual cases of gastrointestinal illnesses could be due to the consumption of tap water. This annual average does not reflect the proportional attributable risk occurring during specific periods and underscores the fact that current regulations still do not provide complete protection of public health. Furthermore, such failures have the potential of causing major outbreaks if raw water microbiological quality degrades significantly after rainfall events.

Similar data from the city of Philadelphia has also been studied (Schwartz *et al*. 1997). In this study the researchers examined the association between daily measures of drinking water turbidity and both emergency visits and admissions to the Children's Hospital of Philadelphia for gastrointestinal illness, controlling for time trends, seasonal patterns, and temperature. The data suggested a relationship between hospital admissions for gastrointestinal illnesses and increases in turbidity at the Philadelphia water treatment plant. At all times, the water produced met federal regulations, perhaps suggesting that the standards need to be re-evaluated. The study has been heavily criticised and several potential confounding factors as well as methodological errors have been raised. The turbidity levels examined were in the range of 0.14–0.22 NTU – considerably below the levels of many water supplies in the US and other developed nations. The turbidity meters used at the time of the study were calibrated at approximately four month intervals using standards from 0.2–1.0 NTU: most of the readings used in the analysis were below the calibration range

and could be considered unreliable. One of the three water treatment plants routinely rounded turbidity readings to the nearest 0.05 NTU, while the others reported to the nearest 0.01 NTU. No consideration was given to the effect of chemical corrosion inhibitors on turbidity. Although the authors were supplied with minimum and maximum turbidity readings as well as mean readings, these were apparently not analysed. If the basic hypothesis is correct, one would expect stronger effects to be seen with maximum readings or turbidity spikes.

The findings from the US and France complement the Canadian studies, which concluded that a fraction of gastrointestinal illness attributable to drinking water arises from microbiological events in the distribution system, but did not discount the treatment plant as a source of pathogens. Beaudeau *et al*. (1999); Morris *et al*. (1996) and Schwartz *et al*. (1997) suggested that variations in rates of illness were due to changes in the numbers of pathogens (carried in or on small suspended particles) coming through the distribution system from the treatment plant. Given that water treatment is a continuous process, constantly responding to changes in demand, that rapid sand filters are not homogeneous and their performance may vary considerably, and that the distribution system is subjected to numerous challenges, the assertion that pathogens may sometimes be present in treated water seems a reasonable one. At most water treatment plants, even if the water produced by the plant always achieves an average turbidity of less than 1 NTU, individual filters may produce water with significantly higher values for short periods. Such a burst of turbidity could be sufficient to introduce pathogens into the treated water at a level sufficient to explain observations such as those in Canada (Payment *et al*. 1991a,b, 1997) and Philadelphia (Schwartz *et al*. 1997).

Turbidity has been suggested by several groups as a potential indicator of waterborne disease. Much remains to be studied on the value of this easy-to-measure parameter, but it is one indicator that promises to better protect public health and one of the rare indicators that could be used in real time.

4.5 WATERBORNE GASTROINTESTINAL DISEASE IN OTHER COUNTRIES

4.5.1 Incidence of endemic gastrointestinal disease

It is even more difficult to get a clear understanding of the incidence of diarrhoea in developing countries than it is for industrialised countries. Nevertheless, several community-based studies have been reported in the literature. These have generally employed regular visits from a health-care worker. It is, however, difficult to use the results of studies to produce an

overall estimate of diarrhoeal disease in developing countries for a number of reasons:

- Levels of diarrhoeal disease may differ markedly between relatively close communities due to different socio-economic factors, such as the availability of a clean water supply and hygiene behaviour.
- The information that is available comes from a variety of sources and has been collected and analysed in different ways.
- The definition of diarrhoea often differs between studies.
- Quite frequently data collection has been part of a prospective epidemiological study designed to investigate the role of some factor such as water supply on health.

In Table 4.2 (see p. 76) we list the estimates of diarrhoeal disease incidence from a variety of prospective epidemiological studies. Where possible the overall incidence of diarrhoea, broken down into broad age groups, has been given. If the study compared two groups during an active intervention such as a health education campaign or improvement in water supply, then we have given the data only for the control group.

