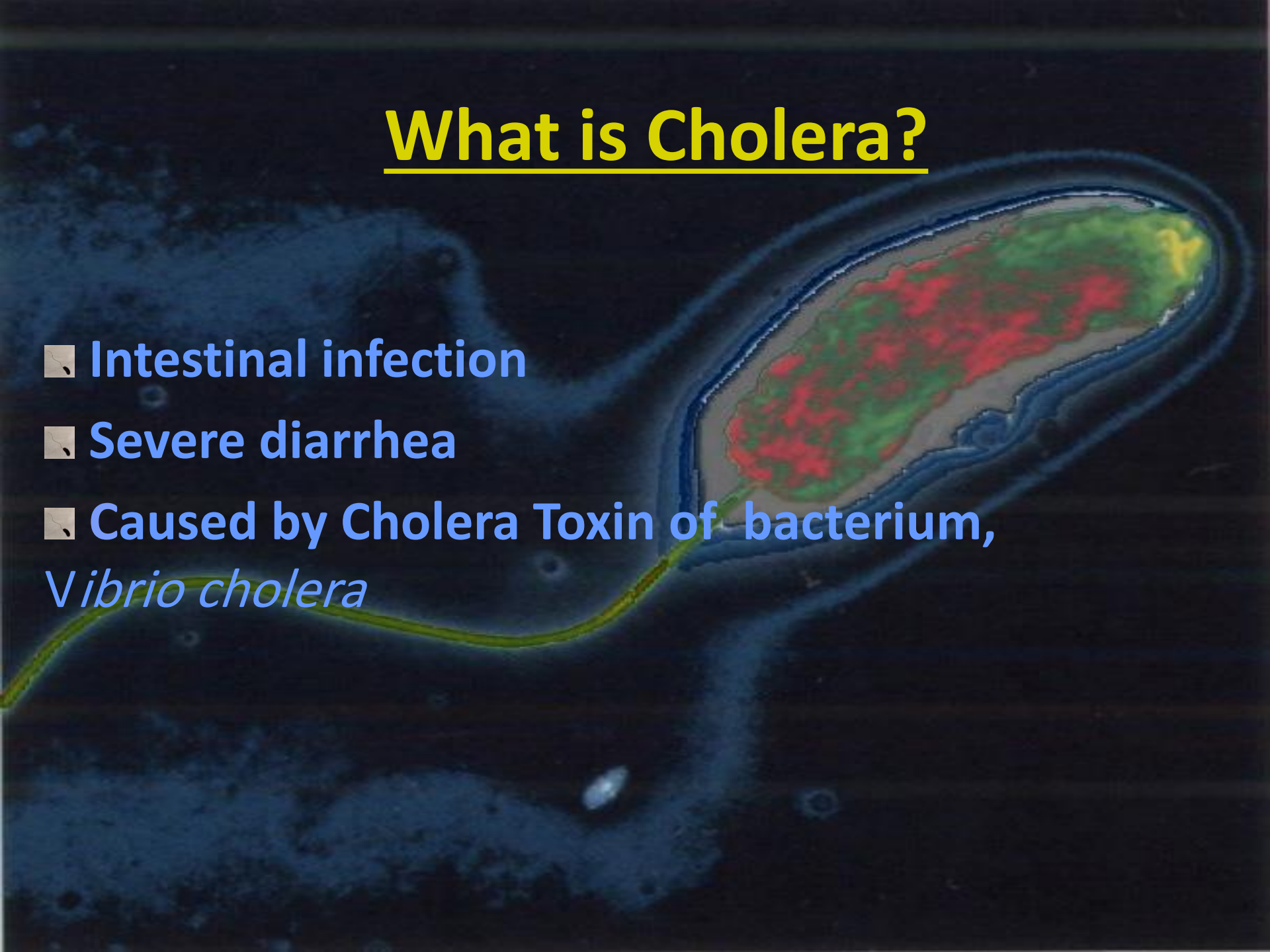
What is Cholera?



- Intestinal infection
- Severe diarrhea
- Caused by Cholera Toxin of bacterium, *Vibrio cholera*

Cholera

- A life-threatening secretory diarrhea induced by enterotoxin secreted by V. cholerae
- Water-borne illness caused by ingesting water/food contaminated by copepods infected by V. cholerae
- An enterotoxic enteropathy (a non-invasive diarrheal disease)
- A major epidemic disease

V. cholerae

- Transmitted by fecal-oral route
- Endemic in areas of poor sanitation (India and Bangladesh)
- May persist in shellfish or plankton
- 7 pandemics since 1817 – first 6 from Classical strains, 7th from El Tor
- 1993: Cholera in Bengal caused by O139 – may be cause of 8th pandemic

Profile of *vibrio cholerae*

- Gram-negative
- Highly motile; polar flagellum
- Brackish rivers, coastal waters
  - Associate with plankton and algae
- Proliferate in summers
- Produce Cholera toxin
- Pathogenic and nonpathogenic strains
  - 206 serogroups

Transmission

- Contaminated food or water
  - Inadequate sewage treatment
  - Lack of water treatment
  - Improperly cooked shellfish
- Transmission by casual contact unlikely

