CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.15366596

Available online at: http://www.iajps.com Review Article

CAUSES AND EFFECTS OF CHOLERA AMONG CHILDREN

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Abstract:

Cholera is a highly infectious waterborne disease caused by Vibrio cholerae, posing a significant public health challenge, particularly in regions with poor sanitation and limited access to clean water. This literature review focuses on the causes and effects of cholera in children, who are especially vulnerable due to weaker immune systems and malnutrition. Cholera results in acute gastrointestinal infection, leading to profuse watery diarrhoea and vomiting, which can cause severe dehydration, electrolyte imbalance, and death if not promptly treated. The major transmission routes include contaminated water and food, poor hygiene, and inadequate sanitation. Malnutrition further exacerbates the severity of the disease in children, increasing the risk of complications and mortality. Clinical presentation includes rice-water stools, dehydration, vomiting, muscle cramps, and in severe cases, hypovolemic shock. Diagnosis is primarily clinical, supported by laboratory tests such as stool cultures or rapid dipstick tests. Effective management includes prompt rehydration therapy and, in some cases, antimicrobial treatment. Preventive measures such as improved sanitation, hygiene education, clean water access, and vaccination are crucial for reducing cholera incidence and improving health outcomes in children, especially in endemic and epidemic-prone areas.

KEY WORDS: *Cholera, Vibrio cholerae, waterborne disease, children, dehydration, malnutrition, diarrhoea, sanitation, hygiene, oral rehydration therapy, cholera toxin, transmission, mortality, endemic, public health.*

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Please cite this article in press *Pooja N. Wayde et* ***al., Causes And Effects Of Cholera Among Children., Indo Am. J. P. Sci, 2025; 12(05).***

INTRODUCTION:

Cholera is a waterborne disease caused by the bacterium Vibrio cholerae. It affects millions of people globally, especially in regions with poor sanitation and limited access to clean water. Children, particularly under the age of five, are highly susceptible to the disease. Understanding the causes and effects of cholera among children is crucial for implementing preventive measures and improving treatment outcomes. This literature review summarizes key findings on the causes and effects of cholera in children.[1]

Cholera is an acute illness caused by Enterotoxin elaborated by Vibrio cholerae which have colonized the small bowel of a susceptible individual. In its most severe form, there is rapid loss of fluid and electrolyte from the gastrointestinal tract, resulting in hypovolemic shock, metabolic acidosis and, if untreated, death. The clinical onset of cholera is generally that of abrupt, painless, watery diarrhoea. In severe cases, several litres of fluid may be lost within a few hours, leading rapidly to profound shock. At varying intervals after onset of diarrhoea, vomiting may ensue. This is characteristically effortless and is not preceded by causes. In the more severe cases, muscle cramps are almost invariably present and commonly involve the calves. When first seen by the physician, the patient who is severely ill with cholera is cyanotic, has sunken eyes and cheeks, a scaphoid abdomen, poor skin turgor, and thready or absent peripheral pulses. The voice is high-pitched or inaudible; the vital signs include tachycardia, tachypnoea and low or unobtainable blood pressure. There may be either low-grade fever or slight hypothermia. The heart sounds are distant, often inaudible, and bowel sounds are usually hypoactive. Major alterations in mental status are not common in adults; the adult cholera patient usually remains oriented, although apathetic, even in the face of severe hypovolemic shock. Central nervous system abnormalities, ranging from stupor to convulsions and coma, are much more common in paediatric patients, and may occur in up to 10% of small children with cholera. In all epidemics there are large numbers of mild cases in which loss of fluid from the gut is not severe enough to require hospitalization. There are even larger numbers of completely asymptomatic people who transiently excrete V. cholerae.[2]

In the absence of antimicrobial therapy, the gastrointestinal loss of fluid and electrolytes may continue for up to seven days, and subsequent manifestations depend upon the adequacy of replacement therapy. With prompt repletion of fluid and electrolyte, physiologic recovery is remarkably rapid and uniform despite continuing voluminous diarrhoea. If therapy is inadequate, the mortality rate in hospitalized cases may exceed 50%. The important causes of death uncompensated metabolic acidosis, and uraemia, hypovolemic shock.[3]

Cholera is a waterborne disease caused by the bacterium Vibrio cholerae. This pathogen leads to acute gastrointestinal infection, which can result in severe dehydration due to profuse diarrhoea. Here's a detailed breakdown of the etiology of cholera:

1.Causative Agent: The bacterium Vibrio cholerae is a gram-negative, comma-shaped organism. Not all strains of V. cholerae cause cholera; the disease-causing ones belong to two serogroups, O1 and O139. These serogroups produce cholera toxin (CT), which is central to the disease's pathogenesis.

V. cholerae O1 is further classified into two biotypes: Classical and El Tor. The El Tor biotype is responsible for most of the recent pandemics, as it is more resistant to environmental stresses and has a longer duration of asymptomatic carriage.

2.Cholera Toxin and Pathophysiology Cholera toxin (CT): is a potent exotoxin composed of two subunits: A (enzymatic) and B (binding).

The B subunit binds to the GM1 ganglioside receptors on the surface of epithelial cells lining the small intestine.

Once bound, the A subunit is internalized into the cell, where it activates adenylate cyclase through a G-protein mechanism. This leads to a massive increase in cyclic AMP (cAMP) levels.

Elevated cAMP levels disrupt the normal electrolyte balance, causing chloride ions (Cl-) to be secreted into the intestinal lumen. Sodium (Na+) and water follow, resulting in massive fluid loss into the intestines.