It can be seen from Table 4.2 that the incidence of diarrhoeal illness varies markedly between studies. While one should not draw too many conclusions from the data as presented here, it seems clear that incidence is higher in rural rather than urban environments and also in poorer communities.

The age distribution of diarrhoeal disease seems to be similar in all regions where reported. Disease incidence is relatively low in the first few months of life, then peaks at about 24 months before declining towards adulthood. Figure 4.1 shows the incidence of disease in various cohorts during the first five years of life in one study (Schorling *et al*. 1990).

One of the issues that has been raised in recent papers has been the role of population immunity on the epidemiology of water-related disease in general and cryptosporidiosis in particular (Craun *et al*. 1998; Hunter and Quigley 1998; Hunter 1999). The implication of this work is that exposure to diarrhoeal pathogens is far more common than observable disease, the difference being due to pre-existing immunity. Evidence for this in developed countries comes from the investigation of outbreaks of waterborne disease which have shown lower attack rates in residents compared to visitors (Hunter 1999).

Table 4.2. Estimates of diarrhoeal incidence in developing countries from various prospective epidemiological studies

Location	Type of area	Study type	Definition of diarrhoea	Age groups	Inc.*
South-eastern China[1]	Rural villages	Prospective community-based	Passing of 2 or more loose or watery stools in 24 h and lasting for less than 5 days	All age groups Children <5 Adult men Adult women	0.730 2.254 0.750 0.627
North-eastern Brazil[2]	Urban slum	Prospective cohort	Increase in stool frequency or a decrease in consistency, as noted by the caretaker, lasting at least 1 day	Children <5	11.29
Bangladesh[3]	Periurban village	Control group from soap hand washing trial	2 or more watery stools or 4 or more loose stools in 24 hours	All ages	1.114
Nicaragua[4]	City	Prospective cohort	Increased frequency to ≥3 liquid stools in 24 h or presence of blood/mucus	Children <2	1.88
Zaire[5]	City	Prospective cohort of control group of HIV negative infants	Change in normal stool pattern with at least one day of increased frequency, blood or mucus	Children <16 m	1.0
Guatemala[6]	Poor rural village	Control group in double blind randomised trial of zinc administration	Mother's definition	Children 6-18 m	23.0
Haiti[7]	Rural	Control group in double blind randomised trial of vitamin A administration	Watery stools four or more times in one day	Children <7	3.29
Columbia[8]	City	Prospective cohort study of diarrhoeal attack rate in those not at day care	3 or more loose stools in 24 hours	Children <24 m 24-35 m 36-60 m	6.8 2.2 1.2

Table 4.2 (cont'd)

Location	Type of area	Study type	Definition of diarrhoea	Age groups	Inc.*
Zambia[9]	City	Retrospective community survey, control group for study of diarrhoea in HIV+ patients	Respondent-defined	Adults	1.74
Bangladesh[10]	Urban	Cohort of children with a non-improved water supply	3 or more loose or watery motions in 24 hours	Children 1–6	3.2
Peru[11]	Poor peri-urban	Prospective cohort	3 or more liquid or semi-liquid stools in 24 hours	0–11 m 12–23 m 24–35 m	8.74 10.18 6.32
Nigeria[12]	Rural	Community survey	Not stated	Children <5	2.12

* Incidence as episodes/person/year (m = months)
[1] Chen *et al*. 1991 [2] Schorling *et al*. 1990 [3] Shahid *et al*. 1996 [4] Paniagua *et al*. 1997
[5] Thea *et al*. 1993 [6] Ruel *et al*. 1997 [7] Stansfield *et al*. 1993 [8] Hills *et al*. 1992
[9] Kelly *et al*. 1996 [10] Henry and Rahim 1990 [11] Yeager *et al*. 1991 [12]Jinadu *et al*. 1991

