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The Whole Program

COTS Program - All Chapters

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Chapter 1 - introduction to diarrhea

Chapter 1.1 - Introduction to diarrhea

This section will serve as a general introduction to diarrheal disease around the world. Diarrhea is defined as loose or watery stools at an increased frequency from normal. Although bowel habits vary, the WHO defines diarrhea as 3 or more loose or watery stools per 24 hours; this presentation is usually associated with other systemic or gastrointestinal symptoms. This program will focus on infectious diarrhea and will use the WHO definition of diarrhea.

In the small sections below, the types, magnitude, and impact of infectious diarrhea will be discussed, as well as the transmission, susceptibility, seasonality, and history of diarrheal epidemics.

- Magnitude of diarrheal disease
- Clinical types of infectious diarrhea
- Transmission and susceptibility of diarrheal infections
- Seasonality of diarrheal disease
- History of diarrheal epidemics
- Chapter conclusion
- Quiz questions

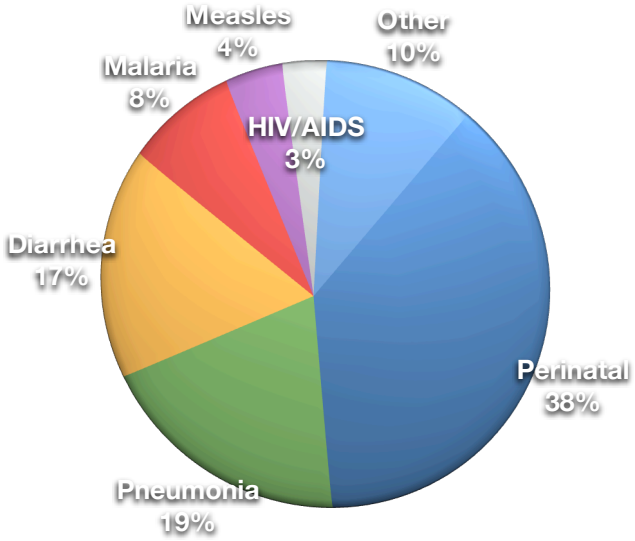
Chapter 1.2 - Magnitude of Diarrheal Disease

Diarrheal disease is a major health problem, especially in refugee camps (1-10). It is an important cause of morbidity and mortality in the developing world. Of infectious causes of death in children, it is the second highest in the world after acute respiratory infection, causing an estimated 1.87 million deaths in children under 5 [(11)]. The morbidity and mortality associated with diarrhea for adults is not well documented, but unsafe water, sanitation and hygiene, which are the main risk factors for diarrhea, cause an estimated 54,158 disability adjusted life years (DALY)[(12)].

Diarrhea is especially risky in the context of malnutrition, which is the underlying cause of death in around 60% of children under 5 [(13)]. Acute disease is often prolonged in malnourished patients due to suppression of the immune system caused by malnutrition. Diarrhea is also considered a disease of nutrition because it contributes to decreased food intake and absorption. Decreased intake is a result of decreased appetite, vomiting, or harmful cultural beliefs that food intake should be restricted during diarrheal episodes. Decreased caloric intake is even more detrimental to nutritional status during diarrheal episodes because the energy requirements are higher in a patient with diarrheal infection.

Diarrheal disease has a large impact on the world, especially in developing countries. Although treatment with ORS (oral rehydration salts) has reduced the mortality due to diarrheal disease, the morbidity may actually be increasing. Recent estimates have suggested that diarrhea morbidity, especially due to repeated episodes in the first 2 years of life, actually outweighs the burden of mortality, with 10-25% of the world's children experiencing long-term disability [(14)]. This long-term disability is in the form of growth faltering, decrease in work productivity, cognitive deficits, and educational performance [(15)]. In addition to morbidity and mortality, diarrheal diseases have a significant economic impact on the communities they infect, which are often already the poorest. [(16)]

Cause of Death for Children under 5 years Worldwide [(17)]



Note: Perinatal mortality includes deaths due to diarrhea during the neonatal period. Including neonatal death due to diarrhea, the total proportion of deaths due to diarrhea in children under 5 is even higher than 17%.

Definition of DALY: the disability-adjusted life year is a calculation based on the time lived with a disability and the time lost due to premature mortality. The duration of time lost due to premature mortality is calculated based on standard life expectancy. The reduction in physical capacity due to morbidity is measured using disability weights. In addition, there is a factor in the calculation that grants a value to different ages, giving more value to those who are of productive working age. This reflects how the young and the elderly are dependant on adults of working age.

Chapter 1.3 - Clinical Types of Diarrhea

When discussing causes of diarrhea it is important to discriminate between the clinical disease and the organism that causes it. In this section, clinical types of diarrhea and the organism or organisms that cause them is discussed in the individual sections. The two main clinical types of infectious diarrhea are generally considered to be:

a) Watery
b) Bloody

Some consider there to be a third clinical type of diarrhea, which is:

c) Diarrhea with severe malnutrition

In terms of duration, diarrhea can be acute, persistent (lasting ≥ 14 days), or chronic. Practically persistent and chronic diarrhea are managed the same. In the different clinical sections mentioned above we will focus on acute diarrhea. However, we will have a separate section on persistent diarrhea since it can be an important issue to address in emergency situations.

1.3.a) Watery Diarrhea: This type of diarrhea is generally of secretory pathophysiology and the main danger is dehydration. There are several different possible infectious causes of this type of diarrhea. The most common pathogens are:

- Rotavirus
- ETEC (Enterotoxigenic *Escherichia coli*)
- *Vibrio cholerae* (different types to be discussed in-depth in the cholera section)

Of the above three, cholera is the most important cause of epidemic watery diarrhea in developing countries in terms of its high rate of morbidity and mortality. Severe ETEC can also cause epidemic diarrhea, but its treatment is essentially the same as cholera.

1.3.b) Bloody Diarrhea (dysentery): This type of diarrhea is generally presumed to be invasive, however not all bloody diarrhea is caused by an invasive organism. Invasive diarrhea is caused by bacteria that invade the intestinal mucosa, which causes inflammation, tissue damage, and often, visible blood. However, watery stool is often present before the appearance of visible blood, which may appear later in the course of the disease. Diarrhea with visible blood can be caused by many different pathogens. Many of these pathogens may also be associated with watery diarrhea, especially early in the illness, including:

- *Shigella* species (often has a history of straining or tenesmus)
- *Salmonella* species
- *Campylobacter jejuni*
- *Clostridium difficile*
- EIEC (Entero-invasive *E. coli*)
- EHEC (Entero-hemorrhagic *E. coli*)
- *E. coli* O157:H7
- *Entamoeba histolytica*
- *Yersinia enterocolitica*
- Amebiasis

Although all of the above organisms can cause dysentery, only *S. dysenteriae* serotype 1 and *E. coli* O157:H7 have been known to cause large epidemics. *S. dysenteriae* is a much more common cause of large-scale epidemics in developing countries, and *E. coli* O157:H7, which is associated with contaminated commercially prepared food, has caused epidemics in industrialized countries.

It is important to note that *E. histolytica* or other pathogens like *C. jejuni* are frequently found in asymptomatic people in developing countries (up to 10% of healthy people in some areas). Although it can cause dysentery, it is not a cause for epidemic disease. Therefore, if *E. hystolytica* is found in stool samples during an epidemic, it is important to continue looking for a more likely pathogenic cause for the dysentery epidemic.

It is also important to distinguish between amebiasis, which is generally a more chronic type of dysentery, and shigellosis, which typically causes acute epidemics. Patients with amebiasis typically have dark brown blood in their stools rather than the bright red blood seen in shigellosis patients. Furthermore, in contrast to amebiasis patients, shigellosis patients typically have a temperature and cramps. Microscopic analysis reveals that shigellosis stools tend to have more white blood cells than red blood cells whereas amebiasis is the opposite.

1.3.c) Diarrhea with severe malnutrition: Although not always considered a separate clinical type of diarrhea, it is important to highlight the fact that malnutrition can be a cause or an effect of diarrheal episodes. Therefore, the management of diarrhea changes with malnutrition. Most importantly, in severely malnourished children, dehydration is corrected more slowly compared to well-nourished children.

Diarrhea can worsen or even cause malnutrition by contributing to decreased food intake, nutrient loss and malabsorption. Thus, diarrhea is often considered a nutritional disease as well as a fluid loss disease. Children eat less because of decreased appetite, vomiting, or harmful cultural beliefs that food intake should be restricted during diarrhea. Decreased caloric intake is even more detrimental to nutritional status during diarrheal episodes because the energy requirements are higher in a patient with diarrheal infection.

Finally, malnutrition can be an indirect cause of diarrhea because children who are severely malnourished have weakened immune systems and are more susceptible to diarrheal disease. This is the vicious cycle of diarrhea and malnutrition.

1.3.d) Persistent diarrhea: Diarrhea is considered to be persistent if it has continued for at least 14 days and up to 4 weeks (at which point it is considered chronic). If there is a break in the diarrhea for 48 hours or more it is considered to be two subsequent infections and not persistent diarrhea. Persistent diarrhea is an important clinical type of diarrhea since it can indicate some underlying problem that a patient may have, and it is dangerous because of the risk of developing, or worsening, malnutrition. Most cases of persistent diarrhea will never be attributed to a specific pathogenic cause. Persistent diarrhea is often due to continuing infection, delayed recovery and sequential new infections and is presumed to be due to malnutrition in most cases. Therefore, the treatment plan primarily becomes one of nutritional support.

Chapter 1.4 - Transmission and susceptibility of Diarrheal Disease

Transmission of diarrheal disease

Most bacterial infectious diarrheal diseases are transmitted by the fecal-oral route. In other words, the main sources of infection are from water or food contaminated with fecal material and from direct contact with hands that are fecally contaminated. Contaminated food (especially seafood) is a more common cause of cholera in developed countries, whereas contaminated water is more common in developing countries [18,19,20].

88% of all diarrheal disease in the world can be attributed to unsafe water, sanitation and hygiene. This translates to >1 million deaths in children under 5 years alone, and 54.2 million DALYs attributable to unsafe water, sanitation and hygiene. Of the deaths associated with unsafe water, sanitation and hygiene, 99.8% occur in developing countries, and of these deaths, 90% are children [21, 22]. The burden of diarrheal disease is also on the elderly, especially in developed countries [23]. An increased probability of transmission occurs in emergency settings due to contaminated water supply, lack of sanitary facilities like latrines, poor hygiene, and improper food preparation and storage.

Some organisms can infect following ingestion of only a few bacteria, while others require a much larger number. For example, *V. cholerae* requires an infectious dose of 10,000 to 1,000,000 organisms [24] versus *Shigella* spp., which can infect a person who has ingested as few as 10 organisms [25]. However, the severity of sickness associated with the growth of the organism in the host is determined by the virulence of the pathogen. Virulence is the degree of sickness caused by the pathogen. The virulence is a product of the pathogen's skill in attacking the host and the host immune system's ability to defend itself.

Increased Susceptibility to Diarrheal Disease

There are a few common factors that increase a person's susceptibility to diarrheal disease, which are common in developing countries and/or emergency settings:

- Malnutrition – people who are severely malnourished are immunosuppressed and therefore do not have an adequate defense against diarrheal diseases in the environment
- Immunodeficiency/immunosuppression – especially HIV/AIDS and other chronic disease
- Reduced gastric acidity – common in old age
- Decreased intestinal motility – common in diabetes
- Recent history of measles - leads to an immunosuppressed condition for several months

Chapter 1.5 - Seasonality of Diarrheal Disease

In each area of the world, the epidemiology of diarrheal disease varies during the course of the year. However, as a general rule, there are two main climates, temperate and tropical, which have their own distinct diarrheal disease seasons. Please use this as a rough guide to begin to analyze the pattern in your area. It is not intended to imply that the "off-season" is a time period when you can ignore epidemic diarrhea.

Temperate Climate:

- Bacterial diarrhea: warm, humid season
- Rotavirus diarrhea: winter, drier season

Tropical Climate:

- bacterial diarrhea: rainy season (including pre and post monsoons)
- rotavirus diarrhea: year-round, with increased prevalence during the cooler season

For example, Bangladesh typically has two cholera peaks, one just before the rainy season and one just following the rainy season [(26)]. Knowing the incidence curve in your area would be helpful in anticipating an outbreak.

Definition of incidence: incidence is the number of new cases of a disease or condition divided by the population at risk for the disease or condition during a specified time period. Incidence is usually expressed as a percentage per year.

Chapter 1.6 - Prevention

Prevention of all bacterial diarrheal disease is the same. Simple improvements in water, hygiene and sanitation can significantly reduce the incidence of diarrhea cases. This section will serve as a general overview of the necessary steps to prevent diarrhea cases. A more detailed discussion on these prevention measures will be in the "Before an Outbreak" section.

The two most important public health measures to prevent diarrhea are ensuring a clean water supply and personal hygiene [(27)]. Safe water is theoretically the easiest to control, despite the fact that in practice it may be quite difficult. Because water contamination can occur at the source, during transport or at the home during storage, site and household visits by a health inspection team are essential to determine the best way to stop the transmission of disease. Depending on the situation, chlorination in the general water system, at the source, the common water tank, or in the home, as well as boiling water in the home, are all viable methods for ensuring safe water. Personal hygiene can be promoted through community health promotion messages and ensuring that every family has supplies of soap and at least one clean towel.

Equally important as clean water and hygiene is the focus on having an adequate number of proper safe latrines, and further sanitation efforts, including health education and promotion, food safety and funeral practices. In addition to being an adequate distance from water sources, latrines must also be culturally and environmentally appropriate and inexpensive in order to ensure their use. Family latrines have the added advantage that the family is responsible for their own latrine. In the case of communal latrines maintenance must be organized and responsibilities delegated throughout the community. Personal hygiene behavior is the hardest to change and may take longer and require more community involvement, but is very effective if it can be implemented [(28)].

In addition to public health prevention efforts, simple messages should be given to the community in a locally and culturally sensitive manner to prevent diarrhea at the household level.

The WHO recommends the following messages [(29)]:

- Wash your hands with soap:
  - After using toilets and latrines
  - Before preparing food
  - Before eating
- Boil or disinfect water with chlorine solution
- Only eat freshly cooked food ("cook it, peel it, or leave it")
- Do not defecate near the water sources
- Use latrines and keep them clean

Chapter 1.7 - Conclusion Box

- With adequate therapy (especially ORS) we can reduce the mortality of watery diarrhea diseases.
- The most important measures to prevent diarrhea diseases are personal hygiene and clean water.
- Some factors, like malnutrition or measles, may increase the susceptibility of persons for diarrhea diseases.
- There are two main clinical types of infectious diarrhea: watery and bloody. Additionally, persistent diarrhea and diarrhea with malnutrition are important to keep in mind in emergency settings because of their prevalence and specific treatment considerations.

Chapter 1.8 - References

1. Goma Epidemiology Group. Public health impact of Rwandan refugee crisis: what happened in Goma, Zaire, in July, 1994? 1995 *Lancet* 345:339-44.

2. Anand, J. K. 1995. Cholera treatment in Goma. *Lancet* 345:1568.

3. Boelaert, M., C. Suetens, M. van Soest, M. Henkens, J. Rigal, and P. de Graaf. 1995. Cholera treatment in Goma. *Lancet* 345:1567.

4. Burns, D. A., and C. B. Wood. 1995. Cholera treatment in Goma. *Lancet* 345:1568.

5. Lacey, S. W. 1995. Cholera: calamitous past, ominous future. *Clin Infect Dis* 20:1409-19.

6. Pelly, M. D., and C. Besse. 1995. Cholera treatment in Goma. *Lancet* 345:1567-8.

7. Roberts, L., and M. J. Toole. 1995. Cholera deaths in Goma. *Lancet* 346:1431.

8. Siddique, A. K. 1994. Cholera epidemic among Rwandan refugees: experience of ICDDR,B in Goma, Zaire. *Glimpse* 16:3-4.

9. Siddique, A. K. 1995. Failure of treatment centres to prevent cholera deaths in Goma. *Lancet* 346:379.

10. Siddique, A. K., A. Salam, M. S. Islam, K. Akram, R. N. Majumdar, K. Zaman, N. Fronczak, and S. Laston. 1995. Why treatment centres failed to prevent cholera deaths among Rwandan refugees in Goma, Zaire. *Lancet* 345:359-61.

11. *World Health Report*, World Health Organization, 2005

12. WHO, World Health Report 2002-Reducing Risks, Promoting Healthy Life

13. Caulfield LE, deOnis M, Blossner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria and measles. *American Journal of Clinical Nutrition*. 2004. 80(1):193-198

14. Guerrant RL, Kosek M, Lima A, Lorntz B, Guyatt H. Updating the DALYs for diarrhoeal disease. *Trends in Parasitology* 2002, 18(5):191-193

15. ibid.

16. Bloom DE, Canning D, The Health and Wealth of Nations, *Science*. 2000. 287(5456):1207-1209

17. *World Health Report,* World Health Organization, 2005; statistics are estimates from member countries for 2000-2003

18. Shapiro RL, Otieno MR, Adcock PM, et al. Transmission of epidemic *Vibrio cholerae* 01 in rural western Kenya associated with drinking water from Lake Victoria: an environmental reservoir for cholera? *Am J Trop Med Hyg* 1999; 60: 271-76

19. Hughes JM, Boyce JM, Levine RJ, et al. Epidemiology of El Tor cholera in rural Bangladesh: importance of surface water in transmission. *Bull World Health Organ* 1982; 60: 395-404

20. Glass RI, Claeson M, Blake PA, Waldman RJ, Pierce NF. Cholera in Africa: lessons on transmission and control for Latin America. *Lancet* 1991; 338: 791-95

21. WHO, World Health Report 2002-Reducing Risks, Promoting Healthy Life

22. Ashbolt NJ, Microbial contamination of drinking water and disease outcomes in developing regions. *Toxicology* 2004. 198 (1-3):229-38

23. Lew JF, et al., Diarrheal deaths in the US 1979-1987. A special problem for the elderly. *JAMA* 265

24. Hornick RB, Music SI, Wenzel R. The Broad Street pump revisited: response of volunteers to ingested cholera vibrios. *Bulletin of the New York Academy of Medicine*, 1971, 47:1192-203

25. Du Pont HL, Levine MM, Hornick RB, Formal SB. Inoculum size in shigellosis and implications for expected mode of transmission. *J. Infect. Dis.* 1989; 159:1126-1128

27. Khan MU, Interruption of shigellosis by hand washing. *Trans R Soc Trop Med Hyg.* 1982;76(2): 164-8

28. World Health Organization, Acute diarrhoeal diseases in complex emergencies: critical steps. 2004 WHO Global Task Force on Cholera Control. WHO/CDS/CPE/ZFK/2004.6

29. World Health Organization, First steps for managing an outbreak of acute diarrhea. 2004 WHO Global Task Force on Cholera Control. WHO/CDS/CSR/NCS/2003.7 Rev.1

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Chapter 2 - introduction to Cholera

Chapter 2.1 - Introduction to Cholera

This section will serve as a general introduction to cholera around the world. *Vibrio cholerae* is the causative agent of the acute watery diarrheal disease cholera. Cholera is dangerous because it can cause rapid dehydration, electrolyte loss, and death if it is not treated promptly and effectively. *V. cholerae* sparks outbreaks that can affect thousands of patients within a few days from the first sentinel case of infection.

In the small sections to follow, the following topics will be discussed:

- History and taxonomy of cholera epidemics
- Epidemiology of cholera disease
- Introduction to *Vibrio cholerae*
- Pathophysiology of cholera
- Clinical presentation of cholera
- Chapter conclusion
- Quiz questions

For the principles of management and complications of cholera, please see Chapter 4 – Clinical Management of Cholera.

Chapter 2.2 - History and Taxonomy of Cholera Epidemics

The history of cholera can, in many ways, be told through its taxonomy. *V. cholerae* taxonomy is not easy because of the great diversity of strains within the species classification (200+ groupings). In the COTS program, we try to limit the information provided to that which is relevant in the clinic.

Strains of *V. cholerae* are classified by their serogroup (and in the case of O1 *V cholerae*, their serotype), and their biotype. There are more than 200 serogroups of *V. cholerae,* but only two of these, serogroup O1 and O139 have been associated with epidemic disease, even though the others may cause illness in individual patients. A serogroup is defined by its agglutination with a specific antiserum. When the specific antiserum is mixed with the bacteria on a slide, the serum binds to the outside of the bacteria causing bacterial agglutination. Thus, in the laboratory, when a strain of *V cholerae* is isolated, the first test the technician carries out is the bacterial agglutination test with O1 and O139 antisera.
If the strain agglutinates with either of these sera, the strain is then known to be a *V. cholerae* O1 (or O139). If it does not agglutinate with the antisera, it is known as a non-O1, non-O139 *V. cholerae.* If the strain is found to agglutinate with O1 antiserum, the technician should then test the strain to see if it agglutinates with an even more specific antiserum to see if the strain is of the Inaba or Ogawa serotype (rarely, there are strains that agglutinate with both Ogawa and Inaba antisera, and these strains are called serotype Hikojima). Unlike strains of the O1 serogroup, strains of O139 are not further subdivided (1).

The biotype is another way to classify the strain. The biotype depends on biological properties of the bacterium, rather than on its agglutination to antisera. The two biotypes of *V. cholerae* include the classical and the El Tor. The 5th and 6th pandemics of cholera were caused by the classical biotype, but the 7th (current) pandemic is caused by El Tor. Strains from earlier pandemics are not available so it is not confirmed which biotypes were responsible.

Often, in addition to the serotype and biotype, it is important to know if the *V. cholerae* strain produces cholera toxin – the toxin primarily responsible for fluid loss. Strains that do not produce the toxin are not associated with epidemics even though they may be an O1 or O139 serogroup.

Thus, a strain of V cholerae O1 may be classified according to the following grid. A strain may be a classical Inaba, a classical Ogawa, an El Tor Inaba or an El Tor Ogawa. In each case, it can be either a producer or a non-producer of cholera toxin.

	Classical**	El Tor
Inaba	Classical-Inaba	El Tor-Inaba
Ogawa	Classical-Ogawa	El Tor-Ogawa

For strains of the serogroup O139, the strains are only subdivided as being a producer or non-producer of cholera toxin. Serogroup O139 may have evolved from strains of O1 El Tor, as they share many properties with El Tor strains. Yet, they have a different outer surface, which causes a different agglutination reaction with antisera.

As microbiology modernizes, serology may become less important as molecular tools, such as PCR, provide better and faster means of classifying bacteria.

V. cholerae has been endemic in South Asia and Africa from the time of recorded history. It is believed to have originated in the Bengal region, or what are modern-day Bangladesh and the state of West Bengal in India. The first pandemic of cholera in recorded history began in 1817 and reached Europe by the 1830s. It was not until the famous epidemiologic study by John Snow in London in 1854 that it was known that cholera was spread by contaminated water (2). John Snow hypothesized that cholera was transmitted by contaminated water. In a move to stop the epidemic and test his hypothesis, he removed the water pump handle from a contaminated well. The number of cholera cases surrounding the pump dropped and John Snow became a public health legend.

As previously mentioned, there have been 7 major pandemics in modern, recorded history. It was not until the 5th pandemic that Robert Koch discovered the causative agent of cholera in Kolkata in 1883 (3). The seventh pandemic was caused by the El Tor biotype, which was first isolated in 1905 in El Tor, Egypt from Indonesian pilgrims traveling to Mecca. In the 1960s El Tor spread from Indonesia, throughout Asia, to the eastern Mediterranean, Africa, Europe and North and South America. Today, the El Tor biotype has replaced the Classical biotype as the dominant cause of cholera (4). Currently, O1 and O139 co-exist on the Indian subcontinent. In the spring of 2002 in Dhaka, Bangladesh, O139 cholera cases exceeded the number of cases of El Tor cases (5) and therefore it is postulated that 0139 might be the cause of an 8th pandemic of cholera. However, more recently, O1 cases have been much more commonly seen.

Chapter 2.3 - Epidemiology of Cholera

During cholera outbreaks in non-endemic areas, children and adults both contract the disease. However, because adults are more mobile and have more of an exposure risk outside the home, they are typically infected more often than children. In endemic areas the situation is reversed. Because most adults in an endemic area have been previously exposed to cholera, the children have higher rates of infection (6). Note that the absolute number of cases however is higher in the adult population because there are more adults than children in the population. For reasons that are not clear, stains of O139 have tended to have higher rates in adults than children.

The attack rate (percentage of cases per susceptible population per year) is approximately 0.2% in endemic areas. This estimate is used to assess the minimum amount of needed supply stocks before an epidemic happens in any area, which should cover supplies needed during the first few weeks of an epidemic. However, attack rates (AR) can be much higher. In an endemic area with very poor sanitary conditions, the attack rate is generally 0.6% (7). The attack rate can be even higher in rural communities with 5000 people or less (2%) and in refugee camps with a high-risk population due to a significant percentage of malnourished people (5-8%) (8).

Chapter 2.4 - Introduction to *Vibrio cholerae*

There are unique and important elements to the biology of *V. cholerae* that drive outbreaks. Almost all members of the genus *Vibrio* are pathogens of marine (saltwater) animals. *V. cholerae* is unique in that it has a very low Na^+ requirement that allows the bacterium to live in fresh and brackish water – a key factor in disease transmission. *V. cholerae* can persist for years in freshwater through establishing associations with phytoplankton and zooplankton. Once a person consumes this contaminated water, a vicious cycle of disease begins (9). Humans are the only known vertebrate host for *V. cholerae*.

V. cholerae is a Gram-negative bacterium and shares many colonization factors with normal gut flora, including its close relative *E. coli*. These factors range from the ability of the bacterium to grow both with and without oxygen as well as its ability to detect when it has entered its human host. Within the species of *V. cholerae*, there are many diverse strains that have varying pathogenicity. As mentioned, the O1 and O139 serogroups contain the major strains responsible for cholera outbreaks (10). *V. cholerae* survives passage through the stomach by initiating an acid tolerance response (ATR) and ultimately (11,12), initiates infection by binding gut epithelium with the aid of projections from the sides of the bacterium called Toxin Co-regulated Pili (TCP) (13,14). Shortly after binding, cholera toxin is produced (see pathophysiology section) and massive amounts of fluid are lost into the lumen of the small intestine.