This manifests clinically as profuse, watery diarrhoea, often described as "rice-water stool" because of its pale, cloudy appearance containing mucus and epithelial cells.[5]

3.**Modes of Transmission:**

Waterborne Transmission: Cholera is typically transmitted through drinking water contaminated with faeces containing V. cholerae. This is common in areas with inadequate sewage disposal, or following environmental disasters (e.g., floods, earthquakes) that compromise water sanitation.

Foodborne Transmission: Consumption of food contaminated with V. cholerae, either through direct

contamination by faecal matter or indirectly through unsanitary handling or preparation, can lead to infection.

Human to Human: While not common, cholera can spread via direct contact, particularly in household where a cholera patient is being cared for and hygiene practice are insufficient.[6]

TYPES OF CHOLERA

Cholera is an infectious disease caused by the bacterium Vibrio cholerae. There are two main types of Vibrio cholerae that cause the disease, classified based on the sero groups of the bacteria. These are

1. Classical Cholera (Serogroup O1)

The Vibrio cholerae serogroup is the most common cause of cholera outbreaks and is responsible for major pandemics. There are two biotypes of the O1 serogroup Classical Biotype: This strain caused several pandemics in the 19th and early 20th centuries but is less common today. El Tor Biotype: This is the predominant strain in modern times and has been responsible for the 7th cholera pandemic, starting in the 1960s and continuing to the present. The O1 serogroup itself has two major serotypes Ogawa: This strain produces a specific type of O antigen. Inaba Another variation of O antigen. There is also a rare third serotype called HI Kojima, which expresses both Ogawa and Inaba antigens.[7]

2. Serogroup

This strain emerged in the 1990s in South Asia and caused significant outbreaks. Unlike O1, O139 strains have a different surface antigen, making it distinct.O139 is less widespread but still poses a threat, particularly in regions where O1 cholera is also present.[8]

CAUSES OF CHOLERA IN CHILDREN

1.Contaminated Water and Food

One of the primary causes of cholera is the ingestion of water or food contaminated with Vibrio cholerae. According to WHO reports, cholera outbreaks are most common in areas where access to clean water is limited, and sanitation infrastructure is inadequate. In regions where sewage and drinking water systems are not well separated, children are more vulnerable to consuming contaminated water and food, especially in slums.[9]

2. Poor Hygiene Practices

Poor personal and community hygiene practices are significant contributors to cholera transmission, particularly among children. Studies by Curtis and Cairn cross (2003) suggest that handwashing with soap can reduce diarrheal disease by 42-47%, but in many low-income regions, access to soap and water is limited. Children, who are often unaware of hygiene protocols, are more likely to engage in behaviour's that increase their risk of infection, such as playing in contaminated environments or handling food without washing hands.[10]

3. Inadequate Sanitation

Lack of proper sanitation infrastructure in many low-income and conflict-affected regions exacerbates cholera outbreaks. Research indicates that cholera thrives in environments where open defecation is common, leading to the contamination of nearby water sources. In rural areas of sub-Saharan Africa and South Asia, poor sanitation has been a key factor in the high incidence of cholera cases among children (Clasen et al., 2014).2.4 Malnutrition and Weakened Immune Systems Children suffering from malnutrition are at higher risk of contracting cholera. Malnutrition weakens the immune system, making it harder for the body to fight off infections, including Vibrio cholerae. Several studies have shown that malnourished children tend to have more severe symptoms and higher mortality rates than well-nourished children (Bhutta et al., 2017)[11]

EFFECTS OFCHOLERA ON CHILDREN

1. **Acute Dehydration**

Cholera leads to severe diarrhoea and vomiting, causing rapid fluid loss, which can lead to dehydration. In children, dehydration is particularly dangerous due to their smaller body size and greater vulnerability to electrolyte imbalances. If untreated, severe dehydration can cause death within hours. UNICEF has documented that dehydration is the leading cause of death in children with cholera.[12]

2. **Malnutrition Cholera**

exacerbates malnutrition in children, particularly in regions where food insecurity is already prevalent. The loss of fluids, essential electrolytes, and nutrients during a cholera infection can cause weight loss and nutritional deficiencies. Research shows that repeated bouts of cholera and other diarrheal diseases can lead to chronic malnutrition, stunted growth, and cognitive impairment (Guerrant et al., 2013[13])

3 **Increased Mortality Children**

under five are disproportionately affected by cholera-related mortality. Data from the Global Task Force on Cholera Control indicates that 20-30% of all cholera deaths worldwide occur in children under the age of five. High mortality rates are associated with delayed treatment, lack of access to oral rehydration solutions (ORS), and coexisting conditions like malnutrition and other infectious diseases (Rochelle et al.,2017[14])

4 **Long-term Health and Cognitive Impacts**

Although cholera is typically an acute illness, children who survive severe cases may experience long-term health consequences. Persistent malnutrition caused by recurrent cholera can impair physical and cognitive development. Studies have shown that children who survive severe diarrhoea episodes, including cholera, are more likely to suffer from cognitive delays, impaired learning, and developmental issues (Checkley et al., 2008)[16]

CLINICAL PRESENTATION

SIGNE OF CHOLERA

Cholera is primarily characterized by acute gastrointestinal symptoms, which can range from mild to severe. Here are the main signs and symptoms.

Watery Diarrhoea

The hallmark symptom of cholera is profuse, watery diarrhoea often described as "rice water stools" due to its pale, cloudy appearance. Diarrhoea can be sudden and extreme, leading to rapid fluid loss.

Dehydration

Severe dehydration is a common complication due to the massive loss of fluids and electrolytes. Signs of dehydration include: Dry mouth and skin Excessive thirst, Sunken eyes, Reduced urine output, Lethargy or fatigue.