People Most at Risk

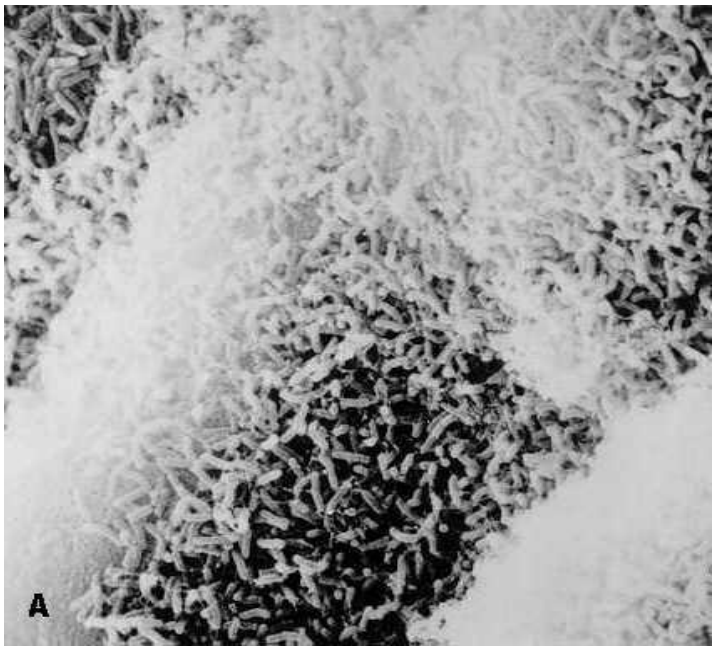
- People with low gastric acid levels
  - Children: 10x more susceptible than adults
  - Elderly
- Blood types
  - O more risk to infection>> B > A > AB less

Period of Communicability

- During acute stage
- A few days after recovery
- By end of week, 70% of patients non-infectious
- By end of third week, 98% non-infectious

Incubation

- Ranges from a few hours to 5 days
- Average is 1-3 days
- Shorter incubation period:
  - High gastric pH (from use of antacids)
  - Consumption of high dosage of cholera



How Does Cholera Toxin Work?

- G proteins stuck in “On” position
- 100 fold increase in cAMP
- Activation of ion channels
- Ions flow out and water follows
- animation

Infectious Dose

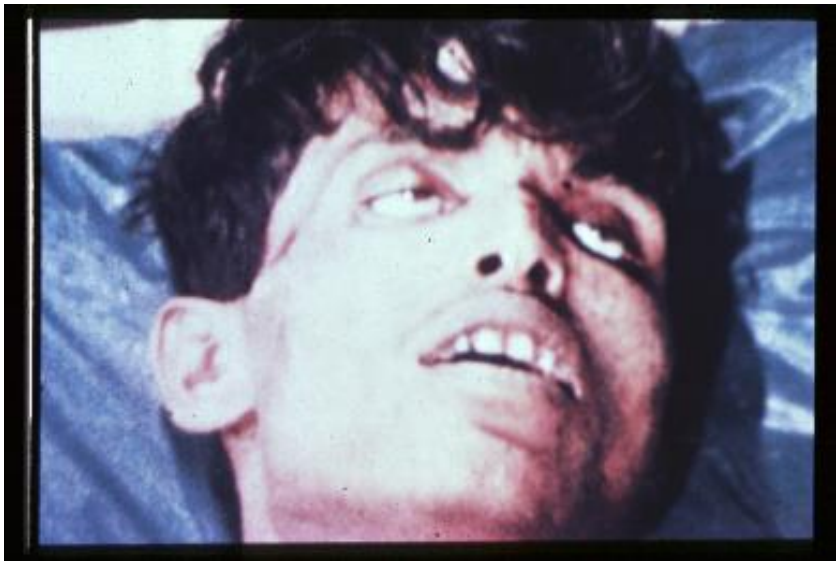
- 10^6-10^{11} colony-forming units
- Why such a high dosage?
  - Series of changes as moves from aquatic environment to intestine
    - Temperature, acidity
  - Acidic environment of stomach
  - Intestinal environment
    - Bile salts, organic acids, complement inhibit bacteria growth
    - Must penetrate mucous lining of intestinal epithelial cells

Symptoms

- Occur 2-3 days after consumption of contaminated food/water
- Usually mild, or no symptoms at all
  - 75% asymptomatic
  - 20% mild disease
  - 2-5% severe
- Vomiting
- Cramps
- Watery diarrhea (1L/hour)
- Without treatment, death in 18 hours-several days

Consequences of Severe Dehydration

- Intravascular volume depletion
- Severe metabolic acidosis
- Hypokalemia
- Cardiac and renal failure
- Sunken eyes
- Almost no urine production

