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section 8 Infectious diseases 1060 moxifloxacin has demonstrated moderate to good in vitro activity against most anaerobes. There are recent reports of isolates of the Bacteroides fragilis groups that were multidrug resistant and also of an isolate of Bacteroides thetaiotaomicron that was resistant to both metronidazole and carbapenems. These increasing reports of resistance raise the con- cern for gene transfer from resistant aerobic Enterobacteriaceae to anaerobes. Updated data on anaerobic resistance in the United States is available in the CLSI M100-S22 document that was last published in 2012. Anaerobes from the non-Bacteroides group are generally more susceptible to antianaerobic antibiotics. Antibiotic resistance among anaerobes is less predictable than with aerobic and faculta- tive anaerobes. Institutions should perform susceptibility testing at least annually to establish patterns of resistance to be reported with the hospital's yearly antibiogram. When susceptibility testing is per- formed, the routine antimicrobials recommended for testing both Gram-negative and Gram-positive anaerobic organisms are peni- cillin/β-lactamase inhibitor combinations, the carbapenem class of antibiotics, metronidazole, and clindamycin. Additionally, routine testing against penicillin is recommended for Gram-positive an- aerobes. When indicated, susceptibility testing to cephalosporins, carboxy- or ureidopenicillins, chloramphenicol, moxifloxacin, or tetracycline can also be performed. Susceptibility of individu- ally recovered isolates should be considered if they were cultured from otherwise sterile sites, in cases of severe infections, those re- quiring long-term antibiotics, or those not responding to initial empiric therapy. The choice of empiric antibiotics for anaerobic in- fections should be based on the hospital or regional susceptibility antibiograms if the individual isolate susceptibility is not available. Surgery Often, antimicrobial therapy alone is not sufficient to cure anaerobic infections. Since many infections are associated with abscess forma- tion or occur in areas with tissue ischaemia, surgical intervention frequently becomes imperative with drainage of abscesses and resec- tion of devitalized tissue. Surgical antimicrobial prophylaxis In cases where contamination of surgical wounds by the local flora could result in infection, it has become common practice for sur- geons to use antimicrobial prophylaxis in the perioperative period. In intra-abdominal procedures, prophylaxis against anaerobic bac- teria significantly reduces postoperative infection rates. The regi- mens cover both aerobes and anaerobes. The choice and duration of therapy depends on the nature of the surgery and whether it is an elective or emergency procedure. These decisions are based on timing, type of clinical presentation, and intraoperative findings. The antimicrobials used include cephamycins such as cefoxitin or the addition of other more specific antianaerobic agents such as metronidazole. Ertapenem has proven to be effective in the prophy- laxis of infections for elective colorectal surgery. FURTHER READING Aldape MJ, Bryant AE, Stevens DL (2006). Clostridium sordellii in- fection: epidemiology, clinical findings and current perspectives on

diagnosis and treatment. Clin Infect Dis, 43, 1436–46. Brook I, Wexler HM, Goldstein, EJC (2013). Antianaerobic antimicrobials: spectrum and susceptibility testing. Clin Micro Rev, 26, 526–46. CLSI (2012). Performance standards for antimicrobial susceptibility testing; twenty-second informational supplement. CLSI document M100-S22. Clinical and Laboratory Standards Institute, Wayne, PA. Finegold SM, George WL (eds) (1989). Anaerobic infections in humans. Academic Press, New York, NY. Hecht DW (2004). Prevalence of antibiotic resistance in anaerobic bacteria: worrisome developments. Clin Infect Dis, 39, 92–7. Nagy E, et al. (2011). Antimicrobial susceptibility of Bacteroides fra- gilis group isolates in Europe: 20 years' experience. Clin Infect Dis, 17, 371–9. Sadarangani SP, et al. (2015). Metronidazole- and carbapenem-resistant Bacteroides thetaiotaomicron isolated in Rochester, Minnesota, in 2014. Antimicro Agents Chemother, 59, 4157–61. Snydman DR, et al. (2011). Update on resistance of Bacteroides fragi- lis group and related species with special attention to carbapenems 2006–2009. Anaerobe, 17, 147–51. 8.6.12 Cholera Aldo A.M. Lima and Richard L. Guerrant ESSENTIALS Vibrio cholerae is a Gram-negative organism that can be subdivided into over 200 serogroups based on the somatic O antigen, with only serogroups O1 and O139 causing epidemic and pandemic disease. Historically it has killed millions from dehydrating diarrhoea, encour- aged the birth of modern epidemiology, the sanitary revolution, and oral rehydration therapy; it persists today as a glaring reminder of poverty and inadequate water/sanitation. Contaminated food (es- pecially undercooked seafood) is the usual route of transmission in developed countries; contaminated water and street food vendors are more common vehicles in less developed countries. Clinical features and diagnosis—typical presentation is with sudden onset of voluminous, painless, watery diarrhoea, which can exceed 500 to 1000 ml/h, leading to severe dehydration in a couple of hours and risk of death. Definitive diagnosis is by isolating V. cholerae from stool or rectal swab samples. Treatment—oral rehydration therapy with sugar or starch, water, and salts must be provided in the community and at field stations, clinics, and hospitals where most patients present: this reduces the case fatality of untreated severe cholera from about 50% to 1% or less. Antibiotics can shorten the illness and decrease diarrhoeal purging: tetracycline, cotrimoxazole, ciprofloxacin, or azithromycin have been effective, but there is increasing resistance. Prevention—effective preventive measures include (1) ensuring a safe water supply; (2) improving sanitation; (3) making food safe for consumption by thorough cooking of high-risk foods, es- pecially seafood; and (4) health education through mass media. Newer-generation killed oral cholera vaccines have been licensed