Vomiting

Frequent vomiting is often associated with cholera, contributing further to fluid loss.

Rapid Heartbeat (Tachycardia)

Due to dehydration, the heart may beat faster as the body tries to maintain circulation.

Low Blood Pressure

Significant fluid loss can result in hypotension (low blood pressure).

Muscle Cramps

As electrolytes are depleted (especially sodium, potassium, and chloride), painful muscle cramps may occur.7. Cold, Clammy Skin The body may struggle to maintain temperature, and the skin may feel cold and moist due to circulatory issues.

Restlessness or Irritability

Severe dehydration can also lead to confusion, irritability, or restlessness, particularly in children.

Shock

In severe cases, when fluid loss is not replaced, the patient can go into hypovolemic shock, characterized by cold skin, weak pulse, and loss of consciousness, which can be life threatening. [17]

DIGNOSIS

Most people who contract cholera have mild or asymptomatic disease although they can shed vibrio's in their stool for 7-14 days. Only 10-20% will develop diarrhoea severe enough to cause dehydration. Clinically, cholera presents with acute watery diarrhoea and painless vomiting, without blood in the stool or (usually) abdominal cramps. The majority of cases are clinically indistinguishable from other causes of watery diarrhoea and require only oral rehydration fluid as treatment. However, some will progress to classical or severe cholera.

The classical picture is of the rapid onset of profuse watery diarrhoea (rice-water stool) and vomiting which is painless which can result in circulatory collapse within hours without effective treatment. The history is usually less than 24 h although it may be longer if oral rehydration solution is being taken by the patient. Abdominal cramps may occur. Fever is absent. Patients usually remain alert but severe electrolyte abnormalities such as hypoglycaemia and hyponatraemia can cause a reduced level of consciousness or convulsions, especially in children. Acidosis is often severe and results in tachypnoea. A common mistake is to misdiagnose this as pneumonia. Patients should be reassessed for the presence or absence of pneumonia 1-2 h after adequate rehydration.

The diagnosis of cholera can be confirmed by rapid dipstick tests, the presence of rapidly motile vibrios by dark-field microscopy, or by stool or rectal swab culture. However, the classical his- tory, appearance of the stool and rapid presentation mean that the diagnosis is usually clinical. Blood tests are not usually needed although serum electrolytes and blood glucose may be useful in patients with more severe symptoms such as confusion or convulsions, those with an ileus, or those with anuria that doesn't respond to fluid resuscitation. [22]

In cholera endemic or epidemic areas, the working diagnosis of cholera should be made on the basis of the clinical picture of severe saline depletion in a patient with a history of abrupt onset of watery and generally painless diarrhoea. Therapy should be initiated immediately on the basis of the clinical diagnosis. It is very important to recognize the fact that, although a cholera like illness may be caused by micro-organisms other than V, cholerae, the resulting physiologic and metabolic abnormalities are essentially the same, so that identical therapy is indicated in all such cases."

Diagnostic culture techniques are relatively simple. A reliable and practical method consists of direct plating of faces on TCBS agar. Typical opaque yellow colonies appear in 18 hours. Final identification

requires agglutination with group and type-specific antisera and demonstration of characteristic biochemical reactions. Rapid, tentative diagnosis may be made by direct observation of the characteristic rapid motility of the comma-shaped bacilli in fresh faces by dark-field micros copy. Group and type-specific antisera will immobilize homologous strains and clearly distinguish them from other vibrios. [22]

MANEGMENT

A clinical syndrome of acute watery diarrhoea (3 or more watery stools in last 24 h) of short duration (24-48 h) with or without vomiting associated with dehydration in anyone over 2 years of age in an endemic or epidemic situation should be treated as cholera.

In children under 2 years of age with acute watery diarrhoea the likelihood of other diagnoses such as rota virus increases. However, the management of the clinical syndrome is the same unless there are comorbidities such as malnutrition. In children less than 1 year of age or less than 2 years of age with malnutrition the rate of rehydration needs to be slowed.

The mainstay of management (whatever the causative organism) is appropriate early rehydration and time should not be wasted worrying about investigations or which antibiotic to use. The initial assessment should be brief but must.

1. Confirm the diagnosis of acute watery diarrhoea
2. Assess the level and severity of dehydration
3. Assess the presence or absence of malnutrition
4. Recognise any other co-morbidities

Accurate assessment and rapid appropriate treatment of dehydration is critical to the management of cholera. A simple scoring system based on five clinical signs is sufficient and can accurately predict patients with 5-10% (some) dehydration and >10% (severe) dehydration. Common include over-reliance on individual clinical signs resulting in either an inappropriate diagnosis of severe dehydration or, conversely, missing severe dehydration in an alert patient.

Clinicians who are not used to treating cholera often underestimate the amount of fluid that has been lost and the rapidity with which it needs to be replaced. This results in giving too little intra- venous fluid during the initial phase which can have a negative impact on the outcome.

Further, inexperienced clinicians underestimate the ability to rehydrate patients orally and this results in the unnecessary use of intravenous fluid during the recovery phase. While this does not usually have a negative impact on the patient it can result in the unnecessary use of scarce intravenous fluids in an epidemic situation and also requires a greater use of staff time which, again, may be in short supply.

Patients with <5% (no) dehydration and 5-10% (some) dehydration can be managed with oral rehydration alone unless there is a reduced level of consciousness or inability to take fluids by mouth. Those with 5-10% (some) dehydration must be reassessed every 1-2h to make sure that hydration is improving. Breastfeeding should be continued in infants and young children.