At some point during infection, *V. cholerae* changes gene expression via an unknown mechanism and enters an 'escape response' (15). Subsequently, cholera toxin shuts off, and the bacteria exit in the rice-water stool in what is called a hyper-infectious state – meaning that bacteria exiting the body are more infectious than they are when the bacteria are grown in the laboratory (16). The role hyper-infectivity plays in an outbreak is modeled to be a significant driving force for the explosive nature of cholera. An opposing force to outbreaks is the presence of bacterial viruses called phage that seem to block the propagation of *V. cholerae* (17,18). The exact role that hyper-infectivity and phage play during outbreaks is still debated and studied.

After ingestion, *V. cholerae* passes through the acidic environment of the stomach and enters the small intestine where the bacteria colonize. (The bacteria are killed by acid; thus, persons with little acid in their stomach are more susceptible. For persons with normal stomach acid production, the numbers of bacteria ingested must be high enough so that some can survive to reach the small intestine.) *V. cholerae* is propelled by a single polar flagellum and uses chemotaxis to swim to food, or away from danger, by sensing changes in the chemical environment. Once *V. cholerae* reaches the small intestine, it uses filamentous proteins called toxin co-regulated pili (TCP) to attach to receptors on the intestinal mucosal surface. *V. cholerae* does this without inducing an overt inflammatory response from the host (19). This intimate relationship between the bacterium and the mucosa allows cholera toxin to be efficiently delivered to the mucosal cells to cause secretory diarrhea.

The cholera toxin consists of β subunits, which bind to the GM1 ganglioside receptors on mucosal cells, and one active α subunit, which is transported into the cell to activate adenylate cyclase (20). In the cytosol, the α subunit catalyzes the transfer of an ADP-ribose from NAD to stimulatory α subunits of G proteins. After ADP-ribosylation, the G proteins bind and constitutively activate adenylate cyclase. The activation leads to increased concentrations of intracellular cyclic adenosine mono-phosphate (cAMP). This rise in cAMP causes an increase in chloride secretion and inhibition of sodium chloride absorption in the mucosal cells.

The result is a net outpouring of fluid into the lumen of the small intestine (21). The fluid secretion induced by cholera toxin is too much for the bowel to reabsorb (described below), especially given that the toxin may also inhibit water absorption from the colon (22). This secretion leads to what is referred to as acute secretory diarrhea. Secretory diarrhea is characterized by the active secretion of fluid and solutes. Osmotic diarrhea, on the other hand, is the passive shift of water to the lumen of the intestine when the lumen harbors a non-absorbable osmolyte.

Water is absorbed from the lumen of the colon in an attempt to aid the renal system by retaining fluid when the body faces dehydration. Unlike in more proximal regions of the gastrointestinal tract, the epithelial tight junctions in the colon do not permit the passive diffusion of Na^+. However, K^+ can diffuse across the tight junctions. During states of hypovolemia, aldosterone stimulates the absorption of Na^+ in active exchange for K^+ (click here for diagram). To balance charge, Cl^- exchanges with HCO_3^- across the lumenal surface, and the Cl^- continues across the baso-lateral surface to follow Na^+ into the bloodstream. At the same time, K^+ slips through tight junctions into the lumen (23).

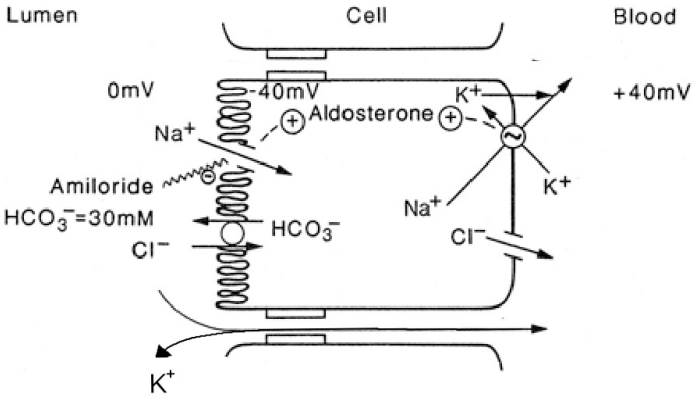
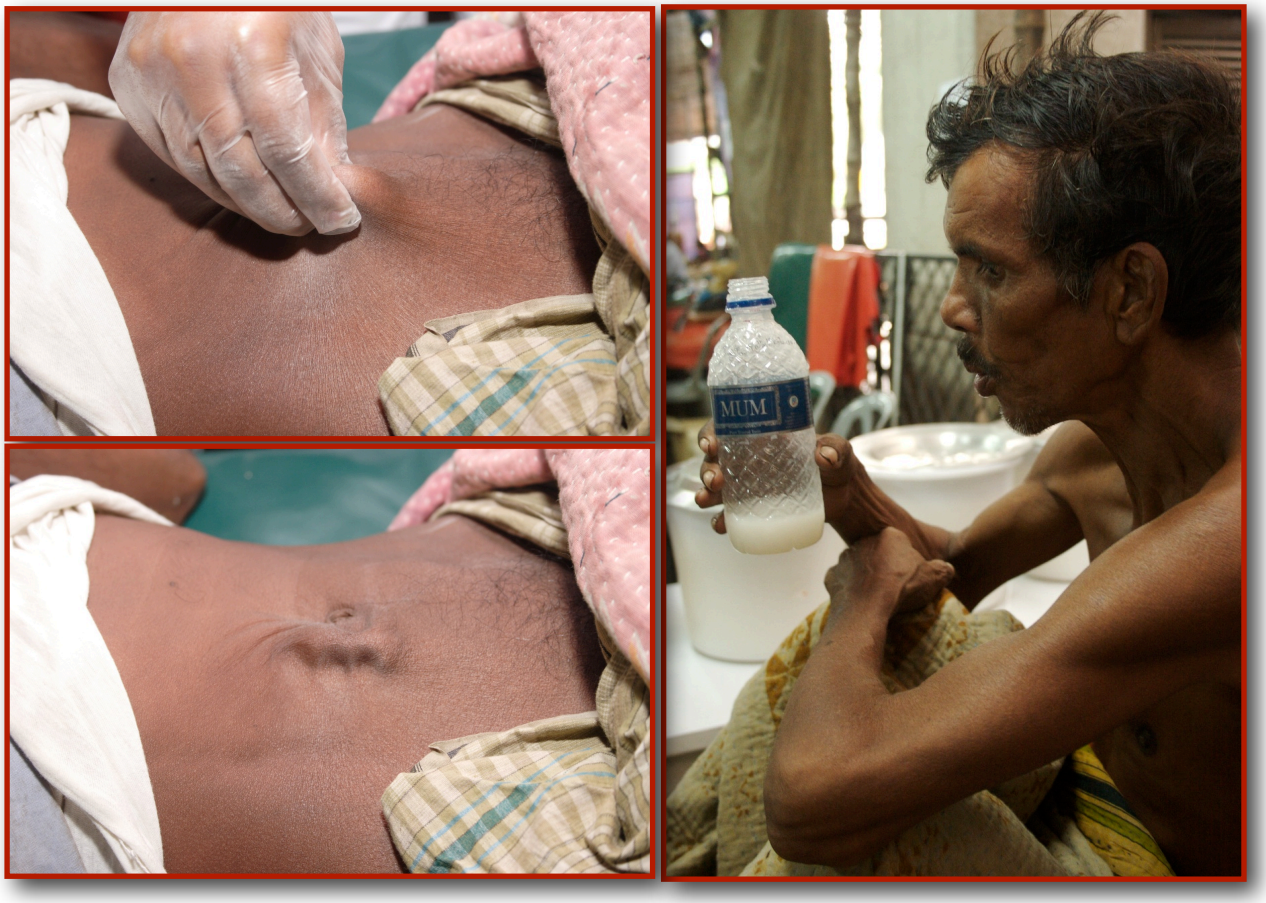


Figure adapted from First Principles of Gastroenterology by A.B.R Thomson and E. A. Shaffer; AstraZeneca Canada Inc. 2000.

Electrolyte composition of stool, IV fluids, and ORS (mmol/L): (24)					
	Na^+	K^+	Cl^-	HCO_3^-	Citrate
Adult cholera stool	135	15	100	45	-
Child cholera stool	105	25	90	30	-
Child non-cholera gastroenteritis	52	25	55	14	-
Lactated Ringers	131	4	109	28	-
Cholera Saline	133	13	98	48	-
Normal Saline	154	0	154	0	-
Low-osmolarity ORS (245 mOsm)	75	20	65	-	10
Traditional WHO ORS (311 mOsm)	90	20	80	-	10

The net result is that some water is absorbed, and K^+ and HCO_3^- are lost in the lumen. Because of the dramatic nature of cholera and the finding that cholera toxin may actually disrupt the Na^+/K^+ pumps, the colon fails to adequately retain water, and large amounts of K^+ and HCO_3^- are lost in the rice-water stool. The stool ultimately becomes isotonic with blood. The electrolyte losses result in potassium depletion and metabolic acidosis, and may present with ileus and rapid respiratory rates, respectively (see clinical management section). For these reasons, the ICDDR,B developed Cholera Saline for IV transfusion that replaces the required K^+ and HCO_3^- (see clinical management section).

Note that even though the patient experiences K^+ depletion, usually the serum K^+ concentration is normal when the patient first presents for treatment. However with correction of the metabolic acidosis, the serum K^+ can fall quickly if the rehydration solution does not replace K^+. This is due to the movement of K^+ into the cells when the metabolic acidosis is corrected.



"A cholera patient typically presents with severe dehydration"

Chapter 2.6 - Clinical Presentation of Cholera

The most common presentation of cholera is a very acute onset of profuse watery diarrhea and vomiting without abdominal pain or cramping. However, spasmodic abdominal pain might occur. Muscle cramps in the extremities can cause severe pain; it is thought that these cramps may be due to calcium abnormalities. Typically the onset of diarrhea is in the middle of the night or the very early hours of the morning, but the reason for this is poorly understood. Dehydration can occur rapidly -- severe dehydration can occur after approximately 4-6 hours of purging. As a result, many patients may present to health centers with severe dehydration in the early morning (within 18 hours after symptoms start). A short duration of profuse watery diarrhea ("rice-water stool") with signs of dehydration, especially severe dehydration, must be assumed to be cholera.

Vomiting is common and can also be a significant source of fluid loss and dehydration, especially if excessive vomiting prevents the patient from taking enough ORS. Patients with severe cholera can purge 500-1000mL of diarrhea in an hour (25). This stool typically looks like rice water and is relatively homogeneously light-colored. Click here to view a picture of typical cholera stool.

Signs of severe dehydration include having a low-volume or absent radial pulse, sunken eyes, extremely reduced skin turgor, and anuria. Patients may be restless and thirsty with moderate dehydration, but when they progress to severe dehydration they become lethargic or may lose consciousness and they may be unable to drink. They might also have Kussmaul breathing due to metabolic acidosis from the loss of basic diarrheal fluid. Kussmaul breathing is a deep rapid respiration typical of acidosis.

Dehydration Criteria:	Observation		
General Condition	Well/ alert	Restless/ irritable	Lethargic/ unconscious
Eyes	Normal	Sunken	Very sunken
Thirst	None	Drinks eagerly and/ or is thirsty	Drinks poorly or unable to drink
Radial pulse	Full volume	Low volume	Weak/absent
Skin pinch	Goes back quickly	Goes back slowly (≥2 seconds)	Goes back very slowly (≥3 seconds)
Dehydration Status	NO Dehydration	SOME Dehydration (if ≥2 criteria above present)	SEVERE Dehydration (if ≥2 criteria above present)
% Dehydration	0-5%	5-<10%	≥10%
Treatment plan	Maintenance Hydration:	Correction of SOME Dehydration:	Correction of SEVERE Dehydration:
	ORS volume to match stool volume. If no danger signs (see below), then NO need for hospitalization	Hydration with ORS. KEEP for observation	Rapid IV hydration. Monitor closely in treatment center

Chapter 2.7 - Conclusion Box

- Tracking the serogroup and biotype of *V. cholerae* is important for epidemiology, but the clinical course for O1 and O139 serogroup infections may be quite similar.
- Because *V. cholerae* has a low Na^+ requirement, the bacterium can survive in brackish or freshwater tanks and ponds where it is likely to be ingested by humans.
- Cholera toxin is the agent responsible for the massive loss of fluid in cholera disease.
- Patients lose K^+ and HCO_3^- in rice-water stool, which presents with metabolic acidosis.

Chapter 2.7 - References

1. Wachsmuth, I. K., P. A. Blake, et al. (1994). *Vibrio cholerae* and cholera: molecular to global perspectives, *ASM Press*

2.Snow J, Frost WH, Richardson BW. Snow on cholera. New York: Commonwealth Fund, 1936

3. Koch R. An address on cholera and its bacillus. *BMJ* 1894; **2**:453-59

4. Ramamurthy T, Garg S, Sharma R, et al. Emergence of novel strain of *Vibrio cholerae* with epidemic potential in southern and eastern India. *Lancet* 1993; **341**: 703-04

5. Faruque SM, Chowdhury N, Kamruzzaman M, et al. Reemergence of epidemic *Vibrio cholerae* 0139, Bangladesh. *Emerg Infect Dis* 2003; **9**: 1116-22

6. World Health Organization, Guidelines for Cholera Control. 1993 (reprinted 2000), Geneva, Switzerland WHO. p. 30

7. WHO Global task force on cholera control, Acute diarrhoeal diseases in complex emergencies: critical steps, decision-making for preparedness and response. 2004. Geneva, Switzerland. World Health Organization

8. World Health Organization, Cholera Outbreak: assessing the outbreak response and improving preparedness, Geneva, Switzerland WHO. p. 27

9. Wachsmuth, I. K., P. A. Blake, et al. (1994). *Vibrio cholerae* and cholera: molecular to global perspectives, ASM Press

10. Faruque SM, Ahmed KM, Siddique AK, Zaman K, Alim AR, Albert MJ, Molecular analysis of toxigenic *Vibrio cholerae* O139 Bengal strains isolated in Bangladesh between 1993 and 1996: evidence for emergence of a new clone of the Bengal vibrios. Journal *of Clinical Microbiology*, 1997. 35(9): 2299-306

11. Merrell, D. S. and A. Camilli (1999). "The cadA gene of Vibrio cholerae is induced during infection and plays a role in acid tolerance." *Mol Microbiol* **34**(4): 836-49

12. Merrell, D. S. and A. Camilli (2002). "Acid tolerance of gastrointestinal pathogens." *Curr Opin Microbiol* **5**(1): 51-5

13. Rhine, J. A. and R. K. Taylor (1994). "TcpA pilin sequences and colonization requirements for O1 and O139 vibrio cholerae." *Mol Microbiol* **13**(6): 1013-20

14. Tacket, C. O., R. K. Taylor, et al. (1998). "Investigation of the roles of toxin-coregulated pili and mannose-sensitive hemagglutinin pili in the pathogenesis of Vibrio cholerae O139 infection." *Infect Immun* **66**(2): 692-5

15. Nielsen, A. T., N. A. Dolganov, et al. (2006). "RpoS controls the Vibrio cholerae mucosal escape response." *PLoS Pathog* **2**(10): e109

16. Merrell, D. S., S. M. Butler, et al. (2002). "Host-induced epidemic spread of the cholera bacterium." *Nature* **417**(6889): 642-5

17. Faruque, S. M., M. J. Islam, et al. (2005). "Self-limiting nature of seasonal cholera epidemics: Role of host-mediated amplification of phage." *Proc Natl Acad Sci* **102**(17): 6119-24

18. Faruque, S. M., I. B. Naser, et al. (2005). "Seasonal epidemics of cholera inversely correlate with the prevalence of environmental cholera phages." *Proc Natl Acad Sci* **102**(5): 1702-7

19. Prinz H, Sribhibhadh R, Gangarosa EJ, Benyajati C, Kundel D, Halstead S. Biopsy of small bowel of Thai people with special reference to recovery from Asiatic cholera and to an intestinal malabsorption syndrome. *American Journal of Clinical Pathology* 1962, 38:43-51

20. Lonnroth I, Holmgren J. Subunit structure of cholera toxin. *Journal of General Microbiology* 1973, 76:417-27

21. Field M, Fromm D, Al Awqati Q, Greenough WB III. Effect of cholera enterotoxin on ion transport across isolated ileal mucosa. *J Clin Invest* 1972, 51:796-804

22. Speelman P, Butler T, Kabir I, Ali A, Banwell J. Colonic dysfunction during cholera infection. *Gastroenterology* 1986, 91:1164-70

23. First Principles of Gastroenterology by A.B.R Thomson and E. A. Shaffer; AstraZeneca Canada Inc. 2000

24. Molla AM. Rahman M. Sarker SA. Sack DA. Molla A. Stool electrolyte content and purging rates in diarrhea caused by rotavirus, enterotoxigenic E. coli, and V. cholerae in children. *Journal of Pediatrics. 98(5):835-8, 1981 May.*

25. Sack DA, Sack RB, Nair GB, Siddique AK. Cholera, *The Lancet* 2004, 363: 223-3.

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Chapter 3 - introduction to Shigellosis

Chapter 3.1 - Introduction to Shigellosis

This section will serve as a general introduction to shigellosis around the world. *Shigella* spp. are among the causes of acute bloody diarrhea.

In the small sections to follow, the following topics will be discussed:

- History of shigellosis epidemics
- Epidemiology of shigellosis
- Introduction to *Shigella* spp.
- Pathophysiology of shigellosis
- Clinical presentation of shigellosis
- Chapter conclusion
- Quiz questions

For the principles of management and complications of shigellosis please see the “clinical management of shigellosis” chapter.

Shigellosis is a form of invasive diarrhea caused by bacteria in the genus *Shigella*. Shigellosis may be endemic (especially in developing countries) and may cause epidemics. There are four pathogenic species of *Shigella*, and each of the four species (except *S. sonnei*) is divided into multiple serotypes. All four species cause shigellosis, but the most severe form of shigellosis is caused by *Shigella dysenteriae* serotype 1 (SD1 or Shiga bacillus) which can occur in large epidemics and cause significant morbidity and mortality. *Shigella* spp. are frightening to public health officials because of the low infectious dose (as few as 10 bacteria). This low infectious dose creates a tremendous potential for outbreaks when sanitation, hygiene and the water supply are compromised. In addition, *Shigella* spp. can rapidly acquire antimicrobial resistance, which complicates case management and requires knowledge of current sensitivity patterns.

Chapter 3.2 - History and taxonomy of Shigellosis Epidemics

S. dysenteriae type 1 was the first of the *Shigella* species isolated in 1896 by Kiyoshi Shiga, a Japanese scientist. At the time, dysentery outbreaks were occurring periodically in Japan, affecting tens of thousands of people with a high mortality rate. For example, the 1897 epidemic affected >91,000 people and had a mortality rate of >20%. After Shiga's discovery from a stool isolate of one of 36 patients he studied at the Institute of Infectious Diseases, other investigators reported other similar organisms. The genus was called *Shigella* after Shiga and his bacillus was termed *S. dysenteriae*. The following 3 species were named *Shigella flexneri, Shigella boydii*, and *Shigella sonnei* after the discoverers Flexner, Boyd and Sonne, respectively. (1).

Over the past forty years, shigellosis pandemics have spread worldwide. SD1 outbreaks tend to occur at approximately decade-long intervals (2). Large-scale epidemics and pandemics have occurred in Central America in 1969-1971 and in South Asia in 1984-1985. The last SD1 epidemic in Bangladesh was in the mid 1990's, but as of 2007, the expected 10-year cycle has not repeated in Asia. Outbreaks have continued to occur in Africa, but because there is no ongoing routine surveillance in Africa, the cyclic pattern is less apparent on this continent. In Asia, each new epidemic in recent times has occurred with strains with increasing antibiotic resistance. A few isolates of ciprofloxacin-resistant SD1 were found in India and Bangladesh and these isolates were predicted to be the possible start of a new epidemic for this decade, but so far, the epidemic has not occurred.

In the past few years there have not been very many reported outbreaks of shigellosis, however there is no reason to believe that outbreaks won't occur again since many places still have the predisposing conditions that led to shigellosis outbreaks in the past. Since 2000, the WHO Epidemic and Pandemic Alert and Response (EPR) department reported outbreaks in Sierra Leone, Lesotho, Liberia, Central African Republic and Sudan (3).

Chapter 3.3 - Epidemiology of Shigellosis

Shigellosis causes an estimated 164.7 million cases of diarrhea every year (4). Despite the agreement on the overall morbidity burden of shigellosis, the mortality burden, which likely exceeds 1 million annually, has dropped considerably in Asia. However, there is little data from Africa. Just like the overall picture of infectious diarrhea, 163.2 million of these cases are in developing countries, of which most have endemic *Shigella* spp. Children under five suffer the majority (69%) of cases and the majority (61%) of fatal outcomes (5).

Shigella spp. are also present endemically in many developing countries, especially in Africa and Asia. S. dysenteriae type 1 is seen most often in South Asia and sub-Saharan Africa. In developing countries, the most common species is *S. flexneri*, followed by *S. sonnei* (6). In developed countries the most common species is *S. sonnei* (median 77%) followed by S. flexneri (median 16%) (7). In endemic countries, the incidence of shigellosis peaks in the first 5 years of life, suggesting that immunity is conferred later in life (8).

Emergency settings are especially at risk for shigellosis outbreaks. Outbreaks of *S. dysenteriae* type 1 typically occur in areas which are overcrowded, impoverished, have inadequate hygiene, and inadequate safe water supplies; all of which apply to refugee camps (9).

However, outbreaks of shigellosis have occurred in many places around the world. Outbreaks are not limited to emergency settings, albeit, most cases in non-emergency settings are non-SD1 strains of *Shigella*. In addition to the usual spread of shigellosis through food, water, and daily contact, there have been some reports of it spreading through men who have sex with men (10, 11, 12)

Chapter 3.4 - Introduction to *Shigella* spp.

There are four species in the genus Shigella:

Species	Serogroup	Serotypes	Notes
S. dysenteriae	A	1-15	most severe disease
S. flexneri	B	1-6 (with 15 subtypes)	main cause of endemic shigellosis
S. boydii	C	1-18	mild disease with bloody or watery stools
S. sonnei	D	1	mild disease with bloody or watery stools

Comment: On average - S. boydii and S. sonnei cause less severe illness, but they can also cause equally severe disease as S. flexneri

S. dysenteriae type 1 is also called SD1 or Shiga bacillus. It is important to be familiar with this Shigella sp. as it causes the most severe disease of all the *Shigella* spp. because it causes a longer duration of illness, and is frequently the most fatal species. In addition to these factors, there are other important ways that SD1 differs from the other *Shigella* spp.:

1. It produces a cytotoxin called Shiga toxin
2. It has a higher frequency of antimicrobial resistance
3. It causes large epidemics which frequently have high attack rates and high case fatality rates (CFR)

The Shiga toxin can cause life-threatening complications such as hemolytic uremic syndrome (HUS), which is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and renal insufficiency.

Although SD1 is the most virulent of the species/ serotypes, *S flexneri* actually presents a greater public health burden because it is endemic and causes a majority of the dysentery in developing countries.

The *Shigella* spp. are very sensitive to environmental conditions. Drying and exposure to direct sunlight causes the bacterium to die rapidly. However, *Shigella* spp. are easily transmitted by person-to-person contact, contaminated food and water, or flies (13). The ease of transmission is aided by its low infectious dose; as few as 10 ingested organisms can cause disease (14).

Chapter 3.5 - Pathophysiology of Shigellosis

As mentioned before, shigellosis causes invasive diarrhea. More specifically, the bacteria invade the epithelium of the colon. This invasion causes destruction in regions that may become micro-ulcers and evoke an inflammatory response; the type of lesion associated with shigellosis may be more diffuse than the localized lesions associated with amebiasis. An anoscopy may aid in diagnosis. As a result of the shigellosis ulcers, blood from destruction and ulceration and inflammatory cells (specifically polymorphonuclear leukocytes or PMNs) can be found in the stool of a shigellosis patient. In fact, the stool may appear to have blood and pus. Typically, shigellosis stool will contain 10^6 - 10^8 bacteria per gram of stool, and the infectious dose for shigellosis can be as low as 10 organisms! (15)

Shigella spp. invade and colonize the intestinal epithelium through a complex mechanism involving possible enterotoxic and/or cytotoxic mechanisms and followed by cytokine-mediated inflammation of the colon and necrosis of the epithelium. (16)

Toxins:

Many *Shigella* spp. produce toxins, but only *S. dysenteriae* type 1 has a neurotoxin, called Shiga toxin. Shiga toxin is not essential for virulence but contributes to the severity of the disease. Shiga toxin can cause HUS and leukomoid reactions in *S. dysenteriae* type 1 infections (17).

Chapter 3.6 - Clinical Presentation of Shigellosis

The typical presentation of a shigellosis patient is diarrhea with frequent liquid or loose stools with blood and sometimes mucous. As a general rule, shigellosis produces small volume diarrheal stools. The case definition of shigellosis for surveillance and reporting during an outbreak is "diarrhea with visible blood in the stool" (18). However, it is possible to have only watery diarrhea, especially at the onset of the disease. In addition to the diarrhea, it is common to have abdominal cramps, tenesmus (painful straining which is unproductive) and the non-specific signs of fever and anorexia. The pain is typically localized in the lower quadrant of the abdomen. The incubation period is generally 1-4 days, but it can be up to 8 days in the case of S. dysenteriae type 1 (19).

Severe dehydration is uncommon and most patients recover within 5-7 days without complication. However, complications do exist, including metabolic and electrolyte abnormalities (especially hyponatremia), sepsis, convulsions, rectal prolapse, toxic megacolon, intestinal perforation, and hemolytic uremic syndrome (HUS) (20). These complications will be discussed further in Chapter 5 – Clinical Management of Shigellosis. Shigellosis can become persistent in a few patients with dysentery symptoms lasting weeks, and occasionally months, especially in malnourished children.

The following groups have an increased risk of death and complications (21):

- Infants
- Adults older than 50 years
- Non-breastfed children
- Children recovering from measles
- Malnourished patients
- Any patient who presents with dehydration, unconsciousness, hypo- or hyper- thermia, or a history of convulsions

Shigella stool in a transparent bucket

Chapter 3.7 - Conclusion Box

- For the clinical diagnosis of shigellosis, visible blood in the stool must be present.
- Blood in the stool is caused by the invasion of the pathogen into the epithelium of the colon with subsequent micro-ulceration.
- Hygiene is crucial to stop shigellosis outbreaks because the infectious dose is as low as ten bacteria.
- *S. dysenteriae* type 1 causes the most severe cases of shigellosis, but *S. dysenteriae* is not the most common species.