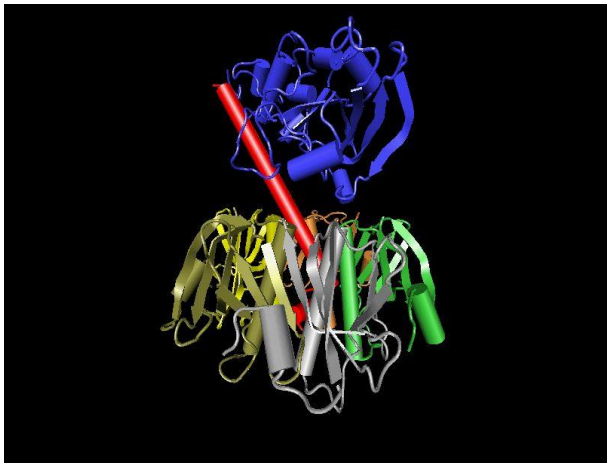


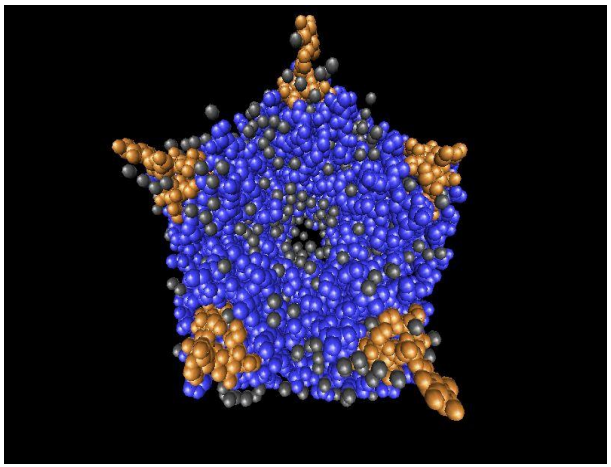
Mortality Rate

- Causes 120,000 deaths/year worldwide
- With prompt rehydration: <1%
- Without treatment: 50%-60%

Pathogenesis: Cholera Toxin (CT) Structure

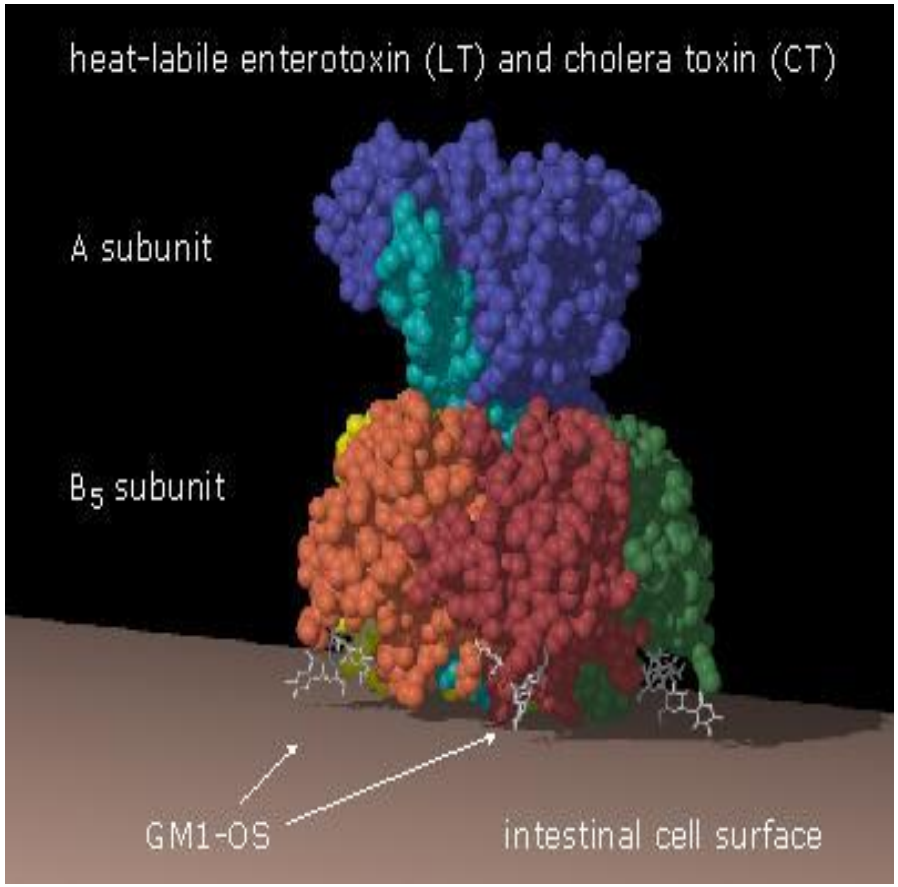
- CT is a prototype A/B subunit toxin, consisting of one A subunit and 5 B subunits.
- The B subunit weighs 11.6kDa each and multimerize to form a pentameric ring, which binds the holotoxin to a eukaryotic cell surface receptor.





Pathogenesis: Mechanism of Action cont.

