3. CHOLERA

Cholera is one of man's great calamities. The causal vibrio was discovered by R. Koch *at Alexandria in 1883.*

Well before that time, cholera had been the focus of an original investigation by John Snow *(1849), who demonstrated the role of water from the Broad Street pump in London at a time when medical opinion was divided between miasmata and soil contamination. This important discovery became a model for later epidemiological surveys and is commemorated in the pub on the corner of Broadwick and Lexington Street.*

For centuries, cholera remained confined to its presumed birthplace, the deltas of the Ganges and of the Brahmaputra. Then, starting in 1823, seven epidemic waves swept eastward across China and Japan and westward through Europe. Following the routes of caravans and sailing ships, then those of steam-powered vessels and aircraft, each successive pandemic spread further and further afield.

Africa was not spared. First the islands in the Indian Ocean were afflicted, then the East African coast and North Africa.

The successive pandemics, bringing diarrhoea and causing hundreds of thousands or even million of deaths, were one of the factors leading to the conclusion of international health conventions aimed at limiting the spread of infections, which were since then called quarantine diseases. There were originally six, later four, and finally three of these, all subject to mandatory reporting under International Health Regulations.

Cholera, whose sinister reputation is now no more than a memory in the industrialized world, became after the seventh worldwide pandemic (caused by Vibrio cholera el Tor*), a painful reality in tropical Africa.*

Whereas the previous epidemics caused by Vibrio cholerae *were self-limiting, the* el Tor *variant found the right ecological conditions in tropical Africa to establish itself.*

A better understanding of the pathogenesis of cholera has led to the development of a simple, inexpensive and effective form of treatment. An effective vaccine is not yet available.

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1. Introduction

Cholera was until recently defined as an acute diarrhoeal disease caused by infection of the small intestine with *Vibrio cholerae*, serogroup 0:1. It is one of the quarantine diseases subject to the International Health Regulations. This disease, which affects only man, can vary from slight diarrhoea to a fulminant syndrome causing death through rapid dehydration within a few hours after onset of the disease. Cholera often strikes in epidemics. Although Egypt was struck by a major epidemic in 1947, Central Africa was spared. Now, however, cholera is endemic throughout Africa, where it was introduced in 1970.

2. Transmission

2.1. *Agent*

V. cholerae is a curved, comma-shaped Gram-negative bacillus 0.5 nm in diameter of the family *Vibrionaceae*. It owes its motility to a single polar flagellum. It yields a positive oxidase reaction and uses both fermentative and respiratory metabolic pathways. Its guanine + cytosine ratio (G+C) is 47%. *V. cholerae* is easily grown on simple peptone broths and on nutritive gelose, on which colonies appear after 8 to 10 hours at 37°C. It grows at neutral and alkaline pH (pH 9-10) and is very sensitive to acidification of the medium. Optimal growth occurs on a medium containing 1 to 3% NaCl.

The interaction between *V. cholerae*, its aquatic environment and its human host is a complex one. So is the bacteriology of the genus Vibrio. Until recently, it was a well-established fact that only classical and El Tor *V. cholerae*, both agglutinated by the 01 antiserum, caused extensive epidemics. The epidemiology and pathogenicity of the numerous non 01-agglutinable (NAG) vibrios have been well described, and, until recently, their epidemic potential has been considered as limited (Sangal, 1992).

V. cholerae can be differentiated from the other *Vibrionaceae*, as, *V. parahaemolyticus, V. algynolyticus*, and *Aeromonas hydrophila*, by a series of biochemical, antigenic, and genetic features.

Four biotypes have been described. The classic cholera vibrio and the El Tor variant (responsible for the current pandemic) were the most important biotypes from an epidemiological point of view. The strains are distinguished by the Voges-Proskauer reaction, by haemolysis of chicken erythrocytes and by sensitivity to polymyxin.

More than 138 serogroups of *V. cholerae* have been described on the basis of their somatic 0 antigens, which are proteins. Strains belonging to serogroup 0:1 are pathogenic and cause epidemics. The other serogroups belong to the non-cholera vibrios (NCV) or non-agglutinable vibrios (NAGs). Usually, strains of these serogroups may cause non-epidemic diarrhoea if they have the necessary virulence factors. Serogroup 0:1 has been subdivided in turn into three serotypes: Ogawa, Inaba, and Hikojima. The classification scheme is displayed in Table 1 (Popoff et al., 1982).