Chapter 3.8 - References

1. Niyogi SK, Shigellosis, The Journal of Microbiology. 2005, 43(2):133-143

2. World Health Organization, Weekly Epidemiological Record. 2005, 80(11): 94-99

3. World Health Organization, Epidemic and Pandemic Alert and Response. www.who.int/csr/don/archive/disease/shigellosis/en/

4. Kotloff KL, Winickoff JP, Ivanoff B, Clemens JD, Swerdlow DL, Sansonetti PJ, Adak GK, Levine MM. Global Burden of Shigella infections: implications for vaccine development and implementation of control strategies. Bulletin of the World Health Organization 1999, 651

5. ibid.

6. Kotloff KL, Winickoff JP, Ivanoff B, Clemens JD, Swerdlow DL, Sansonetti PJ, Adak GK, Levine MM. Global Burden of Shigella infections: implications for vaccine development and implementation of control strategies. Bulletin of the World Health Organization 1999, 651

7. ibid.

8. Taylor DN, Echeverria P, Pal T, Sethabutr O, Saiborisuth S, Sricharmorn S, Rowe B, Cross J, The role of Shigella spp., enteroinvasive Escherichia coli, and other enteropathogens as causes of childhood dysentery in Thailand. Journal of Infectious Diseases. 1986. 153(6):1132-8

9. ibid.

10. Marcus U, Zucs P, Bremer V, Hamouda O, Prager R, Tschaepe H, Futh U, Kramer M, Shigellosis – a re-emerging sexually transmitted infection: outbreak in men having sex with men in Berlin. International Journal of STD and AIDS. 2004. 15(8):533-7

11. O'Sullivan B, Delpech V, Pontivivo G, Karagiannis T, Marriott D, Harkness J, McAnulty JM, Shigellosis linked to sex venues, Australia. Emerging Infectious Diseases 2002. 8(8):862-4

12. Anonymous, From the Centers for Disease Control and Prevention. Shigella sonnei outbreak among men who have sex with men—San Francisco, California, 2001-2002. JAMA 2002. 287(1):37-8

13. Levine, OS; and Levine MM. 1991. House flies (Musca domestica) as mechanical vectors of shigellosis. Rev. Infect. Dis. 13, pp. 688-696

14. Du Pont, HL; Levine, MM; Hornick, RB; and Formal, SB. 1989. Inoculum size in shigellosis and implications for expected mode of transmission. J. Infect. Dis. 159, pp. 1126-1128

15. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to Shigella dysenteriae 1. World Health Organization 2005 Geneva.

16. Sansonetti PJ. Egile C. Molecular bases of epithelial cell invasion by Shigella flexneri. Antonie van Leeuwenhoek. 74(4):191-7, 1998 Nov.

17. Niyogi SK, Shigellosis, The Journal of Microbiology 2005, 43(2):133-143

18. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to Shigella dysenteriae 1. World Health Organization 2005 Geneva.

19. Levine MM, et al. Pathogenesis of Shigella dysenteriae 1 (Shiga) dysentery. J. Infect. Dis 1973. 127:261-270

20. Bennish ML. Potentially lethal complications of shigellosis. Rev Infect Dis 1991. 13 (Suppl. 4): S319-324

21. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to Shigella dysenteriae 1. World Health Organization 2005 Geneva.

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Chapter 4 - Clinical Management of Cholera

Chapter 4.1 - Clinical Management of Cholera Introduction

This section will serve as an overview of the clinical management of cholera. The 'Clinical Management of Cholera' section is geared toward physicians and other health care personnel who have formal training in clinical medicine. Although the chapter stresses cholera, the same treatment principles apply with severe watery diarrhea due to other causes, such as enterotoxigenic E. coli or rarely other bacteria.

In the small sections to follow, the following topics will be discussed:

- Assessment of a patient with watery diarrhea
- Case management of cholera
- Critical aspects of the pathophysiology of cholera which are important to understanding the clinical management, especially related to fluid and electrolyte balance
- Avoiding clinical mistakes
- Common complications of cholera

Chapter 4.2 - Cholera Management Overview

The most important actions for managing patients with cholera and other severe dehydrating diarrheal diseases is rapid and appropriate rehydration to make up for the fluid losses that have occurred prior to coming for treatment, and maintenance hydration to compensate for the ongoing fluid losses. For most patients, the use of oral rehydration solution (ORS) is a simple and effective way to prevent dehydration and to treat some dehydration. It can be used at home or in the clinic. Though ORS is effective for most patients, an estimated 20 to 50% of cholera patients during epidemics present with severe dehydration (shock) because of the severe rapid purging. For these patients, rehydration with IV fluids is required.

When a patient comes for treatment with complaints of severe watery diarrhea, the following steps are key to the successful management of the case. Additional practical worksheets for the management of cholera will be provided in the virtual hospital section and separated by job type.

- Assessment of dehydration status and classifying the patient as having:
  - No Dehydration
  - Some Dehydration
  - Severe Dehydration
- Rehydration
  - ORS for patients with no dehydration or some dehydration
  - Intravenous fluids with polyelectrolyte solution for patients with severe dehydration
- Reassessment of fluid balance periodically and administer fluids sufficient to replace ongoing fluid losses
- Antibiotic treatment for patients with some or severe dehydration clinically suspected of having cholera.
- Avoiding and/or managing complications
- Zinc daily for 10 days for children under 5 years of age
- Determining when to discharge the patient
- Avoiding ineffective treatment
- Considering other conditions that may be confused with cholera

Assessment of dehydration:

This should be done initially at the triage station (e.g. when the patient first arrives at the treatment center) to determine the initial treatment plan, and then providers should routinely assess hydration status if the patient stays in the treatment center. The assessment should be documented on the patient's chart, and the following table is a useful tool to assess the severity of dehydration. This table (the Dhaka Method) differs from the WHO documents only in that it adds the palpation of the radial pulse as one of the criteria in assessing the severity of dehydration.

Assessment and plan for dehydration

Dehydration Criteria:	**Observation:**		
General Condition	Well/ alert	Restless/ irritable	Lethargic/ unconscious
Eyes	Normal	Sunken	Very sunken
Thirst	None	Drinks eagerly and/ or is thirsty	Drinks poorly or unable to drink
Radial pulse	Full volume	Low volume	Weak/absent
Skin pinch	Goes back quickly	Goes back slowly (≥2 seconds)	Goes back very slowly (≥3 seconds)
Dehydration Status	**NO** Dehydration	**SOME** Dehydration (if ≥2 criteria above present)	**SEVERE** Dehydration (if ≥2 criteria above present)
% Dehydration	0-5%	5-<10%	≥10%
Treatment plan	**Maintenance** Hydration: ORS volume to match stool volume. If no danger signs (see below), then NO need for hospitalization	Correction of **SOME** Dehydration: Hydration with ORS. KEEP for observation	Correction of **SEVERE** Dehydration: Rapid IV hydration. Monitor closely in treatment center

Note that patients may have lost clinically significant volumes of fluid but they do not show clinical signs of dehydration until they have lost fluids equivalent to ≥5% of their body weight.

Rehydration:
For patients with no evidence of dehydration or some dehydration, rehydration treatment using ORS is generally sufficient. Either glucose based or starch (e.g. rice) based ORS is appropriate, though for cholera, rice ORS is best. For a more in-depth discussion of the different types of ORS, see the ORS section later in this chapter. ORS is the mainstay of diarrheal treatment, and it is easier to discuss when IV solution should be used rather than ORS.

Intravenous, rather than ORS rehydration, should be used in the following circumstances:

- With severe dehydration
- With severe vomiting
- With ileus
- In cases of glucose malabsorption (very rare)
- If stool output is more than 10ml/kg/hour and the patient cannot drink sufficient fluids to match the purging
- With an unconscious patient or a patient that is not able to drink

No dehydration:
Patients with no dehydration can be managed as outpatients. In the clinic or treatment center, patients will be shown how to make ORS and, depending on their situation, they should stay at the treatment centre for an hour or two so they can drink an amount of ORS in a volume equivalent to about 5% of their body weight. (Example: a 5 Kg child should drink about 250 ml of ORS.) During this time at the clinic, family members are taught how to make and administer ORS. It is also a time of observation to be sure that the clinical situation is not deteriorating. The patient can then be discharged with additional ORS packets to continue to use at home with instructions to continue to drink ORS in volumes to approximate the ongoing fluid losses. The following table provides some guidance as to the volumes of ORS to administer during the maintenance phase of treatment.

Maintenance Rehydration with ORS*

Age	Approximate ORS amount following each stool; By milliliters (ml)	Approximate ORS amount following each stool; By household measures
Children <2 years	50-100ml	10-20 teaspoons
2-10 years	100-200ml	½ - 1 glass
>10 years	As much as is tolerated	Minimum 1 glass

* In children: if the caretaker knows the weight of the patient, advise the patient caretaker to administer one teaspoon per kilogram of ORS for each loose stool. ORS should be given in small amounts (small spoons of 5ml for children <2 years and sips from a cup for older patients) frequently (every 1-2 minutes). If the patient vomits, wait 10 min. and continue to give ORS but more slowly.

Some dehydration:
For patients with some dehydration, calculate the amount of fluid needed to replace the fluid volume that has been lost, assuming that the patient has lost about 7.5% (75 ml/Kg) of his/her body weight. (Example: a patient weighing 10kg will require 750 ml for rehydration.) Ideally the patient should be weighed, but if a scale is not available, the weight can be estimated based on the patient's age. This volume of ORS should be given within the first four hours. The rate of fluid for rehydration is slower for severely malnourished children (please see Chapter 6.3).

ORS general guidelines for rehydration of patients with "SOME" dehydration with ORS

Age	Weight (kg)	Amount of ORS in first FOUR* or SIX* hours (ml)
<4 months	<5	200-400
4-11 months	5-7.9	400-600
1-2 years	8-10.9	600-800
2-4 years	11-15.9	800-1200
5-14 years	16-29.9	1200-2200
>14 years	≥30	2200-4000
	60	4200
	70	About 5 liters

* The correction fluids of 75ml/ kg should be given within the first FOUR HOURS FOR ADULTS/ CHILDREN and within the first SIX HOURS FOR INFANTS (<1 yr), with regular follow-up. Give fluids more slowly (half the rate) for severely malnourished children/ infants.

The caregiver should give ORS in small amounts frequently, as this will reduce the common complaint of vomiting on taking ORS caused by giving too much in one serving. Older children and adults should be given as much additional fluid (e.g. water) as they want. Infants should continue breastfeeding in addition to consuming ORS. Infants who are not breastfed should receive their normal feeding of nutritional foods or milk formula and fluids in addition to the required amount of ORS.

In addition to the volume of ORS needed to rehydrate, additional ORS fluids are needed to replace the ongoing losses from the continued diarrhea; therefore continue to give maintenance ORS as suggested in the previous section.

Severe Dehydration:
Patients with severe dehydration are estimated to have lost ≥10% of their body weight and are in danger of death from hypovolemic shock. They require immediate and rapid replacement of fluids by the intravenous route. Immediate rehydration can decrease the case fatality rate in cholera from over 50% in such patients to <1%. (If intravenous treatment is not available and the patient cannot drink, ORS can be given via nasogastric tube; hopefully, this situation will occur extremely rarely.)

The intravenous solution to use for these cases is an isotonic polyelectrolyte solution containing the appropriate concentrations of sodium chloride, potassium chloride, and a base to correct the acidosis. The ICDDR,B in Dhaka, Bangladesh has developed an intravenous solution called Cholera Saline, which it uses routinely. This rehydration fluid is formulated specifically to replace the electrolytes lost during severe diarrhea. However, because Cholera Saline is not available in most areas, Lactated Ringers is commonly used as it is widely available and is close to being ideal. In addition to the saline, which is needed to quickly replace the volume deficit, a base and potassium are important components of the fluid to correct acidosis and potassium depletion. Cholera Saline contains acetate as the base while Ringers contains lactate as the base. The concentration of potassium in Cholera Saline is 13 mEq per liter while it is lower, only 4 mEq per liter in Ringers. Dextrose and water (without electrolytes) is not appropriate since it does not contain the needed salts. In an emergency when Ringers Lactate is not available, normal saline can be given; however, if it is used, ORS should be added quickly to the treatment to compensate for the lack of base and potassium in the saline.

The volumes needed to rehydrate these patients are 10% of the patient's weight. (Example: A 50 kg patient will require 5 liters of intravenous fluid.) If the patient has no pulse or a very feeble pulse, the intravenous fluid should be given as rapidly as possible to restore the pulse. Sometimes two IV lines are needed, using large bore needles. Once the pulse is re-established, the remaining volume can be given such that the total rehydration requirements are given within the first three hours. If the patient is less than one year old, this time is extended to 6 hours.

Correction of SEVERE dehydration with IV hydration*

Age	Amount of time to give first 30ml/kg	Amount of time to give remaining 70ml/kg
≤ 1 year	1 hour	5 hours
> 1 year	½ hour	2 ½ hours

*Severe dehydration requires rapid replacement of a total of 100ml/ kg of fluids by IV.

Such patients should be reassessed continuously - at least every 1-2 hours. The rate of fluids can be increased if he/she is not improving. In a large patient setting this can best be accomplished by having strict times at which to round on every patient sequentially.

ORS should be given as soon as the patient can drink (within 2-3 hours). Most of these severely dehydrated patients will also be vomiting which, of course, inhibits drinking ORS. Generally within a few hours, with correction of the acidosis, the vomiting will stop and ORS can be given to replace the ongoing fluid losses. This is especially important if the IV fluid is non-ideal as ORS will replace the base and potassium lost in cholera diarrheal fluids.

ORS is especially formulated for intestinal absorption during a diarrheal episode. The sodium and other electrolytes in ORS are only absorbed because of the carbohydrate contained in the ORS. For this reason, IV rehydration solutions should never be given orally.

Severely dehydrated patients must be closely monitored, especially during the first 24 hours. Sometimes, after they have been rehydrated with intravenous fluids and then switched to ORS, their purging is so great that the volume of ORS for maintenance is not sufficient to maintain hydration. They then risk becoming severely dehydrated again and intravenous fluids must be reinstituted, following which they can resume ORS.

Cholera cot:
Reassessment of patients is most efficiently done if patients are placed on a "cholera cot." These are cots with a whole in the middle and a bucket underneath. Patients are able to lie on the cots and pass their liquid stool into the bucket without getting up walk to the toilet. For patients in shock, this has the obvious advantage of comfort. For the health care providers, the amount of liquid stool being passed can easily be assessed so that a similar amount can be given to the patient. Generally the cot is covered with a plastic sheet with a funnel shaped sleeve going into the bucket. While not essential, the bucket is best made of translucent plastic with calibration marks so that the volume of stool can be easily appreciated. A cholera treatment centre should have different sized cots for both children and adults.

Regular reassessment of patients:
Patients should be examined regularly by monitoring hydration status, vital signs and general well being. Most important in this reassessment are the general appearance of the patient and the volume of stools and vomit. During the general physical exam, the health provider should look for co-morbid conditions that may complicate the clinical course. Taking the pulse, including the pulse strength, provides important information on state of hydration since a weakened pulse is a sign of continued dehydration. Cholera does not cause a fever; thus, if a patient has an elevated temperature, consider a co-morbid condition like malaria or pneumonia. Kussmaul breathing is commonly seen in cholera due to metabolic acidosis, however, this should not continue after the rehydration has been completed. If there is continued abnormal breathing, consider other conditions, such as pneumonia. Blood pressure, if taken, can be an important indicator of shock. Rarely, when patients have been in shock for a prolonged time without sufficient rehydration, acute renal failure can occur; thus, it is important to note that the patient is producing urine.

Antibiotics:
Appropriate antibiotics should be given to patients suspected of having cholera with some or severe dehydration. Patients with no detectable dehydration need not be treated with antibiotics. The antibiotics are not as important as the rehydration therapy since patients will recover even without antibiotics if they are kept hydrated; however, effective antibiotics reduce the duration and severity of the illness. This can be important for the patient to return to health more quickly, and it is important for a busy hospital to reduce costs and requirements for clinical supplies and manpower. For example, during epidemic seasons, 700 patients may seek treatment at the ICDDR,B hospital. The use of antibiotics can shorten the hospitalization time by 1 or 2 days, and this drastically reduces the costs and logistical requirements for treating such a large number of patients. The benefits of antibiotics in treatment centers in refugee camps may be even greater since the resources in this setting may be even more limited. Detailed regimens of antibiotics are provided in the virtual hospital.

Unfortunately, the antibiotic resistance pattern is varied by geographic region and it changes over time; therefore, it is important to monitor for antimicrobial sensitivity, using the resistance patterns of the most recent information to guide treatment. In most parts of the world doxycycline is the drug of choice for adults and erythromycin is the drug of choice for children and pregnant women (1). Other antibiotics that can be used in patients with cholera resistant to these first line drugs include ciprofloxacin and azithromycin.

Recommended antibiotics used for CHOLERA. Appropriate antibiotics should be given to patients suspected of having cholera with SOME or SEVERE dehydration. Patients with no detectable dehydration need not be treated with antibiotics (this conserves resources). ALWAYS check antimicrobial sensitivity patterns in your area before dispensing drugs for cholera:

Antibiotic*	Dose in children**	Dose in adults**
Doxycycline	Not drug of choice	300 mg single dose (seek alternative for pregnant women)
Erythromycin	12.5 mg/ kg 4 times a day for 3 days	Not drug of choice (exception is pregnant women at 250 mg 4 times a day for 3 days)
Ciprofloxacin	15 mg/ kg 2 times a day for 3 days	500 mg 2 times a day for 3 days***
Azithromycin	20 mg/ kg single dose with max of 1 g	1 g single dose
Trimethoprim (TMP)-Sulfamethoxazole (SMX)	TMP 5 mg/ kg and SMX 25 mg/ kg 2 times a day for 3 days	TMP 160 mg and SMX 800 mg 2 times a day for 3 days

* Antibiotic selection must depend on the sensitivity pattern determined for the specific cholera outbreak. Do not use anti-diarrheal drugs as they have not been shown to benefit patients.
** Refer to references (2-5) for more information. All doses are given in the oral formulation.
*** Dose recommendation reflects changes in ciprofloxacin resistance patterns as of 2007 in Bangladesh.

Zinc:
All children aged 5 years and younger should be given zinc treatment in addition to fluids and antibiotics as needed. Zinc treatment has been shown to decrease the severity and duration of an acute diarrheal episode (7) and to decrease the severity and incidence of subsequent diarrheal episodes for 2-3 months (8) in children under 5. The recommended treatment regimen is 20mg once daily for 10-14 days for children 6 months to 5 years of age (10 mg once daily for 10-14 days for children 0-6 months old). At the ICDDR,B zinc sulfate is given in a readily dispersible tablet for 10 days. The specific type of zinc salt (zinc acetate, zinc gluconate, and zinc sulfate) does not appear to have an impact on results (9), though most use zinc sulfate.

Zinc supplementation		
Age	**Dose of zinc**	**Duration**
0-6 months	10mg once a day	10-14 days
6 months- 5 years	20mg once a day	10-14 days

***** All children <5 years old with diarrhea should receive zinc.

Feeding:
Patients should be fed as soon as they can eat (within a few hours in the case of severe dehydration). Breastfed children should continue breastfeeding throughout treatment. In the past, providers were told to withhold feeding for a few days, but there is no reason to do this. There should be no restriction on the diet.

Discharge criteria:
The ICDDR, B recommends discharging as soon as possible to reduce patient load and nosocomial infection. As a general rule, a patient can be discharged when his/her purging has decreased to a level at which he/she can keep up with fluid losses by drinking ORS. In other words, the patient must have no dehydration, be able to take ORS adequately, and have a decreased level of purging so that fluids losses can be easily corrected with home fluids and ORS in the home. If the patient was on intravenous fluids, the patient should be observed on ORS for a time to insure that he/she can maintain hydration status by drinking ORS only.

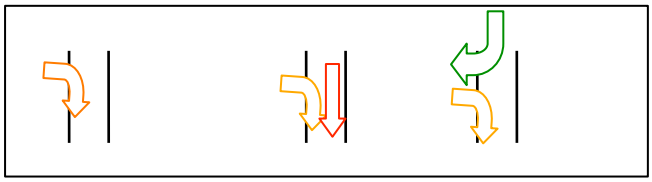
Ineffective treatments:
- Never use anti-diarrheal drugs, they have not been shown to benefit the patient.
- Never use sweetened drinks in place of ORS (e.g. sweetened fruit drinks or soft drinks) as these can cause an osmotic diarrhea and hypernatremia.
- Never use Dextrose in water as the IV fluid for patients with diarrhea and severe dehydration. It does not contain saline, base or potassium and therefore cannot correct the hypovolemia or the electrolyte imbalance.

More about ORS:
ORS is a specially formulated mixture of water with salts and carbohydrate. Though it is a simple mixture, it is actually based on a scientific understanding of the rather complex process of the absorption of salts and water from the intestine. Previously, it was assumed that since patients were loosing so much fluid in the stool, the intestine was not capable of absorbing oral solutions. However, during the 1960's, it was learned that an important mechanism for absorption of sodium is its co-transport with glucose. If solutions with sodium and glucose are given to patients using a proper concentration, sodium can be absorbed even in the face of diarrhea. If the salt solution is given without glucose, it will pass through the intestine, and it will increase the volume of diarrhea. Thus, it is critical that the salt and the glucose be given using the correct concentrations.

In addition to the glucose-mediated absorption, a second mechanism affecting the absorption of ORS is its osmolarity. Solutions with concentrations of salt or glucose that are too high (osmolarity > 300 mMol) produce an "osmotic penalty" in which fluid is drawn into the gut, making the diarrhea worse. If the ORS has a lower osmolarity, more fluid will be absorbed; thus, ORS is now prepared in a way such that it has a low osmolarity (<250). The standard ORS as recommended by WHO now has lower sodium and lower glucose concentrations than the previous formula to take advantage of the lower osmolarity.

Diagram of the absorption of ORS

The first figure shows the intestine during the state of watery diarrhea during which fluid is being secreted from the intestinal mucosal (yellow arrow) and excreted in the stool. If the patient drinks saline (red arrow) in an attempt to replace the fluids being lost, the saline is added to the fluid already being secreted and the diarrhea worsens as illustrated in the middle figure. If (as illustrated in the right hand figure) the patient drinks a salt solution with glucose, the salt and water are absorbed and the patient is rehydrated even though the diarrhea continues.



Note: the absorption (green arrow) is greater than the secretion (yellow arrow) in this 3rd figure, indicating a net absorption, even though the diarrhea continues.

The search for an improved ORS that has a higher glucose content (to increase the sodium carrying capacity), while still having a low osmolarity, led to the development of starch based solutions, e.g. rice ORS. The advantage of rice ORS is its higher content of glucose but in a polymeric form that does not add to its osmolarity. When rice ORS is used in cholera patients, its improved efficiency reduces purging rates by about 30%. Because of this benefit as well as the personal preference for rice in Bangladesh, rice ORS is routinely used at the ICDDR,B. At the Centre, the rice ORS is prepared freshly each day, but for centers where this is not possible, it is also available in a packaged form, which can be prepared just like the glucose ORS. However, some packets of rice ORS require cooking, so follow the instructions on the package.

Oral solutions can also be made from ingredients found in the home. The simplest is a sugar salt solution (half teaspoon of salt and 3 Tablespoons of sugar in a liter of water – don't get the measurements of the two mixed up: it may be dangerous!!). Others prepare other home-based fluids or soups (e.g. chicken rice soup) that can provide salts and carbohydrates. Although these home based fluids do not contain potassium or base, they are very useful for diarrheal illnesses that are not severe.

In preparing an oral solution, one should avoid solutions that have excessive amounts of sugars (e.g. soft drinks) or have excessive salt. Water by itself is not appropriate as a rehydration drink for diarrhea because it does not contain sodium or glucose.

Meat-Wash Stool:

Occasionally you will come across a patient with striking large volume, watery stool with a red tinge, often termed "meat-wash" stool. This is a clinical type of diarrhea that is treated exactly the same way as cholera. The bacterium that causes this diarrheal manifestation is generally *Vibrio parahaemolyticus.* Again, although striking, this type of diarrhea is not any more worrisome than the typical cholera disease and should be treated in the same manner.

Chapter 4.3 - Complications of Cholera

The major complications of cholera can be divided into immediate complications, such as dehydration, and later complications, such as acidosis and electrolyte imbalances, that result from diarrheal losses and improper correction of these losses.

Other Co-morbidities:
Complications can also be due to co-morbidities, some of which are also discussed in chapter 6.2 entitled "Co-morbidities". These cases should be treated for their co-morbid illness as best as possible when they are dehydrated, and then transferred to the general ward or hospital to be treated per the protocol for that condition once their diarrhea is stabilized. This is especially true if the co-morbid disease is not life threatening, because dehydration can be life threatening.

Hyponatremia:
Some electrolyte abnormalities, such as hyponatremia, can occur from improper use of rehydration fluids. Diarrhea and vomiting cause gastrointestinal loss of sodium (termed extra-renal). Without adequate replacement, hyponatremia from diarrhea and vomiting is generally hypovolemic hyponatremia. In the case of extreme excess free water intake (about 10L/day for an adult), there can be euvolemic hyponatremia. The definition of hyponatremia is <130mEq/L and severe hyponatremia is <120mEq/L (10).

Signs/Symptoms: Mild: generalized **weakness**, muscle **cramps**, **nausea** and **vomiting**, **anorexia**, **lethargy**; Severe: **delirium**, **coma**, **depressed deep tendon reflexes**, Cheyne-Stokes respiration, pseudobulbar palsy, seizures, cranial nerve palsies (11)
Treatment: IV hypertonic 3% saline 12ml/kg over 4 hours and, only after dehydration has been corrected, free water restriction (to 1L/day) until it reaches a normal level.

Pseudobulbar palsy definition:
Pseudobulbar palsy is a problem with voluntary control of the lower cranial nerves (V, VII, X, XI and XII), which results in difficulties in chewing, swallowing and speech.

