“Cholera: Calamitous Past, Ominous Future”

Stephen W. Lacey (1995)

CHOLERA:

Greek: chole (bile) + rheein (to flow)

EPIDEMIOLOGY

Together with acute respiratory infections, diarrhoeal diseases are the greatest killers in the world today. The major toll is amongst infants and young children and diarrhoeal diseases are particularly prevalent in developing countries where overcrowding, with inadequate living conditions and poor hygiene, prevails.

Cholera is a historically feared epidemic diarrhoeal disease. New epidemics continue to affect different regions of the world. Excellent descriptions of a disease resembling cholera are extant in the Suhruta Samshita from India which was written in Sanskrit around 500 to 400 BC. Because earlier descriptions of the disease confused cholera with other diarrhoeal diseases, the modern history of cholera begins with a description by Thomas Sydenham in 1817. Seven pandemics, the first between 1817 and 1823 and the latest which started in 1961, have been identified and have caused the deaths of millions of people.

The seventh pandemic was caused by the biotype El Tor of Vibrio cholerae O1. It started in Indonesia and eventually spread to Africa, down the east coast, eventually reaching South Africa in 1981.

Some consider the outbreak of V. cholerae of the new serogroup O139 to be the eighth pandemic. This epidemic started in 1992 in Madras, but has remained confined to India and Bangladesh.

Cholera usually follows the consumption of contaminated water but has been associated with contaminated foods, surviving for up to 14 days in some foods, especially when contamination occurs after preparation. Examples are leftover rice, raw fish, cooked crab, raw oysters, fresh vegetables and fruits. Cooking and heating food eliminates the bacteria. In outbreaks, many infected people have few or no symptoms. Almost all cases of cholera occur in the tropics and imported cases are rare, partly because of the short incubation period (from several hours to 5 days) and partly because the risk to travellers is small. Person-to-person transmission is less likely to occur because a large inoculum is required to transmit the disease.

Some host factors are important in transmission of cholera. People infected by Helicobacter pylori are at a higher risk of acquiring cholera due to the chronic gastritis and hypochlorhydria induced by H. pylori. An unexplained predisposition towards severe disease is found in persons with the O blood group.
EPIDEMIOLOGY: SOUTH AFRICA

Previous outbreaks

Three outbreaks occurred in the 1980s. Each peaked between January and February, when higher rainfalls and temperatures combined to facilitate the spread of the bacterium.

- September 1980: Mpumalanga. 4000 cases and 42 deaths along the Crocodile River.
- August 1981: KwaZulu-Natal. >11 000 cases and 218 deaths.

Why the outbreak now?

The organism seems to follow a cycle of about four years' activity, followed by dormancy in water and estuaries of between 8 and 10 years. The dormancy/activation could possibly be linked to a rise in water levels and heat during the summer months. For an outbreak to occur in a region where cholera is not endemic, the following three factors are probably involved:

- The organism must be introduced into the region: In South Africa the disease was most likely introduced from Moçambique where an epidemic is still raging. Molecular testing has shown that the South African Strain is extremely closely related to the Moçambique strain.
- The environmental conditions must be favourable, e.g. the rise in water levels and heat during summer months.
- The population must be susceptible: This is also an explanation for the cycling phenomenon. After an epidemic, a large portion of the exposed population will develop immunity to the strain, thus curbing the epidemic. (Unfavourable environmental factors may also be involved in curbing the epidemic). After 8 to 10 years, this immunity wanes and new, non-immune people are also introduced into the region, thus creating an “immunologically favourable” environment for the organism.

About the latest outbreak

The first cases were reported in August 2000. By mid-January, 22 000 people were infected in South Africa, with 69 deaths. At the peak of the epidemic about 475 new cases were recorded every 24 hours in KwaZulu-Natal. The disease spread to Mpumalanga and cases were also recorded in Gauteng, North West Province and the Free State. Late in January the Jukskei River tested positive for cholera. This posed a great threat to the millions of people in Alexandra township who depend on the river for daily water. The South African epidemic is not under control yet. During March 2001 about a thousand cases a day were reported. At the moment cases seem to be tapering off slightly. This is actually not unusual for this time of year with winter approaching and does not necessarily mean that the outbreak is under control.

What was done about it?

The WHO credited the swift response of the South African health authorities for an “unusually low” death rate of less than 0,5%.
Measures that were taken include:

- Delivery of 200 new water tanks to affected rural areas
- 45 roving water delivery trucks
- 17 rehydration centres

**What biotype / serotype / serogroup is involved?**

The El Tor biotype is involved and both the Ogawa and Inaba serotypes have been identified. The first isolates were Ogawa, and then later on Inaba was also picked up. Serotype switching is a well-known phenomenon and the Ogawa serotype can convert to the Inaba serotype and vice versa. Only the O1 serogroup has been identified.

**THE CAUSATIVE ORGANISM**

**The bacterium:** Vibrio cholerae

**Life cycle**

The organisms live in aquatic environments, their natural reservoirs, attached to a particular kind of algae or to crustacean shells and zooplankton. When environmental conditions are suitable (temperature, salinity, nutrient availability) organisms multiply and can survive for years in a free-living cycle without the intervention of humans. Otherwise, when conditions are not suitable for its growth, it switches from a metabolically active state to a dormant state.