Table 1
Serotypes of *V. cholerae* 0:1

Specific serotype	Antigenic specificity	Serum agglutination	
		Anti-B	Anti-C
Ogawa	AB	+	–
Inaba	AC	–	+
Hikojima	ABC	+	+

Pathogenicity of *V. cholerae* depends on the action of its numerous extracellular enzymes and above all its enterotoxin. An haemagglutinin and/or a still poorly defined *colonization factor* plays probably a role in the vibrio's adhesion to the intestinal mucosa. In addition, the various strains produce a neuraminidase, a protease, and a chitinase.

Although antibiotic-resistant strains, especially to tetracycline and sulphonamide, were found in Tanzania in 1978 (Mhalu et al., 1979), the *V. cholerae* strains isolated in Zaire and Rwanda in 1978 were sensitive to antibiotics (Colaert et al., 1979). However, resistant strains have recently been isolated in Zaire (Vandepitte, personal communication).

In 1992 and 1993, some of these concepts changed dramatically. In October 1992, an outbreak of clinically typical and severe cholera occurred at Madras, in India. It quickly spread to Madurai and Vellore. A team of Indian and Japanese scientists identified the cause as a hitherto unknown, non 01-agglutinable *V. cholerae* (Ramamurthy et al., 1993). They also showed that the new strain had the gene for cholera toxin, and produced the toxin. In mid-January 1993, the same NAG vibrio had reached southern Bangladesh. In one month's time, 10,000 people had been affected and an estimated 500 had died (Albert et

al., 1993a). Researchers at the International Centre for Diarrhoeal Disease Research in Bangladesh (ICDDR,B) isolated the germ in Dhaka and confirmed its toxigenicity. The epidemic reached Bangkok in April and Karachi in June 1993 (Albert et al., 1993a). In the mean time, members of the Cholera Working group at ICDDR,B (Albert et al., 1993b; Hall et al., 1993) had further characterized this new agent of cholera gravis as *Vibrio cholerae* 0139 Bengal, a mutant of *V. cholerae* El Tor.

In the span of less than one year, the history of cholera, scholarly reviewed by Barua in 1992, has seen a new chapter added to it. Furthermore, health workers and health officials will have to take into account several new aspects of the disease. First, in the homeland of the disease, *V. cholerae* Bengal attacks mainly adults, indicating the absence of cross immunity with classical or El Tor cholera and the lack of protection acquired by prior exposure to cholera toxin. Second, the further search for an effective and efficacious vaccine has become even more difficult, but also more important. Third, routine laboratory methods detecting *V. cholerae* 01 do not detect *V. cholerae* Bengal. A commentary in The Lancet (Swerdlow and Ries, 1993) has aptly asked whether the emergence of *V. cholerae* Bengal does not herald the beginning of the eighth pandemic, which could superimpose itself on the seventh pandemic still afflicting many areas in the world, amongst others Kivu (Zaire).

2.2. *Sources of contamination*

In nature the human being is the only source for the spread of *V. cholerae*. Transmission occurs primarily through drinking water and also via contaminated food or by contact with patients and healthy carriers. Therefore populations lacking fresh water supplies are particularly vulnerable, especially since they are often debilitated by malnutrition.

2.3. *Mode of spread*

Transmission is also favoured by the high number of carriers who are either slightly ill or asymptomatic but excrete the vibrios for up to fourteen days. Colaert, working in Bukavu in 1978, found that 14% of the healthy subjects tested were excreting *V. cholerae* and that there were 18 healthy excretors for each patient with cholera (Schyns et al., 1978). The existence of chronic carriers has not been demonstrated and their importance is probably limited.

3. **Epidemiology**

Africa has been free of cholera for close to a century. Livingstone mentioned the presence of cholera in the Congo, on the edges of Lake Tanganyika, in 1869-1807, during the third pandemic. Cholera was not reintroduced into Zaire, nor from Angola nor from the route described by Livingstone until the 1970s. It is the increased participation to the Mecca pilgrimages that played the main role in its introduction and dissemination through Africa. (Pollitzer, 1960).