Hypernatremia:
Hypernatremia can also occur depending on the relative amount of solute to water lost and consumed. This can happen when caregivers mix the ORS improperly in too little water. The definition of hypernatremia is >145mEq/L.

Signs/Symptoms: thirst, confusion, hyperreflexia, seizures, coma (12)
Treatment: if patient is hypovolemic (i.e. dehydrated), the dehydration must be treated first by choosing to rehydrate with a hypotonic fluid. In the case of dehydration with hypernatremia, the ICDDR,B recommends giving ORS and plain water in a ratio of 1:1; this means that for every glass/spoon of ORS one glass/spoon of plain water is given. However, in cases of shock, the patient must be given isotonic fluid to manage the volume status prior to the sodium. After the patient is euvolemic, he/she should be given water either orally or intravenously with 5% dextrose in water until the sodium level has normalized and/or the symptoms resolve. You can calculate the water deficit in liters by this formula (13):

[(0.6 x wt in kg) x (serum Na - 140)] / 140

To avoid cerebral edema, do not correct Na rapidly; it should normalize between 48-72 hours or at a rate of ≤0.5 mEq/L/hr

Hypoglycemia:
In patients with cholera, hypoglycemia is generally triggered by inadequate gluconeogenesis in light of malnutrition, or sepsis. Severe hypoglycemia is considered to be blood glucose of <2.2mmol/L or 40mg/dl. In the case of convulsions or loss of consciousness, glucose can be given immediately. Other causes of convulsions or loss of consciousness (meningitis, encephalitis, etc.) should be subsequently ruled-out, especially if the patient doesn't recover rapidly with the glucose infusion.

Signs/Symptoms: Mild cases will have headache, nausea, sweating, dizziness, and hypotension. Severe cases will have convulsions and loss of consciousness (14).
Treatment: In mild cases, when the patient is alert, give oral carbohydrate (a glass of water with 2-3 tablespoons of sugar, fruit juice, 1-2 cups of milk, a piece of fruit, crackers). Severe cases, especially with convulsion or loss of consciousness, should be given IV dextrose or glucose, 5.0ml/kg of 10% glucose (15), or an IV bolus of 25-50g of 50% glucose solution (16), or the equivalent. To prevent recurrence, ORS should be given or 5% glucose solution added to the IV fluid until feeding restarts (17).

Hypokalemia:
Diarrheal fluids will cause potassium losses. In mild cases of diarrhea, this will not be clinically significant because the kidneys can compensate and will correct the abnormality. However, in cases of significant potassium loss with severe diarrhea, impaired renal function due to prolonged hypovolemia, or other pre-existing impairment, the kidneys will not be able to compensate and the hypokalemia will become clinically significant. This is most likely to occur if inappropriate fluids, which do not contain enough replacement potassium, are given. Mild hypokalemia is considered to be 3-3.5mEq/L and severe hypokalemia is considered to be <2.5mEq/L.

Signs/Symptoms: Mild hypokalemia can cause muscle cramps, impaired smooth muscle function leading to ileus and abdominal distension, and possibly a reduced heart rate and arrhythmias. Severe hypokalemia causes hyperpolarization of the cardiac conduction tissue leading to EKG changes (ST segment depression, decreased amplitude or inverted T waves, increased height of the U wave >1 mm, widened TU wave, and prolongation of the QTc) and arrhythmias such as AV block and tachyarrhythmias, including ventricular fibrillation (18).
Treatment: In mild cases ORS is usually sufficient. Oral potassium may also be used to correct mild cases (children 1-4mEq/kg/24 hours in 2-4 divided doses, and adults 40-100mEq/24 hours in 2-4 divided doses). In severe cases with EKG changes give IV KCl (children 0.5-1mEq/kg/dose, and adults 10mEq/hour). When IV KCl is given you must monitor the patient closely for arrhythmias. Bananas have a lot of potassium. You can advise the caretaker to feed bananas to the patient to prevent hypokalemia.

Miscarriage/premature Delivery:
This is an unfortunate consequence of severe dehydration in a pregnant woman and is due to inadequate blood flow to the placenta because of shock. If dehydration status is quickly corrected and hydration is maintained, cholera usually does not cause any complications of pregnancy. With pregnant women, you may tend to use more IV fluids rather than ORS to guarantee continued maintenance of hydration. Diarrhea treatment centers may need resources to deliver pregnant women should premature delivery occur.

Muscle/abdominal Cramps:
Muscle cramps occur commonly in patients with severe dehydration and can be very painful. They are thought to be due to abnormalities of serum calcium.
Signs/symptoms: tetany
Treatment: The symptoms will resolve with standard rehydration treatment of cholera with intravenous and oral fluids.

Pulmonary Edema:
Giving too much IV fluid without correcting the metabolic acidosis can lead to pulmonary edema. It is never caused by ORS, which is one of the reasons that patients should be switched to ORS hydration as soon as they are not severely dehydrated. It is more likely if metabolic acidosis is not corrected, as is the case when Normal Saline is given in place of Cholera Saline or Lactated Ringers.

Metabolic Acidosis:
Patients presenting with severe cholera will inevitably have metabolic acidosis because the diarrheal fluid being lost is basic. The acidosis is corrected by proper rehydration solutions and by the ability of the kidneys to compensate and correct the abnormality. However, in cases of impaired renal function due to prolonged hypovolemia or other pre-existing impairment, the kidneys will not be able to compensate and it will become clinically significant.
Signs/Symptoms: bicarbonate <10mmol/L, academia pH <7.3, respiratory compensation in the form of Kussmaul breathing, vomiting. In a patient with an increased respiratory rate, make sure to include pneumonia in your differential diagnosis.
Treatment: correction with a fluid that contains base such as Cholera Saline or Lactated Ringers.

Acute Renal Failure:
Acute renal failure can occur due to prolonged hypoprofusion from dehydration. This most commonly occurs if patients with severe cholera are given enough fluids to keep them alive, but not enough to correct the dehydration during a long transit time to the treatment center.
Signs/Symptoms: decreased urine output, increased BUN (blood urea nitrogen) and serum creatinine
Treatment: fluids; may need dialysis if it does not resolve spontaneously.

Ischemia:
Myocardial infarction, stroke, or mesenteric artery thrombosis can occur because of the hypovolemic state, which will stress vessels that already have compromised perfusion. Consider screening all patients with a pre-existing cardiac condition on initial evaluation to avoid these complications.

Chapter 4.4 - Conclusion Box

- The major complications of cholera result from electrolyte imbalances; either from the diarrheal fluid loss or from improper fluid management
- Rapid rehydration is essential; give IV fluid for severe dehydration and ORS for everyone

Chapter 4.5 - References

1. WHO, First steps for managing an outbreak of acute diarrhea, WHO Global Task Force on Cholera Control, 2004.

2. Khan WA, Saha D, Rahman A, Salam MA, Bogaerts J, Bennish ML. Comparison of single-dose azithromycin and 12-dose, 3-day erythromycin for childhood cholera: a randomised, double-blind trial. Lancet. 2002 Nov 30;360(9347):1722-7.

3. Khan WA, Bennish ML, Seas C, Khan EH, Ronan A, Dhar U, Busch W, Salam MA. Randomised controlled comparison of single-dose ciprofloxacin and doxycycline for cholera caused by Vibrio cholerae 01 or 0139. Lancet. 1996 Aug 3;348(9023):296-300.

4. Sack AS, Lyke C, McLaughlin C, Suwanvanichkij. Antimicrobial resistance in shigellosis, cholera and campylobacteriosis. WHO/CDS/CSR/DRS/2001.8

5. Saha D, Khan WA, Karim MM, Chowdhury HR, Salam MA, Bennish ML. Single-dose ciprofloxacin versus 12-dose erythromycin for childhood cholera: a randomised controlled trial. Lancet. 2005 Sep 24-30;366(9491):1085-93.

6. Saha D, Karim MM, Khan WA, Ahmed S, Salam MA, Bennish ML. Single-dose azithromycin for the treatment of cholera in adults. N Engl J Med. 2006 Jun 8;354(23):2452-62.

7. The Zinc Investigators' Collaborative Group. Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. Am J Clin Nutr 2000;72:1516–22.

8. Zinc Investigators' Collaborative Group. Prevention of diarrhea and pneumonia by zinc supplementation in children in developing countries – pooled analysis of randomized trials. J Paediatr 1999; 135(6):689-97

9. Zinc Investigators' Collaborative Group. Effect of Zinc Supplementation on Clinical Course of Acute Diarrhea: Meeting Report, J Health Popul Nutr, 2001 Dec. 19(4):338-346

10. Internal Medicine, Stein - 5th Ed. (1998)

11. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

12. Merck Manual - 17th Ed. (1999) Centennial Edition

13. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

14. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

15. World Health Organization. The Treatment of diarrhea : a manual for physicians and other senior health workers. -- 4th rev. 2005

16. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

17. World Health Organization. The Treatment of diarrhea: a manual for physicians and other senior health workers. -- 4th rev. 2005

18. Internal Medicine, Stein - 5th Ed. (1998)

Chapter 5.1 - Clinical Management of Shigellosis Introduction

This section will serve as an overview of the clinical management of shigellosis. The 'Clinical Management of Shigellosis' section is geared towards physicians and other health care personnel who have formal training in clinical management.

In the small sections to follow, the following topics will be discussed:

- Case management of shigellosis
- Common complications of shigellosis

Chapter 5.2 - Shigellosis Management Overview

The main difference between shigellosis management and cholera management is that shigellosis generally causes less dehydration, especially severe dehydration, but can lead to many other complications as a result of its invasiveness and therefore an effective antibiotic treatment is essential. The following steps are the main points in the assessment and management of shigellosis. Additional practical worksheets for the management of shigellosis will be provided in the virtual hospital section and separated by job type.

- Antimicrobial Treatment
- Reasons for Hospitalization
- Hospital Management
- Home Management
- Post-shigellosis Treatment

Antimicrobial treatment:
Any patient that has acute bloody diarrhea, most often with fever, should be treated promptly with an antimicrobial that is known to be effective against shigellosis. Effective antibiotic treatment will reduce the chance of serious complications and death, shorten the duration of symptoms and reduce the amount of time that *Shigella* spp. are eliminated in the stool, causing further spread.

Certain antibiotics should NOT be used for the treatment of shigellosis for various reasons (1):

Antibiotics:	Rationale for NOT using:
Ampicillin, chloramphenicol, cotrimoxazole, tetracycline	Used in the past, most *Shigella* spp. are now resistant
Nitrofurans, aminoglycosides, first and second generation cephalosporins, amoxicillin	Poor penetration into the intestinal mucosa, these are not clinically effective
Nalidixic acid	Used in the past, most *Shigella* spp. are now resistant Use may increase resistance to ciprofloxacin

Recommended antibiotics used for SHIGELLOSIS (2)

Antibiotic*	Dose in children	Dose in adults
Ciprofloxacin	15 mg/ kg 2 times a day for 3 days (oral)	500 mg 2 times a day for 3 days (oral)
Pivmecillinam	15-20 mg/ kg 3 times a day for 5 days (oral), Max dose 300 mg	400 mg 3 times a day for 5 days (oral)
Ceftriaxone	50-100 mg/ kg once a day for 2-5 days (IM or IV)	2 g once a day for 3 days (IM or IV)
Azithromycin	20 mg/ kg once a day for 3 days (oral)	500 mg once a day for 3 days (oral)

* Antibiotic selection must depend on the sensitivity pattern determined for the specific shigellosis outbreak; Ciprofloxacin is the first line drug.

Danger signs specific to shigellosis patients (patients at an increased risk of death)

- Patients not improving on conservative treatment after two days
- Age (infants and adults >50 years old)
- Children who are not breastfed
- Children recovering from measles
- Malnourished patients
- Dehydrated patients (see the cholera management section for an explanation of dehydration assessment and management)
- Unconscious patients
- Hypo- or hyperthermic patients
- Patients who have had a convulsion with their illness

Hospital management:
Patients who are evaluated and found to have the above complications are at an increased risk of death and should be hospitalized if possible. In the hospital they should be given appropriate antibiotics and supportive care. Antipyretics and analgesics should be given for fever and pain, respectively per the regular treatment schedule. Patients should be reassessed and monitored frequently. For a discussion on the common complications of shigellosis and their management please see the “Shigellosis Complications” section.

Home management:
Most patients who do not have the above complications will do fine at home with an antibiotic, zinc (if the patient is 5 years old or younger), and ORS. In fact, if there is a shortage of antibiotics, they should be saved for those that require hospitalization. Most patients will improve within 48 hours and recover fully within 7-10 days. Caregivers should be given antibiotics, zinc (if needed) and instructions on how to care for the patient, including disinfecting the patient's clothing and bedding, hygienic practices to prevent spread to other family members, and danger signs, which should prompt them to return to the health facility immediately.

Danger signs for at home caregivers of shigellosis patients:

- Patient becomes unconscious
- Patient has a convulsion
- Patient is unable to eat or drink or vomits everything

After 48 hours the patient should return to the facility for reassessment. If the patient shows signs of improvement, the treatment is finished.

Signs of improvement:

- Less fever
- Less blood in the stool
- Less frequent stools
- Improved appetite

If the patient is not improving or is doing worse after 48 hours of home treatment, he/she should be hospitalized.

Patients with shigellosis are at an increased risk for malnutrition and therefore should be fed frequent small meals.

Post-shigellosis treatment:
Shigellosis patients are at an increased risk for malnutrition. They typically have a decreased appetite at a time when their nutritional requirements are the highest. This is in addition to the general risk of malnutrition during other diarrheal episodes. For this reason, it is recommended that patients be fed frequent small meals during their illness. Following a shigellosis episode, children should be fed at least one extra meal per day for 2 weeks to recover from any nutritional deficit they may have acquired during their illness.

A child with danger signs.

Chapter 5.3 - Common Complications of Shigellosis

Some of the complications of shigellosis are the same as with cholera and other diarrheal illnesses. However, because *Shigella* spp. are invasive and severe dehydration is less common than cholera, there are some complications that are unique to shigellosis.

Common Complications Unique to Shigellosis:

- Severe Hypoglycemia
- Encephalopathy
- Toxic Megacolon
- Intestinal Perforation
- Hemolytic Uremic Syndrome
- Rectal Prolapse
- Convulsions
- Septicemia
- Malnutrition

Complications of Shigellosis Shared with Other Diarrheal Illnesses:

- Hyponatremia
- Hypernatremia
- Hypokalemia

Severe Hypoglycemia:
In patients with shigellosis, hypoglycemia is generally triggered by inadequate gluconeogenesis in light of fever, malnutrition, or sepsis. Severe hypoglycemia is considered to be blood glucose of <2.2mmol/L or 40mg/dl. In the case of convulsions or loss of consciousness, glucose can be given immediately. Other causes of convulsions or loss of consciousness (meningitis, encephalitis, etc.) should be subsequently ruled-out, especially if the patient does not recover rapidly with the glucose infusion.

With an infant or child shigellosis patient, you should ask the mother when the infant/child was last breastfed or ate because of the high risk of hypoglycemia with a prolonged period of not eating. However, in shigellosis, hypoglycemia can occur very soon after the last meal. Children with shigellosis and hypoglycemia have 6 times higher mortality risk than children with shigellosis and normoglycemia (3).

Signs/Symptoms: Mild cases will have headache, nausea, sweating, dizziness, and hypotension. Severe cases will have convulsions and loss of consciousness (4).
Treatment: In mild cases, when the patient is alert, give oral carbohydrate (a glass of water with 2-3 tablespoons of sugar, fruit juice, 1-2 cups of milk, a piece of fruit, crackers). Severe cases, especially with convulsion or loss of consciousness, should be given IV dextrose or glucose, 5.0ml/kg of 10% glucose (5), or an IV bolus of 25-50g of 50% glucose solution (6), or the equivalent. To prevent recurrence, ORS should be given or a 5% glucose solution should be added to the IV fluid until feeding restarts (7).

Encephalopathy:
In many cases of encephalopathy, the cause is never known. In some cases it is caused by metabolic abnormalities brought on by the diarrhea. The standard treatment for encephalopathy should be taken.

Toxic Megacolon:
This is caused by mucosal inflammation, which leads to ulceration and then ileus and severe distension. Complications of toxic megacolon include perforation and hemolytic uremic syndrome. If toxic megacolon occurs in shigellosis it has a 33% case fatality rate (8).
Signs/Symptoms: ileus with severe distension
Treatment: nasogastric tube decompression, broad-spectrum antibiotics.

Intestinal Perforation:
The cause of intestinal perforation is ulceration and vasculitis that penetrates the mucosal wall. It results in peritonitis and sepsis. The only effective treatment is emergency surgery.
Signs/Symptoms: peritonitis (rebound tenderness)
Treatment: surgery, broad-spectrum antibiotics, and supportive care.

Hemolytic Uremic Syndrome (HUS):
Signs/Symptoms: microangiopathic hemolytic anemia, thrombocytopenia, renal failure, with or without a leukomoid reaction; decreased or no urine output, increased BUN/creatinine, abnormal bleeding, decreased hematocrit/RBC count, fragmented RBC and few or no platelets on blood smear.
HUS is also caused by E. coli O157:H7, Echovirus, Coxsackie virus, HIV, and malignant hypertension.
Treatment: blood transfusion (for anemia); restrict fluids including ORS and potassium rich foods (because of renal failure); dialysis may be required.

Rectal Prolapse:
This is a complication of shigellosis that often recurs, however it will stop after recovery from the diarrheal disease. Most cases can be manually retracted and very few require surgery.
Signs/Symptoms: visible rectal mucosa outside of the anal sphincter
Treatment: place the patient in a "knee-chest" position for gravity to help the rectal tissue retract. With a glove or soft, warm, wet cloth, place the rectal tissue back into the anal canal. In some cases the significant mucosal edema will prevent replacement. In these cases, soak the prolapsed tissue in a warm solution of saturated $MgSO_4$ to reduce the edema before replacing.

Convulsions:
Patients with shigellosis may have one brief convulsion. This resembles febrile convulsions, however it occurs in patients that are older and who do not usually have febrile convulsions. Treatment is not necessary unless it is prolonged or repeated. Rule out meningitis and hypoglycemia.
Treatment: Initial treatment for refractory seizures in children: lorazepam 0.05 to 0.1 mg/kg IV should be administered at a rate of 2 mg/min. If seizures continue, additional doses of lorazepam may be given 5-10 min after the previous dose, up to a cumulative dose of 10 mg over twenty minutes (9). If IV lorazepam is not available, avoid rectal delivery of other seizure medicines because of the risk of rectal prolapse and impaired absorption through an inflamed mucosal surface.

Septicemia:
This occurs most commonly in severely malnourished children with shigellosis but may also occur as a result of intestinal perforation. Patients can have *Shigella* spp. bacteremia or bacteremia with other organisms such as *Enterobacteriaceae* or other Gram-negative bacilli (10).
Treatment: Treat as per usual protocol including broad-spectrum antibiotics and fluids to maintain intravascular volume.

Malnutrition:
A long-term complication of shigellosis is malnutrition, especially in children. This occurs due to significantly increased energy requirements in the face of anorexia and cultural beliefs that prevent feeding diarrheal patients. Non-breastfed infants are especially vulnerable. Recommend feeding all children with shigellosis 1 extra meal per day for 2 weeks to avoid this complication.

Hyponatremia:
Some electrolyte abnormalities, such as hyponatremia, can occur from improper use of rehydration fluids. Diarrhea and vomiting cause gastrointestinal loss of sodium (termed extra-renal). Without adequate replacement, hyponatremia from diarrhea and vomiting is generally hypovolemic hyponatremia. In the case of extreme excess free water intake (about 10L/day for an adult), there can be euvolemic hyponatremia. The definition of hyponatremia is <130mEq/L and severe hyponatremia is <120mEq/L (11).

Signs/Symptoms: Mild: generalized **weakness**, muscle **cramps**, **nausea** and **vomiting**, **anorexia**, **lethargy**; Severe: **delirium**, **coma**, **depressed deep tendon reflexes**, Cheyne-Stokes respiration, pseudobulbar palsy, seizures, cranial nerve palsies (12)
Treatment: IV hypertonic 3% saline 12ml/kg over 4 hours and, only after dehydration has been corrected, free water restriction (to 1L/day) until it reaches a normal level.

Pseudobulbar palsy definition:
Pseudobulbar palsy is a problem with voluntary control of the lower cranial nerves (V, VII, X, XI and XII), which results in difficulties with chewing, swallowing and speech.

Hypernatremia:
Hypernatremia can also occur depending on the relative amount of solute to water lost and consumed. This can happen when caregivers mix the ORS improperly in too little water. The definition of hypernatremia is >145mEq/L.

Signs/Symptoms: thirst, confusion, hyperreflexia, seizures, coma (13)
Treatment: if patient is hypovolemic (i.e. dehydrated), the dehydration must be treated first by choosing to rehydrate with a hypotonic fluid. In the case of dehydration with hypernatremia, the ICDDR,B recommends giving ORS and plain water in a ratio of 1:1; this means that for every glass/spoon of ORS one glass/spoon of plain water is given. However, in cases of shock, the patient must be given isotonic fluid to manage the volume status prior to the sodium. After the patient is euvolemic, he/she should be given water either orally or intravenously with 5% dextrose in water until the sodium level has normalized and/or the symptoms resolve. You can calculate the water deficit in liters by this formula (14):

[(0.6 x wt in kg) x (serum Na - 140)] / 140

To avoid cerebral edema, do not correct Na rapidly; it should normalize between 48-72 hours or at a rate of ≤0.5 mEq/L/hr

Hypokalemia:
Diarrheal fluids will cause potassium losses. In mild cases of diarrhea, this will not be clinically significant because the kidneys can compensate and will correct the abnormality. However, in cases of significant potassium loss with severe diarrhea, impaired renal function due to prolonged hypovolemia, or other pre-existing impairment, the kidneys will not be able to compensate and the hypokalemia will become clinically significant. Hypokalemia is most likely to occur if inappropriate fluids, which do not contain enough replacement potassium, are given. Mild hypokalemia is considered to be 3-3.5mEq/L and severe hypokalemia is considered to be <2.5mEq/L.

Signs/Symptoms: Mild hypokalemia can cause muscle cramps, impaired smooth muscle function leading to ileus and abdominal distension, and possibly a reduced heart rate and arrhythmias. Severe hypokalemia causes hyperpolarization of the cardiac conduction tissue leading to EKG changes (ST segment depression, decreased amplitude or inverted T waves, increased height of the U wave >1 mm, widened TU wave, and prolongation of the QTc) and arrhythmias such as AV block and tachyarrhythmias, including ventricular fibrillation (15).
Treatment: In mild cases, ORS is usually sufficient. Oral potassium may also be used to correct mild cases (children 1-4mEq/kg/24 hours in 2-4 divided doses, and adults 40-100mEq/24 hours in 2-4 divided doses). In severe cases with EKG changes, give IV KCl (children 0.5-1mEq/kg/dose, and adults 10mEq/hour). When IV KCl is given you must monitor the patient closely for arrhythmias. Bananas are an excellent source of potassium. You can advise the caretaker to feed bananas to the patient to prevent hypokalemia.

Chapter 5.4 - Conclusion Box

- The significant complications of shigellosis are due to the invasiveness of the bacterium
- Antimicrobial treatment is essential to shigellosis management; use appropriate antibiotics based on known resistance patterns

Chapter 4.5 - References

1. WHO, Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* type 1, WHO 2005

2. ibid.

3 Bennish ML. Potentially lethal complications of shigellosis. *Reviews of Infectious Diseases. 13 Suppl 4:S319-24, 1991 Mar-Apr.*

4. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

5. World Health Organization. The Treatment of diarrhea : a manual for physicians and other senior health workers. -- 4th rev. 2005

6. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

7. World Health Organization. The Treatment of diarrhea : a manual for physicians and other senior health workers. -- 4th rev. 2005

8. Bennish ML. Potentially lethal complications of shigellosis. *Reviews of Infectious Diseases. 13 Suppl 4:S319-24, 1991 Mar-Apr.*

9. Chin RF, Verhulst L, Neville BG, Peters MJ, and Scott RC. Inappropriate emergency management of status epilepticus in children contributes to need for intensive care. J Neurol Neurosurg Psychiatry 2004 Nov; 75(11): 1584-8.

10. Bennish ML. Potentially lethal complications of shigellosis. *Reviews of Infectious Diseases. 13 Suppl 4:S319-24, 1991 Mar-Apr*.