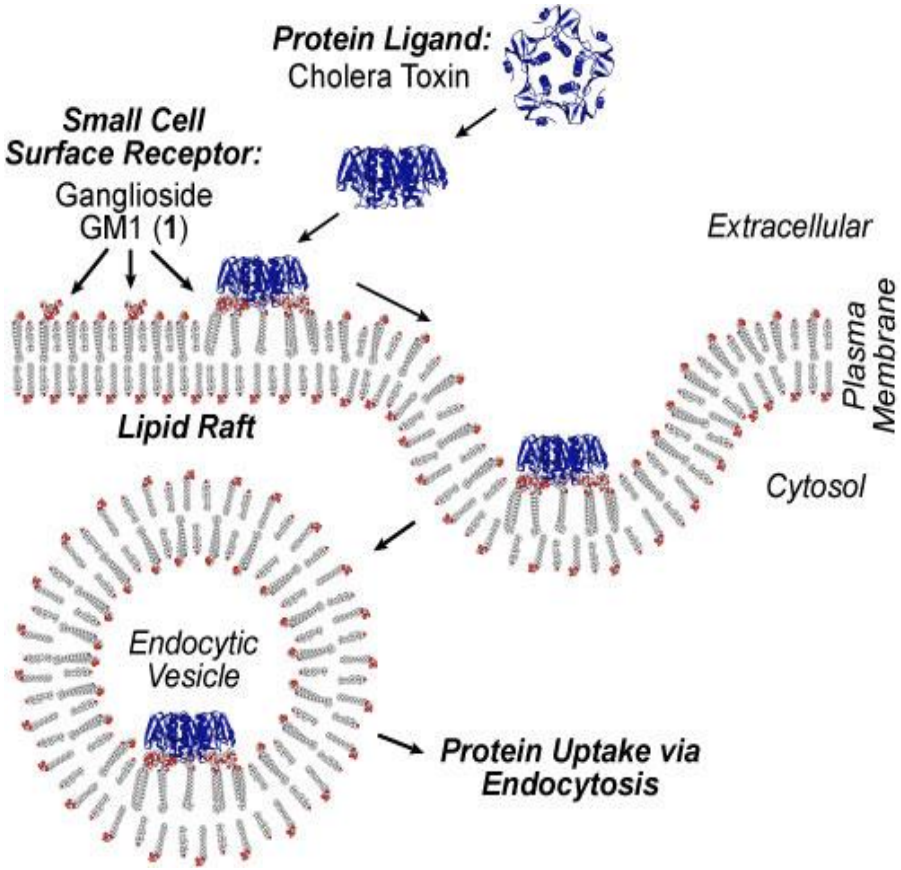
- The biological activity of CT is dependent on binding of the holotoxin B pentamer to specific receptors on the eukaryotic cell.
- The B oligomer binds with high affinity exclusively to GM1 ganglioside.



B subunits bind to GM1 Receptor

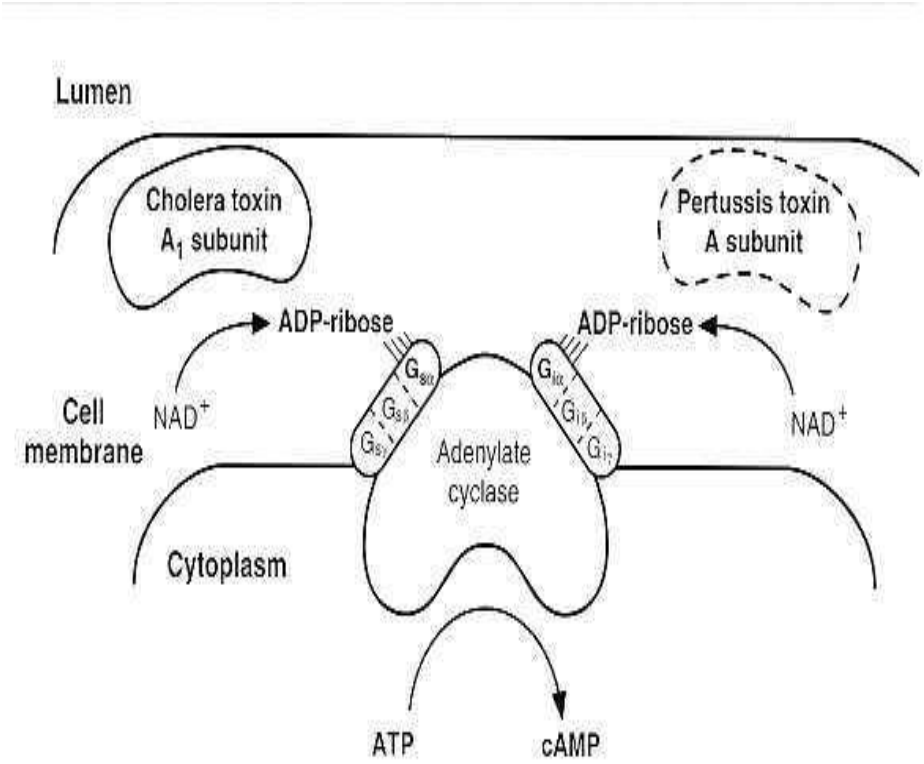
Pathogenesis: Mechanism of Action cont.

- Internalization is initiated once CT-GM1 complexes cluster which then invaginate to form apical endocytic vesicles.



Pathogenesis: Mechanism of Action cont.

- Thus, the net effect of the toxin is to cause cAMP to be produced at an abnormally high rate which stimulates mucosal cells to pump large amounts of Cl- into the intestinal contents.