Patients with severe dehydration require an immediate intra- venous fluid bolus of 100 ml/kg given over 3 h with 1/3 in the first 30 min (double the duration in children less than 1 year and in those with malnutrition). If possible, the intravenous fluid should contain sodium, potassium and bicarbonate Ringers Lactate is usually the fluid of choice (or Cholera Saline), but normal saline with 5-10 mmol/L of potassium may also be used. Oral rehydration should start at the same time. If potassium is not avail- able the ORS, which contains potassium, will compensate to some extent. Once the intravenous fluid bolus has finished further intra- venous fluids are usually not required.

Reduced osmolarity ORS is recommended by WHO for use in children with cholera and non-cholera diarrhoea. Initial concerns that when used in adults with cholera there may be a higher risk of hyponatraemia have been disproved in large scale field studies and this is also the fluid of choice for oral rehydration in adults. ORS can be made at home if sterile water and ingredients are available and certain traditional drinks are also suitable. However, properly prepared reduced osmolarity ORS is the fluid of choice.

After an initial assessment has been made and fluids started a fuller clinical assessment can take place. Patients with significant co-morbidities may require individually tailored treatment plans. In patients with moderate or severe dehydration antibiotics reduce the duration of illness and fluid loss and can shorten the

excretion of vibrio by 1-2 days. Thus, they reduce the length of stay and fluid requirement in patients with severe dehydration due to cholera. A single dose is usually sufficient and is given once any vomiting has stopped. It should be repeated if the dose is vomited back. Doxycycline is still the most commonly used drug world- wide but drug resistance is common thus the choice of antibiotic should be guided by local sensitivities where these are available. If not, a single dose of azithromycin 1 g in adults and 20 mg/kg in children is recommended. If ciprofloxacin is used a daily dose for 3 days is now recommended as the MIC is now higher than previously observed and single dose is not as effective. All children between 6 months and 5 years should receive zinc 20 mg/day for 10 days as this reduces subsequent mortality and further episodes of diarrhoea. [19]

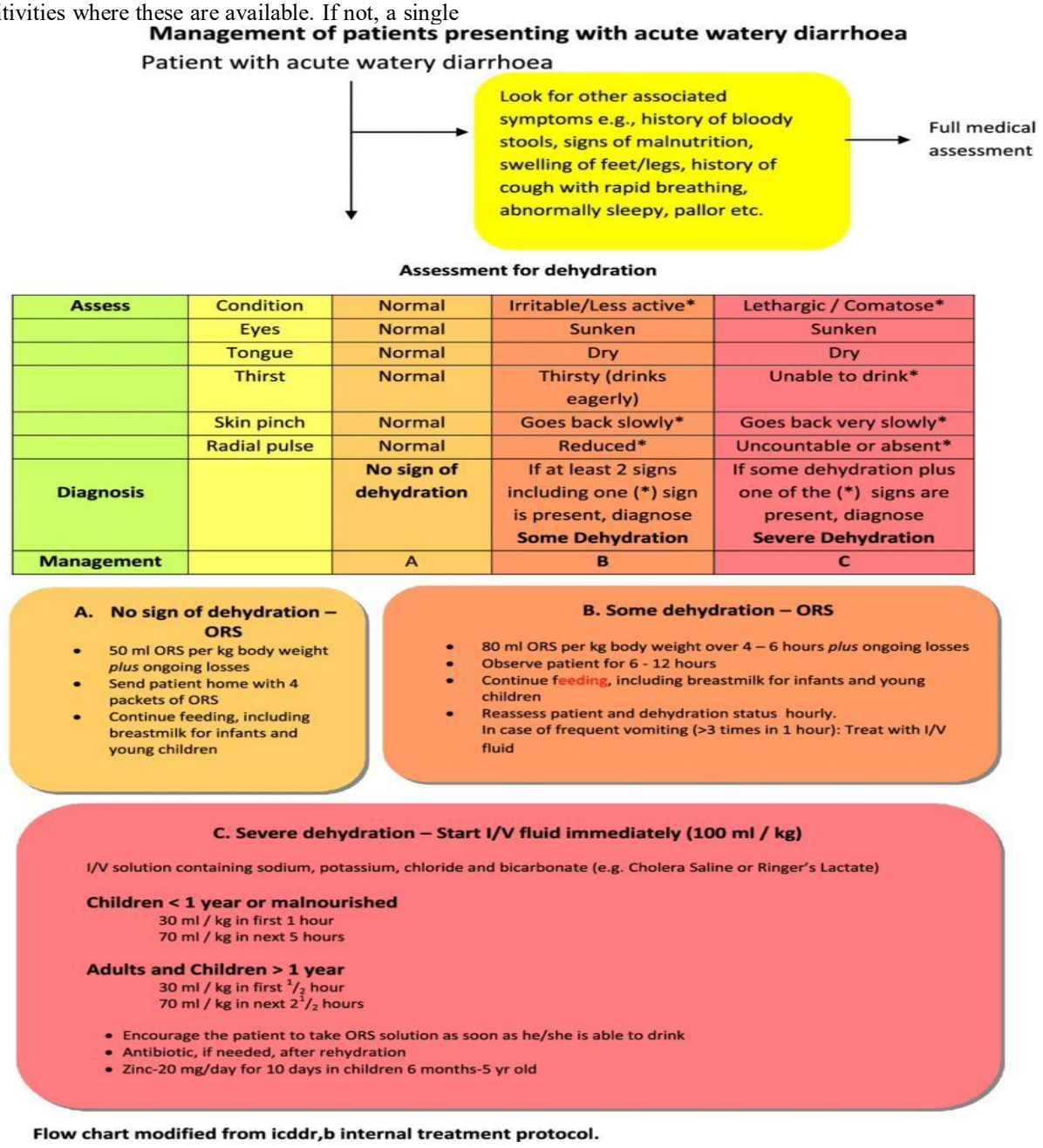

Fig. 1. Flow Chart For The Management of Patient Presenting With Acute Watery Diarrhoea.