11. Internal Medicine, Stein - 5th Ed. (1998)

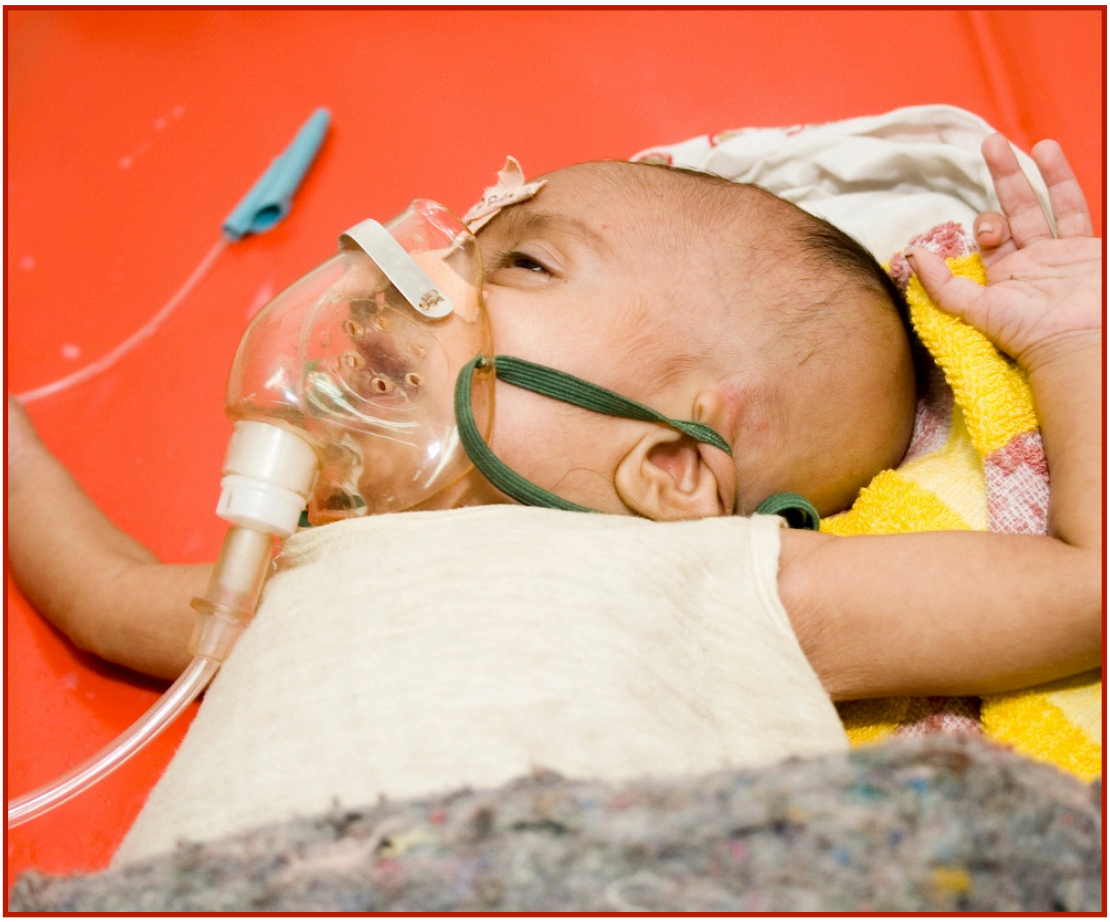
12. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

13. Merck Manual - 17th Ed. (1999) Centennial Edition

14. Griffith's 5-Minute Clinical Consult - 14th Ed. (2006)

15. Internal Medicine, Stein - 5th Ed. (1998)

Chapter 6 - Co-morbidities and Prevention



Chapter 6.1 - Introduction to Co-Morbidities and Prevention

This section will serve as a supplement to the clinical management sections on cholera and shigellosis, respectively. This section will discuss the co-morbid diseases that can complicate epidemic diarrhea and the means of preventing further diarrheal cases during an outbreak. This section is geared towards physicians and other health care personnel who have formal training in clinical management as well as those public health managers who might start a prevention campaign.

In the small sections to follow, the following topics will be discussed:

- Co-morbidities of cholera and shigella
- Common complications of cholera and shigella

Chapter 6.2 - Co-Morbidities

In this section, we will discuss a few key co-morbid conditions that may affect the treatment of patients with epidemic diarrhea. The diseases were chosen based on their high prevalence in areas where diarrheal epidemics are common and based on their impact on diarrheal disease.

Malnutrition is the most important co-morbidity since it is part of the viscous cycle of malnutrition and diarrhea. However, malnutrition will be discussed separately since it requires more involved treatment considerations. The co-morbidity discussion in this section will include malaria, HIV/AIDS, measles, and TB. During a diarrheal outbreak a patient should first be treated for any acute diarrheal presentation. If a co-morbidity is suspected or discovered, the patient should be stabilized for their acute diarrheal disease and then he or she should be treated for his/her co-morbidity according to general medical protocols, preferably in a general hospital separate from the diarrhea ward or tent.

- Malaria
- Measles
- HIV/AIDS
- Tuberculosis

Malaria:
With malaria, gastrointestinal symptoms can be common, especially in children and naïve travelers. However, diarrhea due to malaria rarely (if ever) has blood or pus, so diarrhea with blood or pus should never be initially attributed to malaria. Because malaria can cause such a wide spectrum of disease symptoms, clinical diagnosis alone is known to be inaccurate and therefore blood smears should be done for confirmation whenever possible. This is a situation where a rapid test for malaria can be useful. During an outbreak of diarrhea, some patients may have malaria depending on the location and the season. However everyone who fits the established case definition for the outbreak-causing diarrhea should be recorded and treated empirically regardless of their malaria status.

During a cholera outbreak, malaria may be considered as an additional diagnosis if the patient has an elevated temperature, since cholera patients typically do not have fever (1). Do a blood smear if possible or treat empirically for malaria according to local protocol. Do NOT discontinue life-saving cholera treatment such as rehydration! This will not affect malaria treatment and can save lives.

During a shigellosis outbreak, diarrhea can usually be distinguished from malarial diarrhea by the existence of blood and pus in the stool. Suspect malaria in endemic areas when the diarrhea improves but the fever continues. In these cases, attempt to confirm the malaria and treat accordingly.

Measles:
Diarrhea is an important complication of measles and typically occurs within 2-4 weeks of the rash. However, the patient continues to be at increased risk of severe diarrhea or dysentery for up to 6 months. Because a child recovering from measles is immunocompromised, he/she is at an increased risk of death from shigellosis and should be hospitalized if possible. A diarrheal outbreak also might be a good impetus to start or scale-up a measles vaccination campaign and a vitamin A supplementation program. Even within 72 hours after exposure, the live measles vaccine has been shown to provide protection (2).

Any child with measles who is older than 6 months of age should receive two doses of supplemental Vitamin A 24 hours apart. The dose is 200,000 IU for those 12 months and older and 100,000 IU for those from 6 months to 12 months of age. Infants less than 6 months rarely develop measles (3).

HIV/AIDS:
Patients who are HIV+ are more susceptible to infection than patients without HIV. In addition, they are known to have more severe clinical courses in many cases. The interaction of epidemic *S. dysenteriae* type 1 and *V. cholerae* and HIV/AIDS is not fully understood.

One study investigated *Shigella* and *Vibrio* infections (mostly *S. flexneri* and *Vibrio vulnificus*) in the US population. This study was inconclusive as to whether HIV+ patients were at an increased risk of contracting shigellosis compared to the sexually active homosexual population (4). However, HIV+ patients may be at increased risk for bacteremia and recurrent infection, as presented in a case study (5). Furthermore, in a study in Nairobi, they found that HIV + patients generally had the same spectrum of pathogens in stool samples and blood cultures as the general population. The two pathogens that occurred significantly more commonly in the HIV+ population and not the general population were *Cryptosporidium parvum* and *Cryptococcus neoformans*. This study reinforced the need for health professionals to know which pathogens are causing disease in the community and to have a similar differential diagnosis of pathogens for the diseases of HIV+ patients as for the HIV- population (6).

The key point regarding treatment of patients with HIV during a diarrheal epidemic is that the initial management of patients is the same regardless of their HIV status.

Tuberculosis:

Tuberculosis (TB) is a major cause of morbidity and mortality in the developing world, especially in HIV+ populations. TB is a chronic disease; a patient with untreated TB may be at risk for new infectious diseases, such as diarrhea which may present with more severe diarrhea.

Modified Kenneth Jones Criteria for the Diagnosis of TB

7 or more points = unquestionable TB
5-6 points = probable TB, therapy may be justified
3-4 points = further investigations are needed

In the case of abdominal TB, the TB itself may cause diarrhea. One study on a population of HIV negative patients found that 17% of TB+ patients had a chief complaint of diarrhea as their presenting symptom of abdominal TB, although the most frequent symptom was abdominal pain (28.4%) (6).

Score +3	Score +2	Score +1	Score -1
Recovery of AFB from sputum, gastric lavage, laryngeal swab, etc.	**X-Ray suggestive of lymphadenitis** with or without parenchymal lesions	**Non-specific X-Ray changes**	**BCG vaccination** in last 2 years
Tuberculosis **granuloma**, granulomatous lesions in lymph node biopsy or choroids tubercles on fundoscopy	**Suggestive physical findings**: skin lesion, osteomyelitis, Pott's spine, etc.	**Compatible physical findings**: erythema nodosum, phlyctenular conjunctivitis, meningitis, cervical lymphadenitis, arthritis, hemoptysis, etc.	
Positive Tuberculin skin test (TST)	**Recent TST conversion** from negative to positive	History of **contact with a patient suffering from TB**	
	Contact with sputum positive person	**Non-specific granuloma**	
		Age < 2yrs	
		Non-response to therapy	
		Severe malnutrition	

Adapted from: Prof. MS Akbar. Synopsis of Child Health, Dhaka

Chapter 6.3 - Identification and Treatment of Malnutrition

Malnutrition is a serious cause of morbidity and mortality worldwide, especially in children. It affects the clinical outcome in every disease, and thus treatment plans should be changed accordingly. Unfortunately, the same disasters that may cause an increased risk for diarrheal outbreaks may also put the population at risk for malnutrition. There are different ways of determining the cut-off point for the admission of a patient with malnutrition. In addition, there are different ways of treating malnourished children. The management of malnutrition in disaster situations and refugee camps is a very important issue because acute malnutrition is often a co-morbid condition of these humanitarian emergencies. From the management point of view, the most important points are:

- Determining the nutrition status of a patient
- Determining when intervention is necessary
- Determining what type of intervention to plan

The former classifications of malnutrition in terms of kwashiorkor and marasmus are used less in favor of edematous malnutrition and wasting.

There are different ways of measuring the nutrition status of a patient. The most widely accepted way for children is to measure weight and height and determine the relationship of this child's weight for height (WFH) to the median. If a child has a low WFH he/she is considered wasted. Low height for age is called stunting and is the best marker of chronic malnutrition, but not as useful as an indication for treatment. Weight for age (WFA or underweight) is also used, although this could be inappropriately low in a child who is stunted from chronic malnutrition. For clinical treatment and follow-up, it is useful to use a growth curve to monitor the child's growth over time as well.

For adolescents and adults (≥10 years old) body mass index (BMI) is recommended as a measure of malnutrition. BMI is the weight (in kilograms) over the height (in meters) squared.
BMI = kg / m2

Finally, there is a quick and easy estimate for wasting termed the "mid-upper arm circumference" or MUAC. This can be used for children and adults in screening, surveillance or in an area with large numbers of malnourished patients and low numbers of trained staff, weighing machines or height boards. It is also a good marker for the nutritional status of pregnant women.

	Classification	
	Moderate Malnutrition	Severe malnutrition (type)
Symmetrical edema (adults and children)	Not present	Yes (edematous malnutrition—for adults rule out non-nutritional causes)
WFH (children)	-3 ≤ SD[a] < -2 or 70-79%	< -3 SD[a] or <85% (severe wasting)
Height for age (children)	-3 ≤ SD[a] < -2 or 85-89%	< -3 SD[a] or <85% (severe stunting)
MUAC (children)	110-125 mm	<110 mm
BMI (adults)	16 – 16.99	<16 (severe malnutrition)
MUAC (adults)	160-185mm	<160mm (severe wasting)
MUAC (pregnant and lactating women)	170-185mm	<170mm (severe wasting)
BMI (adolescents 10-18)		<5th percentile (severe malnutrition) except in cases of stunting where cut-off is <3rd percentile

[a] = standard deviation from the mean

The following are the most common interventions used:

Therapeutic Feeding Center
A therapeutic feeding center (TFC) is the traditional approach for treating severely malnourished children. In this approach, children are fed at the center (often a separate section of the hospital) until they reach discharge criteria. The treatment is broken into the initial phase, the rehabilitation phase, and follow-up.

Because the greatest risk for death is at the beginning, or the initial phase, it is very important that children be assessed and treated promptly for severe malnourishment. The initial phase includes treating and preventing hypoglycemia, hypothermia, dehydration, as well as correcting electrolyte imbalances, starting feeds and treating infections. Patients should be fed every 2-3 hours both day and night to prevent hypoglycemia. The total amount of feeds per day should equal 80-100 Kcal/kg during the initial phase. This initial phase lasts until the patient has stabilized and has regained his/her appetite; usually within 2-7 days. Finally, iron supplementation should NEVER be given during the initial phase because of the risk of worsening the infection by providing iron that can be sequestered by pathogenic bacteria.

The WHO recommends that a TFC be created in any place where >10% of all children aged 6 months-5 years are <-2SD weight for height. In the TFC, management should follow the WHO guidelines, or national adapted guidelines based on research. Children usually stay 4-6 weeks until they are considered rehabilitated enough to be discharged home.

WHO entrance criteria: WFH <-3SD (or <70% of the median) or symmetrical edema
WHO exit criteria: WFH –1SD and no edema.

Feeding programs
Feeding programs are more of a public health approach to widespread malnutrition and are generally reserved for emergency settings. There are two types of feeding programs: a general feeding program in which everyone in the community receives full dietary requirements, and supplementary feeding program in which a portion of the daily dietary requirements are given. General feeding programs are reserved for populations that have no access to food and should provide at least 2100kcal per person per day.

Supplementary feeding programs are recommended for populations with high rates of malnutrition. They provide supplementary food (not a complete daily ration) to vulnerable groups, such as children with a WFH <-2SD (targeted), or to other groups including pregnant and lactating women, twins, orphans, etc. whether or not the individual is malnourished. Either 500-700kcal of cooked food (sometimes a porridge or gruel) or 1000-1200kcal of dry rations (generally staples like rice or wheat) is given per person per day. There are two types:
Blanket supplementary feeding: when rates exceed 15% or they are >10% with risk factors such as poor food availability, epidemic of diarrhea or measles, etc.
Targeted supplementary feeding: when rates exceed 10% or 5% with risk factors

Community Therapeutic Care Program (CTC)
This is a relatively new approach (started in Ethiopia in 2000) to treating malnourished children and CTC is particularly suited to disaster situations. This approach uses a paste with the nutritional equivalent of F-100 to feed children, who are at least 6 months of age, with signs of severe acute malnutrition without complications. Children are initially screened for nutrition status and complications. If they are found to have severe acute malnutrition, they are either referred to the hospital or "stabilization center," or included in the "outpatient therapeutic program" and given a broad-spectrum antibiotic and other locally relevant empiric treatments as well as a week's supply of paste. The children return weekly for a check-up and the next week's supply of paste. The paste is called Ready to Use Therapeutic Food (RUTF); it is commercially available as PlumpyNut and is made locally in some places as well.

Children with complications are first admitted to the hospital to be stabilized and then transferred back to the outpatient program. The average length of stay is 2-10 days compared to 4-6 weeks. The opportunity cost to the mother is lower than traditional TFC's because there is a significantly shorter stay, if any, in the hospital away from the rest of the family. The child must then only return one time per week for treatment.

Opportunity Cost Definition
An opportunity cost is the cost of something in terms of an opportunity forgone (and the benefits which could be received from that opportunity). In other words, the opportunity cost of doing one thing is the lost benefit of doing the alternative.

Children with moderate malnutrition are also included in this program and receive supplementary feeding.

This program was initially designed to treat children from the age of 6 months to 5 years, but it is now being adopted for adults, especially those with HIV.
To read more about the program go to http://www.validinternational.org/pages/sub.cfm?id=1492)

General comments about the management of severely malnourished children with diarrhea:

Correction of severe dehydration in a severely malnourished child:

- First hour 20ml/kg (compared to 30mL/kg)
- Hour 2-10 10ml/kg (compared to 70ml/kg in 5 hours) with 5-10ml ORS after each watery stool

The WHO recommends that severely malnourished children receive a diluted ORS solution because the regular solution contains too much sodium and too little potassium. Although the new WHO low osmolarity diluted ORS has not been tested, the prior formulation, called ReSoMal, was tested at the ICDDR,B. Malnourished children on ReSoMal had a faster correction of potassium depletion but had a longer persistence of hyponatremia and an increased chance for severe hyponatremia causing adverse complications. This was especially true in children with diarrhea with high purging rates, such as those caused by *V. cholerae* and ETEC. Furthermore, this study found no significant difference in the risk of over hydration, which was one of the major concerns that led to the development of ReSoMal (8). For this reason, the ICDDR,B does not use a different formulation of ORS for malnourished patients.

- Always calculate drug doses based on the child's weight and not on their age.
- Never give a severely malnourished child iron in the acute phase as this can actually exacerbate infections, both sub-clinical and clinically apparent.

For the complete management of severely malnourished children please refer to the WHO guidelines for physicians and other senior health care workers. This also covers some basic points about the management of severely malnourished adults and adolescents, and the management of malnutrition in disaster situations and refugee camps. The quiz at the end of the chapter includes questions that cover the material in this document.

Chapter 6.4 - Prevention of Cholera and Shigellosis

Prevention of cholera and shigellosis is best achieved by providing safe water, sanitation and hygiene measures. These topics will be discussed in chapters 7.6 and 8.6. There are certain measures, however, that are **not useful** and actually distract from the important and effective measures. For this reason we will address the ineffective/distraction methods here as things to avoid in a cholera or shigellosis control program (9).

1. Mass Chemoprophylaxis
   This is not recommended because it leads to antibiotic resistance and is not effective from public health standpoint.

2. Quarantine
   Although it is useful to keep patients of a diarrhea outbreak (especially shigellosis) separate from other patients in the hospital, quarantine is not required.

3. Excessive personal protective gear
   a. Masks and gloves are not routinely necessary for close contact of patients and only serve to cause undue fear
   b. BUT hand washing, especially among health care workers, should be enforced for personal protection as well as the control of spread to other patients. Hands should be washed after each patient exam.
   c. Gloves are recommended under universal precautions for direct encounter with bodily fluids, including collecting fecal samples, cleaning patient vomit and stool and handling blood products.

4. Travel and trade restrictions
   a. These do not prevent the spread of cholera and shigellosis. It is not possible to detect every infected person and it diverts substantial resources to an activity that is ineffective.
   b. Because restrictions disrupt the economy of a country, cholera and shigellosis epidemics may not be reported by government officials, which hampers efforts to control the outbreak.

Vaccinations for Cholera and Shigellosis:
The types, formulations, and recommendations for cholera vaccinations are changing rapidly (10). Although an injectable cholera vaccine was used earlier, it was found to be impractical for public health use; thus, its use was strongly discouraged. Recently, oral vaccines have been developed that are proving beneficial, and the WHO is now recommending the use of vaccines in certain high-risk situations, especially among refugees at high risk. There are two types of oral cholera vaccines: those with dead *V. cholerae* and those with living *V. cholerae*. Dukoral is an inactivated (not-living) vaccine that is given as two doses, two weeks apart along with a buffer; Dukoral is a mixture of the classical serogroup (both Inaba and Ogawa serotypes) and the El Tor serogroup (only the Inaba serotype) plus purified cholera toxin B subunit. Another inactivated vaccine is made in Vietnam and other Asian countries and is similar to Dukoral except that it does not require a buffer and is less expensive. The implementation of this vaccine is centered in Asia and the scope is not intended to have global impact. The other major type of vaccine is a live-attenuated vaccine (Orochol), which requires only a single dose. A second live-attenuated vaccine, called Choleraguard, is under development but it is not yet licensed. To date, Dukoral is the main vaccine considered for use in high-risk populations.

Recommendations from the WHO are still evolving because of ongoing clinical research. However, "Since 1999, WHO recommends the use of killed oral WC/rBS (Dukoral) vaccine as a tool to prevent cholera in populations at risk of a cholera epidemic. Such high-risk populations may include, but are not limited to, refugees and urban slum residents." In addition, in 2002, WHO recommended that demonstration projects with oral cholera vaccines be performed in populations at risk living in endemic settings" (11). The WHO is in the process of developing guidelines to determine when either of these vaccines should be used in refugee situations or in endemic areas. The ICDDR,B feels that a cholera vaccine should be used in endemic areas when the rate of cholera is > 1/1000 annually; however, the currently licensed vaccines are still too expensive and require complex logistics (cold chain and systems for distributing and administering the vaccine). As newer vaccines or improvements in formulations become available, it is likely that vaccinations will be used widely for both refugees at high risk and for endemic areas.

DUKORAL CHOLERA VACCINE RECOMMENDATION:

Because of limitations in terms of transport, formulation, and cost of the current Dukoral vaccine, the COTS program does **NOT** require the utilization of the vaccine during an outbreak; it is **NOT** necessary to vaccinate to overcome an outbreak.

However, if Dukoral is readily available and staff are properly trained in its use according to the guidelines that come with the vaccine, the COTS program **PERMITS** Dukoral's use (ideally before an outbreak) in the following high-risk populations: refugee populations in which cholera is present, health care workers managing cholera cases, and communities in which the incidence rate is greater than 1 in 1,000 annually.

Regarding shigellosis, there is **NO VACCINE COMMERCIALLY AVAILABLE** against shigellosis. Unfortunately, there are many species and serotypes of Shigella and a vaccine appears to be specific against these types. Although there is likely to be some cross protection, a large number of vaccine antigens will still be needed. Despite current research, it will be some time before an effective and broad-reaching vaccine debuts on the market (12-15).

Chapter 6.5 - Conclusion Box

- As in any medical setting, it is important to be aware of the other prevalent diseases in your area as well as known chronic diseases your patient has and how these interact with the acute diarrheal disease
- Emergency settings increase the population's risk for malnutrition. Malnutrition should be screened for, treated appropriately, and taken into consideration when treating patients for diarrheal disease
- The prevention of most diarrheal disease can be achieved through simple acts of sanitation, clean water, and personal hygiene

Chapter 6.6 - References

1. WHO, Cholera outbreak: assessing the outbreak response and improving preparedness. Global Task Force on Cholera Control. 2004

2. American Academy of Pediatrics. [Measles]. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006:[441-452]

3. http://www.unicef.org/immunization/files/Vit_A_strategy.pdf and D'Souza RM, D'Souza R. Vitamin A for the treatment of children with measles--a systematic review. J Trop Pediatr. 2002 Dec;48(6): 323-7. Review.

4. Angulo FJ, Swerdlow DL. Bacterial Enteric Infections in Persons Infected with HIV. *Clinical Infectious Disease*. 1995 21(Supp 1): S84-93

5. Kristjansson M, Viner B, Maslow JN. Polymicrobial and Recurrent Bacteremia with Shigella in a Patient with AIDS. *Scand. J. Infect. Dis.* 1994. 26:411-416

6. Batchelor BI, Kimari JN, Brindle RJ. Microbiology of HIV associated bacteremia and diarrhea in adults from Nairobi, Kenya. *Epidemiol. Infect.* 1996. 117:139-144

7. Bolukbas C, Ovunc O, et al. Clinical presentation of abdominal tuberculosis in HIV seronegative adults. BMC Gastroenterology 2005, 5:21

8. Alam NH, Hamadani JD, Dewan N, Fuchs GJ, Efficacy and safety of a modified oral rehydration solution (ReSoMal) in the treatment of severely malnourished children. J Pediatr 2003. 143:614-9

9. WHO. Guidelines for Cholera Control. World Health Organization 1993

10. Hill, D. R., L. Ford, and D. G. Lalloo. Oral cholera vaccines: use in clinical practice. *Lancet Infect Dis* 2006. 6:361-73.

11. WHO Initiative for Vaccine Research reference; Vaccine recommendation updated in 1999: http://www.who.int/vaccine_research/diseases/diarrhoeal/en/index3.html.

12. Niyogi, S. K. Shigellosis. *J Microbiol* 2005. 43:133-43.

13. Ashkenazi, S., J. H. Passwell, E. Harlev, D. Miron, R. Dagan, N. Farzan, R. Ramon, F. Majadly, D. A. Bryla, A. B. Karpas, J. B. Robbins, and R. Schneerson. Safety and immunogenicity of Shigella sonnei and Shigella flexneri 2a O-specific polysaccharide conjugates in children. *J Infect Dis* 1999. 179:1565-8.

14. Cohen, D., S. Ashkenazi, M. S. Green, M. Gdalevich, G. Robin, R. Slepon, M. Yavzori, N. Orr, C. Block, I. Ashkenazi, J. Shemer, D. N. Taylor, T. L. Hale, J. C. Sadoff, D. Pavliakova, R. Schneerson, and J. B. Robbins. Double-blind vaccine-controlled randomised efficacy trial of an investigational Shigella sonnei conjugate vaccine in young adults. *Lancet* 1997. 349:155-9.

15. Noriega, F. R., G. Losonsky, C. Lauderbaugh, F. M. Liao, J. Y. Wang, and M. M. Levine. Engineered deltaguaB-A deltavirG Shigella flexneri 2a strain CVD 1205: construction, safety, immunogenicity, and potential efficacy as a mucosal vaccine. *Infect Immun* 1996. 64:3055-61.

Chapter 7 - Before an Outbreak

Chapter 7.1 - Before an Outbreak Introduction

This section will serve as an introduction to preparing for an outbreak before it occurs. This section is important for the creation of a plan for outbreak management and control from an administrative perspective.

In the small sections to follow, the following topics will be covered:

- Coordination in an emergency
- Surveillance of diarrheal disease
- Communication in an emergency
- Preparing to establish treatment centers
- Emergency water, hygiene, and sanitation needs
- Operating a diagnostic laboratory
- Chapter conclusion
- Quiz questions

Chapter 7.2 - Coordination in an Emergency

In an emergency setting, whether natural or man-made, the numerous needs of the community must be met. Coordination is required between different NGOs and governmental bodies in the area to ensure delivery of services without redundancy. The best outcomes result when a system for a coordinated response is already in place before an emergency happens. The three most important steps in coordination are determining who is affected by the emergency, the services that are needed, and who is able to provide the needed services.

There are two main situations in which a disaster may happen and the coordination steps may vary slightly in these two situations:

1. In an area where there are **already many aide/ governmental agencies** working

   Example: a flood in Bangladesh where the government has an extensive health system network and where many international NGOs are working year-round.

   a. Create records of NGOs and governmental organizations working in the area before an emergency (1) including:
      i. Contact information
      ii. Their current activities
      iii. Available resources in terms of staff, infrastructure, supplies, and funding that could be re-appropriated in times of emergencies
   b. Disseminate the above information to all concerned parties, including private health care facilities, and all organizations on the list

2. In an area in which **aide/governmental agencies have not been working**
   - In this case there should be a government coordinating body that will call for help and coordinate disaster relief efforts.

Example: Hurricane Katrina affected communities in the southern United States in which there are not NGOs actively working in the area and where government agencies do not directly provide healthcare.

Once aide agencies and governmental organizations are working in an emergency setting, it is important to prepare for a potential diarrheal outbreak. Not all emergencies settings have diarrheal outbreaks. However, because emergency settings are prone to outbreaks of diarrhea and other diseases, it is important to plan ahead so that you are prepared for an outbreak when and if the time comes.

Long before an outbreak of diarrheal illness occurs, a coordinating body must be formed in areas where cholera or shigellosis outbreaks have been known to occur or in emergency situations where the risk of a diarrheal outbreak is high to address the following important topics (2,3). For example, in regions with a high density of people with poor sanitation and contaminated drinking water, there is a high risk of a diarrheal outbreak.

