CHOLERA

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CHOLERA

- Cholera is an acute diarrhoeal disease caused by V. Cholerae 01 (classical or El Tor) and 0139.
- It is now commonly due to the El Tor biotype and 0139.
- Cases range from symptomless to severe infections.
- The majority of infections are mild or asymptomatic.

CHOLERA

- Typical cases are characterized by the sudden onset of profuse, effortless, watery diarrhoea followed by vomiting, rapid dehydration, muscular cramps and suppression of urine.
- Unless there is rapid replacement of fluid and electrolytes, the case fatality may be as high as 30 to 40 per cent.

Problem statement

- The number of cholera cases reported to WHO continues to rise.
- For 2016 alone, a total of 132,121 cases were notified from 38 countries, including 2,420 deaths. Many more cases were unaccounted for due to limitations in surveillance systems and fear of trade and travel sanctions.
- The true burden of the disease is estimated to be 1.3-4.0 million cases and 21,000-143,000 deaths annually.

- Two serogroups of V. cholerae - 01 and 0139 - cause outbreaks.
- Non-O1 and non-O139 V. cholerae can cause mild diarrhoea but do not generate epidemics.
- Recently, new El Tor variant strains cause more severe cholera with higher case fatality rates.

- Global warming creates a favourable environment for the bacteria.
- Cholera transmission is closely linked to inadequate environmental management.
- Typical at-risk areas include peri-urban slums.
- Cholera remains a global threat to public health and a key indicator of lack of social development.

- **INDIA** - West Bengal has lost its reputation as the "home" of cholera. Many of the States became endemic foci of El Tor infection.
- There has been no large scale epidemic of classical cholera since 1964.
- The El Tor biotype of V. Cholerae 01 has rapidly replaced the classical biotype in all parts of the country, which belong to the serotype Ogawa.
- During 2017, about 494 cholera cases were reported in India with 3 deaths.

Epidemiological features

- Cholera is both an epidemic and endemic disease depending on the characteristics of the agent, and those of the environment.
- Agent - its ability to survive in a given environment, its virulence, the average number of organisms required to cause infection, etc.
- System - include the number of susceptible, and the opportunities it provides for transmission of the infection.

