

# CASE 1: Travelling In India

*Vibrio cholerae*

THE BODY SYSTEM

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PATH 417

# *Vibrio cholerae*

- **HOW IT IS CONTRACTED**

- Can infect an individual by means of ingesting fecal-contaminated:
  - Food
  - Water

- **DISEASE CAUSED**

- Cholera

- **ISOLATION**

- Stool Culture → Best Method
  - Examined microscopically with the use of antibodies to inhibit bacteria motility
- Rectal swab samples
- Agglutination Test
- Polymerase Chain Reaction (PCR)

# SIGNS AND SYMPTOMS

- **DIARRHEA**
  - Severe
  - Watery
- **VOMITING**
  - In large Volumes
- **MINOR CRAMPING**
  - In patient's leg

# AFFECTED BODY SYSTEM

- **GASTROINTESTINAL TRACT**
  - Particularly colonizes the small intestine
- **IN THE SMALL INTESTINE**
  - *V. cholerae* releases an enterotoxin
    - Cholera Toxin

# EFFECTS ON PHYSIOLOGICAL FUNCTION

## NORMAL FUNCTION OF SMALL INTESTINE:

- **NUTRIENT AND FLUID ABSORPTION**
  - Nutrient-Dependent Salt Absorption
  - Nutrient-Independent Salt Absorption
- **SECRETION**
  - Done mainly by crypt cells
  - Cl<sup>-</sup> exits out of the cell (Main electrolyte driving secretion)
    - Through the Cystic Fibrosis Transmembrane Conductance Regulator

# EFFECTS ON PHYSIOLOGICAL FUNCTION

## NUTRIENT-DEPENDENT SALT ABSORPTION

- Mediated by sodium-dependent cotransporters
  - Glucose, galactose, and amino acid transport is coupled to that of sodium
  - Transported down their concentration gradient

## NUTRIENT-INDEPENDENT SALT ABSORPTION

- Mediated by  $\text{Na}^+/\text{H}^+$  and  $\text{Cl}^-/\text{HCO}_3^-$ -parallel exchangers
  - $\text{Na}^+$  and  $\text{Cl}^-$  transported in
  - $\text{H}^+$  and  $\text{HCO}_3^-$  transported out
  - $\text{Na}^+/\text{K}^+$  ATPase pumps  $\text{Na}^+$  out to maintain the intracellular concentration of  $\text{Na}^+$
  - Water transported from lumen because of osmotic gradient

# EFFECTS ON PHYSIOLOGICAL FUNCTION

## HOW FUNCTION IS ALTERED BY CHOLERA TOXIN:

- **MODE OF DISRUPTION**
  - Binds to the ganglioside receptor on epithelial cells
    - Activates Adenylate Cyclase
      - Which in turn increase the intracellular concentration of cAMP
    - Inhibits Na<sup>+</sup>/H<sup>+</sup> Exchangers (NHEs)
      - Leading to inhibit absorption
    - Increased secretion of Cl<sup>-</sup> through CFTR
  - Ultimately leads to WATER AND ELECTROLYTE LOSS

# TREATMENTS

## OPTION 1: REHYDRATION



- **ORAL REHYDRATION**
  - To replace fluid and electrolyte loss
  - Oral Rehydration Salts (ORS) [or low-osmolarity and cer ORS]
  - Amount administered calculated by:
    - $\text{body weight (kg)} * 75\text{mL} = \text{volume in mL}$
- **INTRAVENOUS REHYDRATION**
  - For severe dehydration, vomiting, and inability to drink water
  - Amount administered in first 24 hours by:
    - 200mL/kg (Ringer's Lactate or Saline solution)
  - Return to ORS treatment when patient recovers enough to drink



# TREATMENTS

## OPTION 2: ANTIBIOTICS

For severe cases of cholera

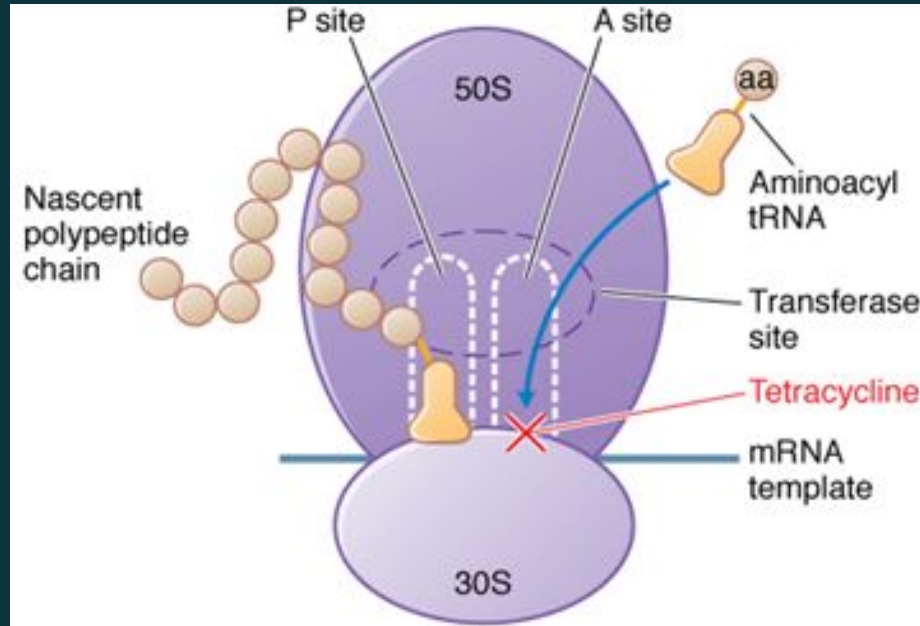


- **TETRACYCLINE**

- Enters the gram-negative bacteria by use of porin channels
- Bacteriostatic
  - Stops bacterial reproduction without killing the bacteria
- Doxycycline
  - A tetracycline that is more effective and longer-acting