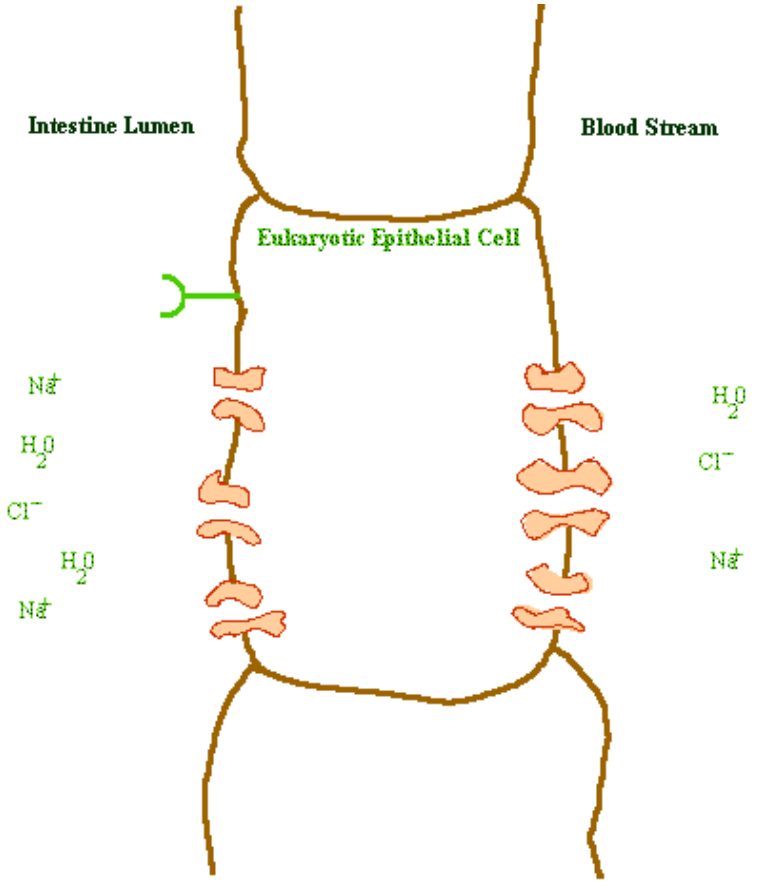


Pathogenesis: Mechanism of Action cont.

- H_2O, Na^+ and other electrolytes follow due to the osmotic and electrical gradients caused by the loss of Cl^-.
- The lost H_2O and electrolytes in mucosal cells are replaced from the blood.
- Thus, the toxin-damaged cells become pumps for water and electrolytes causing the diarrhea, loss of electrolytes, and dehydration that are characteristic of cholera.

Pathogenesis: Mechanism of Action cont.

- Normally, the epithelial cells of the inner lining of the intestines (lumen) transfer sodium and chloride ions from the inside of the intestines to the blood stream.
- The "B" subunit of cholera toxin is bound by a host receptor (like a specific "landing pad") allowing the "A" subunit to enter the cell.
- Once inside the cell the "A" subunit causes a change in the regulation of the cells genes and as a result, the flow of ions and water is reversed.



Treatment

Even before identifying cause of disease, rehydration therapy must begin Immediately because death can occur within hours

- Oral rehydration
- Intravenous rehydration
- Antimicrobial therapy

Treatment: Oral Rehydration

- Reduces mortality rate from over 50% to less than 1%
- Recover within 3-6 days
- Should administer at least 1.5x amount of liquid lost in stools
- Use when less than 10% of bodyweight lost in dehydration

Treatment: Oral Rehydration Salts (ORS)

- Reduces mortality from over 50% to less than 1%
- Packets of Oral Rehydration Salts
  - Distributed by WHO, UNICEF
  - Dissolve in 1 L water
  - NaCl, KCl, $NaHCO_3$, glucose

Treatment: Antibiotics

- Adjunct to oral rehydration
- Reduce fluid loss by half
- Reduce recovery time by half
  - 2-3 days instead of 4-6
- Tetracycline, Doxycycline
- Not recommended
  - Short duration of illness
  - Antibiotic resistance
  - Limited gain from usage

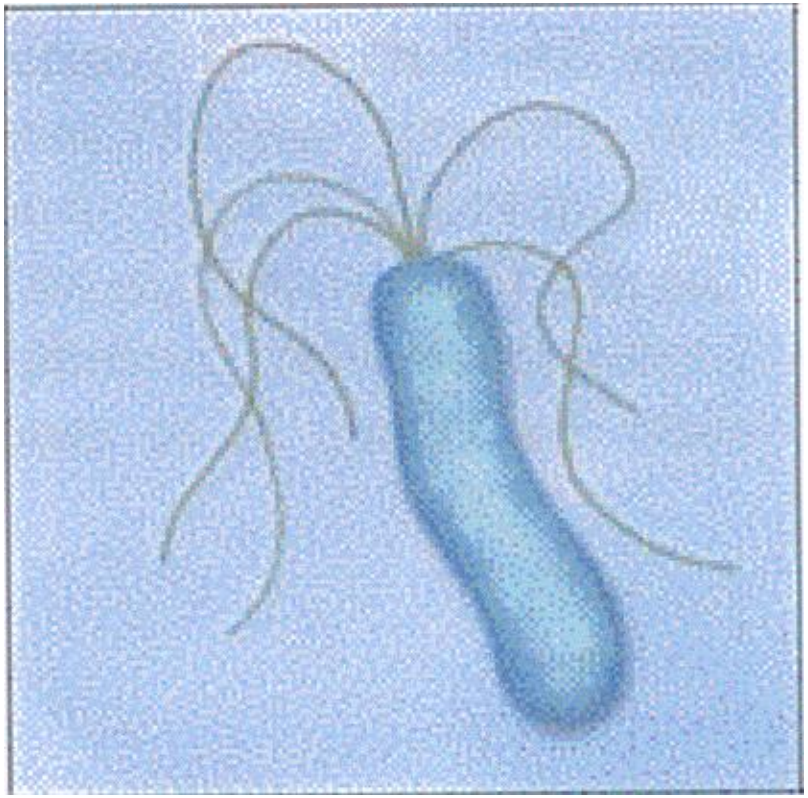
Helicobacter pylori

Abdulelah A Almayah

Helicobacter pylori

History

- **In 1982 ,spiral-shaped bacterium from gastric biopsies of patients with gastritis was isolated**
- **The discovery was by Dr.Robin Warren and Dr.Barry Marshall**