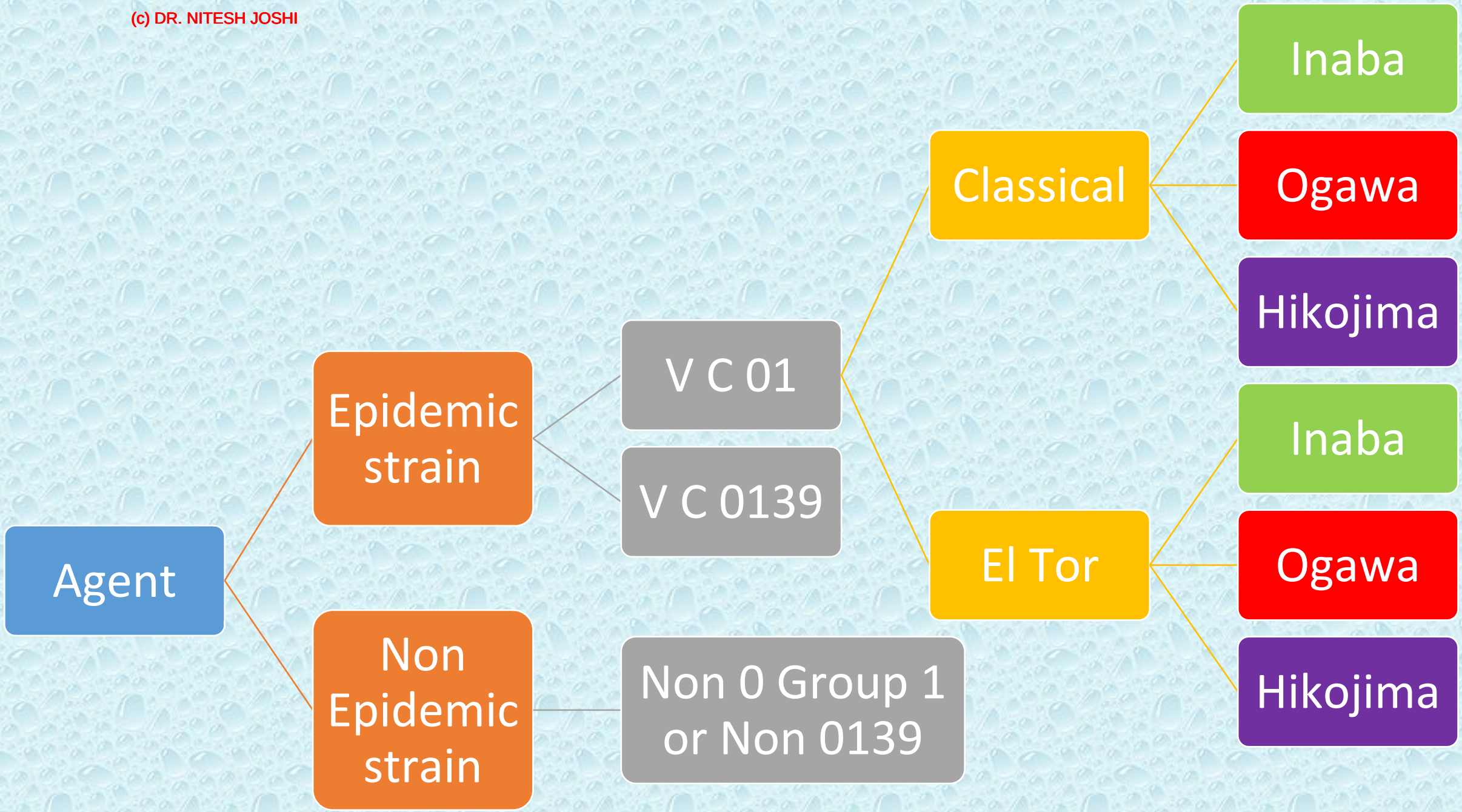
- Epidemics of cholera are characteristically abrupt and often create an acute public health problem.
- They have a high potential to spread fast and cause deaths.
- The epidemic reaches a peak and subsides gradually as the "force of infection" declines. Thus, cholera epidemic in a community is self-limiting.
- This is attributed to the acquisition of temporary immunity, as well as due to the occurrence of a large number of subclinical cases.

- The "force of infection" is composed of 2 components, namely the force of infection through water and the force of infection through contacts.
- In areas where cholera is endemic, it does not show a stable endemicity like typhoid fever. It undergoes seasonal fluctuations as well as epidemic outbreaks.
- The El Tor biotype, has become endemic with periodic outbreaks. It appears to have greater "endemic tendency" than its classical counterpart in that it causes a higher infection-to-case ratio (i.e., inapparent infections and mild cases).

Epidemiological determinants - Agent factors

- **(a) AGENT** : The organism that causes cholera is labelled as V. cholerae O Group 1 or Vibrio cholerae 01 and 0139.
- The term "epidemic strain" has also been used for these vibrios.
- Vibrios that are biochemically similar to the epidemic strains but do not agglutinate in V. cholerae 01 and 0139 antiserum have been referred to in the past as non-agglutinating (NAG) vibrios or as non-cholera vibrios (NCV).

- These are now included in the species V. cholerae and are referred to as non-O Group 1 V/ 0139 cholerae (non-epidemic strains), which include some species that are pathogenic for humans
- Within the O-Group 1, two biotypes - **classical and El Tor**, have been differentiated.
- Cholera is now caused mostly by the El Tor biotype and 0139.
- Classical and El Tor vibrios are further divided each into 3 serological types namely **Inaba, Ogawa and Hikojima**.



- **(b) RESISTANCE** : killed within 30 minutes by heating at 56 deg. C or within a few seconds by boiling.
- They remain in ice for 4-6 weeks or longer.
- Drying and sunshine will kill them in a few hours.
- They are easily destroyed by coal tar disinfectants such as cresol.
- Bleaching powder is another good disinfectant which kills vibrios instantly at 6 mg/litre.
- The El Tor biotype tends to be more resistant than do classical vibrios.