1.**Intravenous fluid therapy**

Successful therapy of cholera and the cholera like diarrheal illnesses requires only prompt and adequate replacement of the fluid and electrolytes which have

been lost from the gastrointestinal tract. Several inter-related factors are critical to appropriate replacement of these losses of electrolyte fluid. These include the solute concentrations of the fluid used to replace these losses, the route of administration of the replacement fluids, and the rate at which the replacement fluids should be administered.

Adults. Table I shows typical stool electrolytes in the severely ill adult cholera patient. The stool is nearly isotonic with plasma, the bicarbonate concentration is roughly twice that of normal plasma, and the potassium concentration is nearly five times that of plasma. The patient who loses this fluid therefore develops an isotonic extracellular fluid deficit and metabolic acidosis, and may develop a clinically significant degree of hypokalaemia.

The potassium concentration in the stool varies inversely with the rate of fluid loss, and the figures shown in Table I represent values obtained at a time when the mean stool output was 15% of body weight per 24 hours. With stooling rates of less than 5% of body weight per 24 hours, the stool potassium concentration may be as high as 40 mEq/A, but the absolute loss of potassium with acute diarrheal disease of such magnitude is not great enough to be of major clinical significance, Re- placement of fluid in adults should therefore be designed roughly to replace the electrolytes outlined in Table I. In the treatment of the adult patient, there is a fair amount of leeway which will be discussed below.

Based on the known gastrointestinal electrolyte losses, the ideal re- placement solution in the adult cholera patient should be roughly isotonic with plasma, with a sodium concentration nearly equal to that in plasma, and a bicarbonate concentration twice that of plasma. When replacement is by the intravenous route a concentration of potassium of 8 το mEq/1. is usually employed, because of the danger of hyperkalaemia if fluids with higher potassium concentrations are infused at the rates sometimes required for treatment of the seriously saline-depleted individual. In actual fact, intravenous potassium therapy is seldom essential in the adult patient. There are two reasons for this. First, symptomatic hypokalaemia is rarely seen in adults with acute diarrheal disease, despite relatively large potassium losses. Second, absorption of potassium by the small bowel is not significantly impaired during cholera, and repletion of potassium can be achieved effectively by the oral route. In actual fact, 100% recovery of adult patients severely ill with cholera has been achieved by the simple intravenous administration of an isotonic intra- venous solution containing two parts sodium chloride to one part sodium lactate. The left column in Table II shows the mean admission blood chemical determinations on 38 consecutive hypotensive, adult cholera patients. Observe the striking elevation in plasma protein concentration, reflecting the loss of roughly half the extracellular fluid volume, and the marked metabolic acidosis. The right column of Table II shows the same values four hours later, after administration of the 2:1 saline: lactate mixture in amounts equal to to% of the body weight of the patients. Observe that the mean plasma protein concentration and arterial blood pH are now within normal limits, and that, concomitant with extracellular fluid volume expansion and correction of the acidosis, the plasma.

Potassium level has fallen sharply. A more ideal adult replacement solution, outlined in Table III, can be prepared by the simple addition of 5 gm. sodium chloride, 4 gm. sodium bicarbonate, and 1 gm. potassium chloride to 1. of sterile, pyrogen-free distilled water. In the preparation of this solution the sodium bicarbonate must be added after the bottle is autoclaved. Even this relatively simple problem can be overcome by substituting equimolar amounts of sodium acetate, which readily stands autoclaving, for the sodium bicarbonate. The acetate, like the lactate, is rapidly metabolized after intravenous administration, yielding mole of bicarbonate for each mole of acetate which is administered. The rate of intravenous fluid administration is determined by the degree of saline depletion. In hypotensive adult patients the initial infusion is given rapidly (at rates of go to 100 ml./min.) until a strong radial pulse has been restored. Subsequently the fluids are infused in quantities equal to the gastrointestinal losses, Ideally, each patient should be placed on a "cholera cot," with the buttocks positioned over a hole leading directly to a collecting bucket. If the fluid losses cannot be accurately measured (ie., if cholera cots and calibrated buckets are not available), intravenous fluids should be given at a rate sufficient to maintain a normal radial pulse volume and normal skin turgor. Over hydration can be avoided by careful observation of the neck veins and auscultation reduced level of consciousness or inability to take fluids by mouth. Those with 5-10%

(some) dehydration must be reassessed every 1-2h to make sure that hydration is improving. Breastfeeding should be continued in infants and young children.

Patients with severe dehydration require an immediate intra- venous fluid bolus of 100 ml/kg given over 3 h with 1/3 in the first 30 min (double the duration in children less than 1 year and in those with malnutrition). If possible, the intravenous fluid should contain sodium, potassium and bicarbonate Ringers Lactate is usually the fluid of choice (or Cholera Saline), but normal saline with 5-10 mmol/L of potassium may also be used. Oral rehydration should start at the same time. If potassium is not avail- able the ORS, which contains potassium, will compensate to some extent. Once the intravenous fluid bolus has finished further intra- venous fluids are usually not required.