Establish a national coordinating committee for acute diarrheal disease (cholera and shigellosis) to be responsible for creating a plan for dealing with outbreaks in a systematic and coordinated way to avoid duplication or unmet needs. Based on the country's size and health services structure, a working group can be established at a more local level (instead of or in addition to the national committee) as needed. It is important to include the relevant **sectors of government** including **health**, **emergencies**, **water**, **sanitation**, **food**, and **communication** as well as relevant **United Nations** agencies (WHO and UNICEF) and **NGO**s involved in the same sectors in the area. For large countries, it may be that state or district level coordinating committees will be more appropriate.

1. Initial Response to a Suspected Outbreak

Form an emergency team to confirm suspected outbreaks of diarrheal illness and to take the first steps in controlling the outbreak.

In an ideal setting, an emergency response team should consist of:

1. A **physician** who can confirm clinical signs and symptomes and who can train health workers in proper case management.
2. A **microbiologist** to take stool samples for laboratory confirmation, train health workers in correct sampling and confirm proper techniques by laboratory technicians.
3. An expert in **behavior change communication** (BCC) who can assess the populations' reaction to the outbreak and create and disseminate appropriate health messages.
4. An **epidemiologist** to monitor proper data collection and surveillance procedures.
5. A **water and sanitation expert** who can assess the situation and develop a plan to reduce sources of contamination (4).

There may be cases where only 1-2 people are available to be a part of the response team. In that case, the team members must be aware of all the necessary investigations and the priority interventions, even if these are not their field of expertise.

2. Epidemiology and Surveillance
3. Case Management
4. Water and Sanitation
5. Laboratory Services
6. Communication

During an outbreak, this committee should meet at least once a week to monitor outbreak control. A lead organization should be clearly designated before a time of crisis. In addition, in order for the committee to be able to implement its plan for cholera control, funds should be appropriated before an outbreak occurs (5).

7.

Chapter 7.3 - Surveillance of Diarrheal Disease

Once a system for coordination is established, a surveillance program can help to determine when an outbreak is happening and when systems already in place to deal with an emergency should be mobilized.

1. Establish a surveillance system
Surveillance can be accomplished in a passive way or in an active way. Passive surveillance is where the outbreak team relies on information to be reported to them, mostly by individual health care providers. This form is easier on the part of the outbreak team, but a lot of cases can be missed if the health care providers do not report cases promptly. To reduce the cases missed, you can also collaborate with journalists or establish a hotline where regular citizens can call with questions about disease.

In active surveillance, cases are sought out through random (or at least representative) clinical information on hospitalized patients or through home visits. Ideally, this should be substantiated with laboratory information on a sample of patient specimens.

2. Create a case definition for surveillance for cholera and shigellosis.
The WHO has created clinical case definitions for cholera and shigellosis to aide in suspecting an outbreak or a case. These clinical case definitions are used for monitoring purposes to detect an outbreak when it starts, monitor the course of an outbreak, and can be used during an outbreak to clinically diagnose particular cases.

3. Establish a reporting system.
Create a universal reporting form for treatment centers to use (see sample WHO form)

- Classify the number of cases and number of deaths in at least two age groups; under 5 years and 5 years and older for reporting to WHO
- Establish a person responsible for registering and reporting cases in each treatment facility
- Reports should be given to the surveillance team at the district or national level on a weekly basis so that outbreaks can be dealt with early and monitored closely
- Ensure that all hospitals/health centers are reporting to the next highest level of the health system

4. Establish a method for compiling data.
Consider downloading a free copy of EpiInfo (8) as well as using a mapping program to track cases and "hot spots" (9). EpiInfo is a program that makes it easy to develop questionnaires or forms, customize the data entry process, and enter and analyze data through statistics, tables, graphs and maps. Click here to go to the EpiInfo web site. (http://www.cdc.gov/EpiInfo/)

5. Identify likely contributors to the transmission of diarrheal disease that should be investigated by the team at the time of a suspected outbreak.

- Water sources
- Foods
- Cultural practices (funeral rites)

6. Identify groups at high risk for mortality during an outbreak and methods of tracking them by the team at the time of a suspected outbreak.

- Poor access to health services
- Extreme poor
- Racial/ethnic/religious minorities
- Malnourished
- Pregnant and lactating women
- Children not vaccinated against measles
- Elderly
- Non-breastfed infants

WHO definition for suspected cholera:

1. A person older than 5 years with severe dehydration from acute watery diarrhea (usually with vomiting)
2. Any person older than 2 years with acute watery diarrhea where there is a confirmed outbreak of cholera
3. Any sudden increase in the daily number of patients with acute watery diarrhea, especially patients who pass typical rice-water stools (6)

WHO definition for suspected shigellosis:
Diarrhea with visible blood in the stool (7).

Chapter 7.4 - Preparing a Communication Strategy

Although much of the health communication that will need to occur during an outbreak will depend on the specifics of the outbreak, there are planning steps that can be taken by the coordinating committee prior to the outbreak.

1. Assign a person or an organization to be in charge of health communication for ease during an emergency. This is usually a government-appointed official. Having a single spokesperson to deal with the media minimizes confusion. Preferably, this spokesperson will have a clear understanding of the whole situation and be able to deliver the information in a culturally sensitive manner.

2. Establish a way to disseminate important epidemiological findings
   a. To the health care community
   b. To the public
   c. To partners responding to the epidemic

Identify partners early and create a list of contact information (address, phone numbers, e-mail, etc.). Contact information should be frequently updated.

3. Devise a plan for disseminating information to the public. Take into account cultural and logistical factors specific to the local setting.

Determine what methods for information dissemination are already in use and what is effective. Some examples are:

- Media (TV, radio, newspaper)
- Flyers (need to determine where they will be disseminated. Include pictures to aid those who are unable to read.
- Posters (need to determine where they will be hung and include pictures to aid those who are unable to read).
- Loudspeaker announcements
- Announcements at religious gatherings
- Door-to door announcements (time-consuming)
-
-

4. Create a list of basic health messages that will apply to all diarrheal disease prevention.

Consider using the existing WHO messages for prevention in a diarrheal outbreak. If you do use these, remember to present them in a culturally appropriate way, including using pictures, the local language, and making them religiously and ethnically neutral.

WHO messages for the community to avoid diarrhea (10):

- Wash your hands with soap
  - After using toilets/latrines
  - After disposing of children's feces
  - Before preparing food
  - Before eating
  - Before feeding children
- Boil or disinfect water with chlorine solution
- Only eat freshly cooked food
- Do not defecate near water sources
- Use latrines and keep them clean
- Peel it, cook it, or leave it

5. Devise a plan to disseminate updated information during the outbreak

Remember to give enough information so that rumors will not evolve out of confusion, but not too many details, as to cause confusion. Messages should be simple and clear and might include the following:

- Who is getting sick
- What disease is causing sickness
- Where people are getting sick
- When and where people should seek medical help
- How to prevent illness
- What to do at home if someone is sick

Summary of Health Communication Necessary Characteristics (the 5 C's)

- Clear and simple
- Correct (so both the sender and the receiver of the message interpret it the same)
- Concise and specific (minimum words, no ambiguous or extraneous information)
- Complete (no room for assumptions)
- Credible

Chapter 7.5 - Preparing to Establish Treatment Facilities

During an outbreak, there will be a significant increase in the number of patients that health care facilities and workers will see in a day. It will be the responsibility of the coordinating committee or of the health care managers to determine if the current facility can accommodate for this new influx of patients or if new facilities need to be established (reminder: you can use the estimated attack rate calculations in section 2.3-Epidemiology of Cholera, and the population to determine how many patients you expect to see). Furthermore, in coordination with the epidemiology team, it should be determined if there are areas affected by the outbreak that do not have adequate access to treatment and how to address this issue.

Based on the needs of the community, there are two types of treatment facilities that can be established. The first type is an "outpatient ORS site" where low-level heath care workers can give ORS and antibiotics (in the case of shigellosis), record attack rate information and instruct the community on using ORS and good hygiene practices. This is best suited to treat mild cases of cholera, identify cases that need to be transferred to the health facility, and treat cases of shigellosis that do not need to be hospitalized.

The second type of treatment facility is the treatment center/hospital where a group of health care workers, including physicians, nurses and aides, can care for patients who need hospital care. This facility would care for cases of dehydration in the case of cholera, and for cases of shigellosis that require hospitalization. The treatment center may be a section of an existing hospital or health center or it may be a makeshift facility.

Rapid access to treatment centers is crucial in the management of cholera; many deaths are easily avoided if treatment is delivered promptly. For remote areas where travel to a hospital is difficult or in areas where there is no hospital, many deaths from both cholera and shigellosis can be avoided by establishing a makeshift treatment center during an epidemic (11). Most cholera deaths occur when patients do not seek medical care or when a facility is too far away. It is best to have country-specific guidelines established before an epidemic so that the makeshift treatment center can be up and running promptly.

1. Designate specific treatment facilities
2. Provide locally appropriate case management charts to treatment facilities including current recommendations for antibiotic use
3. Ensure that proper supplies are available in treatment centers (see WHO minimum supplies list)
4. Determine at risk populations due to medical complications and/or lack of access to treatment facilities because of money, cultural reasons, or distance and formulate a plan to provide services to these populations
5. Conduct regular refresher courses on managing acute diarrheal outbreaks

Where to set up a center

A treatment center is most useful when it is in a central location to maximize utilization in an area that has low access. Although an existing health post or outpatient facility would be ideal, any place that is central and has room for large numbers of people will suffice if an existing facility is not available. Options include schools, religious centers, or community centers, which can be designated before an emergency and supplied with buffer stocks for rapid initiation of treatment. Tents can also be built if there is a lack of existing facilities, but this is not ideal.

An “ORS station” should be in areas that have low access to the full treatment center, or in areas where the burden of disease is too high for the hospital to manage. This can be located anywhere from a health workers house, to a table under a tree, or to a school or other community building.

Resources needed:

The resources needed to operate a treatment center during an outbreak of diarrhea are on the WHO supply list, however, the main essential components of a treatment center are the following:

1. Running water/close proximity to water source
2. Large quantities of safe water (40-60 liters per patient per day)
3. Adequate waste disposal system
4. Shelter from weather
5. Recording form for demographic information and patient status
6. Medicines, IV and oral rehydration fluids and other supplies
7. Trained staff including physicians, nurses, and aides

The main resources needed for an “outpatient ORS site” are the following:

1. ORS packets
2. Clean water
3. Recording form for demographic information
4. Antibiotics (in the case of a shigellosis outbreak)
5. Zinc
6. Trained staff (health workers or nurses)

Additional items for an “outpatient ORS site” if the budget allows:

1. Soap to give to families (especially in the case of a shigellosis outbreak)
2. Means of transport to the site (ambulance, horse, rickshaw, etc.) and communication (radio, telephone) with the treatment facility for patients that need to be transferred

Chapter 7.6 - Emergency Water, Hygiene and Sanitation Needs

Although sanitation plays a pivotal role in every kind of disaster, there are important factors to consider that are specific to cholera and shigellosis outbreaks. For both diseases, clean water and waste management are crucial as well as attention to hand washing and personal hygiene. For both diseases it is crucial to develop a system for monitoring and collecting data. For example, determine how much clean water per person per day the community is able to provide and the incidence and prevalence of cases.

One very effective way of providing clean water to a large population during an outbreak is to use point of use water purifying techniques. For example, Procter and Gamble makes a product called PuR, which is a packet that can be distributed to households to reduce turbidity and purify water so that it is safe for drinking. Generic versions of this may become available in the near future. Products like PuR are especially useful in an acute situation to provide clean water without the need for bacteriological or chemical studies and to prevent contamination at a centralized site.

There are many ways to supply clean water (boiling, ozonation, filtration, etc.), but chlorine is the most readily available and widely used chemical disinfectant for water supplies. The aim of chlorination is the destruction of pathogens and the protection of the water supply. Leaving a residual chlorine dose gives protection against further contamination. However, if the chlorine levels are too low, some pathogens may still survive. A free chlorine residual of 0.2-0.5 mg/liter in the disinfected water after a contact time of 30 minutes will inhibit the subsequent growth of organisms. A higher residual will also inhibit growth, but may give an unpleasant taste so that people do not want to drink the “safe water”.

In developing countries and specifically in disaster situations it can sometimes be difficult to ensure that the supplies you buy are what their label claims they are and that the items have not spoiled. For this reason, it is essential to test the chlorine residue even if you are using standard amounts of chlorine, because the potency may be lower. It may also be useful to buy name brand chlorine to ensure potency, albeit at a higher price.

A precondition for effective chlorination is that the turbidity of the water is low. In an emergency water supply, the aim is to have a turbidity of less than 5 NTU (nephelometric turbidity units). Chlorination will function relatively effectively up to 20 NTU but steps should be taken to reduce turbidities as soon as possible. At higher turbidity levels, larger quantities of chlorine are needed to oxidize the organic matter present. Some pathogens inside the organic matter particle may survive the oxidizing effect.

- Immerse your arm totally into the water and if you can see your fingertips the turbidity is probably less than 5 NTU.

The microbiologist should test the water for the bacterial coliform, chlorine and aluminum concentrations. In some parts, it may be necessary to test for iron. If the camp has a pipe water system, always make sure that the water is chlorinated.

- The easiest way to get rid of iron is to add air, by, for example, letting the water flow over some clean steps.

Chapter 7.7 - Operating a Diagnostic Laboratory

The role of a diagnostic laboratory in an outbreak of diarrhea is important and multi-faceted. During an outbreak, the laboratory should not be focused on the individual patient, but on its public health role in developing the best overall treatment policy based on the most common organism identified and its antimicrobial sensitivity.

Communication between laboratories and public health professionals is very important because of their inter-dependency. In some cases, the outbreak will be suspected by clinical suspicion, which then needs laboratory confirmation. In other cases, the laboratory may notice an increase in a certain type of specimen, which needs a clinical correlation. In either case, good bilateral communication is necessary. Finally, the lab can provide data on changing antimicrobial sensitivities, which can occur during the same outbreak and which can directly affect treatment efficacy.

In the past, 'laboratory confirmation' has been limited to growth on selective media. However, a rapid dipstick is now available for detecting cholera directly from rice water stool. This dipstick is available from Span Diagnostics (12) and the test does not need to be performed by a specialist. This dipstick can be used on a representative sample of specimens to confirm *V. cholerae* as the cause of the outbreak and the test results are available in only 5 minutes. A sample of the positives samples MUST still be sent to a reference laboratory for confirmation by culture and antibiotic sensitivities. The dipstick is incredibly useful for rapid diagnosis of cholera, but the gold standard for diagnosis is still growth on selective media for *V. cholerae*.

At least one laboratory in the country should have the capability to isolate and identify pathogens that cause epidemic diarrhea (especially *V. cholerae*, *S. dysenteriae* type 1, other shigella species and *E. coli* O157:H7 (13)) and perform antimicrobial sensitivity tests. In some cases, smaller laboratories may have the capability to isolate and identify organisms but need to send samples to the national laboratory for antimicrobial sensitivity testing. If there is no laboratory in the country with this capability, then a partnership can be established with an international reference laboratory (see "contacts" section for a complete list). The international reference laboratory should also be used to confirm findings and to further investigate atypical strains or unusual antibiotic resistance patterns.

Either the national laboratory or the international reference laboratory can train technicians at other laboratories in the country, or health personnel where there is not a laboratory, on how to properly collect and transport specimens, and sometimes on how to run the analysis themselves. This "training" laboratory should also be involved in quality control and improvement, as it is better to have only one good quality laboratory than many bad laboratories that give erroneous results, which could adversely affect the clinical treatment plan (14).

The coordinating committee for diarrheal outbreaks should ensure that laboratories designated to investigate potential outbreaks have an adequate amount of supplies. In addition, treatment facilities should have adequate supplies for the collection and transport of samples at all times.

A protocol should be developed before an outbreak occurs to determine how many samples should be investigated at the laboratory. The main steps of clinical investigation are confirmation of the outbreak, initial antimicrobial sensitivities, monitoring antimicrobial sensitivities, and monitoring the duration of the outbreak. It is important to mention that standard monitoring of environmental samples for *V. cholerae* by growth on selective media or by use of a dipstick are often ineffective because of the high rate of false negatives in environmental sampling for *V. cholerae*. Therefore, environmental monitoring for *V. cholerae* is often ineffective. Culture methods and dipsticks are best used for patient diarrheal samples.

The following general suggestions can be adapted to local practice:

1. If there is a clinical suspicion of an outbreak a minimum of **5-10** initial stool specimens should be sent to the laboratory for confirmation
2. To create an antibiotic use policy, the first **30-50 isolates** from an outbreak should be tested for antimicrobial sensitivity
3. After the initial antibiotic pattern is established, a representative **20-30 samples should be sent every month** (before antibiotic treatment given) from both hospitalized and non-hospitalized patients with the clinical syndrome to monitor changing antibiotic resistance
4. A representative sample of **10-20 isolates** (or 5% of all patients, whichever is more) should be sent periodically to an international reference laboratory for confirmation of the antimicrobial resistance pattern and possibly for additional studies (sub-typing and further molecular analysis)
5. At the end of the outbreak, about **20 samples** should be collected to confirm that new cases of diarrhea are not epidemic cholera or shigellosis.
6. Collect a representative sample by collecting a systematic sample. One method is to collect from every 10th patient. Another method is to collect specimens from all diarrhea patients every 15 days. These numbers can be adjusted according to the size of the outbreak so that the 10-20 samples needed are collected. If you find that you are having less than 100 patients a month, then collect more frequently (i.e. every 5th patient).
7. An area can be declared cholera-free after two times the incubation period (10 days) has passed without isolating cholera. However, due to seasonal variation in both cholera and shigellosis, monitoring in hospitals should continue for a year because of the notorious nature of these diseases to arise long after they have been declared 'gone.'
8. Remember that *V. cholerae* keeps well if it is kept moist and can survive a week in a Cary-Blair medium. However, *Shigella* spp. are fragile and difficult to recover if transport time exceeds 1 day.

See Appendix 7A and 7B for a list of Laboratory Supplies for cholera and Shigellosis

Summary of planning steps for the coordinating committee: Laboratory Facilities

1. Obtain rapid test (dip sticks) and have on hand in case an epidemic occurs.
2. Create a list of all available laboratories which have the capacity to:
   a. Culture and type both *V. cholerae* and *Shigella* spp.
   b. Determine antimicrobial sensitivities
3. Create a system for where stool samples should be sent, either locally or abroad and contact information
4. Provide information/training on collection and transport of samples where there is no on-site laboratory services
5. Provide information/training on how many and which samples should be sent for laboratory diagnostics.

Chapter 7.8 - Conclusion Box

1. Assessment and coordination between the local community and local and foreign aide are essential to ensure that the community receives what is needed without duplication or neglecting areas of need.

2. Surveillance programs should be established in order to categorize the extent of the outbreak and analyze who is at risk (and why) in order to stop the spread, provide appropriate services and prevent future outbreaks.

3. Effective communication between different aide partners and with the local community is essential to any epidemic control situation.

4. Either current facilities, new temporary facilities or both should be prepared to treat the suspected number of outbreak patients with adequate supplies and staff.

5. A system that is appropriate to the setting must be established to provide sanitary living conditions and a minimum of 20L of water per person per day in an emergency situation.

6. Determine which laboratories have the capabilities to isolate/identify and determine the antimicrobial sensitivity of *V. cholerae* and *Shigella* spp. Establish a system for where and when to send samples.

7. Utilize rapid test (Dip sticks) to confirm a representative sample of specimens as being cholera. It is not necessary to test every patient, only a sufficient number to confirm the outbreak.

Appendix 7A - Laboratory Supplies for cholera

Laboratory Supplies Cholera (15)
Assumptions:
Each district will collect and transport 50 samples
Each regional laboratory will process 100 specimens
Each national reference laboratory will confirm 500 specimens

Cholera

District level:

- 100 cotton swabs
- 50 bottles or tubes of Cary-Blair or other transport media
- Transport for specimens to regional laboratory

Optional: Rapid test for *V. cholerae* by cholera dipstick (12)

Regional Level:

- 200 sterile cotton or polyester swabs
- 500 g of Cary-Blair or other transport media
- 500 g TCBS medium
- 25 g sodium desoxycholate
- Glass slides for serologic testing (at least 500 or 20 boxes of 25 slides)
- 5 g *N,N,N',N'*-tetramethyl-D-phenylenediamine dihydrochloride (oxidase reagent)
- Filter paper for oxidase test
- Sterile wooden sticks or platinum inoculating loops for oxidase test
- 500 g nonselective agar (not nutrient agar because some formulations have no added salt and do not allow for optimal growth of *V. cholerae*)
- 4 x 2 ml polyvalent *V. cholerae* O1 diagnostic antiserum
- 500 g Bacto-peptone medium
- 500 g NaCl
- NaOH
- pH paper or pH meter
- 500 disposable petri dishes (9 cm)
- 1,000 disposable test tubes (e.g. 13 x 100 mm or 16 x 125 mm)
- Transport for specimens to reference laboratory
- Materials and postage for production and dissemination of reports

Optional: Rapid test for *V. cholerae* by cholera dipstick (12)

National Level:

Confirmation

- 500 sterile cotton or polyester swabs
- 5 x 500 g Cary Blair or other transport media
- 5 x 500 g TCBS medium
- 5 x 25 g sodium desoxycholate
- Glass slides for serologic testing (at least 500 or 20 boxes of 25 slides)
- 5 x 5 g *N,N,N',N'*-tetramethyl-D-phenylenediamine dihydrochloride (oxidase reagent)
- Filter paper for oxidase test
- Sterile wooden sticks or platinum inoculating loops for oxidase test
- 5 x 500 g nonselective agar (not nutrient agar because some formulations have no added salt and do not allow for optimal growth of *V. cholerae*)
- 20 x 2 ml polyvalent *V. cholerae* O1 diagnostic antiserum
- 5 x 2 ml *V. cholerae* O139 diagnostic antiserum
- 5 x 2 ml *V. cholerae* O1 serotype Ogawa diagnostic antiserum
- 5 x 2 ml *V. cholerae* O1 serotype Inaba diagnostic antiserum
- 5 x 500 g Bacto-peptone medium
- 5 x 500 g NaCl
- NaOH
- pH paper or pH meter
- 5 x 500 disposable petri dishes
- 5 x 1000 disposable test tubes (e.g. 13 x 100 mm or 16 x 125 mm)

Optional: Rapid test for *V. cholerae* by cholera dipstick (12)

Antimicrobial susceptibility for 100 isolates

- 2 x 500 g Meuller-Hinton Agar
- 200 disposable petri dishes (9 cm)
- Antimicrobial disks (100 of each)
    - Chloramphenicol
    - Tetracycline
    - Erythromycin
    - Trimethoprim-sulfamethoxazole
    - Azithromycin
- Control strains (susceptible and resistant)
- 0.5 McFarland turbidity standard
- Sterile cotton swabs
- Sterile saline
- Forceps and 95% alcohol for flaming
- Zone size criteria chart
- Materials and postage for production and dissemination of reports

Appendix 7B - Laboratory Supplies for Shigellosis

Laboratory Supplies Shigellosis (15)
Assumptions:
Each district will collect and transport 50 samples
Each regional laboratory will process 100 specimens
Each national reference laboratory will confirm 500 specimens

Shigellosis:
District level:

- 100 cotton swabs
- 50 bottles or tubes of Cary-Blair or other transport media
- Transport for specimens to regional laboratory

Regional Level:

- 200 sterile cotton or polyester swabs
- 100 bottles or tubes of Cary-Blair or other transport media
- 500 g XLD medium
- 500 g MacConkey medium
- 500 g Kliger iron agar
- 500 g motility agar
- 500 g nonselective agar
- Diagnostic anti-sera:
    - 4 x 2 ml monovalent *S. dysenteriae* serotype 1 (not Group A polyvalent)
    - 2 x 2 ml polyvalent *S. flexneri* (Group B)
    - 2 ml polyvalent *S. sonnei* (Group D)
- Glass slides for serologic testing (at least 500 or 20 boxes of 25 slides)
- 500 disposable petri dishes (9 cm)
- 1,000 disposable test tubes (e.g. 13 x 100 mm or 16 x 125 mm)
- Transport for specimens to reference laboratory
- Materials and postage for production and dissemination of reports

National Level:
Confirmation

- 500 sterile cotton or polyester swabs
- 5 x 500 g Cary Blair or other transport media
- 5 x 500 g XLD medium
- 5 x 500 g MacConkey medium
- 3 x 500 g Kliger iron agar
- 3 x 500 g motility agar
- 3 x 500 g nonselective agar
- Diagnostic anti-sera:
    - 20 x 2 ml monovalent *S. dysenteriae* serotype 1 (not Group A polyvalent)
    - 10 x 2 ml polyvalent S. *flexneri* (Group B)
    - 5 x 2 ml polyvalent *S. sonnei* (Group D)
- Glass slides for serologic testing (at least 500 or 20 boxes of 25 slides)
- 5 x 500 disposable petri dishes
- 5 x 1000 disposable test tubes (e.g. 13 x 100 mm or 16 x 125 mm)

Antimicrobial susceptibility for 100 isolates

- 2 x 500 g Meuller-Hinton Agar
- 200 disposable petri dishes (9 cm)
- Antimicrobial disks (100 of each)
    - Pivmecillinam
    - Ciprofloxacin (or other fluoroquinolones)
    - Ceftriaxone
    - Azithromycin
- Control strains (susceptible and resistant)
- 0.5 McFarland turbidity standard
- Sterile cotton swabs
- Sterile saline
- Forceps and 95% alcohol for flaming
- Zone size criteria chart
- Materials and postage for production and dissemination of reports

Chapter 7.9 - References

1. World Health Organization, Cholera Outbreak: assessing the outbreak response and improving preparedness. Global Task Force on Cholera Control,

2. These topics will be discussed more completely in the relevant sections of “Before an Outbreak” and “During an Outbreak.” For a more complete list please see, “Controlling Cholera: a checklist for planners” created by BASICS in the ‘virtual classroom’ section.

3. BASICS, Controlling Cholera: A checklist for planners. Basic Support for Institutionalizing Child Survival 1996

4. WHO. Cholera Outbreak: assessing the outbreak response and improving preparedness. 2004 Global task force on cholera control, World Health Organization.