- **(c) TOXIN PRODUCTION** : The vibrios multiply in the lumen of the small intestine and produce an exotoxin (enterotoxin). This toxin produces diarrhoea through its effect on the adenylate cyclase-cyclic AMP system of mucosal cells of the small intestine.
- The exotoxin has no effect on any other tissue except the intestinal epithelial cells.

- **(d) RESERVOIR OF INFECTION**: Only The human
- may be a case or carrier.
- (i) Cases : range from inapparent infections to severe ones.
- About 75 per cent do not develop any symptoms, and about 20 per cent develop acute watery diarrhoea with severe dehydration.
- It is the mild and asymptomatic cases that play a significant role in maintaining endemic reservoir.

- (ii) Carriers : The carriers are usually temporary, rarely chronic.
- They also make an important contribution to the reservoir of infection.
- Since carriers excrete fewer vibrios than clinical cases, carriers are best detected by bacteriological examination of the purged stool induced by the administration of 30-60 gram of magnesium sulphate in 100 ml of water by mouth.

- **(e) INFECTIVE MATERIAL** : The immediate sources of infection are the stools and vomit of cases and carriers.
- **(f) INFECTIVE DOSE** : Cholera is dose related. Infection occurs when the number of vibrios ingested exceeds the dose that is infective for the individual.
- **(g) PERIOD OF COMMUNICABILITY** : A case of cholera is infectious for a period of 7-10 days. Convalescent carriers are infectious for 2-3 weeks. The chronic carrier state may last from a month up to 10 years or more.

Carriers in cholera

1. PRECLINICAL OR INCUBATORY CARRIERS : The incubatory carriers are potential patients.
2. CONVALESCENT CARRIER : The patient who has recovered from an attack of cholera may continue to excrete vibrios, during his convalescence for 2-3 weeks.

Convalescent state has been found to occur in patients who have not received effective antibiotic treatment. The convalescent carriers can often become chronic or long-term carriers.

Carriers in cholera

3. CONTACT OR HEALTHY CARRIER: result of subclinical infection. The duration of contact carrier state is usually less than 10 days; the gall bladder is not infected, and the stool culture is frequently positive for V. cholerae 01. Contact carriers probably play an important role in the spread of cholera.
4. CHRONIC CARRIER : A chronic carrier state occurs infrequently. The longest carrier state was found to be over 10 years. Gall bladder is infected in chronic carriers.

Host factors

- **(a) AGE AND SEX** : all ages and both sexes. In endemic areas, attack rate is highest in children.
- **(b) GASTRIC ACIDITY** : An effective barrier. The vibrio is destroyed in an acidity of pH 5 or lower.
- **(c) POPULATION MOBILITY**: Movement of population (e.g., pilgrimages, marriages, fairs and festivals) results in increased risk of exposure to infection.

Host factors

- **(d) ECONOMIC STATUS** : The incidence of cholera tends to be the highest in the lower socio-economic groups, and this is attributable mainly to poor hygiene.
- **(e) IMMUNITY** : An attack is followed by immunity to reinfection, but the duration and degree of immunity are not known.

Vaccination gives only temporary, partial immunity for 3-6 months.

Environmental factors

- poor environmental sanitation.
- contaminated water and food.
- Flies may carry V. cholerae.
- human habits favouring water and soil pollution.
- low standards of personal hygiene.
- lack of education and
- poor quality of life.

Mode of transmission

- (a) FAECALLY CONTAMINATED WATER : Uncontrolled water sources pose a great threat.
- (b) CONTAMINATED FOOD AND DRINKS : Bottle-feeding could be a significant risk factor for infants. Fruits and vegetables washed with contaminated water, cooked food through contaminated hands and flies.
- (c) DIRECT CONTACT : secondary transmission, i.e., person to person transmission through contaminated fingers while carelessly handling excreta and vomit of patients and contaminated linen and fomites.

Incubation period

- From a few hours up to 5 days, but commonly 1-2 days.

Pathogenesis

- The vibrio - mucus of intestinal epithelium - secretes mucinase, which helps it move rapidly - gets attached to the intestinal epithelial cells - produces its enterotoxin - the light or L toxin and the heavy or H toxin.
- The L toxin combines with gangliosides and binds the vibrio to the cell wall. Binding is irreversible.
- H toxin activated adenyl cyclase causes a rise in 3, 5-adenosine monophosphate, cAMP provides energy which drives Isotonic fluid and ions into the lumen of the intestine. The increase in fluid is the cause of diarrhoea.