Epidemiology

- **Infection occurs worldwide**
- **Overall *prevalence* strongly correlates with socio-economic conditions**
- **In Middleaged adults in developing countries prevalence is 80%, in industralised countries 20-50% (rate of acquistion decreasing)**
- ***Acquisition:*Oral Ingestion of the bacterium**
- ***Transmission:*Within families in early childhood, not isolated from water etc, e**

Pathogenesis

- ***H. pylori*** **is found only on gastric epithelium where the organisms tend to cluster around the junctions between cells and virtually never penetrate the cells themselves.**
- ***H. pylori*** **is able to survive in the gastric environment which is hostile to growth of most bacteria.**

Standard triple therapy-Eradication therapy, which is probably the most widely used treatment for eradication of *H. pylori for* 7days minimal

Proton pump inhibitor **B.D. (e/g Lansoprazole 30 mg BD)**
+
Clarithromycin 500mg **B.D.**
+
Amoxycillin 1g **B.D.**
Or If penicillin allergic
Proton pump inhibitor **B.D. (e/g Lansoprazole 30 mg)**
Clarithromycin 500mg B.D.
Metronidazole 400 mg B.D
If treatment failure refer to Gasterenterologist

BRUCELLOSIS

Etiology

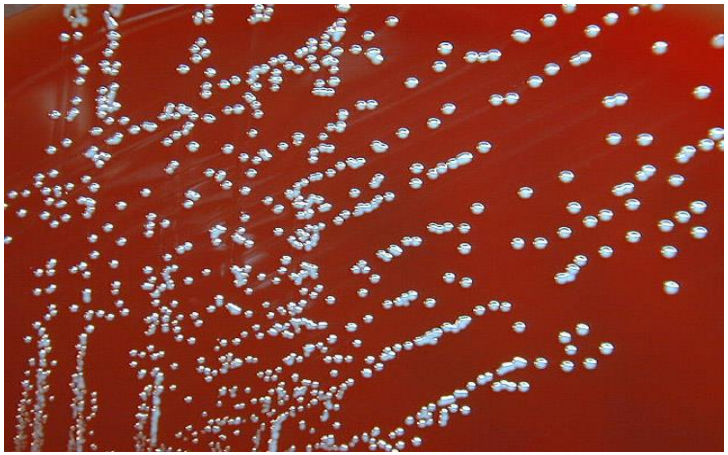
- *Brucella:*
- *Brucella abortus*(infect Cattle),

Brucella melitensis (infect Sheep,Goat)

- *Brucella suis*(Swin),Canins(Dog)

Brucella are

- G-ve Coccobacilli
- Aerobic, Non-spore forming
- Non motile
- Grown on Blood or Chocolate agar



Clinical Manifestations

- GIT : anorexia, abd. pain, vomiting, diarrhea,constipation, hepatosplenomegaly.

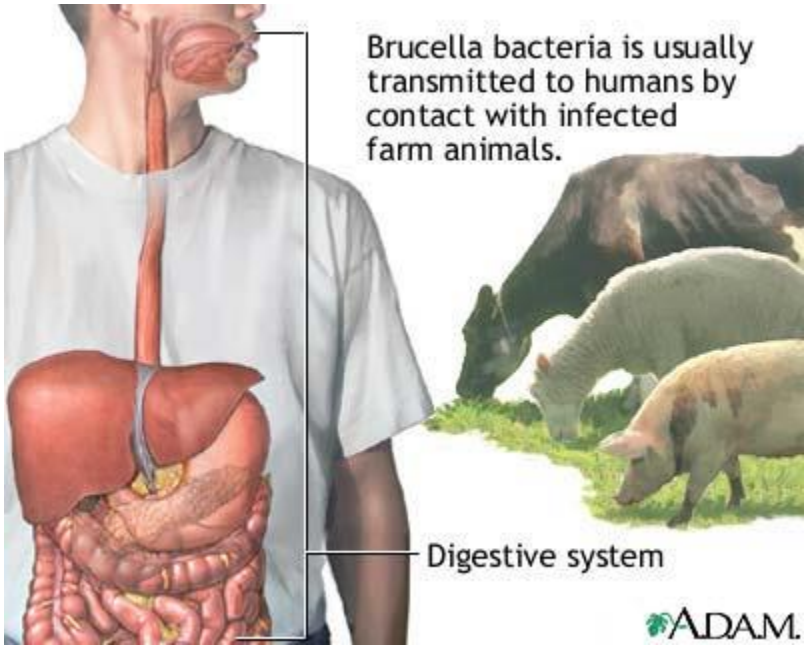
- LIVER : Involved in most cases .
  - granulomas (*B. abortus*).
  - hepatitis (*B.melitensis).*
  - abscesses (*B.suis)*.