 and proved to be well tolerated, protective, cost-beneficial, and a potential tool to control cholera together with the other preventive recommendations. Introduction and historical perspective Cholera, the dreaded scourge causing death from dehydrating diar- rhoea, existed for centuries in South Asia until, in 1817, it broke out along trade routes; since then there have been seven pandemics across all six inhabited continents. The whole-genome sequences of globally and temporally representative V. cholerae isolates, including the Haitian outbreak in 2010, have shown that since the 1950s these isolates have spread from the Bay of Bengal in three independent waves with a common ancestor. Analysis of the whole- genome sequences of Vibrio cholerae strains also demonstrated that genomic changes and alterations in CTX phage, particularly in the gene encoding the B subunit of cholera toxin, were major changes in the evolution of V. cholerae. Cholera was largely responsible for encouraging the birth of modern epidemiology and for driving the sanitary revolution in Western Europe and North America in the 19th century. In the last one-third of the 20th century, it helped drive scientific discoveries of cell signalling, intestinal ion trans- port, and oral rehydration therapy, which have brought global diar-

rhoea mortality down from over 5 million/year to below 2 million/ year. Yet cholera persists today as a disease of poverty, along with other faecally transmitted pathogens, a sign of inadequate water and sanitation among the desperately poor and displaced around the world. Aetiology, genetics, and pathophysiology Thirty years before the causative agent Vibrio cholerae was discovered during the fifth pandemic in 1884 in Kolkata, India, by Robert Koch, John Snow's classic epidemiological study of cholera in London in 1854 suggested that it was transmitted by contaminated drinking water. Snow even postulated that a toxin might cause the dramatic fluid loss.
V. cholerae is a halophilic flagellated curved Gram-negative organism classified by biochemical tests and fur- ther subdivided into serogroups based on the somatic O antigen. Among over 200 serogroups, only O1 and O139 cause epidemic and pandemic disease. The other strains are classified as non-O1 and non-O139 V. cholerae. Serogroup O1 is further subdivided into three serotypes (Inaba, Ogawa, and Hikojima) and into two phenotypically different biogroups (Classical and El Tor). The latter is named for the Egyptian village quarantine station where it was first isolated in 1905 from Indonesian pilgrims travelling to Mecca. This strain then became the cause of the seventh pan- demic that continues around the world today. The O139 serogroup, first seen in 1992, appears to have emerged from horizontal gene transfer of a fragment of DNA that encodes O-antigen biosynthesis from another serogroup (perhaps O22) into the seventh pandemic V. cholerae O1 El Tor strain. O139 and O1 (both Classical and El Tor biotypes) now coexist and continue to cause large outbreaks in India and Bangladesh. V. cholerae O1 (biotype El Tor) has two circular chromosomes and the entire genome sequence has been described. The large chromosome has most of the genes required for growth and pathogenicity and the small chromosome encodes components of several essential metabolic and regulatory path- ways. Critical to the pathogenicity of V. cholerae (and distinct from environmental isolates) is the acquisition of two distinct phages. The first contains a 'pathogenicity island' (VPI) encoding the 'toxin coregulated pilus'. Remarkably, toxin coregulated pilus serves as both a major intestinal colonization factor and as the receptor for the second phage, CTXϕ, that encodes for cholera toxin and ac- cessory proteins (including ACE and Zot) as well as containing genes required for phage replication, integration, and regulation in the RS2 region. Genes encoding colonization factors or toxin are regulated in response to environmental conditions. The 32- kDa transmembrane protein ToxR binds upstream of ctxAB to increase transcription and synthesis of cholera toxin. ToxR also regulates the expression of other genes in the ToxR regulon; hence, the expression of ToxR is controlled by environmental factors. Characterization of V. cholera O1 El Tor biotype variant clinical isolates from Bangladesh and Haiti showed that all strains pro- duced increased cholera toxin (2–10-fold) compared to the wild type El Tor strains and also produced more toxin coregulated pilus and ToxT. These essential virulence factors are regulated primarily by ToxT via the ToxR virulence regulon. Vibrios are acquired from contaminated water or food and they must pass though the acidic stomach before they are able to col- onize the upper small intestine. Colonization occurs with fila- mentous protein fimbriae, called toxin coregulated pili, which extend from the vibrio wall and attach to receptors on the mucosa. V. cholerae adhere to the M cells without causing tissue damage and rapidly multiply to 107 to 108 cells/g of tissue. Attached vib- rios efficiently deliver cholera toxin directly to the epithelial cells (Fig. 8.6.12.1). The A subunit consists of two peptides linked by a disulphide bond. The larger, A1, containing the toxic activity, is endocytosed following toxin binding via its B subunit to GM1 ganglioside. The A1 subunit catalyses the covalent bonding of adenosine diphosphoribose from nicotinamide adenosine di- nucleotide to the α-subunit of Gs, the heterotrimeric adenylyl cyclase-stimulating G protein, thus activating adenylate cyclase to form cAMP. cAMP then acts to open the cystic fibrosis transmem- brane conductance regulator chloride

