

## CHOLERA

### METHOD OF PAKISTAN-SEATO CHOLERA RESEARCH LABORATORY\*

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The copious "rice water" diarrhea which characterizes cholera may result in the loss of as much as one liter of body fluid per hour. This causes a typical clinical syndrome marked by dehydration, acidosis and shock. Vascular collapse can result within two hours of the abrupt onset of disease. Death may occur within four hours, but more often after 24 hours of illness. *Vibrio cholerae* can often be isolated in nearly pure culture from the stools of early cases. Sometimes, cases clinically indistinguishable from cholera occur in which no pathogen can be isolated. On the other hand, *V. cholerae* infection may also be associated with mild, self-limited diarrhea, or an asymptomatic carrier state. Thus, although isolation of the causative organism may be useful for investigation of the disease, or control of an outbreak, it is not useful as a guide to treatment of the individual case.

\* The methods described in this paper have been arrived at independently and are also in standard use by the Johns Hopkins University International Center for Medical Research and Teaching, Chittaranjan Avenue, Calcutta, India.

The signs and symptoms of cholera are readily explained by profound losses of water and electrolytes. Recent careful studies of the composition of cholera stool by Capt. R. A. Phillips' group (Watten and associates, *J. Clin. Invest.*, 38:1879, 1959) showed that the stool is isotonic and contains on the average 137 mEq./l.  $\text{Na}^+$ , 16 mEq./l.  $\text{K}^+$ , 107 mEq./l.  $\text{Cl}^-$  and 45 mEq./l.  $\text{HCO}_3^-$ . Other ionic components are present in approximately the same concentration as in plasma. Insignificant amounts of plasma proteins and glucose are found.

The treatment of cholera is fundamentally simple. The basic objectives are to replace losses of water and electrolytes by infusions, and to destroy the causative organism. If fluid and electrolyte losses are promptly and adequately replaced there should be no deaths or serious complications. Satisfactory replacement can be effected with isotonic solutions containing approximately 100 mEq./l. of sodium chloride and 50 mEq./l. of either sodium bicarbonate or sodium lactate. Although losses of potassium are large, intravenous

replacement has not yet been shown to be essential to survival. Moreover, potassium replacement may be easily accomplished by the oral route.

Bedside observations suffice to determine the quantity of replacement fluid to be given. The most reliable and convenient indices are the quality of the radial pulse, blood pressure (particularly pulse pressure), facial appearance, auscultation of lungs, urine output and, if possible, body weight. It is important to recognize that in uncomplicated cases there is considerable latitude on either side of the state of "ideal hydration" consistent with a favorable result. 177 consecutive cases of cholera were successfully treated in Dacca at the Pakistan-SEATO Cholera Research Laboratory and 62 cases in Calcutta by Carpenter and associates without using laboratory data to judge intravenous fluid needs. Thus, although laboratory measurements such as plasma protein, plasma specific gravity and electrolyte concentrations are useful for studying the disease, they are not essential in guiding the therapy of an uncomplicated case of cholera. This is particularly important since cholera so often occurs on a large scale and in situations in which adequate laboratory support is not available.

Studies both at the Pakistan-SEATO Cholera Research Laboratory (*Lancet* 1:355, 1964) and by Carpenter and associates (*Bull. Calcutta School Trop. Med.* 12:30, 1964) have shown that early administration of tetracycline to patients with cholera will not only kill *V. cholerae* but also significantly shorten the duration of diarrhea. Some patients treated by fluid replacement alone may continue to pass large volumes of liquid stool for seven or eight days, and require as much as 70 liters of intravenous fluid replacement; therefore, an agent capable of shortening the duration of the disease greatly simplifies management.

Although cholera is an infectious disease it is not highly contagious. Medical personnel attending cholera patients are protected by observing simple rules of hygiene such as washing hands after being in contact with infected material. Elaborate isolation techniques interfere with patient management and are not necessary. Immunization of ward personnel is recommended although its efficacy remains unproven despite many years of use.