The epidemiological pattern of cholera is that of an endemic disease with large epidemic outbreaks. How these epidemic outbreaks are triggered remains unclear. Climatic factors, the introduction of *V. cholerae* into non-immune populations, and variations in the bacterium's antigen make-up are probably all involved. The first Central African epidemics in the years 1973 and 1978-79, can be explained by the total lack of herd immunity in the region. Seasonal variations are observed in most of the affected regions: the epidemics peak in some cases during the rainy season and in others during the dry season. The 1978-79 Central African epidemics raged primarily in the dry season.

Zaire was struck by the seventh pandemy in 1973. The epidemic, which had been imported from Angola, was limited to Mayumbe (a coastal region) but was never officially reported. Cholera reappeared five years later, on this occasion at the same time in Mayumbe and in eastern Kivu (Malengreau et al., 1979; Schyns et al., 1979; Stock et al., 1976). The eastern epidemic began in a village near Kalemie, on the shores of Lake Tanganyika, where a fisherman from Tanzania died from cholera in May 1978. The epidemic spread north and then south along the lake, affecting Kivu, Upper Zaire and Shaba. More than 1,000 cholera deaths were registered in Kivu in 1978. That same year more than 10,000 cases of cholera were treated in special centres at Bukavu, Katana, Kirotshe, Uvira, Ubembe, and in the Rusizi Plain. The case-fatality rate was 3.2 to 3.5% for the patients treated in Bukavu and Katana and 7.8% in the other rural centres. The highest incidence was in adult females.

Since this first epidemic, cholera has become endemic in eastern Zaire, giving rise to regular epidemic outbreaks. Ogawa was the initial serotype in Kivu Region, but later the Inaba and Hikojima serotypes were also detected.

In May 1978 cholera was introduced in Burundi from Tanzania (Eyckmans, 1979; Storme, 1979). The epidemic started at Rumonge, but remained confined within a 15-km radius of this town. A second wave

broke out in Uvira (Zaire) and reached Bujumbura, from which it spread chiefly across the Rusizi Plain and along Lake Tanganyika. In Burundi 8,615 cases of cholera with 256 deaths, were registered between May 1978 and April 1979. The case-fatality rate (3.0%) was comparable to the observed one in Bukavu five years earlier.

The epidemic spilled over, from Lake Tanganyika (Uvira) to Cyangugu, in Rwanda. In July 1979 a new wave struck the country, crossing over from the Zairean shore of Lake Kivu via Idjwi and Nkombo Islands and Goma. Between June 1978 and April 1980, 3,886 cases, with a case-fatality rate of 4.0%, were reported. The overwhelming majority of these cases (95%) occurred in the second half of 1978, and 85% of the patients were from the Cyangugu Prefecture.

4. Pathogenesis

To produce cholera in healthy volunteers 10^8 to 10^{11} vibrios are required. The infective dose is much lower in subjects presenting hypo- or achlorhydria and/or suffering from malnutrition. After multiplying in the intestinal lumen the vibrios penetrate the mucus layer to adhere to the brush border of the intestinal cells. They do not invade the mucosa, but the enterotoxin that they secrete is responsible for massive losses of water and electrolytes. The toxin consists of an A or H (for heavy) fragment, molecular weight 28,000, and 6 B or L (for light) subunits, each with a molecular weight of 8,000. The B subunits attach themselves irreversibly to the membrane's GM1 receptor, allowing the A fragments to exert their enterotoxic effect by activating adenylcyclase production. The adenylcyclase transforms ATP in the membrane into 3'5-cyclic AMP (cAMP). This process raises the cAMP level fifteenfold, stimulating an ion pump responsible for chloride ion excretion. Thus, due to ion imbalance, abnormally large amounts of water and positive ions are secreted into the intestine. The result is acute watery diarrhoea (see also the chapter Diarrhoeal Diseases, p. 614). To complete the picture, a new, even more poorly defined enterotoxin, has been discovered (Sanyal et al., 1983). No morphological changes occur in the mucosa and the stools are free of leucocytes.

5. Clinical description

The onset of cholera, after an average incubation period of 1 to 2 days (12 hrs to 6 days), is marked by soft stools progressing quickly to watery diarrhoea, accompanied by violent abdominal and epigastric pain and projectile vomiting. The illness becomes quickly an untreatable watery diarrhoea – the so-called rice-water diarrhoea – containing mucosal debris. The rice-water diarrhoea is isotonic, the stools containing higher levels of bicarbonate and potassium than the serum. The stools also contain 10^6 to 10^9 vibrios per ml. If not treated immediately, the diarrhoea causes serious dehydration with cyanosis, severe asthenia, muscle cramps (mainly in the calves), extreme emaciation, and a drop in body temperature to 35 to 36°C.