Clinical features

- The severity of cholera is dependent on the rapidity and duration of fluid loss.
- More than 90 per cent of El Tor cases are mild and clinically indistinguishable from other acute diarrhoeas.
- However, a typical case of cholera shows 3 stages :

- (a) STAGE OF EVACUATION :
- The onset is abrupt with profuse, painless, watery diarrhoea followed by vomiting.
- The patient may pass as many as 40 stools in a day.
- The stools may have a "rice water" appearance.

- (b) STAGE OF COLLAPSE : The classical signs are : sunken eyes, hollow cheeks, scaphoid abdomen, sub-normal temperature, washerman's hands and feet, absent pulse, unrecordable blood pressure, loss of skin elasticity, shallow and quick respirations.
- The output of urine decreases and may ultimately cease. The patient becomes restless, and complains of intense thirst and cramps in legs and abdomen.
- Death may occur at this stage, due to dehydration and acidosis resulting from diarrhoea.

- (c) STAGE OF RECOVERY : If death does not occur, the patient begins to show signs of clinical improvement. The blood pressure begins to rise, the temperature returns to normal, and urine secretion is re-established. If anuria persists, the patient may die of renal failure.
- The classical form of severe cholera occurs in only 5-10 per cent of cases. In the rest, the disease tends to be mild characterized by diarrhoea with or without vomiting or marked dehydration. As a rule, mild cases recover in 1-3 days.

- Epidemiologically, El Tor biotype differs from classical cholera in the following respects :
- (a) a higher incidence of mild and asymptomatic infection
- (b) fewer secondary cases in the affected families
- (c) occurrence of chronic carriers, and
- (d) since El Tor vibrios are more resistant than classical cholera vibrios, they survive longer in the extra-intestinal environment.

Laboratory diagnosis of cholera

- The diagnosis can never be made with certainty on clinical grounds. Laboratory methods of diagnosis are required to confirm the diagnosis :
- DIRECT EXAMINATION : In the dark field of microscope, the vibrios evoke the image of many shooting stars in a dark sky.
- CULTURE METHODS
- CHARACTERIZATION : V. cholerae appears as translucent, moist, raised, smooth and easily emulsifiable colonies about 1 mm in diameter.

- Serological test: Slide agglutination test is done to determine the subtype.
- FURTHER CHARACTERIZATION biotypes organisms are identified by slide agglutination tests using anti - 01 or group 139 antisera.

CONTROL OF CHOLERA

- **1. Verification of the diagnosis**
- It is important to have confirmation of the outbreak as quickly as possible.
- All cases of diarrhoea should be investigated even on the slightest suspicion.
- For the specific diagnosis of cholera, it is important to identify V. cholerae 01 in the stools of the patient.

- **2. Notification**
- Cholera is a notifiable disease locally and nationally. Since 2005 cholera notification is no longer mandatory internationally.
- Under the International Health Regulations, cholera is notifiable to the WHO within 24 hours of its occurrence by the National Government; the number of cases and deaths are also to be reported daily and weekly till the area is declared free of cholera.
- An area is declared free of cholera when twice the incubation period (i.e., 10 days) has elapsed since the death, recovery or isolation of the last case.

- **3. Early case-finding**
- An aggressive search for cases (mild, moderate, severe) should be made in the community to be able to initiate prompt treatment.
- Early detection of cases also permits the detection of infected household contacts and helps the epidemiologist in investigating the means of spread for deciding on specific intervention.

- **4. Establishment of treatment centres**
- To provide prompt treatment, it is necessary to establish easily accessible treatment facilities in the community.
- The mildly dehydrated patients should be treated at home with oral rehydration fluid.
- Severely dehydrated patients, requiring intravenous fluids, should be transferred to the nearest treatment centre.

- **4. Establishment of treatment centres**
- If there is no hospital within a convenient distance, a local school or public building should be taken over and converted into a temporary treatment centre, as close to the site of epidemic as possible.
- Transportation of cases over long distances is not desirable; it has been linked with the spread of the disease.
- mobile teams should be established at the district level. When needed, should be brought promptly into the epidemic area to assist the local workers.