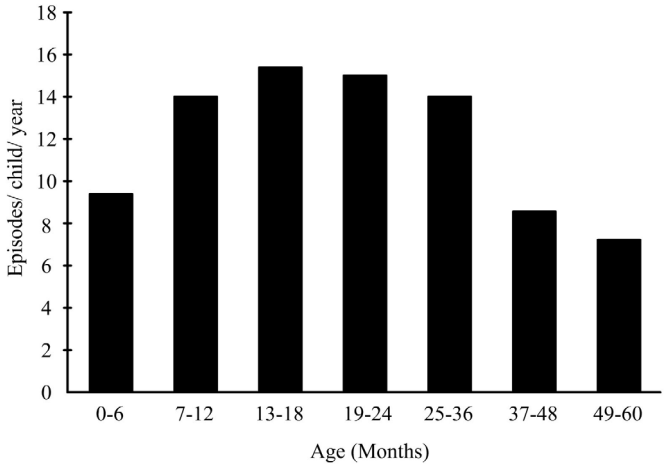

Figure 4.1. Age distribution in incidence of diarrhoea in children in an urban slum in north-eastern Brazil (Schorling *et al*. 1990).

For those interested in the impact of prior immunity on the epidemiology of diarrhoeal disease in developing countries, we are fortunate in having access to a considerable literature on travellers' diarrhoea (Table 4.3).

Table 4.3. Estimated incidence of travellers' diarrhoea from various studies[a]

Home country	Destination country	Study population	Inc.*	Reference
US	Mexico	Adult students	15.64	Johnson *et al*. 1984
US	Mexico	Adult students	9.21	Ericsson *et al*. 1985
US	Mexico	Adult students	6.95	DuPont *et al*. 1987
US	Thailand	Peace core volunteers	4.95	Taylor *et al*. 1985
Sweden	Various	Various age 10+	4.68	Ahlm *et al*. 1994
Various	Jamaica	>16 years	11.3	Steffen *et al*. 1999
Switzerland	Various	0–2	5.00	Pitzinger *et al*. 1991
		3–6	1.45	
		7–14	4.86	
		15–20	5.57	
Netherlands	Various	Adults	11.5[b]	Coeblens *et al*. 1998

* Incidence in episodes/person/year.

[a] Figures usually represent number of affected individuals and so do not count repeated episodes in the same individual and consequently underestimate incidence.

[b] Includes multiple episodes.

Although the studies of travellers' diarrhoea are not directly comparable with studies of local people, it clear that the attack rate in travellers is several-fold higher. This difference is even more notable considering that travellers usually live in rather more hygienic surroundings then do locals. Thus the evidence presented here would support the hypothesis that local people build up a substantial immunity to those enteropathogens circulating in their communities. However, to achieve this level of immunity there is a substantially higher incidence of illness in young children in developing countries than in developed nations. This high incidence of gastrointestinal disease in children is one of the reasons behind the high childhood mortality in developing countries. Consequently there is no place for any argument that allows less than the highest achievable standards of hygiene or water quality in order to build up population immunity. Such arguments would, if implemented, inevitably lead to a rise in childhood morbidity and mortality.

4.5.2 Waterborne disease

Clearly, determining the proportion of diarrhoeal disease in developing countries that is due to contaminated water is problematic. As with the determination of incidence rates, the proportion of diarrhoeal disease due to water consumption varies substantially between communities because of varying water quality and other behavioural and socio-economic factors. An estimate of the proportion of diarrhoeal disease due to water consumption comes from those studies that have compared illness rates between two communities with different water supply or in the same system before and after improvements in water supply.

Esrey and colleagues (1991) published a review of studies that investigated the impact of improved water supply and sanitation on various waterborne diseases. They were able to identify 16 studies that examined the health impacts of pure water over contaminated water. Of these studies, ten reported a positive effect. In only seven studies was it possible to calculate the percentage reduction, the median being a 17% reduction.