### Treatment Program

1. Place the patient on a cot that has a hole located under the patient's buttocks. The cot can be made of canvas or burlap on a wooden frame; a rubber sheet with a sleeve through the hole channels the stool into a bucket. This permits collection of total output and avoids contamination of the area. The bucket should have a capacity of 7 liters. A dipstick or the bucket itself should be calibrated to measure the volume contained.

2. A single isotonic solution containing 50 mEq./l. of sodium bicarbonate or sodium lactate and 100 mEq./l. of sodium chloride is effective replacement for all uncomplicated cases. If such a solution is not available isotonic saline can be alternated with isotonic sodium lactate or bicarbonate in a ratio of 2:1. Infusions containing physiologic concentrations of other solutes may be beneficial but have not been shown to be necessary for survival.

3. Establish an intravenous route through which fluid can be given as fast as 1 liter in 15 minutes. In adults, if a peripheral vein cannot be located either the external jugular or femoral vein may be used. In infants and children a 21 gauge thin-walled scalp vein needle is helpful for placement in an external jugular vein. If all else fails the subclavian vein can be used.

4. Infuse fluid as rapidly as possible until a full radial pulse is obtained and pulse pressure is at least 20 to 30 mm. Hg. Subsequently, fluid is given at the same rate as the stool output. Further regulation of intravenous fluid should be based on observation of the patient's radial pulse, blood pressure, lung bases, facial appearance, urine output and, if possible, body weight, as well as the stool volume.

5. Oral fluids should be given to cover insensible water losses and provide supplements of potassium, carbohydrate and other components. Green coconut water, frequently available in cholera prone areas, contains on the average 70 mEq./l. of potassium, and 2.5 grams per 100 ml. of reducing substances. Water, other fruit juices, bananas, milk and other soft foods or liquids may be given as soon as the patient desires, which often is shortly after rehydration.

6. Tetracycline, 100 mg. intravenously may be given immediately and repeated 6 to 12 hours later. As soon as the patient can swallow, a dose of 500 mg. every 6 hours should be administered for at least 48 hours. It is very likely, on the basis of more recent studies, that the intravenous injection is unnecessary and may be omitted without loss of effect. Other vibriocidal antibiotics have not yet been properly tested; they may also work.

7. Vasopressor agents, cardiac stimulants, anticholinergic drugs and steroids are not indicated and may be harmful.

### Complications

1. Acidosis, although a feature of all cases, may at times be extreme, particularly in instances of prolonged vascular collapse or after previous treatment with saline alone. Profound hyperventilation occurs and rales suggestive of pulmonary edema may develop. In such cases infusion of isotonic sodium bicarbonate solution is effective in

treating the acidosis. When the acidosis is corrected, hyperventilation and pulmonary rales diminish despite the added fluid volume and sodium.

2. Oliguria lasting 12 to 36 hours is a feature of some cases of cholera. If shock has been prolonged and therapy inadequate, renal failure ensues and may last for several weeks. The treatment of such patients is the same as for acute renal failure due to other causes.

Laboratory measurements, such as carbon dioxide, electrolytes and blood urea nitrogen, non-protein nitrogen or creatinine, are desirable in treating the complications mentioned in (1) and (2) and greatly improve the accuracy of the therapy rendered.

3. Hypokalemia may be severe if the diarrhea is prolonged and potassium replacement neglected. In such instances electrocardiographic changes occur and renal tubular damage has been demonstrated by renal biopsy.

4. Hypoglycemia, sometimes resulting in coma, has been seen, particularly in children. Oral administration of carbohydrate in the form of soft foods or juices is recommended and will avert this complication.

5. Hypocalcemia and tetany occur rarely and require intravenous calcium.

6. Burning abdominal pain, transient hearing loss and dizziness may occur in convalescence but resolve spontaneously.