The most frequent cause of death is cardiovascular shock plus acidosis and renal failure with none or minimal urine production.

This classic pattern of acute cholera is seen in a minority of patients. Mild and even asymptomatic forms are up to fifty times more frequent than the extremely serious, lethal forms.

6. Diagnosis

The aetiological diagnosis of cholera relies on the finding of *V. cholerae* in the stools. *V. cholerae* can easily be detected in fresh stools examined by dark-field microscopy. *V. cholerae* survive only a few hours in stool specimens unless these are kept at 4°C or in a transport medium such as Venkatraman-Ramakrishnan sea salt liquid medium, alkaline peptone water, or Carry-Blair semisolid medium.

In the case of healthy carriers or patients with mild forms of the disease, the stools contain only 10^2 to 10^5 bacteria per gramme. Therefore an enrichment medium, such as alkaline peptone water at pH 9.0, must be used. Following 6 to 8 hours' incubation at 37°C the cultures are plated on a solid medium, usually thiosulfate-citrate-bile salt-saccharose (TCBS). Watery cholera stool specimens can be plated directly on this medium, which is very selective for *V. cholerae* and *V. parahaemolyticus*. Moreover, this medium does not have to be sterilized, a considerable advantage in the field. The *V. cholerae* colonies will appear after 6 to 12 hours incubation under aerobiosis. They are bulging on TCBS by acidification of the saccharose. The diagnosis of *V. cholerae* is confirmed by biochemical and serological identification tests.

Serological testing is not useful for individual diagnosis. When an epidemic occurs each case does not have to be identified bacteriologically, but it is essential that the first cases are. Afterwards, mere clinical examination and inspection of the stools should be sufficient for a correct diagnosis of tropical cases. Hence, of the 3,336 cases treated in the health centres

of Cyangugu Prefecture (Rwanda) in 1978, 38 cases (1.1%) were confirmed by laboratory analysis (Rugamba et al, 1982, Pierce, 1984; Pollitzer, 1960; Popoff et al., 1982).

7. **Treatment**

The treatment for cholera consists first and foremost of rapid intravenous and/or oral rehydration. The fluid and electrolyte losses can be extremely severe, leading to circulatory shock and death within hours. Shock is easily recognized clinically by inspection of the patient and by the absence of radial pulse. Intravenous rehydration has to be started without delay. Properly conducted, this treatment can save even an apparently dying patient. The volume of fluid must be 10% to 15% of the patient's body weight, to be administrated in not more than four hours. If an intravenous line cannot be installed, fluid can be given intraperitoneally, as fast as possible.

Special *cholera beds* have been used to cope with the problem posed by the copious, uncontrollable diarrhoea. A strategically placed hole in a cot allows the watery stools to be collected directly in a (graduated) bucket which is placed under the bed and should contain an antiseptic.

Once the circulation is restored, patients recover very quickly and rehydration should be continued via the oral route. The amount of ORS must be based on the ongoing faecal losses, which have to be monitored thanks to the graduated bucket.

In cholera gravis, adult patient may require up to 25 to 30 litre of ORS during the first day of their treatment. Feeding should be resumed within 12 hours after the onset of treatment. In infants, standard ORS must be alternated with breastmilk and plain water to prevent hyperchloraemia.

Intravenous solution suitable for all ages are Hartmann's Ringer-lactate (in mEq/l: Na 130, K 5.4, Ca 1.8, Mg 2, Cl 112.2, lactate 27) or, preferably, the very efficient Dhaka solution (Na 133, K 14, Cl 99, bicarbonate 48, Greenough et al., 1964; Rahman et al., 1988).

The fluids used during the 1978 epidemic in Kivu contained 1.5 g potassium chloride, 3.5 g sodium chloride, 2.5 g sodium bicarbonate, and 20 g glucose per litre of drinkable solution; for injectable solution the content was 1 g potassium chloride, 4 g sodium chloride, 6.5 g sodium acetate, and 10 g glucose per litre. WHO has recently recommended a more stable formula for the oral rehydration salts, namely, 3.5 g sodium chloride, 2.9 g dihydrate trisodium citrate, 1.5 g potassium chloride, and 20 g glucose per litre of oral solution ORS (WHO, 1984). Obtaining sufficient supplies of salts and rehydration solutions often pose a major logistic problem.