Despite the importance of sanitation and hygiene behaviours a significant proportion of diarrhoeal disease due to waterborne transmission will be related to water quality. Perhaps the source with the poorest quality is river water. Two relatively recent studies have examined diarrhoeal illness in people taking river water. In a study in south-eastern China, the incidence of diarrhoea was related to the source of drinking water (Chen *et al*. 1991). The attack rate was 0.575 per person per year in those drinking piped water, 0.846 in those drinking well water and 4.580 in those drinking river water. Thus, other things being equal (which they most likely were not) about 87% of illnesses in people drinking river water were waterborne. This figure of 87% is similar to the reduction in diarrhoea in a more recent study of families in Uzbekistan (Semenza *et al*. 1998). In those families without a piped mains supply the incidence was 2.15 episodes per person per year, and it was 0.91 in those with a piped supply. If those without a piped supply were taught to chlorinate their water, the incidence fell to 0.35, a reduction of 85%.

Moe *et al*. (1991) reported on a particularly elegant study done in Cebu, the Philippines. They looked at the relationship between the microbiological quality of drinking water and the prevalence of diarrhoeal disease in 690 children under two years old. Faecal pollution, as measured by microbiological indicator organisms, was common. The authors reported that: 21% of 123 spring waters, 21% of 131 open dug wells, 14% of 52 wells with pumps, 6% of 751 boreholes, and 60% of 5 non-municipal piped water supplies all yielded water

containing more than 1000 faecal coliforms/100 ml. By contrast, only 5% of 138 municipal piped water samples yielded a count of >1000 faecal coliforms/100 ml. The prevalence of diarrhoea ranged from 5.2–10.0% over the six subsequent two-month periods. It appeared that there was little change in the prevalence of diarrhoea if indicator counts rose to 100/100ml. There was a significant association between diarrhoea and >1000 *E. coli*/100ml (Odds Ratio (OR) 1.92, Confidence Interval (CI) 1.27–2.91), enterococci (OR 1.94, CI 1.20-3.16) and faecal streptococci (OR 1.81, CI 1.10–3.00). The association with faecal coliforms was borderline significant (OR 1.49, CI 1.00–2.22). The probability of diarrhoea in a child during a 24-hour period was 0.09 in those exposed to <1000 *E. coli* and 0.15 in those exposed to >1000. The respective probabilities for enterococci were 0.09 and 0.16.

Also from Cebu, VanDerslice and Briscoe (1995) reported that in areas with poor environmental sanitation, improved drinking water would have little or no effect. However, in areas with good community sanitation, reducing faecal coliform counts by two orders of magnitude would reduce the incidence of diarrhoea by 40%, eliminating excreta from around the house by 30% and providing private excreta disposal by 42%.

In conclusion, it is not really possible to give definitive estimates of the burden of diarrhoeal disease due to water consumption in developing communities as this varies substantially depending upon water source and quality as well as other socio-economic and behavioural factors.

4.6 WATERBORNE OUTBREAKS (DEVELOPED COUNTRIES)

An outbreak can be defined as the occurrence of two or more related cases of infection. Usually family outbreaks, where all cases occur in the same family group, are distinguished from general outbreaks. The reasons for this separation are that person-to-person spread within a family is more likely and members of a family are more likely to be exposed to the same risk factors. Both of these reasons make epidemiological investigation of family outbreaks very difficult.

Unfortunately the definitions given in the previous paragraph do not help greatly when identifying potential outbreaks of waterborne disease. Early in a waterborne outbreak, obviously related cases are rare. The exception to this observation is with small supplies providing water for a few homes, or an institution such as a hotel or hospital. The detection of waterborne outbreaks is further hampered by the fact that the most common waterborne infections are also endemic in the community. Consequently most waterborne outbreaks are

first identified by noting a general increase in cases over what would be expected for the time of year.

A more useful definition is an increase of cases of a particular infection above what would be normally expected. The detection of a potentially waterborne outbreak now becomes a question of identifying an increase in cases as early as possible when still only a few cases have occurred. One approach that has recently been suggested is to define check and alert values based on the usual weekly rate within a population (DETR and DoH 1998). The check and alert values have been calculated to give only a 1/20 and 1/100 probability of occurring by chance in any week. To have cases that exceed the alert value on two consecutive weeks is very strong evidence of an outbreak. Clearly, if numbers are large early on in the outbreak then such statistical tests are not needed. In this case it is usually obvious that there is an outbreak.

