Cholera

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History

- Originated in Ganges River
- 19th century—six subsequent pandemics
  - Spread to all continents
  - Probably killed President James Polk in 1849 shortly after he left office
Epidemiology

• 3-5 million cases per year, 100-120,000 deaths
• Endemic in resource poor areas of Asia and Africa
  – Worst cases in young children and elderly
• Epidemics have occurred in Asia, Middle East, South and Central America
  – 1991 Peru
• Mostly imported to US
  – 9% acquired via consumption of contaminated Gulf Coast seafood
The spread of cholera 1950-2004

Transmission events inferred for the seventh-pandemic of cholera phylogenetic tree
Global map of countries reporting cholera in 2010

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Data Source: The Global Task Force on Cholera Control
WHO Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Post-earthquake cholera epidemic in Haiti 2010
Cholera outbreak in Haiti

• Importation by Nepalese battalion (asymptomatic vs. symptomatic carriage)
• Spread through Artibonite river
• 5 clusters: ~440,000 cases by Oct 2011
• Hyper virulent strains

Microbiology

- Gram negative, curved, motile bacillus
- More than 190 serotypes
  - Only O1 and O139 responsible for epidemic cholera
- Cholera toxin—multimeric protein
  - Binds to enterocytes, increases cyclic AMP
  - Increased chloride secretion
  - Reduced sodium absorption
  - Massive loss of fluid and electrolytes
Mode of Infection

- Humans only known natural host
  - Fecal-oral transmission

- Free-living *V. cholerae* in aquatic environments

- Infections generally caused by ingestion
  - Water (infectious dose = $10^9$)
  - Food (infectious dose = $10^3$)
  - Person-to-person
Clinical Manifestations

• Most V. Cholera infections are asymptomatic (75%)
  - 1 case per 30 to 100 infections in the E1 biotype
  - 1 case per 2 to 4 infections with the classical biotype
    - shedding bacteria in feces for 7-14 days
• Mild disease cannot be distinguished from typical gastroenteritis
  – Few episodes of watery diarrhea
  – +/- Nausea and diarrhea
  – Do not become clinically dehydrated
• Incubation—few hours to 5 days
  – Most present between 1-3 days
  – Incubation shortest with higher number of ingested organisms
Characteristic Diarrhea

- Onset sudden or gradual
- "Rice Water"—watery with flecks of mucus
  - Mild "fishy" odor
  - High concentration of Na, K, Cl, bicarbonate
- Abdominal cramping but not severe
- Fever infrequently (non-invasive disease)
Severe Cholera ("Gravis")

- Massive volume loss—500-1000ml/hour
  - Can develop over a few hours
    - Hypovolemic shock within 4-12 hours
  - Most severe over first two days, then gradually improves over 4-6 days
  - Volume loss may be 100% of body weight

- Complications
  - Renal failure due to dehydration
  - Severe hypokalemia
    - Arrhythmias, ileus, and leg cramps
  - Metabolic acidosis
  - Hypoglycemia, seizures
Mortality

- Most infections none or mild symptoms
  - <5% with severe disease
- Untreated patients—50-70% mortality
  - Increased risk in children—10-fold increased
  - Increased risk in pregnant women
    - 50% fetal loss in 3rd trimester
  - Death can occur within 2-3 hours of onset of symptoms
    - Usually after 18 hours to a few days
Microbiological & Molecular Methods of Detection

- Microbiological culture-based methods using fecal or water samples
- Rapid Tests
  - Dark-field microscopy
  - Rapid immunoassays
  - Molecular methods - PCR & DNA probes
Treatment

• ORAL REHYDRATION
  – Reduces mortality to less than 1%
  – Na and water absorption is facilitated by glucose even in the presence of cholera toxin
  – Oral rehydration solution from WHO
    • Make your own: 1 liter water, 1 tsp salt, 8 tsp sugar
    • Don’t use apple juice, chicken broth, tea, ginger ale
    • Approx 10ml/kg for each stool
    • Rice-based ORS may be more effective
  – Use NGT if necessary
IV rehydration

• Ringer’s lactate if available
  – 20ml/kg bolus

• Watch for hypokalemia
  – Use potassium bicarb to correct metabolic acidosis if possible rather than only sodium bicarb (K driven into cells)

• Start oral rehydration as soon as patients able to drink
Preventing Cholera: Vaccines

• Orochol
  – Contains $2 \times 10^8$ viable cells of attenuated strain CVD 103-HgR in a lyophilized form
  – Oral immunization of children older than 2
  – Subunit A of the cholera toxin (CT) has been removed

• Dukoral
  – Protects against O1 Inaba and Ogawa, Classical & El Tor strains
  – Contains $1 \times 10^7$ heat/formalin killed cells of strain WC/rBS

Image from: http://www.pharmeragroup.com/dukoralb.htm
Epidemic Control Measures

- Hygienic disposal of human waste
- Adequate supply of water
- Good food hygiene
  - Thoroughly cooking food
  - Eating food while it’s hot
  - Preventing cooked foods from contacting raw foods (including water or ice)
  - Avoiding raw fruits or vegetables
  - Washing hands after defecation & before cooking

Antimicrobials

- Adjunct to appropriate rehydration
- Use in severe cases
- Reduce volume by about half
- Decrease Vibrio excretion by one day
- Oral not IV/IM
- Consider local resistance patterns
  - Tetracycline 500mg Q6h x 3 days
  - Doxycycline 300mg x 1 dose
  - Ciprofloxacin 1gm x 1 dose
  - Children <8yrs: Erythromycin 10mg/kg TID x 3 days
    - Azithromycin 20mg/kg x 1 dose
Zinc supplementation

- Reduces stool output and duration in children
- 179 Bangladeshi children with cholera
  - Erythromycin + zinc 30mg or placebo
  - 12% shorter duration of diarrhea
  - 11% less stool output
Antibiotic Prophylaxis

- Appropriate for household contacts
  - Not recommended for mass community
Vaccine

- Oral—not available in US
  - Short-term protection (2 years)
  - Active against 85–90% *V. cholerae* O1 among all age groups
  - Requires two doses 7 days-6 weeks apart
  - Protection 4-6 months after immunization
Anatomy of an Outbreak--Haiti

• Haiti without Vibrio cholerae outbreak for decades
• Catastrophic earthquake in January 2010
  – Displacement of population
  – Disruption of already heavily fractured infrastructure
  – Massive tent communities with poor sanitation
• Outbreak of cholera in October 2010
  – South Asian strain
  – 440 deaths, approx 7,000 cases
• Impact of Tropical Storm Tomas
Requirements for an Outbreak

- Significant breaches in the water, sanitation, and hygiene infrastructure permitting large-scale exposure to food or water contaminated with *Vibrio cholerae*
- Cholera must be present in the population
Prevention

• Clean water
  – Boil water for at least one minute
  – Chlorine tablets commercially available
  – Bleach—8 drops of bleach for 1 gallon
    • 2 drops of bleach for every 1 liter of water
    • Wait 30 minutes before drinking
• Wash hands, use latrines, cook food
Technology in an epidemic

- Free texts in Creole
  - 80% have access to cellular phone
  - Information on symptoms
  - Information on prevention and clean water sources
References


Slide title

• Bullet 1
• Bullet 2