- **5. Rehydration therapy**
- (I) ORAL REHYDRATION THERAPY : The aim of oral fluid therapy is to prevent dehydration and reduce mortality.
- Oral fluid therapy is based on the observation that glucose given orally enhances the intestinal absorption of salt and water, and is capable of correcting the electrolyte and water deficit.
- Inclusion of trisodium citrate in place of sodium bicarbonate made the product more stable and it resulted in less stool output.

- **5. Rehydration therapy**
- improved ORS formulation is focussed on reducing the osmolarity to avoid possible adverse effects of hypertonicity.
- Decreasing the sodium concentration of ORS solution to 75 mmol/l improved the efficacy of the ORS regimen for children with acute non-cholera diarrhoea.
- India was the first country in the world to launch this ORS formulation since June 2004.

Composition of reduced osmolarity ORS

Reduced osmolarity ORS	**grams / litre**
Sodium chloride	2.6
Glucose, anhydrous	13.5
Potassium chloride	1.5
Trisodium citrate, dihydrate	2.9
Total weight	20.5
Reduced osmolarity ORS	**mmol / litre**
Sodium	75
Chloride	65
Glucose, anhydrous	75
Potassium	20
Citrate	10
Total osmolarity	245

Guidelines for oral rehydration therapy (for all ages) during the first four hours

Age (*)	under 4 months	4–11 months	1–2 yrs.	2–4 yrs.	5–14 yrs.	15 yrs or over
Weight (kg)	under 5	5–7.9	8–10.9	11–15.9	16–29.9	30 or over
ORS solution (ml)	200–400	400–600	600–800	800–1200	1200–2200	2200–4000

(*) The patient's age should only be used if weight is not known. The approximate amount of ORS required in ml. may also be calculated by multiplying the patient's weight (expressed in kg) by 75.

As a general guide,

- ✓ After each loose stool, give - children under 2 years of age : 50-100 ml of fluid; children aged 2 up to 10 years : 100-200 ml; and older children and adults : as much fluid as they want.
- ✓ if the child wants to drink more ORS solution than the estimated amount, and does not vomit, there can be no harm in feeding him/her more.
- ✓ If the child refuses to drink the required amount and signs of dehydration have disappeared, rehydration is completed.

If the WHO mixture of salts is not available,

a simple mixture consisting of table salt (one level teaspoon) and sugar (6 level teaspoon) dissolved in one litre of drinking water may be safely used until the proper mixture is obtained.

The infant's usual diet of cereals, vegetables and other foods should be continued during diarrhoea, and increased afterwards.

Food should never be withheld and the child's usual food should never be diluted. The aim is to give as much nutrient rich food as the child will accept.

(II) INTRAVENOUS REHYDRATION

(a) Ringer's lactate solution (also called Hartmann's solution for injection)

(b) Diarrhoea Treatment Solution (DTS): It contains in one litre, sodium chloride 4 g, sodium acetate 6.5 g, potassium chloride 1 g and glucose 10 g.

(c) If nothing else is available, normal saline can be given. Plain glucose and dextrose solutions should not be used as they provide only water and glucose.

Treatment Plan for IV Rehydration		
Age	First give 30 ml/kg in	Then give 70 ml/kg in
Infants (Under 12 months)	1 hour	5 hours
Older	30 minutes	2 ½ hours

(III) MAINTENANCE THERAPY Oral fluid should be used for maintenance therapy. Thirst is an adequate guide for fluid needs.

Amount of Diarrhoea	Amount of fluid
Mild diarrhoea (not more than one stool every 2 hours or longer, or less than 5 ml stool per kg per hour)	100 ml/kg body weight per day until diarrhoea stops
Severe diarrhoea (more than one stool every 2 hours, or more than 5 ml of stool per kg per hour)	Replace stool losses volume for volume; if not measurable give 10-15 ml/kg per hour

- **6. Adjuncts to therapy**
- The commonly used antibiotics for the treatment of cholera are flouroquinolones, tetracycline, Azithromycin, ampicilline and Trimethoprim (TMP) Sulfamethoxazole (SMX). No other medication should be given to treat cholera, like antidiarrhoeals, antiemetics, antispasmodics, cardiotonics and corticosteroids. If diarrhoea persists after 48 hours of treatment, resistance to antibiotic should be suspected.