4.6.1 Factors leading to waterborne outbreaks

The causes behind the occurrence of outbreaks are numerous and have been well described by Craun (1986) and in subsequent reports from the US EPA and US Centers for Disease Control (CDC) (Herwaldt *et al*. 1991, 1992), and are described more fully in Chapter 6. Because of an increasingly contaminated global water resource, there has been a rise in waterborne disease worldwide (Ford and Colwell 1996). In developing countries, treatment of water and wastes is often non-existent or grossly inadequate and until sanitation is improved it will be impossible to impact greatly on the level of waterborne disease. In developed countries, deficiencies in treatment and delivery systems, anthropogenic impacts on source water, and the emergence of resistant and more virulent micro-organisms pose serious threats to human health. In industrialised countries, an increase in waterborne disease is expected because of a number of factors, including:

- Newly recognised agents (*Cryptosporidium*, *Giardia*, *Cyclospora*) that have a high resistance to chemicals used in water treatment and development of antibiotic resistant strains of pathogens.
- Less immunity to pathogens (because of better sanitary conditions and a higher population of immunocompromised individuals) and the resulting higher susceptibility and risk of disease during systems failures.
- Anthropogenic alterations of water systems that have stimulated eutrophication, changes in food chain structure, and unrestricted

growth of 'nuisance species', creating breeding sites for vector-borne diseases.

- Changes in agricultural production methods, including high-density animal operations carried out in proximity to urban development, leading to an increase in transmission of animal pathogens to humans.
- Ageing and deteriorating environmental infrastructure, particularly in inner cities.

4.7 COSTS TO SOCIETY

In developed countries, such as the US, diarrhoeal disease is common but generally not severe. Sufferers frequently downplay its significance and doctors often do not trace the causes of individual cases. Therefore, many illnesses caused by waterborne agents go unreported. Moreover, few physicians are on the look-out for rare or emerging organisms and laboratory analyses that might alert communities to outbreaks of waterborne disease are infrequently done.

The societal cost of the so-called 'mild gastrointestinal illnesses' is several orders of magnitude higher than the costs associated with acute hospitalised cases (Payment 1997). In the US, the annual cost to society of gastrointestinal infectious illnesses was estimated in 1985 as $19,500 million for cases with no consultation by physician, $2,750 million for those with consultations, and only $760 million for those requiring hospitalisation (Garthright *et al*. 1988; Roberts and Foegeding 1991). These estimates, however, do not address the deaths associated with these illnesses, particularly in children and older adults.

From the data collected during the Payment studies the economic costs of endemic waterborne diseases were calculated based on reported symptom and behaviour rates between unexposed and tap water exposed groups (Payment 1997). These estimates were then combined with published figures for the cost of gastrointestinal infectious diseases in the US (Garthright *et al*. 1988; Roberts and Foegeding 1991). Assuming a population of 300 million individuals, the estimate of the cost of waterborne illness ranges from US$269–806 million for medical costs, and US$40–107 million for absences from work. Such figures can only underscore the enormous economic cost of endemic gastrointestinal illnesses, even in societies where they are not perceived to be a problem.

4.8 CONCLUSIONS

In this chapter we have presented evidence examining the levels of infectious intestinal disease in both developed and developing countries. It is clear, however, that deriving such estimates from routinely available data is difficult

because of problems in ascertainment. Nevertheless, we can be certain that the incidence of disease is high in all countries. The proportion of endemic disease due to the water route varies substantially from community to community. The water route seems to increase in importance as general levels of hygiene increase in a community. Indeed, in many poorer tropical countries, the priority is not to improve quality of drinking water supplies but to provide adequate water close to the home, and supply or maintain adequate sanitation.

All developed civilisations depend on an adequate supply of safe water for their continuation. We cannot afford to become complacent about the safety and reliability of our water supplies, nor can we afford not to invest in and maintain our infectious disease surveillance systems.

4.9 IMPLICATIONS FOR INTERNATIONAL GUIDELINES AND NATIONAL REGULATIONS

In terms of the framework and guidelines development this chapter clearly shows that a hazard exists and that there can be no room for complacency even in developed countries. It is also clear that there is very weak understanding of risk with regard to endemic rates of illness attributable to drinking water in developed and developing countries.

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