Clinical Manifestations

- Neurologic
  - Meningitis, encephalitis, radiculopathy & peripheral neuropathy, intracerebral abscesses
  - Meningitis
    - acute or chronic
    - neck rigidity < 50%

Epidemiology

- Unpasteurized milk
- Occupational events



Diagnosis

- WBC Normal or low
- + History of animal or food exposure
- Recovering organisms (blood’ bone marrow’..)
- Serum agglutination test: >1/160

(Antibody against Abortus ,Melitensis, Suis)

Pertussis

(Whooping Cough or Hundred Day Cough)

Epidemiology of Pertussis

Mode of transmission

- Person to person via
  - Aerosolized droplets from cough or sneeze
  - Direct contact with secretions from respiratory tract of infectious person

- 80% - secondary attack rate

- Older children and adults are important sources of disease for infants and young children

- Infants <12 months of age greatest risk for complications and death

-

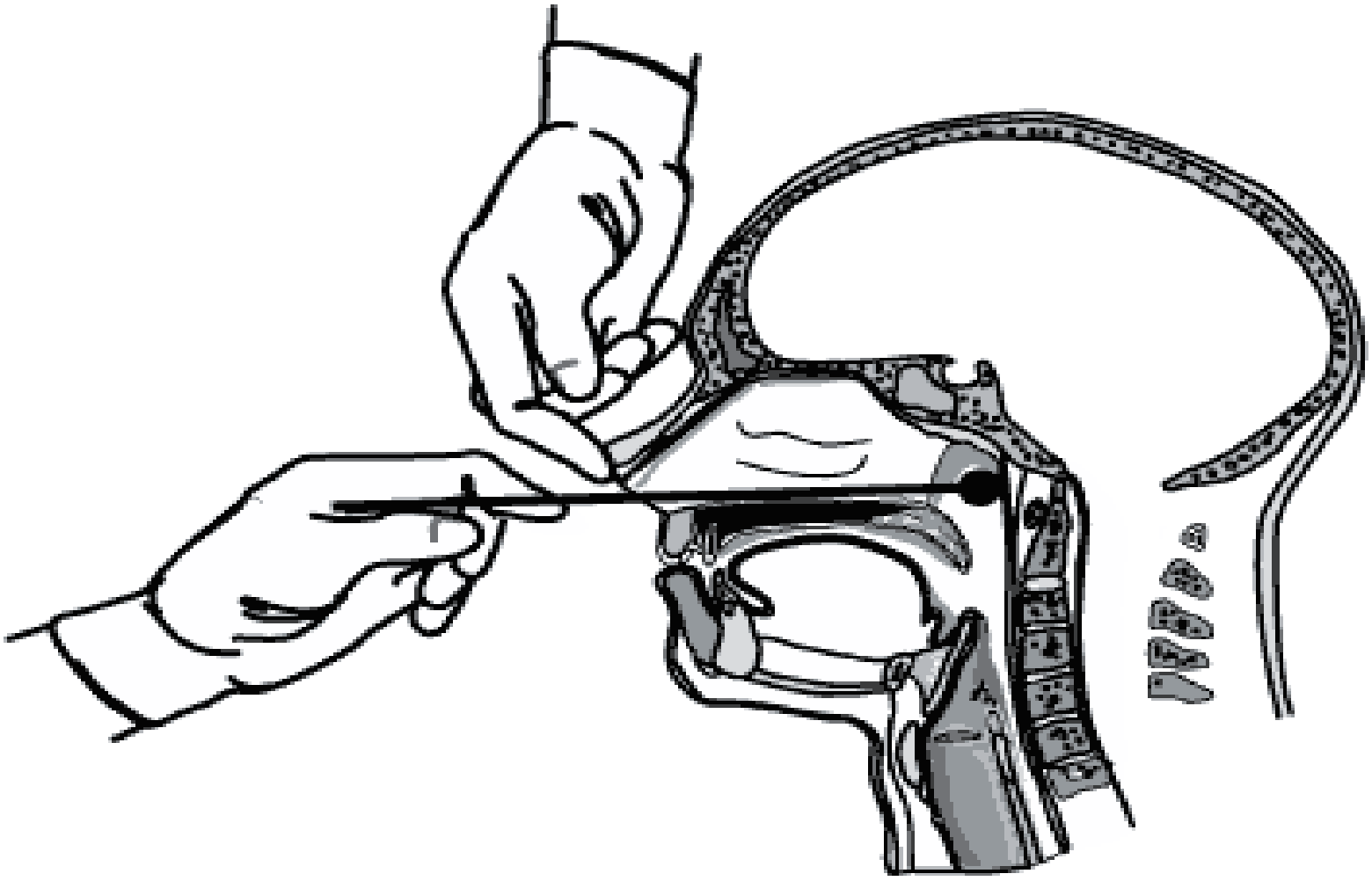
Epidemiology of Pertussis

- Reservoir - Humans
- Incubation period – 7-10 days (5-21 days).
- Infectious period – Most contagious during the first 2 weeks after cough onset
- Duration of illness:
  - Children: 6-10 wks.
  - ~ ½ of Adolescents: 10 wks or longer