**Microbiology**

Vibrio cholerae is a curved Gram-negative bacillus with somatic (O)- and flagellar (H) antigens. The somatic antigens are used to differentiate pathogenic (O1 and O139 strains) from non-pathogenic V. cholerae (often referred to as non-O1 strains).

**O1-strains**

Three serotypes: **Inaba, Ogawa and Hikojima** (related to O-antigens). During an epidemic a shift from one serotype to another may occur. There are no differences in the clinical pictures caused by the different serotypes.

**Two biotypes**

1. **Classic:** Caused the first 6 pandemics and is currently confined to the south of Bangladesh. Causes an approximately equal number of symptomatic and asymptomatic cases.

2. **El Tor:** Causes more asymptomatic infections (20-100 asymptomatic infections to 1 symptomatic case). Responsible for the current pandemic.
The cholera toxin

This is an enterotoxin which binds to the enterocyte by means of its 5 B-subunits, thus facilitating the entry of the A-subunit into the cell, where it can activate adenyl cyclase; this in turn leads to net secretion of chloride ions and water into the gut lumen. This excess secretion overwhelms the normal absorptive capacity of the small and large bowel, leading to diarrhoea. It causes relatively little inflammation in the mucosa.

THE DISEASE

In any patient who has profuse watery diarrhoea and severe dehydration, cholera should be considered. The illness begins with a sudden onset of profuse, watery diarrhoea or anorexia and abdominal discomfort followed by diarrhoea. The stool has a characteristic “rice water” appearance because of the mucus content, and a mild fishy smell. Tenesmus is absent and vomiting often occurs a few hours after onset of diarrhoea. Signs and symptoms result from fluid and electrolyte losses: abdominal pain, muscle- and leg cramps, nausea, vomiting, thirst and faintness. 2-10% of patients develop cholera gravis with tachycardia, hypotension and severe hypovolaemic shock as a result of loss of between 500 ml and a litre of fluid per hour. Patients are typically afebrile, but fever may occur in up to 20% of cases and is more common in children than in adults. Diarrhoea will persist for up to 5 days in the untreated patient.

Complications:

- Altered consciousness
- Acidosis
- Hypoglycaemia
- Hypokalaemia
- Hypernatraemia
- Renal failure

LABORATORY DIAGNOSIS

A case of cholera should be confirmed by a positive stool specimen. Stool specimens should be collected in clear containers with tight-fitting lids and should be refrigerated if not preserved.

What is done in the laboratory?

Microscopy

A Gram’s stain can be done: sometimes curved Gram-negative rods can be observed which are suggestive of V. cholerae.
Culture

May take up to 3 days. The specimen is put into an enrichment medium (peptone water) and incubated for 24 hours. It is then plated out onto selective and differential media (TCBS = thiosulfate-citrate-bile-salt-sucrose) and incubated for up to 48 hours. Vibrio cholerae forms flat yellow colonies on TCBS. Suspect colonies are confirmed biochemically and serologically.

P.S. Enrichment media is useful when the number of bacteria in the stool is small or when environmental samples are evaluated for the presence of V. cholerae.

EVALUATION AND MANAGEMENT

1. Antibiotics have a very limited use and do not significantly affect the course and the spread of the disease, although some studies have shown it to decrease the duration of diarrhoea and to reduce the volume of stool by nearly half. The current strain is also resistant to quite a few of the conventional antibiotics, namely:
   - Tetracycline / doxycycline (given as a single dose of 300 mg)
   - Chloramphenicol
   - Cotrimoxazole
   - Erythromycin
   - Furazolidone
   A reasonable alternative is ciprofloxacin 1 g stat or 250 mg daily for 3 days.

2. The goal of therapy is to restore the fluid losses caused by diarrhoea and vomiting. The mortality from severe cholera should be less than 1% with proper fluid therapy (in contrast to as much as 50% if untreated). The rationale behind ORS (Oral rehydration solution) is that glucose increases the absorption of NaCl in the small intestine even in the presence of secretory toxins. Please refer to the Gauteng Health Department Clinical Guidelines for Management of Patients with Cholera, for details of patient pre-treatment evaluation and fluid replacement therapy.

3. Antimotility drugs should not be used. Feeding should be restarted ASAP and breastfeeding should not be discontinued. Full strength dairy products and caffeine should be avoided.

4. Health education: all patients should be informed about the spread of cholera, the role of personal hygiene, e.g. hand washing and the use of oral rehydration solution. The most effective prevention methods are adequate sanitation and access to clean drinking water. This is proven by the fact that the USA have so few indigenous cases despite the fact that V. cholerae is isolated from the environment. Health authorities have undertaken extensive education programmes to encourage improved basic hygiene by boiling drinking water or treating it with bleach (one teaspoon of household bleach in 25 litres of water allowed to stand overnight).

WHAT ABOUT A VACCINE?

The ideal vaccine is still not available, but significant progress has been made in vaccine development. Oral vaccines seem to be more effective than parenteral vaccines. However, none of the vaccines tested so far have prevented cholera transmission, and none are recommended for general use or are practical for treating large numbers of people. More research on safe, effective vaccines is needed.

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