channel causing increased chloride secretion by the intestinal crypt cells and a blockade of neutral sodium and chloride absorption by villous cells. This leads to voluminous fluid efflux into the small intestinal lumen which exceeds the absorptive capacity of the bowel and results in watery diarrhoea. The diarrhoeal fluid contains large amounts of sodium, chloride, bicarbonate, and potassium, but little protein or blood cells. The loss of electrolyte-rich isotonic fluid leads to blood volume depletion with attendant low blood pressure and shock. Loss of bicarbonate and potassium leads to metabolic acidosis and potassium deficiency. Epidemiology Ever since Snow's seminal epidemiological treatise, cholera has been described as the classic water-borne disease. However, it is also transmitted by contaminated food, especially undercooked sea- food or food mixed with contaminated water. Contaminated food

section 8 Infectious diseases 1062 (especially undercooked seafood) is the usual vehicle for transmis- sion in developed countries, and contaminated water and street food vendors are more common vehicles in less developed coun- tries. V. cholerae is found in brackish surface water and in shellfish, and survives and multiplies in association with zooplankton and phytoplankton independently of infected human beings. There is no known other animal reservoir for V. cholerae. V. cholerae is en- demic in the Indian subcontinent and the re-emergence of cholera in other continents is highly dependent on environmental factors. The association of the bacteria with plankton has led to the sug- gestion that ship ballast is a cause of its global spread. V. cholerae has evolved to survive in the aquatic environment and then in the host. In water, V. cholerae vibrios are free swimming or attached to plants, green algae, copepods, crustaceans, or insects. In humans, the intestinal milieu fosters the acquisition of genetic elements from the toxin coregulated pilus bacteriophage, lacking in most environ- mental strains. Toxin coregulated pilus phage encodes type IV fim- bria which serves as colonization factor and receptor for the CTX phage that carries genes encoding cholera toxin. Thus, both bac- teriophages integrate into the bacterial genome and form episomal replication intermediates. The production of cholera toxin and the biogenesis of CTX phage both depend on a type II secretion appar- atus, encoded within the bacterial genome. In Bangladesh and Peru, where the disease has been endemic and epidemic, cholera tends to occur in the warm seasons, albeit before and after the monsoon rains in Bangladesh. Most V. cholerae infections are asymptomatic (case:infection = 1:3 to 1:100) or associated with mild nonspecific diarrhoea. Since a high inoculum dose is required for infection, person-to-person infection is rare without intervening water or food contamination. Infection and its severity also depend on the gastric acid barrier, local intestinal immunity, and blood group. Those with blood group O are at higher risk of severe El Tor cholera than are those with other blood groups. This susceptibility might explain the lower prevalence of blood group O in the Ganges Delta area. A recent study showed that Lewis blood group antigen type Le(a + b –) are more susceptible and Le(a – b +) are less susceptible to V. cholerae O1 associated symp- tomatic disease. This might be important in evaluating population risk factors for cholera and in vaccine efficacy studies. In cholera-en- demic areas, the highest attack rates are in children aged 2 to 4 years. Cholera toxin A1 GM1 Na+ Na+ H+ H+ PKA cAMP AC ATP α Golgi ERD2 A1 ARF ERAD G-Protein CFTR NHE3 NHE2 Cl— B Fig. 8.6.12.1 Pathophysiology of cholera. V. cholerae produces a major virulence factor, cholera toxin, an 84-kDa protein consisting of a dimeric A subunit and five identical B subunits. Cholera toxin binds to a monosialoganglioside GM1 receptor at the host mucosal surface and triggers endocytosis of the holotoxin. The A1 domain of the A subunit is transported through the Golgi and endoplasmic reticulum to activate the Gsα subunit of G protein. This A1 domain interacts with ADP-ribosylating factors (ARFs) to ADP-ribosylate this Gsα subunit leading to activated G