5. WHO. Cholera outbreak: assessing the outbreak response and improving preparedness. 2004 World Health Organization

6. WHO. Guidelines for cholera control. 1993 World Health Organization

7. WHO. Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* type 1. 2005 World Health Organization

8. Free epidemiology software available at: www.cdc.gov/epiinfo.

9. Mapping tools: http://www.who.int/health_mapping/tools/healthmapper/en/index.html.

10. WHO. First steps for managing an outbreak of acute diarrhea. 2004 WHO Global task force on cholera control. WHO/CDS/CSR/NCS/2003.7 Rev.1

11. Siddique AK, Matsuddy P, Akram K, Islam Q, Zaman K, Majumder Y, Guidelines for operating makeshift treatment centres in cholera epidemics. 1997, ICDDR,B Special Publications No. 61, Dhaka, Bangladesh

12. Diagnostic Dip Stick for *V. cholerae*. 173-B, New Industrial Estate, Udhna, Surat - 394 210, INDIA. (Website : www.span.co.in)

13. CDC, Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera, Centers for Disease Control and Prevention, 1999. Atlanta, Georgia.

14. WHO, Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* type 1. World Health Organization 2005. Geneva, Switzerland.

15. CDC, Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera, Centers for Disease Control and Prevention, Atlanta Georgia 1999.

Chapter 8.1 - During an Outbreak Introduction

This section will be the most practical section in that this section will discuss the steps neccessary to take during an outbreak or crisis situation.

In the small sections to follow, the topics discussed will provide practical knowledge in the main aspects of outbreak control for diarrheal disease.

- Coordination and initial response to an outbreak
- Epidemiology and monitoring
- Health communication
- Treatment facilities
- Ensuring proper water and sanitation
- Use of the diagnostic laboratory
- Chapter conclusion
- Quiz questions

Chapter 8.2 - Coordination and Initial Response to an Outbreak

As discussed in the coordination section of "Before an Outbreak," a coordinating committee should exist anywhere that cholera or shigellosis outbreaks have been known to occur, or in emergency situations where the risk of a diarrheal outbreak is high. However, if a coordinating body does not exist when an outbreak occurs, the first priority is to establish a special task force with decision-making capability to coordinate relief efforts.

These categories are not in a particular order of importance; certain activities in each category may be of greater importance than other activities, depending on the location and specifics of the outbreak. Please refer to the sections on each topic.

1. Initial Response to Suspected Outbreak
2. Epidemiology and Surveillance
3. Case Management
4. Water and Sanitation
5. Laboratory
6. Communication

Overview:
The coordinating committee/special task force needs to involve all the stakeholders in a situation to determine the best course of action. The stakeholders who should be involved in varying capacities are the community members (local populations/refugees/ internally displaced persons), neighboring communities, governments, warring parties/army, multilateral agencies and donors, and service providers (such as NGOs and government organizations). The WHO recommends meeting daily at the local level and at least weekly at a national level during an outbreak (1).

1. Initial Response to Suspected Outbreak:

In the case of a suspected outbreak, a team must be sent to confirm the outbreak and make an assessment report of the situation in order to plan accordingly. Ideally an emergency response team would already be formed, but if not, one must be formed immediately.

Intravenous, rather than ORS rehydration, should be used in the following circumstances:

1. A **physician** who can confirm clinical signs and symptoms and train health workers in proper case management
2. A **microbiologist** to take stool samples for laboratory confirmation, train health workers in correct sampling and confirm proper techniques by laboratory technicians
3. An expert in **behavior change communication** (BCC) who can assess the population's reaction to the outbreak and create and disseminate appropriate health messages
4. An **epidemiologist** to monitor proper data collection and surveillance procedures
5. A **water and sanitation expert** who can assess the situation and develop a plan to reduce sources of contamination (2)

There may be cases where only 1-2 people are available to be a part of the response team. In that case, the team members must be aware of all necessary investigations and priority interventions, even if these are not their field of expertise. This response team should confirm the outbreak and then create a brief assessment report to notify the local health board, and the WHO (see "contacts"). Click here for a WHO template for an assessment report. More about updating health professionals and the community will follow in the communication section.

The remaining steps for dealing with an outbreak will all be covered in detail in their respective sections. Here the main activities are briefly explained for management purposes.

WHO list of critical information needed for an assessment (3):

1. Description of the disaster (man-made, natural) and speculative evolution
2. Geographical description of the area (climate, water sources, topography)
3. Accessibility (road quality, especially as changed by weather patterns, harbor and airport access, security issues)
4. Population size (permanent, refugee/displaced persons, age and gender distribution, expectation of new arrivals in terms of numbers and date)

2. Epidemiology and Surveillance

1. Pathogen characteristics: The initial stool samples taken by the Rapid Response/ Confirmation team should be examined for the causative organism as well as antimicrobial resistance. This can be done with a rapid test and then a representative group of the positive samples could be cultured and the sensitivity pattern determined. As the outbreak continues not every patient's stool needs to be examined, but a monthly representative sample should be used to monitor the progress of the outbreak in terms of its antimicrobial resistance pattern. Any changes in the antimicrobial resistance pattern should be announced to the health care providers and incorporated into updated treatment guidelines.

2. Patient characteristics: The epidemiology team should report aggregated figures of cases and deaths grouped by under 5 years and 5 years and older to the coordinating committee at each meeting. In addition, location of patients and accessibility to treatment facilities should be assessed to plan for temporary treatment centers as needed.

3. The case fatality rate (CFR) should not be >1% for cholera or shigellosis outbreaks. If the CFR is >5%, an investigation needs to be undertaken to determine if this is the result of bias or inadequate case management, and then the team must make necessary changes (4).

4. Outbreak longevity: An additional suggested surveillance approach investigates the prevalence of the outbreak pathogen in all patients with diarrhea, both in the hospital AND AT HOME. If this is not done throughout the outbreak, it should be done at the suspected end of the outbreak to confirm that the outbreak pathogen is no longer causing disease in the community.

5. All epidemiological surveillance data should be shared with national and international partners.

3. Case Management

1. Treatment facilities: The coordinating body should ensure that there are adequate treatment facilities available and accessible to the majority of patients. As per the "Before an Outbreak" section, sufficient supplies should be provided before an outbreak. The epidemiological team should be able to provide information as to which vulnerable areas have poor access and need temporary treatment facilities. These treatment facilities should be adequately staffed with trained personnel, and training should be organized if needed.

2. Supplies: It is very important to have a coordinating group that can liaison with suppliers, donors, and diplomatic and consular representatives abroad to inform them of what is needed, identify and screen aide offers, reduce the number of inappropriate donations, and ensure arrival of supplies at the right place and time. Meet with representatives of the affected communities, service providers and government to determine what should be done when, where, and by whom. Exchange information on resource availability to ensure financial support for logistics and supplies and coordinate donations of supplies and personnel as needed. In addition to the procurement of supplies, the supplies need to be mobilized in a timely fashion to the area of need.

3. Treatment guidelines: Create and disseminate a national policy on treatment if one does not exist or if the antimicrobial sensitivities have changed.

4. Water and Sanitation

1. Water: The water team should ensure safe water on the order of 15-20 liters per person per day for the residents in an area/refugee camp, and 40-60 liters per person per day for patients in a diarrheal treatment facility. Additionally, the water team should continue to monitor bacteriological quality to ensure that the supply remains safe.

2. Waste management: In the community, latrines should be provided to all and maintained. In the treatment facilities, waste management is paramount to ensure that the outbreak is not perpetuated. Make sure that all facilities are adequately disinfecting their waste products.

3. Hygiene: Provide health messages to the community to teach personal hygiene practices to prevent the spread of disease. Ensure that the families can follow these recommendations by providing soap for all families.

4. Miscellaneous: Ensure safe practices at funerals. Especially in the case of shigellosis, monitor food quality. If food handling and processing in the streets cannot be safe then stop the selling of pre-cooked or pre-prepared foods.

- In each location, different prevention measures may be controversial depending on the culture of the population and the means of implementing the measure. Please weigh the potential complications of changing funeral practices or prohibiting the sale of prepared food with the benefit they might bring. If you decide that a practice is significantly contributing to the epidemic, make sure you discuss with community leaders as to how best avoid the spread with the least controversy, disruption to daily life, and resistance.

5. Laboratory

1. Partnership: Establish a partnership with an international reference laboratory to confirm results and to use if facilities in the area do not have the necessary capabilities (see the contacts section).

2. Training: Verify that the local laboratories in use have technicians that are adequately trained in the required techniques and consider training if necessary.

3. Supplies: Ensure that all local laboratories in use have adequate stocks of the supplies needed for collection, transport and evaluation based on the national guidelines.

4. Guidelines: Create and disseminate national guidelines on the methods of surveillance, means of collection and transport, and where to send specimens. Laboratories should be identifying the organism and verifying the antimicrobial sensitivity pattern.

6. Communication

1. Messages to the community on healthy practices, hygiene, care seeking, and an update on the situation.

2. Information to health professionals

3. Updates to partners

In areas where mobile networks are widespread, consider giving mobile phones to partners for ease in communication.

Chapter 8.3 - Epidemiology and Monitoring During an Outbreak

Please see the "Before an Outbreak" section if further clarification is needed on the following previously discussed topics:

1. Establishing a national surveillance system
2. Creating a case definition for shigellosis and cholera
3. Establishing a reporting system
4. Establishing a method for compiling data
5. Identifying likely contributors to transmission
6. Identifying groups at high risk for mortality

Cholera/Shigellosis outbreak definition: an increase from previous years or weeks in cases of culture-proven *V. cholerae* or *S. dysenteriae* type 1 in endemic communities, or any culture-proven case where the disease is not endemic

Step 1: Determining if an outbreak is occurring:
The initial "rapid response team" must get laboratory confirmation of an outbreak suspected clinically from the first 10-20 cases. It is not necessary to perform laboratory tests on all cases with the clinical syndrome during an outbreak. The rapid test for cholera can be useful in confirming the cause of the outbreak and representative stool samples can be sent on transport media to the laboratory for confirmation and for antibiotic sensitivity.

Step 2: Describe the outbreak:

1. Begin by describing how the outbreak was suspected, whether from a cluster of cases, a single case, or an incidence greater than the same period in previous years.

2. Using the clinical case definition, collect data about the patients from treatment centers. If possible, data from community health volunteers about patients not coming to the hospital is very useful. It is useful to use a standardized admission information sheet like the one found in our 'virtual hospital' in the 'knowledge base' section. Compile this data and describe the outbreak in terms of:
   a. Attack rate (cases/1000 susceptible population)
   b. Geographical extent
   c. Case fatality rate (CFR), including age and gender CFR distribution
   d. Gender distribution of cases
   e. Age distribution of cases (separate into two groups: under 5 years and 5 years and above)

3. Speculate about the probable evolution of the outbreak (i.e. how many people might be affected, which locations might be affected, how this might influence the economy, health systems, and migration of people, among other factors).

4. Discuss special considerations for this particular outbreak
   a. Cultural issues
   b. Social structure
   c. Political situation
   d. Security
   e. Vulnerable populations
   f. Coping ability of population

- You can practice analyzing an outbreak with the outbreak investigation exercise in the virtual classroom.

Step 3: Coordinate with the communication team
Disseminate important epidemiological findings, including the assessment report, the prediction for how the outbreak might evolve, and special considerations for the population affected.

Step 4: Monitor the progress of the outbreak
Although you don't need laboratory samples on all patients once the organism is defined and you have devised a case definition, you need to know about any changing antimicrobial sensitivity. Therefore, at least every month, about 10-20 samples (or 5% of all patients, whichever is more) should be examined for organism strain type and antimicrobial sensitivity. It is important that these samples are collected randomly. A good way to collect a random sample is to collect from every 10th patient, but other methods can also be used as suggested above. The method chosen should be adjusted according to the size of the outbreak so that the needed 10-20 samples are collected. If you find that you are having less than 100 patients a month, then collect more frequently (i.e. every 5th patient). The results need to be reported to the coordinating committee to update the clinical guidelines if needed.

Also, to confirm the end of the outbreak, collect about 20 samples. Even in an endemic area, cholera or shigellosis should account for less than 5% of all acute diarrhea cases when an epidemic is not occurring.

Step 5 (optional): Active case finding/ Creating a study

Although not required, we recommend active case finding activities. Even if they are not laboratory confirmed cases, it is useful to find patients that fit the case definition during an outbreak who are not presenting to the hospital for some reason (remote area, lack of information, poverty, marginalized population). Minimally trained health volunteers can perform active case finding and disseminate ORS and information on the treatment of diarrhea. Information from active case finding can help to plan for where and when to establish makeshift treatment centers and ORS stations so that the maximum number of people can be treated. Remember that most cholera deaths occur in patients who do not come to the treatment center.

In some areas it will not be possible to complete an active surveillance for diarrheal pathogens. However, where it is feasible to randomly sample all diarrheal patients both at home and in the hospital during the outbreak, this is useful data to have. For example, every 20th patient could be sampled to watch antimicrobial sensitivity patterns, which might vary from inpatient and outpatient samples, and for causative organisms. To read more about creating a study, see the Centers for Disease Control and Prevention guide to "Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera" (5). Other data sources include verbal autopsies and data analysis through cluster surveys.

Active case finding to get more information about the patients that do not reach the treatment center.

Chapter 8.4 - Communication During an Outbreak

During an outbreak, it is important to communicate well with partners as well as with the community. The different approaches to reaching these two populations will be very different. In the "Before an Outbreak" section, we discussed in more detail ways to establish a communication strategy. This section will be a list of main points that need to be addressed immediately, as well as key messages that need to be communicated with the community.

The following are the first three essential steps to an outbreak communication strategy:

1. Assign a person or an organization to be in charge of health communication for ease during an emergency. Often this is a government appointed official with the Ministry of Health or the equivalent. Having a single spokesperson to deal with the media minimizes confusion. Where it is possible the spokesman should be available by mobile phone, e-mail or radio (24 hours a day, 7 days a week).

2. Establish a way to disseminate important epidemiological findings, including the assessment report, the prediction for how the outbreak might evolve, and special considerations for the population affected.

    a. To the health care community
    b. To the public
    c. To partners responding to the epidemic

3. Devise a plan for disseminating information to the public, taking into account cultural and logistical factors specific to the local setting.

Messages for the Community:

The main points for messages to the community should be:

- What the disease is
- Where the disease has been found
- Who has fallen ill from the disease (demographic information and numbers of people)
- How to prevent getting the disease
- What to do if you think you have the disease

Summary of Health Communication Necessary Characteristics

- Clear and simple
- Correct (so both the sender and the receiver of the message interpret it the same)
- Concise and specific (minimum words, no ambiguous or extraneous information)
- Complete (no room for assumptions)
- Credible

The above points 1-3 are situation dependant. Suggestions for points 4 and 5 are below. Remember to always adapt messages in a culturally appropriate manner and to make them relevant to the situation. For example, do not tell people in a refugee camp with few possessions that they should bleach a sick person's clothing and bedding. Instead, come up with practical alternatives such as boiling or burying them

WHO messages for the community to avoid diarrhea (9):

Wash your hands with soap:

- After using toilets/latrines
- After disposing of children's feces
- Before preparing food
- Before eating
- Before feeding children

Boil or disinfect water with chlorine solution
Only eat freshly cooked food
Do not defecate near water sources
Use latrines and keep them clean
Peel it, cook it, or leave it

Care seeking:

Caregivers should be informed to bring family members to a health facility if they have:

1. Many watery stools (more than usual)
2. Blood in the stool
3. Fever
4. Repeated vomiting
5. Marked thirst
6. Eating/drinking poorly

The community needs to know where the nearest health facilities are located. If you are using 'ORS stations' the community should be informed as to where such stations are located as well. In addition, messages about the prevention of dehydration and malnutrition during dehydration are important:

1. Give someone with diarrhea ORS
2. If ORS is not available, give home fluids
3. Continue feeding during diarrhea
4. Continue breastfeeding during diarrhea

ORS guidelines for maintenance hydration*:		
Age	**Approximate ORS amount following each stool; By milliliters (ml)**	**Approximate ORS amount following each stool; By household measures**
Children <2 years	50-100ml	10-20 teaspoons
2-10 years	100-200ml	½ - 1 glass
>10 years	As much as is tolerated	Minimum 1 glass

* In children: if the caretaker knows the weight of the patient, advise the patient caretaker to administer one teaspoon per kilogram of ORS for each loose stool. ORS should be given in small amounts (small spoons of 5ml for children <2 years and sips from a cup for older patients) frequently (every 1-2 minutes). If the patient vomits, wait 10 min. and continue to give ORS but more slowly.

If the caretaker knows the weight of the child advise him/her to give one teaspoon of ORS per kilogram with each loose stool.

The best home fluids to use are those that have salt, including soups like chicken broth, rice broth or gruel, or other fluids like natural juices, or green coconut water. Never give artificially sweetened drinks, like juice or colas, as this can make the diarrhea worse.

Chapter 8.5 - Operating Treatment Facilities

In the “Before an Outbreak” section we discussed the two main types of treatment facilities: “ORS stations” and hospitals/treatment centers. Where and when to establish these sites was also discussed. Please see that section for a review. This section will discuss the organization of both “ORS stations” and treatment centers.

“ORS stations”:
This is a very simple set-up that does not require divisional organization. Basically it entails having a nurse or trained health worker at a table with supplies. If there is active case finding, this person could perform the same tasks and reduce the burden of the station. The number of nurses/health workers should be determined based on the expected catchment area, and on whether there is active case finding. Ideally one person should not see more than 40-50 patients in one day. The worker should be able to perform the triage duties outlined in the ‘virtual hospital’ as well as health education about hygiene and proper ORS use.

Treatment centers:
It is helpful to split the treatment center into several different areas for rapid triage and efficient treatment and distribution of medical supplies and treatments (ORS, IV fluids, antibiotics and zinc, as needed). Please see our interactive ‘virtual hospital’ for more detail and printable job descriptions and sample forms.

1. Registration and Triage: Here there should be at least one person 24 hours a day and 7 days a week (please rotate between different people so nobody becomes overworked), who is trained in triage (preferably a nurse), and who can determine the patient’s level of dehydration and their risk factors (fast breathing, severe malnutrition, shigellosis mortality risk factors) and subsequent need for hospitalization. They should also record demographic information for reporting.

2. Treatment: This area should have an adequate supply of cholera cots for patients to lie on during observation. There should be a system so that physicians visit all patients at least twice a day, and that nurses are not assigned to too many patients. Assigning rows of patients to which you can add as new patients come is one often-used system. Another method, used at ICDDR,B is to tape the patient information to a new patient’s bed with a flag so it is visible and a doctor knows to check that patient. Service personnel should also have a system of removing the waste buckets promptly, but not before the nurse has recorded the amount of fluid purged.

3. ORS making area: There should be a third area in which ORS is prepared on a regular basis (so that it is not stored for more than 6 hours). Care must be taken to use safe water, clean containers and hygienic methods of preparation. Personnel working in this section should avoid contact with patients as much as possible. Preferably you should always assign the same people to this section so they become skilled in the preparation of ORS.

4. Waste management, chlorine solution preparation and laundry: This area will be in charge of waste treatment and disinfection. They can make the appropriate concentrations of chlorine solution at this location. They should also be trained in handling, disinfecting, transporting and disposing of dead bodies.

5. Health education section: Health education will most likely occur in the main hospital or any other space available, but it is an important part of the hospital’s activities in preventing further hospitalizations. This should not deter from life-saving measures, but added as staff time allows.

6. Kitchen: The kitchen area must be separate from the waste treatment area and will prepare safe water as needed and food for patients, if possible. In acute situations, there may not be the facilities or the supplies to prepare food and the patients’ families can provide it. However, in the long-term, it is desirable to control the spread of infection by providing safe food to patients and their caregiver. This can be in the same area as the ORS preparation section. Again, the people working in the kitchen should not be allowed to treat patients.

7. Security: Although not necessarily needing a separate section, security may need to be a vital part of any treatment facility to ensure that supplies are available and that patients and health care workers are not in danger. This is especially important in the case of an emergency setting during a man-made conflict.

8. Supplies: other supplies are managed. Inventory should be taken daily during an outbreak to ensure adequate supplies for the coming days.

See Appendix 8A for a list of supplies.

Chapter 8.6 - Ensuring proper water and Sanitation

This section will share a few important concepts about:

- Hygiene
- Water supply
- Water quality
- Latrines
- Funerals
- Food safety

General Tips:
Water *quantity* is just as important as water *quality*. First, ensure adequate water supplies, and then increase the quality of water.

Residual chlorine levels are very important to inhibit any subsequent growth of bacteria and give further protection depending on the local circumstances (e.g. climate, turbidity, personal hygiene). Make sure chlorinated water has a minimum of 0.2-0.5 mg/l of free residual chlorine. However, if people fetch the water at a central point, the free residual chlorine should be higher at 1.0-2.0 mg/L.

It is important to chlorinate water that is not turbid (dark and cloudy), because organic matter that causes turbidity will trap bacteria and prevent the chlorine from killing the pathogens. A rule of thumb is that if you immerse your arm completely in the water and cannot see your fingertips, you have to reduce the turbidity before chlorination.

Although in every kind of disaster event sanitation plays a pivotal role, there are important differences in the cases of cholera or shigellosis outbreaks. In the case of a cholera outbreak, the focus should be on the provision of clean water and waste management, whereas in case of shigellosis, the focus should be on personal hygiene. The reason is that shigellosis is transmitted more readily by hand-to-hand contact and only needs a low infectious dose for transmission. In both settings it is crucial to develop a system for monitoring and data collection. For example, it is important to collect data on how much clean water per person per day you are able to provide, as well as the incidence of the current disease outbreak.

Hygiene:
Soap should be made available to every household or at least to every patient in a treatment facility. Clean towels might be considered if there is an adequate budget – dirty towels can propagate disease. If you do not have clean towels, air-drying hands is safer. Clear messages should be given to the population to wash hands with soap after using latrines, before eating, before preparing food, before feeding children and after disposing of children's feces. The use of latrines must be emphasized.

Clean the bedding and clothes of anyone who is sick by boiling in water for 5 minutes. This should also happen at health facilities. There should be an area for laundry and for drying clothes and bedding. Ideally cholera cots in treatment facilities should be lined with plastic, which are easy to bleach with 0.05% disinfecting solution. Use the 0.05% disinfecting solution for cleaning the stool collection buckets and other equipment. Click here for information on mixing chlorine solutions.

At the ICDDR,B, there are different colored cot covers so that it is easy to ensure that the covers are replaced and cleaned daily. For example, the green cot cover is used on Monday and then Tuesday is changed to the red cot cover. It is then easy to see that any cots that are still green on Tuesday haven't been changed and need to be changed.

Try to prevent large gatherings of people, such as for celebrations, from happening during an outbreak. If the gathering is going to occur, make sure there are adequate latrines and safe water for the estimated number of people. If the gathering must include food, then ensure sanitary food preparation is practiced.

Making chlorine solution

Chlorine product	Hands and skin	Floors, clothes, bedding, equipment.	Body fluids** (Rice Water stool, Diarrhea, Vomit treated in large containers)
	Final concentration: 0.05% active chlorine	Final concentration: 0.5% active chlorine	Final concentration: 2% active chlorine. Wait at least 2 hours before dumping.
Household bleach (5% active)	0.1 liters of bleach to 9.9 liters of water (WRITE: 0.05%)	1 liter of bleach mixed with 10 liters of water (WRITE: 0.5%)	4 liters of bleach mixed with 6 liters of water (WRITE: 2%)
Household bleach (30% active chlorine)	Add 16 grams or 1 tablespoon to 10 liters of water (WRITE: 0.05%)	16 grams or 1 tablespoon to 1 liter of water (WRITE: 0.5%)	64 grams or 4 tablespoons to 1 liter of water (WRITE: 2%)
Calcium hypochlorite powder or chlorine granules (70% active chlorine)	7 grams or ½ a tablespoon to 10 liters of water (WRITE: 0.05%)	7 grams or ½ a tablespoon to 1 liter of water (WRITE: 0.5%)	28 grams or 2 tablespoons to 1 liter of water (WRITE: 2%)

* ALWAYS label the solutions with a permanent marker.
** Note that if chlorine is limited, body fluids can be treated with a final concentration of 0.5% chlorine, but the fluids must be held and occasionally stirred for at least 6 HOURS before dumping.

Water supply:
In an emergency setting, you should provide water according to the key indicators developed by Sphere (www.sphereproject.org):

- Water used for drinking, cooking and personal hygiene in any household is at least 15 liters per person per day.
- The distance from any household to the nearest water point should be no more than 500 meters.
- No one should wait more than 15 minutes at the water source for water.
- Water sources and systems should be maintained such that appropriate quantities of water are available consistently.

Simplified table of basic survival water needs		
Survival needs; water intake (drinking and food)	2.5-3 liters per day	Depends on: the climate and individual physiology
Basic hygiene practices	2-6 liters per day	Depends on: social and cultural norms
Basic cooking needs	3-6 liters per day	Depends on: food type, social as well as cultural norms
Total basic water needs	7.5-15 liters per day	

In contrast to household needs, you need 40-60 liters per patient per day in a hospital. It is important to also take into account the needs of the caretaker or family (not only the patient), who stay with the patient. For those caretakers you should calculate with 15-20 liters of water per person per day as well.

Water quality:
There are many ways to supply clean water (boiling, ozonation, filtration etc), but chlorine is the most readily available and widely used chemical disinfectant for water supplies. The purpose of chlorination is to destroy pathogens and protect the water supply. It is important to leave a residual chlorine dose to protect against further contamination. A free chlorine residual of 0.2-0.5 mg/liter in the disinfected water after a contact time of 30 minutes will inhibit the subsequent growth of pathogens, however it may not kill all pathogens (particularly *Entamoeba hystolotica*, *Giardia lamblia*). A higher chlorine residual will inhibit growth of all pathogens, but may give an unpleasant taste so that people don't want to drink the "safe water".

The turbidity of the water must be low for effective chlorination. In emergency settings, the aim is to have a turbidity of less than 5 NTU (nephelometric turbidity units). Chlorination will function relatively effectively up to 20 NTU but steps should be taken to reduce turbidities as soon as possible. At higher turbidity levels, larger quantities of chlorine are needed to oxidize the organic matter present. Some pathogens inside the organic matter particle may survive the oxidizing effect.

