Cholera and cholera vaccination

This disease is notifiable in the UK - see **NOIDs** article for more detail.

What is cholera?[1]

Cholera is an acute, secretory diarrhoea caused by infection with Vibrio cholerae of the O1 or O139 serogroup. It is endemic in more than 50 countries and also causes large epidemics. Since 1817, seven cholera pandemics have spread from Asia to much of the world. The seventh pandemic began in 1961 and affects 3-5 million people each year, killing 120,000.

Although mild cholera can be indistinguishable from other diarrhoeal illnesses, the presentation of severe cholera is distinct, with watery diarrhoea that is very profuse and can rapidly lead to severe dehydration and death.

Cholera is a water-borne infection usually caught through ingestion of faecally contaminated water or shellfish. Person-to-person spread via the faeco-oral route can also occur.

There are other types of species of *V. cholerae* which also cause infection in humans. They include *V. parahaemolyticus*, *V. mimicus*, *V. damsela* and *V. hollisae* and they also cause diarrhoea. There are also two other related families called aeromonas and plesiomonas and they cause diarrhoea, wound infections, septicaemia, ocular infections and meningitis.

How common is cholera? (Epidemiology)[2]

Cholera is prevalent in areas with poor sanitation and poor food and water hygiene and constitutes a major global public health problem. The disease is not endemic to the UK and is rarely imported from abroad (an average of only 10 cases of cholera are imported into the UK annually).

The most common serotype is *V. cholerae* El Tor and most infections are acquired on the Indian subcontinent.

The disease is endemic to parts of Africa, Asia, the Middle East and South America. Large outbreaks are common after natural disasters or in populations displaced by war, where there are inadequate sewage disposal and contaminated water.

Most of the recent pandemics have been due to El Tor but O1 classical and O139 are endemic in India and Bangladesh.

Researchers have estimated that every year, there are 1.3 to 4.0 million cases of cholera, and 21,000 to 143 000,deaths worldwide due to the infection.

Risks for travellers

- The risk of cholera for most travellers to endemic areas is very low. The overall incidence of cholera in travellers is only 2–3 per million but, for those staying in areas of outbreaks, the incidence rises to 5 per thousand.[3]
- A high infecting dose (as many as 1,011 organisms) is necessary to cause illness in healthy individuals.
- Drinking untreated water or eating poorly cooked seafood in endemic areas carries a high risk.
- Large outbreaks are common after natural disasters or in populations displaced by war, where inadequate sewage disposal and contaminated water exist.
- Travellers living in unsanitary conditions, such as humanitarian relief workers in disaster areas, are also at risk.

Symptoms of cholera (presentation)

The incubation period is usually 2-5 days. However, it can sometimes be a few hours. 75% of those infected are asymptomatic.[4] However, those who remain asymptomatic excrete the organism for 7 to 14 days.

History

A number develop a moderate form of diarrhoea that is clinically indistinguishable from other forms of gastroenteritis. No more than 10% develop the very profuse diarrhoea that is regarded as characteristic of the disease.

- Severe illness - sudden onset of profuse, watery diarrhoea with nausea and vomiting.
- The volume of fluid lost can be up to 20 litres a day.
- If not replaced, heavy fluid loss rapidly leads to serious dehydration and circulatory collapse.

Examination

The severely dehydrated patient will look very unwell with sunken eyes and possibly impaired level of consciousness. Skin will be dry and lacking turgor. Pulse will be fast but weak with a low blood pressure indicating haemodynamic instability.

Diagnosing cholera (investigations)

- Stool specimen to identify the organism.
- U&E, as the patient is likely to be significantly dehydrated, and to monitor IV fluid replacement. Creatinine may rise if the kidneys fail with circulatory collapse.
- FBC will often show a high Hb with haemoconcentration.
- WCC is likely to be raised but will not aid diagnosis or management.

A good way of estimating net fluid loss or gain if changes are large is to weigh the patient daily. 1 kg of weight represents 1 litre of fluid.

Management of cholera

Resuscitation

- The basis of treatment is the replacement of lost fluid.
- This may be done orally if not very severe or if there is no access to facilities for IV replacement but the latter is required in severe fluid loss.
- Up to 80% of people can be treated successfully through prompt administration of oral rehydration salts.

Antibiotics

- Antibiotic treatment decreases volume and duration of diarrhoea by 50% and is recommended for patients with moderate-to-severe dehydration.[1]
- Tetracycline, doxycycline or ciprofloxacin are often used.
- Mass administration of antibiotics is not recommended, as it has no effect on the spread of cholera and contributes to increasing antimicrobial resistance.[2]

Antidiarrhoeal and antisecretory drugs

- Antidiarrhoeal drugs are not recommended.
- Many antisecretory drugs have been tried as an adjunct therapy but none has been found useful.

Prognosis

Untreated, over 50% of the most severe cases die within a few hours of onset; with prompt, correct treatment, mortality is less than 1%.[5]

Cholera prevention

Oral cholera vaccines serve as a major component of an integrated control package during outbreaks or within zones of endemicity. Water, sanitation, and hygiene (WaSH), health education, and prophylactic antibiotic treatment are additional components of the prevention and control of cholera.[6]

An oral cholera vaccine is available in the UK (see below) . The vaccine is not required by most travellers but may be suitable for those who are unable to take adequate precautions in highly endemic or epidemic settings.