protein and consequent activation of adenylyl cyclase (AC). The AC cleaves ATP to cAMP which subsequently activates protein kinase A which inhibits NaCl absorption (NHE transporters) and increases chloride secretion through the cystic fibrosis transmembrane regulator (CFTR).

8.6.12 Cholera 1063 In newly invaded areas, attack rates are similar for all ages. First illnesses are often seen in adult men, presumably because of greater exposure to contaminated food and water. The current seventh pandemic began in 1961, in Sulawesi (Celebes), Indonesia. By 1966 the disease had spread to other coun- tries in eastern Asia including Bangladesh, India, the former Union of Soviet Socialist Republics, Iran, and Iraq. Cholera reached West Africa in 1970, and in 1991 it appeared in Latin America for the first time in more than a century. Until 1992 only serogroup O1 had been implicated in epidemics while other serogroups had caused only sporadic cases of diarrhoea. However, in late 1992 cholera broke out in India and Bangladesh caused by a previously unrecognized serogroup of V. cholerae, designated O139. It is unclear whether this new serogroup from Southeast Asia will spread to other regions of the world. It is estimated that 1.3–4.0 million cholera cases and 21 000–143 000 deaths occur every year worldwide (Fig. 8.6.12.2). Hence, cholera continues as a significant global public health problem. In 2015, a total of 172 454 cases including 1304 deaths were reported from 42 counties, resulting in a case fatality rate of 0.8%. Cases were reported from 16 countries in Africa, 13 in Asia, 6 in Europe, 6 in the Americas, and 1 in Oceania. Afghanistan, the Democratic Republic of the Congo, Haiti, Kenya, and the United Republic of Tanzania were responsible for 80% of all reported cases. From all cases reported, 41% were from Africa, 37% from Asia, and 21% from Hispanic population. Thirteen countries reported im- ported cholera cases. All cases of suspected cholera should be reported to local and national health authorities, since cholera outbreaks can become massive epidemics. These cases should be confirmed by labora- tory investigation. If a patient older than 5 years develops severe dehydration or dies from acute watery diarrhoea, or if there is a sudden increase in the daily number of patients with acute watery diarrhoea, a cholera outbreak should be suspected. Prevention and vaccines Since contaminated water and food are the main vehicles of trans- mission, effective preventive measures include ensuring a safe water supply (especially for municipal water systems), improving sani- tation, making food safe for consumption by thorough cooking of high-risk foods (especially seafood), and providing health education through mass media (Box 8.6.12.1). Three safe and well-tolerated oral cholera vaccines that pro- vide significant protection have been approved by World Health Organization (WHO) for use in both endemic and epidemic cholera: Dukoral, Shanchol, and Euvichol. Dukoral is a killed Fig. 8.6.12.2 Countries and areas reporting cholera cases in 2015. From Cholera. Weekly Epidemiological Record (2016), 38(91), 433–440, © WHO 2016. Box 8.6.12.1 Prevention of cholera • Ensure a safe water supply. • Wash hands after defecation and before food preparation. • Improve sanitation, making water and food safe for consumption. • Provide health education through mass media. • Vaccination and improvements in sanitation work synergistically.