- Immerse your arm totally into the water. If you can see your fingertips, the turbidity is less than 5 NTU.

You should test the water for the content of bacterial coliforme count, chlorine and aluminum. In some areas it may be necessary to test for iron. If your camp has a piped water system, always make sure the water is chlorinated.

- The easiest way to get ride of the iron is to add air; for example, by letting the water flow over some steps prior to further treatment.

Latrines
Latrines are essential for controlling diarrheal outbreaks. Sphere recommends that a maximum of 20 people use each latrine (Please see the Sphere Handbook in the 'virtual classroom' section for complete recommendations). In the case of cholera or shigellosis outbreaks in areas with no existing infrastructure, building latrines is a top priority. In many settings, it will take some time to provide a toilet for every 20 people. In such cases it is feasible to start with public or community toilets and arrange for the creation of individual household toilets at a later time. There are special concerns for public and community toilets. For example, separate toilets for women and men should be provided in public places (markets, distribution centers, health centers, etc.). Disaggregated population data should be used to plan the ratio of women's latrines to men's latrines (of approximately a 3:1 ratio). When possible, urinals should be provided for men. Shared or public toilets should be cleaned and maintained in such a way that they are used by all intended users. However, it is often difficult to organize the cleaning of community toilets. Make sure you supply enough cleaning materials.

For safety (especially for girls and women at night) and convenience, toilets should not be more than 50 meters from dwellings. This is true for both household toilets and public or communal toilets.

Particular attention should be given to the disposal of children's feces, which are often neglected despite the fact that children are more susceptible to disease. Parents or caregivers need to be involved in the planning of latrines, and facilities should be designed with children in mind. It may be necessary to provide parents or caregivers with information about safe disposal of infant feces and diaper laundering practices.

Before you start building toilets, make sure that users (especially women) have been consulted and approve of the setting and design of the toilet. The Sphere standards recommend that toilets have the following features:

1) They are sufficiently easy to keep clean in order to invite use and do not present a health hazard.

2) They provide a degree of privacy in line with the norms of the users.

3) They allow for the disposal of women's sanitary protection, or provide women with the necessary privacy for washing and drying sanitary protection clothes.

4) They minimize fly and mosquito breeding.

5) All toilets constructed that use water for flushing and/or a hygienic seal have an adequate and regular supply of water.

6) Pit latrines and soak-aways (for most soils) are at least 30 meters from any groundwater source and the bottom of any latrine is at least 1.5 meters above the water table. Drainage or spillage from defecation systems must not run towards any surface water source or shallow groundwater source.

7) People wash their hands after defecation and before eating and food preparation.

8) People are provided with tools and materials for constructing, maintaining and cleaning their own toilets, if appropriate.

Funerals:
Funerals are often an overlooked means of transmission of disease during an outbreak. Make official recommendations about safe funeral practices and consider providing people trained in proper handling of corpses to attend funerals and either dispose of the body properly or supervise the practices of the family. The following are WHO recommendations for safe funerals of people who died of diarrheal disease during an outbreak.

1. Consider canceling all funeral feasts.

2. If the family/society does not agree with canceling feasts, ensure that the people who wash the body do not prepare the food and that the people who do prepare the food wash their hands thoroughly and follow hygienic practices.

3. If the body must be cleaned, use 2% bleach solution to clean the body and soak cotton wool with 2% bleach solution and put this in the mouth and anus.

4. Keep the mouth shut, wrapping a bandage around the head if necessary.

5. Do not empty the intestines.

6. Clean the clothes and bedding of the deceased by boiling in water for 5 minutes and then dry normally.

Remember, as with any changes or restrictions to cultural practices, a balance must be reached between preventing the most disease with the minimum distress to a community. For this reason, it is useful to engage community leaders to ensure acceptance and understanding of any cultural restrictions because if the community does not accept the rules then they will not be followed.

Food Safety:
Determine which local practices might be sources of spread of cholera or shigellosis, such as eating raw seafood or raw fruits and vegetables, and determine a way to control this source of spread. Then, create minimum standards for food handlers and determine a way to enforce these practices.

V. cholerae grows very well in moist foods at room temperature. Never keep milk, cooked rice, lentils, potatoes, beans, eggs, chicken, or seafood at room temperature for longer than one hour before eating. Avoid raw seafood.

Consider shutting down restaurants, markets and street vendors that sell prepared food, especially raw prepared food. If you decide not to restrict prepared food vendors, you can consider displaying a sign at those restaurants or vendors that inform people of the increased risk of diarrhea from eating raw food, especially during the outbreak. In addition, you could encourage sanitary behavior by installing latrines and hand-washing facilities in marketplaces.

Food safety needs to be encouraged in personal kitchens. Means of preventing the spread of infection include promoting kitchen cleanliness and food preparation by posting (or relaying) messages such as “cook it, peel it or leave it”. The kitchen area should be clean and raw and cooked foods should be kept separately to avoid contaminating previously cooked food. Also, canned, acidic and dried foods are generally safe choices to eat.

Breastfeeding is the most hygienic food of all! Breastfeeding should always be encouraged, and mothers should be taught to continue, and even increase, breastfeeding for a child with diarrhea.

Chapter 8.7 - Diagnostic Laboratory Techniques

During an outbreak, the two most important tests that the clinical laboratory can do are (1) identification of the causative organism by culture and/ or dipstick (optional), and (2) antimicrobial sensitivity testing of the pathogen. In an emergency setting there may not be time to train new laboratories how to complete these tasks. Therefore, if there is not a laboratory that is already isolating/identifying and determining the antimicrobial sensitivity of *V. cholerae* and *Shigella* spp., then samples should be sent to the nearest laboratory that has these capabilities. Alternatively, samples should be sent directly to an international reference laboratory (Please see the "contacts" section for a complete list). The coordinating committee should have created a policy to specify which laboratory the samples should be sent to. The laboratory and/or the coordinating committee should ensure that there are adequate supplies. Click here for a list of laboratory supplies.

This section will provide a basic overview for a laboratory, but this section is not meant as a comprehensive training guide for a laboratory. This overview is for a lab that already has the basic capacity to isolate/identify and determine the antimicrobial sensitivity of *V. cholerae* and *Shigella* spp. For more information please refer to the CDC manual on laboratory methods (7).

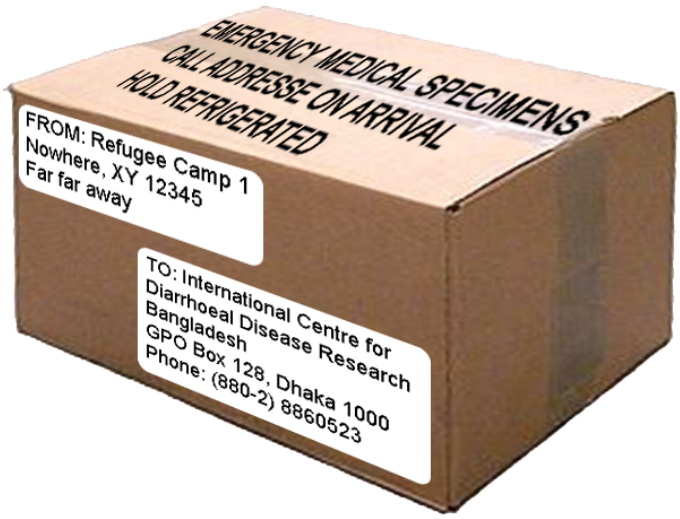
Pop-up text:
Cary-Blair is the recommended medium as it is available commercially and it can be stored for one year after preparation. It can be used for *Shigella* spp., *V. cholerae*, and *E. coli* O157:H7. Although Amies and Stuart's media can be used for *Shigella* spp. and O157:H7, Cary-Blair is better for cholera because of its higher pH (8.4). Alkaline Peptone Water (APW) is acceptable for *V. cholerae*, but only for about 6 hours, after which point other organisms will outgrow the *V. cholerae*. Buffered glycerol saline (BGS) is unsuitable for *V. cholerae*. BGS can be used for *Shigella* spp. However, BGS is not preferred since it is only good for one month and is liquid so it has a higher chance of spillage during transport.

Collection and transport of specimens for laboratory diagnosis (8):	
Who:	From a patient currently ill with diarrhea.
When:	As soon as possible after the onset of illness (preferably within 4 days) and before antibiotics are given.
How:	Rectal swab or fresh stool.
Transport media:	Cary-Blair is recommended if specimen cannot reach the lab within 2 hours. Click for further discussion of transport media.
What to do after collection:	If the specimen can reach the lab within 2 hours, carry in a leak-proof sterile container at ambient temperature. Cholera can be collected with a stool sample on tissue paper and transported if it is kept moist in a plastic bag. If the specimens will be received within 48 hours, refrigerate at 4°C. If it will take longer than 48 hours, freeze at –70°C. You can also run a rapid test for cholera on site prior to sending it for culture and sensitivities.
Transport:	Prevent the sample from leaking by sealing tubes/containers and place in a waterproof container. Ship in an insulted box with ice packs, wet ice (cannot last more than 36 hours) or dry ice by overnight delivery.

Transport:
If specimens are being sent to an international reference laboratory (see the "Contacts" section of the toolbar at the top of the screen) arrangements should be made ahead of time, including arrangements for immediate pick-up at the arrival airport. The receiving laboratory should also be able to help you to navigate the relevant regulations for their country and those regulations that pertain to certain couriers. If you plan to use a rapid test you should understand that some countries may regulate samples of known pathogens more strictly than those of medical samples with an unknown pathogen. The receiving person should be given the following:

1. Air bill number
2. Flight number
3. Times and dates of departure and arrival of the flight

Inside the package you should include a copy of the stool specimen data sheet. On the outside of the package you should clearly label the name and telephone number of the receiving laboratory and "EMERGENCY MEDICAL SPECIMENS; CALL ADDRESSE ON ARRIVAL; HOLD REFRIGERATED". See the example below:



Isolation/Identification Methods for *Shigella* spp.:
To isolate *Shigella* spp. you should use a low selectivity medium first and then a highly selective medium. However, at least 2 media - one of each type - must be used. The low selectivity medium of choice is MacConkey agar. The highly selective medium can either be xylose lysine desoxycholate (XLD), desoxydholate citrate (DCA) or hektoen enteric (HE) agar. Salmonella-Shigella (SS) agar may inhibit the growth of *S. dysenteriae*. No enrichment medium is needed to isolate *Shigella* as enrichment does not provide greater recovery than direct plating. After colony purification, biochemical tests must be performed.

Screening medium	*Shigella* spp. Reaction
KIA or TSI (same results)	Alkaline (red)/acid (yellow); no gas produced (red slant/yellow butt), no hydrogen sulfide produced (no black along the stab line)
Motility	Negative
Indole	Positive or negative
Urea	Negative

Finally, serological tests must be completed on suspected *Shigella* spp. cultures. Each antiserum (in the left-hand column) must be tested. If agglutination occurs, the species of *Shigella* is reported in the corresponding right-hand column. If an organism is found to be *S. dysenteriae,* you should test the type 1 antiserum to see if it is *S. dysenteriae* type 1.

Antiserum	Report if agglutination occurs
Group A	*S. dysenteriae*
If above occurs; test with: Type 1	*S. dysenteriae* type 1
Group B	*S. flexneri*
Group C	*S. boydii*
Group D	*S. sonnei*

Isolation Methods for *V. cholerae*:
The O1 and O139 strains of *V. cholerae* have the same cultural and biochemical characteristics. Therefore, O group antiserum must be used to differentiate the two as well as differentiate these from all the other serogroups of *V cholerae*. Biochemical tests are usually not needed unless there is a limited supply of anti-serum.

V. cholerae will grow on a variety of common media, but specialized media are best for isolation from fecal specimens. The enrichment medium is Alkaline Peptone Water (APW). The selective medium of choice is TCBS (thiosulfate citrate bile salts). Enrichment and selective media should always be used in convalescent patients, suspected asymptomatic carriers, environmental samples, and where there is likely to be a high number of competing organisms and low counts of *V. cholerae*. Samples from patients with active cholera should be cultured with TCBS.

Antimicrobial Sensitivity Testing:
Once the organism is identified, the laboratory should perform antimicrobial sensitivity testing to determine a treatment plan and determine guidelines for future patients. If the lab that performed the isolation/ identification does not have experience or supplies for antimicrobial susceptibility testing, then the samples should be sent to a lab that can perform this testing.

The susceptibility of *Shigella* spp. and *V. cholerae* to the following antibiotics should be tested, as they are indicated for treatment:

Zone size interpretive standards for antimicrobial susceptibility testing of *Shigella* spp. with selected antimicrobial disks

Antimicrobial	Disk potency	Diameter of zone of inhibition (mm) and equivalent MIC breakpoint (µg/ml)			*E. coli* ATCC 25922	*S. aureus* ATCC 25923
		Susceptible	Intermediate	Resistant	(NCCLS QC strain)	(NCCLS QC strain)
Ciprofloxacin	5 µg	≥ 21 mm *(≤1 µg/ml)*	16 – 20 mm *(2 µg/ml)*	≤ 15 mm *(≥ 4 µg/ml)*	30 – 40 mm *(0.004–0.016 µg/ml)*	--
Pivmecillinam	10 µg	≥15 mm	12 mm	≤11 mm	23-29 mm	--
Ceftriaxone	30 µg	≥21 mm	14-20 mm	≤13 mm	29-35 mm	22-28 mm
Azithromycin	15 µg	≥19 mm		≤15 mm	--	21-26 mm

Note: you must run a positive control with the reference strain(s).
Table Adapted from: WHO, Manual for the Laboratory Identification and Antimicrobial Susceptibility Testing of Bacterial Pathogens of Public Health Importance in the Developing World. WHO/CDS/CSR/RMD/2003.6
Source: NCCLS (2002) Performance Standards for Antimicrobial Susceptibility Testing; Twelfth Informational Supplement. NCCLS document M100-S12 [ISBN 1-56238-454-6]. NCCLS 940 West Valley Road, Suite 1400,Wayne, PA 19087 USA.

Zone size interpretive standards for antimicrobial susceptibility testing of *V. cholerae* with selected antimicrobial disks					
Antimicrobial	**Disk potency**	**Diameter of zone of inhibition (mm) and equivalent MIC breakpoint (µg/ml)**			***E. coli* ATCC 25922 (NCCLS QC strain)**
		Susceptible	**Intermediate**	**Resistant**	
Ampicillin[1]	10 µg	≥ 17 mm *(≤ 8 µg/ml)*	14 – 16 mm *(16 µg/ml)*	≤ 13 mm *(≥ 32 µg/ml)*	16 – 22 mm *(2–8 µg/ml)*
Azithromycin	15 µg	≥ 18 mm			
Chloramphenicol[1,2]	30 µg	≥ 18 mm *(≤8 µg/ml)*	13 – 17 mm *(16 µg/ml)*	≤ 12 mm *(≥ 32 µg/ml)*	21 – 27 mm *(2–8 µg/ml)*
Erythromycin	15 µg	≥ 23 mm			
Furazolidone[3]	100 µg	≥ 18 mm	--	< 18 mm	22 – 26 mm[4]
Ciprofloxacin[5]	5 µg	≥ 21 mm *(≤1 µg/ml)*	16 – 20 mm *(2 µg/ml)*	≤ 15 mm *(≥ 4 µg/ml)*	30 – 40 mm *(0.004–0.016 µg/ml)*
Tetracycline[1]	30 µg	≥ 19 mm *(≤ 4 µg/ml)*	15 – 18 mm *(8 µg/ml)*	≤ 14 mm *(> 16 µg/ml)*	18 – 25 mm *(0.5–2 µg/ml)*
Trimethoprim-sulfamethoxazole[1] **(cotrimoxazole)**	1.25/ 23.75 µg	≥ 16 mm *(≤ 2/38 µg/ml)*	11 – 15 mm *(4/76 µg/ml)*	≤ 10 mm *(≥ 8/152 µg/ml)*	23 – 29 mm *(≤ 0.5/9.5 µg/ml)*

Note: you must run a positive control with the reference strain.

Table Adapted from: WHO, Manual for the Laboratory Identification and Antimicrobial Susceptibility Testing of Bacterial Pathogens of Public Health Importance in the Developing World. WHO/CDS/CSR/RMD/2003.6

1. Source: NCCLS (2002) Performance Standards for Antimicrobial Susceptibility Testing; Twelfth Informational Supplement. NCCLS document M100-S12 [ISBN 1-56238-454-6]. NCCLS 940 West Valley Road, Suite 1400,Wayne, PA 19087 USA.
2. Use these interpretive standards for chloramphenicol with caution because the disk diffusion test may misclassify many organisms (high minor error rate) [NCCLS 2002].
3. Proposed interpretative criteria based on multi-laboratory studies; criteria have not been established for V. cholerae by NCCLS.
4. Quality control inhibition zone diameter ranges for furazolidone have not been validated by NCCLS; the ranges presented in this table are based on those suggested by the manufacturer of the antimicrobial disks.
5. Criteria for interpretation of susceptibility of V. cholerae to ciprofloxacin have not been developed; this table presents tentative interpretive criteria based on NCCLS interpretive criteria for Enterobacteriaceae.

Antimicrobials that should not be used for the treatment of shigellosis (do not test) :

- Ampicillin
- Chloramphenicol
- Cotrimoxazole/TMP-SMX
- Tetracycline
- Nitrofurans
- Aminoglycosides
- 1st and 2nd generation cephalosporins
- Amoxicillin
- Nalidixic acid

Chapter 8.8 - Conclusion Box

- There should be a multidisciplinary coordinating team to provide technical assistance during an outbreak, which includes: the initial evaluation, ongoing epidemiology and surveillance, comprehensive and effective case management, appropriate water and sanitation, laboratory services, and effective communication.
- Surveillance programs should be established in order to categorize the extent of the outbreak and analyze who is at risk and why in order to stop the spread, provide appropriate services and prevent future outbreaks.
- Effective communication between different aide partners and with the local community is essential to any epidemic control situation.
- Either current facilities, new temporary facilities or both should be prepared to treat the suspected number of outbreak patients with adequate supplies and staff.
- A system that is appropriate to the setting must be established to provide sanitary living conditions and a minimum of 20L of safe water per person per day in an emergency situation.
- If your local laboratory does not have the capability to isolate/identify and determine the antimicrobial sensitivity of *Shigella* spp. and *V. cholerae,* you should at least know where and how to send samples for processing.

Appendix 8A - Supplies list

Estimated Minimum Supplies Needed During an Outbreak
Assumptions:
These supplies are for 100 patients

- A refugee camp with 2,000 people will have an attack rate of 5% or 100 patients
- An endemic area with 50,000 people will have an attack rate of 0.2% or 100 patients

20 are expected to be severely dehydrated and require IV fluids

Modified WHO List (6)

Rehydration Supplies:

- 650 packets oral rehydration salts (1 liter each)
- 120 bags Ringer's lactate IV solution (1 liter each)
- 120 giving sets (must include large-bore IVs such as 18-19 gauge or larger)
- 10 scalp-vein sets (21 gauge)

Medicine:

- Antibiotics for 20 adults and 20 children

Other Supplies:

- 2 large water dispensers (marked at 5 and 10 liter levels) with tap for making ORS solution in bulk
- 20 bottles (1 liter) for oral rehydration solution (e.g. empty IV bottles)
- 20 bottles (½ liter) for oral rehydration solution
- 40 cups (100-200ml)
- 20 teaspoons
- 5 kg cotton wool
- 3 reels adhesive tape

Optional Supplies

- 3 nasogastric tubes, 5.3 mm OD, 3.5 mm ID (16 French), 50 cm long, for adults
- 3 nasogastric tubes, 2.7 mm OD, 1.5 mm ID (8 French), 38 cm long, for children
- Antibiotics to cover all anticipated patients (up to 100 including both adults and children)

Additional Supplies the ICDDR,B Recommends

Rehydration and medicine:

- Injection of KCl saline
- Injection of 25% Dextrose 25 ml
- Injection of Normal Saline ½ liter
- Injection of Calcium Gluconate 10%
- Readily Dispersible (dissolvable) Zinc Sulfate Tabs (or other zinc preparation appropriate for children, e.g. syrup)

Other Supplies:

- Communication tools appropriate to the region to request more supplies/aide (e.g. a cellular or satellite phone, fax machine, or internet connection)
- Alcohol solution (for disinfection)
- Tincture of iodine
- Swab sticks
- Disposable gloves
- Liquid hand soap
- Bleaching powder (or other bleach product)
- 250 Plastic buckets (for patients)
- 150 Vomit basins
- 100 Cots
- 200 Plastic cot covers
- 2 Book registers
- 50 Pens
- Food to feed all patients and 1 caregiver
- Mops

Regular hospitals also need to be prepared in the case of a diarrheal epidemic. Buffer stocks should be kept at all hospitals and in larger supply at central sites (district and national level) in case of an outbreak. Where outbreaks do not happen very often, staff at these hospitals should be trained and given refresher courses on a regular basis to keep their skill level high and the case fatality rate low.

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Chapter 8.9 - References

1. WHO, Cholera Outbreak: assessing the outbreak response and improving preparedness. Global Task Force on Cholera Control 2004 Geneva, p.21

2. WHO, Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* type 1. WHO 2005

3. WHO, Acute diarrhoeal diseases in complex emergencies: critical steps. 2004 Global Task Force on Cholera Control

4. The Sphere Project, Humanitarian charter and minimum standards in disaster response. 2004 revised edition. Stylus Publishers or www.sphereproject.org

5. CDC, Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera. Centers for Disease Control and Prevention, Atlanta, Georgia 1999.

6. WHO Guidelines for Cholera Control, Geneva 1993

7. Centers for Disease Control and Prevention. Laboratory Methods for the Diagnosis of Epidemic Dysentery and Cholera. Atlanta, Georgia: CDC, 1999. WHO/CDS/EDC/99.8

8. ibid.

9. WHO. First steps for managing an outbreak of acute diarrhea. 2004 WHO Global task force on cholera control. WHO/CDS/CSR/NCS/2003.7 Rev.1

Chapter 9.1 - After an Outbreak

In endemic areas, the time period after an outbreak can also be considered to be the time before the next outbreak. Therefore, it is more appropriate to speak of an intra-epidemic period rather than “after an outbreak”. Although certain situations (i.e. refugee camps) make a population more likely to have a cholera epidemic despite the region, it is still important to recognize a pattern in epidemics and evaluate the future risk after an outbreak occurs. This is especially important in camps where the population becomes semi-permanent and remains in the camp for many years.

In places where cholera is endemic, it is important to establish the seasonality pattern. The easiest way to determine seasonality is by surveillance of clinical samples. Although seasonality patterns might be determined by bacterial surveillance through water samples, such surveillance is not practical because some strains in the environment may not cause clinical symptoms and *Shigella* spp. are rarely isolated from the environment.

It is crucial that the surveillance from patient samples is maintained during the whole year, to identify the serogroup/ biotype and the resistance pattern of the circulating cholera strains. This will allow you to predict the months that might have the highest number of patients. An effective link to a referral laboratory is necessary to establish the resistance pattern in a representative sample of all cholera patients. The strain (e.g. serotype and antibiotic resistance pattern) that has dominated an area for several years/decades may seem to disappear at certain times but may re-emerge later.

In countries where cholera is endemic, outbreaks frequently spread from the coast along the rivers and commerce routes. Artificial changes, such as large fish farms, dams, or soil erosion, may be important factors that influence the course of spreading. In addition, host factors can alter the dynamics of cholera spread or containment. For example, communities that had previous exposure to El Tor cholera have no protection against O139 since they do not confer cross-immunity.

The sequential outbreaks of cholera and shigellosis are often caused by different strains. Therefore, the sensitivity of the pathogens to different antibiotics can differ from one outbreak to the next and the antimicrobial resistance pattern should be assessed at the beginning of each outbreak for both cholera and shigellosis. Assuming that the strain is sensitive, doxycycline is the drug of choice for cholera. Generally ciprofloxacin is the drug of choice for shigellosis.

Ideally, cholera and shigellosis surveillance should be part of the routine national health surveillance for at least several years after an outbreak. Utilize the time between outbreaks to train staff on prompt intervention, promote ORS, refill stocks, and improve sanitation and water supplies.

Ensure that you have adequate stocks of all supplies in the event of a future outbreak. The initial supplies needed are IV fluids, ORS, zinc, antibiotics, and training materials. Stocks of these supplies should be decentralized as much as possible to ensure rapid delivery to isolated areas in the event of an outbreak.

In refugee camps or in internally displaced persons camps (e.g. after a natural disaster), displaced people normally do not stay for years, therefore it might not be possible or necessary to maintain surveillance over several years. In these situations, it is also much more difficult to assess any seasonality.

Learn from the experience of the last outbreak: what was well organized and what went wrong. Adopt policy accordingly and disseminate your major findings. Sometimes small things make big differences (having an established effective communication by fax, phone or email, having already established a link to partners) and may save lives! Since neither socioeconomic status nor the distance to the next health facilities, both of which correlate with increased mortality, can be modified in the immediate future, the effective utilization of village health workers, practitioners and volunteers is a practical solution to access issues.

A follow-up survey should be completed to discover any shortfalls in the treatment, including deaths at treatment facilities or deaths due to lack of access. Addressing the following points will help you to prepare for the next outbreak and should be discussed with the health authorities and disseminated:

- Identify the resistance pattern of the last outbreak. Was this used to provide the ideal antibiotic treatment?
- Identify the geographic areas and age groups that had the highest incidence, and prevalence of cholera and/or shigellosis, and establish why this was the case. Were the treatment centers located amongst areas and groups with the highest need?
- Identify the areas that had the highest mortality rate due to cholera and shigellosis, and establish why this was the case. What could have been done to reduce this high CFR?
- Determine ways to integrate treatment into the permanent health system.
- Identify agencies that were involved and which parts of treatment, preparation or laboratory support did they provide. What additional agencies should have been included?
- Identify the sources of funding. Were sufficient funds available? How can you communicate with the funding agencies to ensure proper funding levels for the next season? Were additional funding agencies willing to provide funding but were unable due to an administrative issue? How can these administrative constraints be addressed? Did the funding come in time?

Try to answer these questions to be better prepared for the next outbreak, wherever and whenever it next occurs.

Chapter 9.2 - Conclusion Box

- Analyze the last outbreak: what can be improved next time and what was managed well. The lessons learned will help you to tackle the next outbreak.