An average of 3 litres of IV solution was given to patients in Katana (Kivu) in 1978, but most of the patients were treated successfully with oral fluids.

As a rule an antibiotic is administered to lessen the length of illness and the period during which the vibrios are excreted. However rehydration alone is sufficient to cure the patients. This adjuvant therapy usually consists of daily 2 g doses of tetracycline for four days. Chloramphenicol and sulphonamides are also used. As mentioned earlier, sulphonamide- and tetracycline-resistant strains of *V. cholerae* have emerged in Africa. Therefore these antibiotics could lose their effectiveness in the future.

8. **Prevention**

8.1. *Vaccination*

The classic vaccine is composed of killed bacteria administered by subcutaneous or intramuscular injection. Other vaccines based on somatic antigen (cell-wall extracts, lipopolysaccharides) and cholera toxoid vaccines have also been developed. All of these vaccines afford only 50% protection; furthermore, the acquired immunity is of short duration (6 months at best). Opinions on their usefulness and cost/benefit in controlling epidemic or endemic cholera are divided.

In 1978 the authorities in Kivu (Zaire) and Rwanda opted for mass immunization, but the impact of this campaign cannot be assessed because the vaccinated and unvaccinated groups were not randomly selected. Malengreau and co-workers (Malengreau et al., 1979) have calculated that, based on 50% effectiveness and a 5% attack rate, vaccination has a lower cost than care to be provided for additional patients (0.85 Belgian francs per dose of vaccine, versus BFr 100 for the cost of treatment per patient). However, as the vaccine affords a very brief protection, immunizing is definitely not a long-term solution.

In Burundi, on the other hand, it was decided not to vaccinate, the total cost of an immunization campaign being judged an excessive expenditure without lasting benefits (Storme et al., 1979). The incidence of and the mortality due to cholera in Burundi in 1978 were of the same magnitude as those observed in Zaire and Rwanda, where the population had been vaccinated. Burundi's courageous decision not to vaccinate was apparently not detrimental to its population.

8.2. *Chemoprophylaxis*

Opinions on preventive therapy with slow-release sulphonamides (sulfadoxine) are divided. French authors have recommended such chemoprophylaxis (Lapeyssonnie et al., 1970), but a controlled study carried out in India failed to show better protection for sulfadoxine as compared to a placebo in reducing the spread of cholera to patients' families (Deb et al., 1976). Mass chemoprophylaxis was instituted in Burundi, whereas in Kivu it was limited to the personnel attending the sick. In Katana sulfadoxine proved ineffective in some individuals, who developed cholera a few days after having definitely taken the drug. On the other hand, its psychological effect on the medical and administrative staff was certain. Tetracyclin is able to protect individuals, but its widespread use is responsible for the development of resistant strains. In any event, WHO does not recommend chemoprophylaxis as it is generally ineffective (WHO, 1985).

8.3. *Other preventive measures*

Other, less specific preventive measures are also recommended to control cholera. Quarantining a region or country is not only questionable in terms of efficacy, but also economically harmful.

In the long run, measures to improve general hygiene and sanitation and reduce faeco-oral transmission such as health education, building latrines and supplying clean drinking water are not only the most cost-effective cholera control strategy but will also reduce the incidence of all diarrhoeal diseases and faeco-oral transmission (Cvjetanovic et al., 1978).

A few unrealistic, even harmful measures are discussed by Malengreau and Storme (Malengreau et al., 1979; Storme et al., 1979). These include recommending that water be boiled or filtered, setting up road blocks, banning fishing or large gatherings of people, or even the sale of banana beer. The useful measures include inspecting and renovating water collectors, speeding up work on water supply schemes, advising the population to get their drinking water only from properly protected sources, epidemiological surveillance, and spreading information or raising public awareness.