section 8 Infectious diseases 1064 whole cell V. cholerae plus recombinant B subunit of cholera toxin (rCTB-WC). Sanchol (Shantha Biotechnics) was devel- oped and licensed in 2009 via a public-private partnership in India as a new killed whole-cell-only oral cholera vaccine, which was modified from an earlier oral cholera vaccine produced in Vietnam. Euvichol (EuBiologics, The Republic of Korea) has the same characteristics as Shanchol and was prequalified by WHO in December 2015. All three vaccines were recommended two doses for full protection. In a trial in Kolkata, India, the two- dose regimen confer 65% cumulative protection at five years of follow-up. The same regimen

in a trial in Dhaka, Bangladesh was found to confer 53% protection over two years of follow- up. A single dose of the killed oral cholera vaccine (Shanchol) was also efficacious in older children (≥5 years of age) and in adults during the initial six months after vaccination in an urban endemic cholera in Dhaka, Bangladesh. Because vaccine efficacy is overcome by larger infectious doses, vaccine should be seen as synergistic with improvements in water, hygiene, and sanitation that reduce the numbers of vibrios ingested. Clinical features The incubation period of cholera usually ranges from 18 h to 5 days. There is a sudden onset of voluminous watery diarrhoea with occasional vomiting. Diarrhoea is severe in 5–10% of those infected. Its most distinctive feature is the painless purging of voluminous stools resembling rice-water with a fishy odour. The vomitus is generally a watery and alkaline fluid. Severe diarrhoea can exceed 500 to 1000 ml/h, leading to severe dehydration in 2 h and risk of death. Dehydration can be classified based on the pres- ence and severity of clinical findings. Table 8.6.12.1 summarizes the clinical assessment of patients with mild, moderate, or severe dehydration. In all cases the key is to rapidly replace fluid deficits, correct metabolic acidosis and potassium losses, and to continue replacing ongoing fluid losses. Because cholera toxin has pro- longed effects, it is imperative to continue replacing fluid losses, for which a ‘cholera cot’ with a central hole, plastic sheet, and bucket to monitor purging can be tremendously helpful to both the patient and medical attendants. Signs of severe dehydration include absent or low-volume peripheral pulse, undetectable blood pressure, poor skin turgor, sunken eyes, and wrinkled hands and feet. Metabolic acidosis can develop and lead to gasping (Kussmaul) breathing. Urine output is diminished or absent until dehydration is corrected. Complications generally result from inadequate fluid replace- ment, acute renal failure due to protracted hypotension, hypogly- caemia, hypokalaemia, and cramps due to electrolyte imbalance. Differential diagnosis Most cases are indistinguishable from other cases of diarrhoeal diseases, but since the treatment of any dehydrating diarrhoea is the same—fluid replacement—identification of the pathogen is not essential for patient management. However, if an adult patient becomes severely dehydrated and is in the right epi- demiological setting or with a history of travelling, the clinician and public health authorities should be alert to the possibility of cholera. Criteria for diagnosis Definitive diagnosis is by isolating V. cholerae from stool or rectal swab samples on selective media. V. cholerae survives in faecal specimens if kept moist. Cary–Blair transport medium should be used for transport to the laboratory for plating onto thiosulphate citrate bile salts sucrose (TCBS) agar that inhibits most other normal faecal flora but supports the growth of the vibrios. Specimens should also be inoculated into alkaline pep- tone water, an enrichment broth that preferentially supports the growth of vibrios. After 6–12 h of incubation, a second TCBS plate is inoculated. These plates are incubated for 18–24 h, and V. cholerae colonies appear as smooth yellow colonies with slightly raised centres. V. cholerae is a Gram-negative polar monotrichous oxidase-positive asporogenous curved rod that ferments glucose, sucrose, and mannitol and is positive in the ly- sine and ornithine decarboxylase tests. The organism is classified by biochemical tests and is further subdivided into serogroups based on the somatic O antigen. Presumptive identification Table 8.6.12.1 Assessment of patients with diarrhoea for dehydration Feature No dehydration Some dehydrationa Severe dehydrationa, b General appearance Well, alert Restless, irritable Lethargy or unconscious; floppy Eyes Normal Sunken* Very sunken and dry* Tears Present Absent* Absent* Mouth and tongue Moist Dry* Very dry* Thirst Drinks normally, not thirsty Thirsty, drinks eagerly Drinks poorly or not able to drink Skin pinchc Goes back quickly Goes back slowly Goes back very slowly a Two or more of these signs including one indicated by *. b Absence of radial pulse and low blood pressure are also signs of severe dehydration in adults and children older than 5 years. c The skin pinch is less useful in patients with marasmus (severe wasting),

kwashiorkor (severe malnutrition with oedema), or in obese patients. From Azurin JC, et al. (1967). A long-term carrier of cholera: cholera Dolores. Bull World Health Organ, 37, 745–9.