- **7. Epidemiological investigations**
- Epidemiological studies must be undertaken to define the extent of the outbreak and identify the modes of transmission so that more effective and specific control measures can be applied.
- National Institute of Communicable Diseases, Delhi.
- All India Institute of Hygiene and Public Health, Kolkata.
- National Institute of Cholera and Enteric Diseases, where the WHO International Centre for Vibrios is located.

- **8. Sanitation measures**
- (a) WATER CONTROL : As water is the most important vehicle of transmission of cholera, all steps must be taken to provide properly treated or otherwise safe water to the community for all purposes.
- As an emergency measure, in urban areas, properly treated drinking water containing free residual chlorine should be made available.
- In rural areas, water can be made safe by boiling or by chlorination.

- (b) EXCRETA DISPOSAL : Sanitary latrines is a basic need of all human settlements. Health education messages should stress the proper use of such facilities and the importance of hand washing with soap after defecation.
- (c) FOOD SANITATION : Steps should be taken to improve food sanitation. Health education must stress the importance of eating cooked hot food and of proper individual food handling techniques. Cooking utensils should be cleaned and dried after use.

- (d) DISINFECTION : Disinfection should be both concurrent and terminal.
- The most effective disinfectant for general use is a coal tar disinfectant such as cresol.
- Bleaching powder, if used, should be of good quality.

- **9. Chemoprophylaxis**
- Chemoprophylaxis is advised only for household contacts or of a closed community in which cholera has occurred.
- Tetracycline is the drug of choice for chemoprophylaxis. Adult 500 mg BD, 4-13 years 125 mg BD, 0-3 years 50 mg BD over 3 days.
- A single oral dose of doxycycline (300 mg for adults and 6 mg/kg for children under 15 years) has proved to be effective.

- **10. Vaccination**
- Two types of oral cholera vaccines are available :
- (a) Dukoral (WC-rBS) is a monovalent vaccine The vaccine is provided in 3 ml single-dose vials together with the bicarbonate buffer.
- Vaccine and buffer are mixed in 150 ml of water for persons aged >5 years and in 75 ml of water for children aged 2-5 years.
- The vaccine has a shelf life of 3 years at 2-8°C and remains stable for 1 month at 37°C.

- Vaccine schedule and administration
- 2 oral doses given ≥7 days apart (but <6 weeks apart) for adults and children aged ≥ 6 years.
- Children aged 2-5 years should receive 3 doses.
- Intake of food and drink should be avoided for 1 hour before and after vaccination.
- Protection may be expected about 1 week after the last scheduled dose.
- 1 booster dose is recommended after 2 years for adults and ≥ 6 years. For children 2-5 years every 6 months.
- Dukoral is not licensed for children aged <2 years.

- (b) Sanchol and mORCVAX - The closely related bivalent oral cholera vaccines are based on serogroups 01 and 0139.
- vaccine should be administered orally in 2 liquid doses 14 days apart for individuals aged ≥ 1 year.
- A booster dose is recommended after 2 years.
- (c) Euvichol – It is prequalified in Dec 2015 and has same characteristics as Sanchol.

- **11. Health education**
- The most effective prophylactic measure is perhaps health education. It should be directed mainly to -
- (a) the effectiveness and simplicity of oral rehydration therapy.
- (b) the benefits of early reporting for prompt treatment.
- (c) food hygiene practices.
- (d) hand washing after defecation and before eating, and
- (e) the benefit of cooked, hot foods and safe water.

Since cholera is mainly a disease of the poor and ignorant, these groups should be tackled first.

Diarrhoeal Diseases Control Programme

- The National Cholera Control Programme is now termed as Diarrhoeal Diseases Control Programme
- Oral Rehydration Therapy Programme was started in 1986-87 in a phased manner.
- The main objective of the programme is to prevent diarrhoea-associated deaths in children due to dehydration.
- ORS is promoted as first line of treatment. ORS is being supplied as a part of the sub centre kits.

THANK YOU !