Cholera vaccination [5] [7]

The only cholera vaccine used in the UK since May 2004 is Dukoral®, a killed V. cholerae whole-cell (WC) vaccine with recombinant B subunit of cholera toxin (rCTB), administered orally. Intramuscular cholera vaccines are no longer recommended for use. [5]

Vaxchora (a live, oral cholera vaccine for prevention of cholera disease in adults and children aged 2 years and older) was granted UK marketing authorisation (licensed) in 2020. The UK Joint Committee on Vaccination and Immunisation (JCVI) are in the process of reviewing the product information. Recommendations on the use of this vaccine will be published in due course. [3]

Shanchol™ and Euvichol® are the vaccines currently available for mass vaccination campaigns through the Global oral cholera virus (OCV) Stockpile, which is supported by Gavi, the Vaccine Alliance. Shanchol™ and Euvichol® are essentially the same vaccine as Dukoral®, produced by two different manufacturers. More than 20 million doses of OCVs have been used in mass vaccination campaigns. The campaigns have been implemented in areas experiencing an outbreak, in areas at heightened vulnerability during humanitarian crises, and among populations living in highly endemic areas, known as “hotspots”.

A mix of live, killed and conjugated vaccines are in development that have the potential of providing longer term protection with an easier-to-administer schedules.

Indications for vaccine - UK recommendations

Immunisation against cholera can be considered, following a full risk assessment, for the following categories of traveller:

- Relief or disaster aid workers.
- Persons with remote itineraries in areas where cholera epidemics are occurring and there is limited access to medical care.

- Travellers to potential cholera risk areas, for whom vaccination is considered potentially beneficial.

Cholera vaccine is not licensed for use as an infection control tool in the management of cholera contacts or for prevention of traveller's diarrhoea.

The vaccination must not be used as an alternative to standard hygiene precautions, which remain the most effective preventative measures for all food- and water-borne diseases.

Vaccine schedule (Dukoral) [3]

- Adults and children from 6 years: 2 doses with an interval of at least 1 week but less than 6 weeks between them. Provides protection for 2 years.
- Age 2 to below 6 years: 3 doses with an interval of at least 1 week but less than 6 weeks between them. Provides protection for 6 months.

If more than 6 weeks have elapsed between doses the primary course should be restarted. If more than 2 years (or 6 months for children aged 2 to below 6 years of age) has elapsed since the last dose of vaccine, the primary course should be repeated.

Certification of vaccination against cholera is no longer a requirement for entry into any country.

Reinforcing immunisation

For continuous protection against cholera, a single booster dose is recommended 2 years after completing the primary course for adults and children over 6 years of age, and after 6 months for children aged 2 to 6 years.

No clinical efficacy data have been generated on repeat booster dosing.

If more than 2 years have elapsed since the last vaccination, the primary course should be repeated.

Efficacy

- The vaccine confers specific protection against *V. cholerae* serotype O1. It is therefore ineffective for prevention of infection with non-O1 strains including *V. cholerae* serotype O139. Oral cholera vaccines are safe and offer good protection.
- The currently available oral killed whole-cell vaccines can prevent 50-60% of cholera episodes during the first two years after the primary vaccination schedule.[8]
- Injectable cholera vaccine provides unreliable protection and is no longer available in the UK.[9]

Administration

Food, drink and oral medications must be avoided for one hour before and one hour after vaccination. Effervescent sodium hydrogen carbonate granules are dissolved in water (150 ml for adults, and pour half away for children aged 2-6 years) and mixed with 3 mls of vaccine suspension.[5] The solution must be ingested within two hours of reconstitution.

The oral cholera vaccine can be given at the same time as other injected vaccines.

Contra-indications

The oral cholera vaccine should not be administered to patients with:[3]

- Confirmed anaphylactic reaction to oral cholera vaccine.
- Confirmed anaphylactic reaction to any of the components of the vaccine.
- Acute gastrointestinal illness - the vaccine should be delayed in those with acute gastrointestinal illness. Pre-existing gastrointestinal illnesses are not contra-indications to the vaccine.

Precautions

Pregnancy and breast-feeding - it is unlikely that vaccination of pregnant or breast-feeding women with inactivated bacteria or toxoids is associated with adverse outcomes. However, no data are available regarding the safety of oral cholera vaccine in such situations. The vaccine should be considered if the risk of cholera exposure is high.

Immunosuppression including HIV - immunosuppressed individuals must be considered for cholera vaccination according to the recommendations above but may not raise adequate immunological responses.

Adverse reactions

- The oral cholera vaccine is generally well tolerated but reported side-effects include:[3]
    - Gastrointestinal symptoms of diarrhoea, nausea, vomiting, abdominal pain or cramps occurring in up to 1 in 100 cases.
    - Arthralgia, rash, paraesthesia and flu-like syndrome which can occur rarely.

Further reading

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