8.6.12 Cholera 1065 of V. cholerae O1 or O139 can be made on the basis of typical colonies, which are oxidase-positive and agglutinate with O1 or O139 antiserum. Rapid tests include dark-field microscopy and rapid immuno- assays which can be useful for monitoring epidemiological patterns in remote areas where cultures are not readily available. New out- breaks must be confirmed by cultures. Polymerase chain reaction and DNA probes are available but are not practicable in many areas where cholera is common. Treatment Treatment must be provided at the community and field stations, clinics, and hospitals where most of the patients present. Oral re- hydration therapy was a major therapeutic breakthrough that has drastically decreased mortality from cholera and other dehydrating diarrhoeal diseases. The case fatality rate of untreated severe cholera approaches 50%, but with oral rehydration therapy it is decreased to 1% or less. The physiological basis for oral rehydration therapy is Na+-coupled transport with glucose; transport from the entero- cyte to the lateral intercellular space creates a local osmotic gradient that initiates water flow (Fig. 8.6.12.3). The oral rehydration salts (ORS) formulation approved by the WHO is based on the electro- lyte composition lost in stool in patients with cholera. Table 8.6.12.2 summarizes the electrolyte concentrations from cholera stool and several oral rehydration formulations, including that approved and recommended by the WHO. Around 5–7.5% of the bodyweight should be given as ORS with additional ORS to compensate for other losses. In patients who are severely dehydrated, having lost at least 10% (5 litres for a 50-kg patient) of their bodyweight, volume replacement must be rapid. Lactated Ringer’s solution is an excellent commercially available intravenous fluid. Other polyelectrolyte solutions with added potas- sium can also be used. Since ORS is the best polyelectrolyte solution to compensate for the acidosis and potassium deficiency, they should be given as soon as possible after initial intravenous fluid resuscitation. A formulation of ORS that uses rice rather than glucose is better for cholera patients because it reduces the purging rate by providing polymeric glucose with lower osmolarity. ORS have been modified to prevent hypernatraemia (more common with S Ouabain Na+ Na+ Na+ Na+ Na+ Na+ Na+ Na+ Na+ Na− K+ K+ K+ CI− CI− CI− CI− CI− CI− CI− 0 mV− S H+ H+ H+ Co2 + H2O HCO3−

- HCO3−
- 40 mV−

- 2–5 mV− Organic substrate H2CO3 Fig. 8.6.12.3 The pharmacological principle and basis for oral rehydration therapy. Na+ coupling permits the organic substrate to be transported ‘uphill’ (i.e. from low luminal to higher concentration), a gradient opposite to that for Na+. The Na+ gradient is the driving force for sugar and amino acids. As these organic solutes are absorbed, salt is absorbed with them, and water follows osmotically—transport from enterocytes to lateral intercellular space creates a local osmotic gradient that initiates water flow. This coupled transport of Na+ and organic substrate is the theoretical basis for oral rehydration therapy in cholera and other diarrheal diseases. Table 8.6.12.2 Composition of cholera stools and electrolyte rehydration solutions used to replace stool losses Fluid Sodium
  (mmol/litre) Chloride
  (mmol/litre) Potassium
  (mmol/litre) Bicarbonate
  (mmol/litre) Carbohydrate

(g/litre) Osmolality
(mmol/litre) Cholera stool Adults 130 100 20 44 – – Children 100 90 33 30 – – Oral rehydration salts Glucose 75 65 20 10a 13.5b 245 Rice 75 65 20 10a 30–50c About 180 Intravenous fluids Lactated Ringer’s 130 109 4 28d – 271 Dhaka solution 133 154 13 48e – 292 Normal saline 154 154 0 0 – 308 a Trisodium citrate (10 mmol/litre) is generally used, rather than bicarbonate. b Glucose 13.5 g/litre (75 mmol/litre). c Depending on degree of hydrolysis, 30–50 g rice contains about 30 mmol/litre glucose. d Base is lactate. e Base is acetate. From Sack DA, et al. (2004). Cholera. Lancet, 363, 223–33, reprinted with permission of Elsevier.

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