9. **Problems for further study**

- Adaptation of surveillance methods to local conditions, especially the adaptation of early screening for cholera among patients with acute diarrhoea, possibly relying on mobile units;
- development of a plan for action as part of each country's national public health programme. It should provide for strategies and an appropriate logistic base for rapid intervention, possibly in specialized or *ad hoc* treatment centres, where quick and efficient links will be made with supporting laboratory facilities;
- special training, retraining, to be provided to all medical and paramedical staff (general practitioners, specialists, nurses, laboratory technicians, and aides) with reliable information updates, especially concerning oral rehydration therapy (ORT);
- information and education of the public, which includes the evaluation of the population's attitude towards oral rehydration salts (ORS) and dissipate unfounded belieg in the effectiveness of vaccination and chemoprophylaxis;
- the need for epidemiological research in the broadest sense, covering both personal hygiene and sanitation as well as the sources and means by which the vibrios are transmitted.

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EYCKMANS L. (1979), Le problème du choléra en Afrique de l'Est, – *ARSOM Bull.*, 25, pp. 445-450.

The author found that cholera, which is traditionally an Asian disease, had reached the African continent a few

years earlier. Starting in 1978 it spread out from Tanzania to eastern Zaire and Burundi. These two regions' experiences prompt comments as to the epidemiology and treatment of the disease. Its transmission in Africa is not exclusively waterborne, although the contamination of lakes and streams has been less dramatic than in Asia. The author also discusses the merits of preventive medication and vaccination and recent developments in this field. A lengthy bibliography completes the article.

MALENGREAU M., GILLIEUX M., DE FEYTER M. & WITTMAN L; (1979), A propos de l'épidémie de choléra à l'est du Zaïre en 1978, – *Ann. Soc. Belg. Méd. Trop.*, 59, pp. 401-412

The authors recount their experience of a cholera epidemic in a rural area in South-Kivu (Zaire) in 1978. They describe the epidemic's spread and impact on the population in connection with the area's geographical and socio-cultural characteristics. The epidemic was controlled mainly by means of local manpower and materials, with imports from outside (vaccines, light medical equipment, antibiotics, and basic ingredients for preparing rehydration solutions locally) and thus keeping the overall cost of the interventions to a minimum. This control effort was incorporated into the areas' normal health and development activities and consisted primarily in informing the population, in deciding with community representatives what measures to take (with reassessment of their efficacy after implementation), and in organizing effective treatment of patients as simply and cheaply as possible. A lengthy bibliography completes the article.

POLLITZER R. (1959), *Cholera*, Monograph series, n° 43, WHO, Geneva, 970p.

This book remains a basic reference, in which each chapter is followed by a large bibliography, although many new data were gathered in the last forty years.

RUGAMBA E. & MUREKEZI J. (1982), Choléra, in: MEHEUS A. & al. (Eds), *Santé et maladies au Rwanda*, AGCD, Bruxelles, pp. 260-274.

The authors trace the history of cholera's invasion of Rwanda in 1978. They take a closer look at the epidemic's development based on observations made in Cyangugu Prefecture, where most of the cases occurred. They discuss diagnosis, sex- and age-group-related vulnerability, complications, immunity, and the treatment and hospitalisation of cholera patients, ending with a list of both the preventive and general measures that should be taken. A map, various tables, and a lengthy bibliography complete the study.

SCHYNS C., FOSSA A., MUTOMBO-NFENDA, KABUYAHIYA, HENNART P., PIOT P. & COLAERT J. (1979), Cholera in eastern Zaire, 1978, – *Ann. Soc. Belg. Méd. Trop.*, 59, pp. 391-400.

The cholera epidemic that swept across eastern Zaire in 1978 came from Tanzania. The most important foci were located close to the Great Lakes and contaminated water was found to be instrumental in transmitting the infection. The article discusses preventive and curative measures. The antibiotic sensitivity of the El Tor strain of *Vibrio cholerae* is established. A lengthy bibliography completes the article.

STORME B. et al. (1979), L'épidémie de choléra au Burundi en 1978, – *Ann. Soc. Belg. Méd. Trop.*, 59, pp. 413-425.

The cholera epidemic that swept across Tanzania reached Burundi in May 1978. This article describes the steps taken by the Public Health Ministry to cope with the epidemic, the epidemic's course, and the factors that played a major role in the control effort.

WHO (1980), *Guide for the control of cholera,* WHO/CDC/SER/80.5, 15 p.

An essentially practical handbook for national public health workers, especially the directors of diarrhoeal disease control programmes, that gives recommendations for the cholera control activities that are conducted within the framework of such programmes. It can also be useful as a source of information about the types of assistance that should be given to countries that are confronted with a cholera epidemic.