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In patients with moderate or severe dehydration antibiotics reduce the duration of illness and fluid loss and can shorten the excretion of vibrio's by 1-2 days. Thus, they reduce the length of stay and fluid requirement in patients with severe dehydration due to cholera. A single dose is usually sufficient and is given once any vomiting has stopped. It should be repeated if the dose is vomited back. Doxycycline is still the most commonly used drug world- wide but drug resistance is common thus the choice of antibiotic should be guided by local sensitivities where these are available. If not, a single dose of azithromycin 1 g in adults and 20 mg/kg in children is recommended. If ciprofloxacin is used a daily dose for 3 days is now recommended as the MIC is now higher than previously observed and single dose is not as effective. All children between 6 months and 5 years should receive zinc 20 mg/day for 10 days as this reduces subsequent mortality and further episodes of diarrhoea.

Recovery from cholera is rapid and mortality extremely low if the dehydration is treated appropriately. The Cholera Hospital run by icddr ,b in Dhaka, Bangladesh treats around 150,000 patients a year, one third of whom present with severe dehydration. The average length of stay is 16h and the mortality rate in patients without comorbidities is zero. the lungs. Close observation of the patient is mandatory during the first two days of therapy; an adult patient can lose up to 1 1. of isotonic fluid per hour during the first 24 hours of illness.

Although determination of whole blood or plasma specific-gravity has been employed historically as a means to estimate fluid deficit in cholera patients, this technique has been found in recent years to be of less value under epidemic conditions than the careful, sequential clinical evaluation of the patient. This specific gravity technique has several important limitations.) This test, like any other, is subject to errors in sampling, handling, and reading which are likely to be multiplied during epidemic situations. 2 The correlation between isotonic fluid deficit and plasma specific gravity is nor a straight-line one, as demonstrated by Figure 1, and the technique therefore fails to provide a consistently accurate means of determining requirements of fluid. 3It is further my strong impression that, in the management of large numbers of cholera patients, emphasis on any technique other than bedside evaluation tends.

To detract from the quality of the care of patients. The route of intravenous fluid infusion is generally no great problem in adult patients, in whom a needle of large bore, No. 16 or No. 18, can generally be inserted in an antecubital vein. Children. The stool electrolyte pattern in children, shown in Table IV, varies significantly from that of the adult in that the mean sodium concentration is significantly lower, and the mean potassium concentration is significantly higher than that in adult patients. The basis for these differences is not yet understood, but they are of critical importance in determining the optimal therapeutic regimen for patients weighing less than 20 kg.

The paediatric patient not only requires a different intravenous solution because of the different composition of the stool, but the patient also requires a more precise correction of the electrolyte losses. Table V shows the composition of fluid which appears

appropriate for the treatment of paediatric diarrhoea. This regimen, developed by the U.S. Naval Medical Research Unit in Manila, takes into consideration the hypotonicity of the paediatric stool losses, the relatively greater potassium requirements, and the fact that serious hypoglycaemia not uncommonly accompanies severe diarrhoea in paediatric patients. There is less leeway in paediatric than in adult patients, both in regard to the tonicity and in regard to the potassium concentration of the administered fluids. Whereas the adult rarely develops serious problems-albeit he gets very thirsty-with moderate degrees of hypernatremia, the paediatric patient may develop organic brain damage when the serum sodium concentration is in the 160 to 170 mEq./1. range. The intravenous administration of an isotonic solution to a paediatric patient with diarrheal disease may therefore cause serious brain damage or death, unless appropriate. amounts of water are given by mouth..

2. Antimicrobial therapy

Although intravenous fluid therapy, when promptly and adequately administered, results in survival of virtually all cholera patients, the intravenous fluid requirements may be staggering, and occasional patients have required intravenous fluids in amounts equal to twice their body weight. In fact, the average intravenous fluid requirement in one carefully studied group of adult cholera patients was 241. The logistic problems presented by such fluid requirements are overwhelming in the impoverished rural areas in which cholera outbreaks most frequently occur. It was therefore a welcome finding, in 1963, that tetracycline therapy results in a 60% reduction in gastrointestinal fluid loss, and an equally great reduction in duration of diarrhoea in the seriously ill cholera patient. Tetracycline, in the dosage of 40 mg./ kg. per day, given in divided doses for two days, also eliminates V. cholerae from the stool in the great majority of cholera patients. Other antimicrobial agents, most notably furazolidone and chloramphenicol, have also proved highly effective in reducing gastrointestinal fluid losses in cholera, but both these agents appear to be slightly less effective than tetracycline.

Tetracycline therapy has therefore more than doubled the number of patients who can be treated adequately with a given amount of intravenous fluids. Since the availability of intravenous fluids is frequently the limiting factor in dealing with outbreaks of cholera, anti- microbial therapy has proved to be a major advance in the management of cholera. Even with appropriate antimicrobial therapy, however, the requirements of fluid remain large. The average intravenous fluid requirement in this group of tetracycline-treated patients.

3. Oral electrolyte therapy

The development of oral therapy for cholera in the late 1960's was, therefore, another milestone in the treatment of this disease, as it further extended by several fold the number of patients to whom adequate treatment could be given in situations in which the supply of intravenous fluids is limited. The development of oral therapy is a particularly interesting one, as it involves the direct clinical extension of an observation which had previously appeared to be relevant only in the realm of basic physiologic research: namely, that intraluminal glucose enhances ab- sorption of sodium by the mammalian small intestine. As expressed earlier in this symposium, the primary problem in cholera is that of the increased secretion of isotonic fluid by the small intestine caused by the cholera enterotoxin. The enterotoxin has no significant effect on movement of sugar from gut lumen to plasma. Nor does the enterotoxin alter the enhancement of lumen-to-plasma movement of sodium which is caused by intraluminal glucose. It has therefore been possible to developed a solution containing both glucose and sodium which, when administered orally to the actively purging cholera patient, can maintain adequate fluid and electrolyte balance. Although solutions with a wide variety of glucose concentrations, as well as certain variations in electrolyte concentrations, have been tested under field conditions, solutions approximating that shown in this table have proved most successful in maintaining fluid balance in both paediatric and adult cholera patients. While all severely saline-depleted cholera patients require intravenous fluids until adequate circulation is restored, the oral route has been used successfully both for maintenance therapy in the more severely ill patients and for the entire requirements of fluid remain large. The average intravenous fluid requirement in this group of tetracycline-treated patients. course of therapy in patients with less severe disease. Although oral therapy has been of greatest value in adults, it can also be effectively employed in children who are alert and able to retain orally administered solutions. It is important to emphasize that successful management of the cholera patient with oral therapy demands just as close supervision, with careful monitoring of pulse volume, skin turgor, and neck veins, as does management with intravenous solutions. Supplemental intravenous fluids must be administered whenever clinical signs of saline depletion recur.