# TREATMENTS

## TETRACYCLINE



# TREATMENTS

## OPTION 2: ANTIBIOTICS

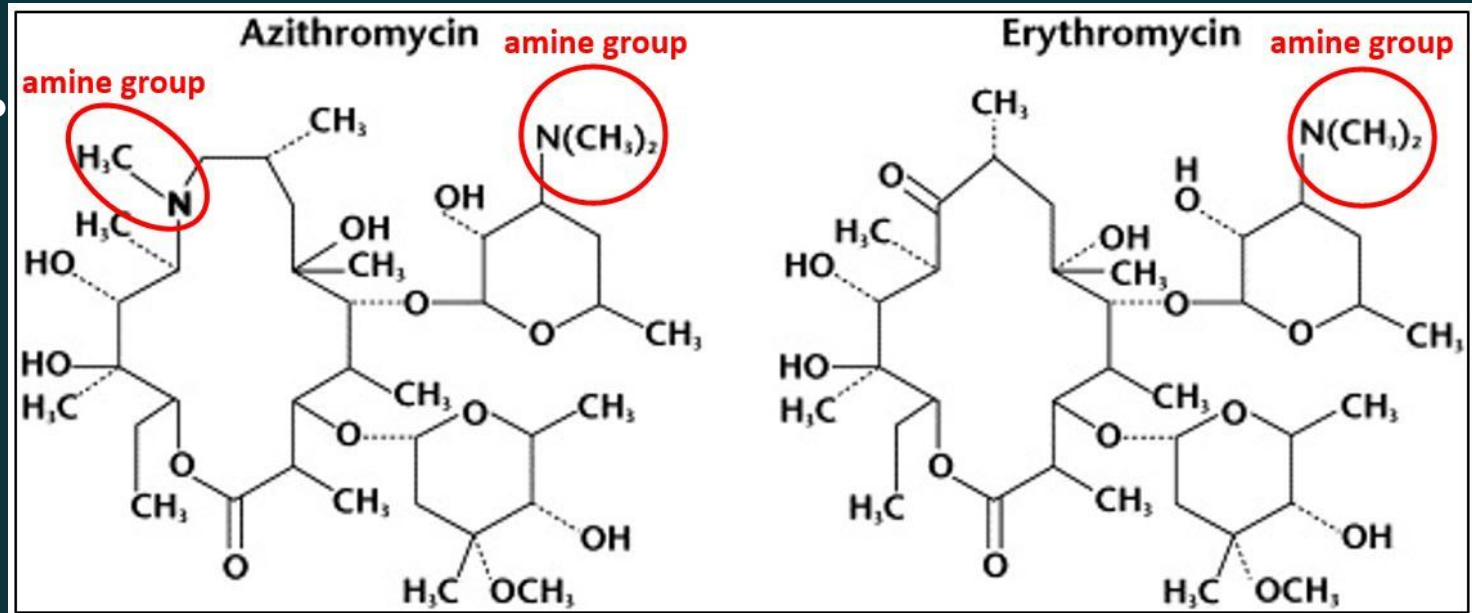
For severe cases of cholera

- **AZITHROMYCIN**

- Good stability at low pH and reaches site of infection rapidly
- Can be synthetically produced from erythromycin
  - By replacing 9a carbonyl in aglycone ring with a methyl substituted nitrogen
- Oral Administration: rapid transport from blood to tissue
- Blocks protein synthesis of *V. cholerae*
  - Therefore blocking production
  - By binding to the 50S ribosome subunit it blocks mRNA translation

# TREATMENTS

## AZITHROMYCIN STRUCTURE vs. ERYTHROMYCIN STRUCTURE



# TREATMENTS

## OPTION 2: ANTIBIOTICS

For severe cases of cholera

### RISKS OF ANTIBIOTICS

- Development of antibiotic-resistant strains of *V. cholerae*
- Disruption of the gut flora balance
  - Making it even more susceptible to other infections

# PREVENTION FOR THE SUBJECT

- **VAXCHORA VACCINE**
  - Approved by the American CDC
  - Single-dose oral vaccine
  - Contain live attenuated O1 serotype vibrios that are non-pathogenic
    - Subunit A was removed, so it only has Subunit B
- **TETRACYCLINE REGIMEN**
  - Only recommended for those with higher risk of cholera exposure
  - Effective prophylactic treatment

# PREVENTION FOR OTHERS

- **SHARED LIVING SPACES, KITCHENS, AND WASHROOMS**
  - Be mindful about fecal-contamination of food and water
  - Even more so when there is an infected person around
- **PREPARATION OF FOOD**
  - Boil
  - Cook
  - Peel