Of critical importance to the proper management of the cholera patient is the knowledge that hypotension, when present, is entirely due to hypovolemia. A number of pharmacologic agents, including cardiotonic drugs, sympathomimetic amines, central nervous system stimulants, steroids and ant peristaltic agents have sometimes been employed in the treatment of this disease. The use of all such agents is strongly contraindicated. Certain of these agents are clearly harmful (e.g., by precipitating cardiac arrhythmias or intensifying renal ischemia in the hypotensive patient), and the use of any such agents detracts from the primary goal of prompt and adequate fluid and electrolyte replacement.

4.New therapeutics approaches

The essence of this discussion has been that every cholera patient should survive if he receives adequate replacement therapy. Adequate therapy for patients in cholera endemic areas has often been, and frequently still is, impossible because of the lack of adequate supplies of sterile, pyrogen-free fluids. The requirement for such fluids has been greatly decreased, first by the use of appropriate antimicrobial therapy and, more recently, by the use of an oral electrolyte replacement regimen. Patients still, however, die of cholera, and the mortality rates in certain of the recent outbreaks in Africa have been extremely high. Even with adjuvant antimicrobial therapy and oral electrolyte replacement, adequate intravenous fluids have often not been available in the areas in which cholera has occurred. The recent advances in our understanding of the mechanism by which the cholera enterotoxin acts has led to the hope of developing an agent which, without causing unacceptable side effects, will rapidly reverse the action of the cholera enterotoxin. Since the enterotoxin appears to achieve its effect by stimulating adenyl cyclase in the gut epithelial cell wall, it is hoped that enterotoxin action may be blocked either by an antagonist of adenyl cyclase or by an agent which lowers intracellular levels of cyclic 3'5' adenosine mono- phosphate. Considerable research is presently being directed toward this goal.[20][21].

VACCINE

Cholera vaccines play an important role in preventing and controlling cholera, especially in areas where access to clean water and sanitation is limited. There are two main types of cholera vaccines: oral cholera vaccines (OCVs) and a lesser-known injectable cholera vaccine that is no longer in use. Most cholera vaccines in use today are oral, and there are several formulations available.

Oral Cholera Vaccines (OCVs): OCVs are the primary type of vaccine used to prevent cholera. They provide immunity by stimulating the body's immune system to produce antibodies against Vibrio cholerae, specifically targeting the cholera toxin or the O-antigen. OCVs are used both for routine immunization in endemic areas and during outbreaks as part of emergency response efforts. They are safe and effective, with minimal side effects.

- **Dukoral Type:** Killed whole-cell Vibrio cholerae O1 strain with recombinant cholera toxin B subunit (CTB). Escherichia coli (ETEC), another cause of travellers' diarrhoea.
- **Formulation:** Contains inactivated (killed) Vibrio cholerae O1 bacteria (both Classical and El Tor biotypes) and cholera toxin subunit.
- **Dosage:** Adults and children aged 6 years and older receive 2 doses, 1-6 weeks apart. Children aged 2-6 years receive 3 doses.
- **Efficacy:** Provides about 85-90% protection in the short term, with immunity lasting for about 2 years. Booster doses are required for continued protection.
- **Administration:** Oral suspension mixed with a buffer solution to neutralize stomach acid.
- **Indications:** Approved for use in travellers and people in endemic regions, though it is also effective against enterotoxigenic

A. Shanchol Type: Killed whole-cell Vibrio cholerae O1 and O139.

- **Formulation:** Contains inactivated Vibrio cholerae O1 (Classical and El Tor biotypes) and O139 serogroups but lacks the cholera toxin subunit.
- **Dosage:** Two doses given 2 weeks apart. Booster doses can be given after 3 years.
- **Efficacy:** Provides around 65% protection for up to 5 years in endemic populations.
- **Administration:** Oral, no need for buffer solution, making it easier to administer in field settings.
- **Indications:** Primarily used in mass vaccination campaigns and endemic areas. Approved by the World Health Organization (WHO) for pre-emptive use in high-risk populations.

C. Euvichol-Plus Type: Killed whole-cell Vibrio cholerae O1 and O139.

- **Formulation:** Similar to Shanchol, it contains inactivated Vibrio cholerae O1 and O139 but is available in a more affordable and easy-to-administer package.
- **Dosage:** Two doses given 2 weeks apart, similar to Shanchol.

- **Efficacy:** Provides similar protection as Shanchol, about 65% efficacy for up to 5 years.
- **Administration:** Oral liquid formulation.
- **Indications:** Mainly used in mass vaccination efforts, particularly in lower-income settings or during outbreaks. [23]

Efficacy of OCVs

- **Short-term Protection:** short-term protection. Within the first year after vaccination, protection rates are high ranging from 60% to 90%.
- **Long-term Protection:** Over time, the protection from OCVs wanes. After two years, protection is around 60%, and after five years, it can drop further. Booster doses can extend protection.
- **Effectiveness During Outbreaks:** OCVs are effective for preventing the spread of cholera during outbreaks, especially when deployed quickly. They are used in combination with improved water, sanitation, and hygiene (WASH) measures.3.
- **Availability and Usage:** OCVs are part of the WHO's cholera control strategy, especially in areas experiencing outbreaks or where cholera is endemic. Mass vaccination campaigns using Shanchol and Euvichol-Plus have been effective in controlling cholera in countries such as Haiti, Yemen, and parts of Africa and Southeast Asia. Travelers to cholera-endemic regions can also receive the vaccine, particularly Dukoral, to protect themselves from infection.
- **Oral Cholera Vaccine Stockpile:** The WHO maintains a global cholera vaccine stockpile to respond to emergencies and outbreaks. It ensures that vaccines are rapidly deployed in areas experiencing cholera outbreaks, usually within a few weeks of an outbreak being declared. Since 2013, millions of OCV doses have been distributed through this stockpile to countries in Africa, the Middle East, and South Asia.
- **Discontinued Injectable Cholera Vaccine:** Injectable Cholera Vaccine: Historically, cholera vaccines were delivered by injection, but they were less effective and provided only short-term immunity. These vaccines were phased out in favour of more effective oral vaccines, which have higher efficacy and fewer side effects. Injectable vaccines offered low efficacy (about 50%) and required frequent boosters. They also did not stimulate mucosal immunity, which is key in preventing cholera in the intestines. [24]

RAPID ADVANCED HEALTHCARE TECHNOLOGIES

Recent innovations in cholera vaccines include the development of Euvichol-S, an oral cholera vaccine that received WHO prequalification in 2024. This vaccine is an optimized version of Euvichol Plus, designed to simplify its production while maintaining its efficacy. The streamlined manufacturing process allows for faster production at a lower cost, making it possible to meet increasing global demand due to the surge in cholera outbreaks since 2021. Euvichol S is expected to add up to 50 million doses to the global stockpile, a significant increase compared to previous years.

Additionally, researchers have developed a novel conjugate vaccine, utilizing a new method for linking bacterial polysaccharides to proteins, which simplifies the production process. This approach, demonstrated in cholera vaccine prototypes, could improve the efficiency and reproducibility of vaccine manufacturing, offering potential for broader applications in vaccine development.

Several ground breaking innovations have emerged across medicine and technology. Here are some key highlights:

1. **Cell Therapy for Melanoma:** In 2023, the FDA approved the first cellular therapy for advanced melanoma. This treatment involves extracting and replicating T-cells from a patient's tumor to boost the immune system's response. It showed promising results, with about 56% of patients responding to the treatment and 24% experiencing complete remission 1991.
2. **Menstrual Blood as a Diagnostic Tool**: In early 2024, the FDA approved the Q Pad, a menstrual pad that collects blood for non-invasive health diagnostics. This pad can track blood sugar levels and potentially diagnose other conditions such as HPV.
3. **Robotic Surgery Innovations**: Advances in surgical robotics include devices like Stryker's Mako for spinal and shoulder surgeries and Zimmer Biomet's ROSA Shoulder robotic system, both launching in 2024. These innovations enhance precision and improve patient outcomes.
4. **Mon-Insulin CGMs:** Dexcom is set to launch a continuous glucose monitor (CGM) tailored for non-insulin users by 2024. This device will provide insights without the alarms typical for insulin users, catering to a large portion of diabetic patients [25]

SUMMARY

Cholera among children is a significant public health concern, particularly in regions with limited access to clean water and proper sanitation. The primary cause is the ingestion of Vibrio cholerae bacteria through contaminated water or food, often due to inadequate waste disposal, poor hygiene practices, or exposure to unsanitary environments following natural disasters like floods. Children are highly susceptible to cholera because their immune systems are not fully developed. The disease leads to rapid dehydration due to profuse watery diarrhoea and vomiting, which can result in shock and death if medical intervention is delayed. Dehydration also worsens malnutrition, a common issue in areas where cholera outbreaks occur, further weakening children's ability to recover. The effects of cholera extend beyond health risks. When children contract cholera, they may miss extended periods of school, affecting their education and social development. In communities with frequent outbreaks, cholera can perpetuate cycles of poverty and under development. Efforts to combat cholera in children focus on improving access to safe drinking water, enhancing sanitation infrastructure, promoting proper hygiene practices such as handwashing, and ensuring prompt treatment through oral rehydration solutions (ORS) or intravenous fluids in severe cases Vaccination campaigns and community awareness programs are also important for preventing outbreaks. The disease leads to severe dehydration due to watery diarrhoea and vomiting, which can be life-threatening if untreated. Children are particularly vulnerable, with cholera worsening malnutrition and increasing mortality rates. The disease also impacts their education, as affected children often miss school. Preventive measures, such as access to clean water, sanitation, and oral rehydration therapy, are crucial to managing and reducing cholera's effects on children.

CONCLUSION:

Cholera among children is a major public health challenge in regions with poor sanitation, inadequate water supply, and high rates of malnutrition. Children, due to their vulnerability, suffer both acute and long-term health consequences from cholera. Preventive measures such as improved sanitation, access to clean water, and hygiene education are critical to reducing cholera incidence. Furthermore, timely treatment with ORS, antibiotics, and nutritional support can reduce mortality and prevent long-term developmental impacts. Ongoing research and intervention efforts must focus on addressing the underlying factors of cholera transmission to protect children in vulnerable communities.

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