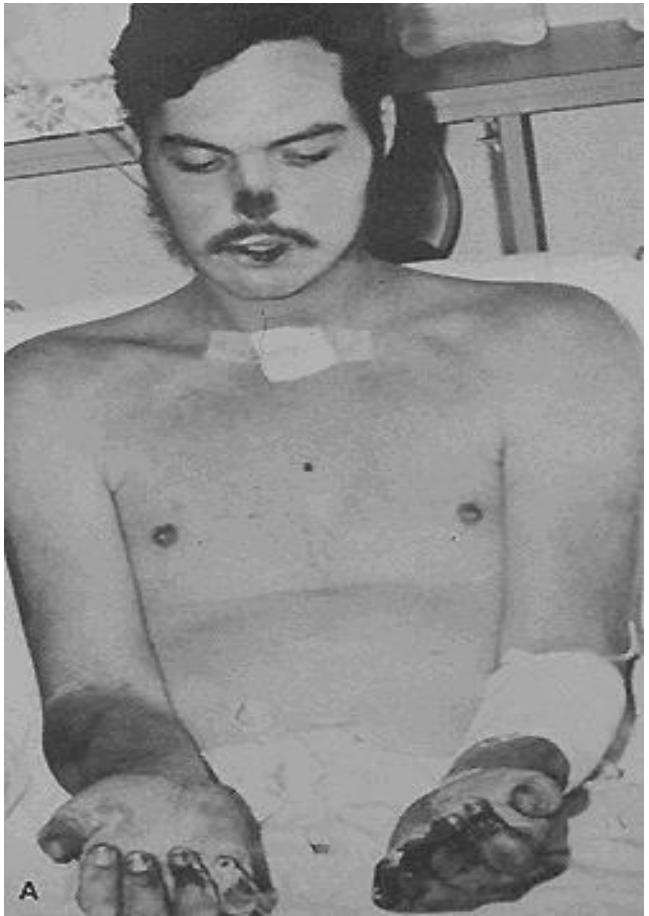
Pertussis Complications

- Syncope (temporary loss of consciousness)
- Sleep disturbance
- Incontinence
- Rib fractures
- Complications among infants
  - Pneumonia (22%)
  - Seizures (2%)
  - Encephalopathy (<0.5%)
- Death
  - Infants, particularly those who have not received a primary vaccination series, are at risk for complications and mortality.

Proper Technique for Obtaining a Nasopharyngeal Specimen for Isolation of *B pertussis*



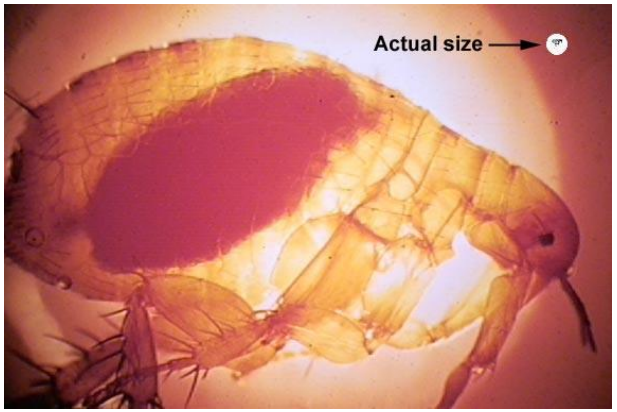
Yersinia pestis



- Member of the *Enterobacteriaceae* family

Yersinia is a Gram-negative coccobacilli

Ecology and Infection Process



Y. pestis **multiply into intestinal Flea.**

Some *Y. pestis* in the flea infect next blood meal thus transferring the infection to a new host.

A few bacilli are taken up by tissue macrophages after they lose their capsular layer. Macrophages can't kill *Y. pestis* and provide protected environment for bacilli so they can re-synthesize their capsular layer.

The re-encapsulated organisms then kill the macrophage and are released into the extracellular environment where they travel to draining lymph nodes.

Symptoms

Bubonic Plague

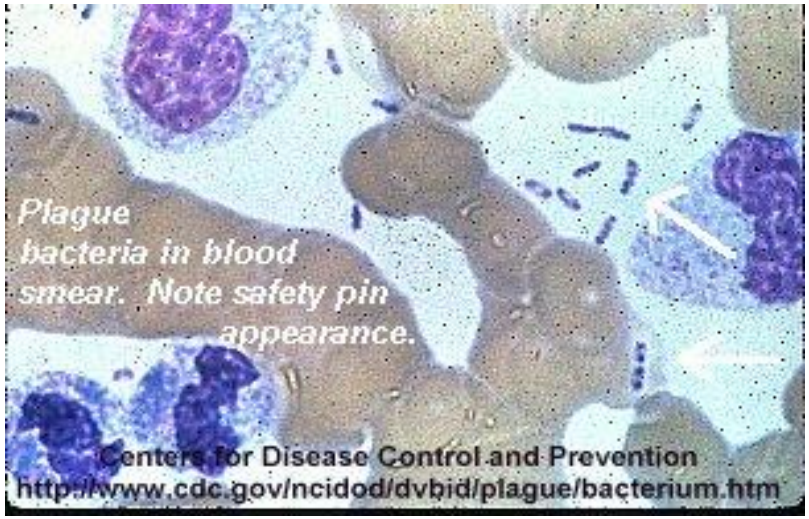
bacteria infect lymph nodes

- Bubos

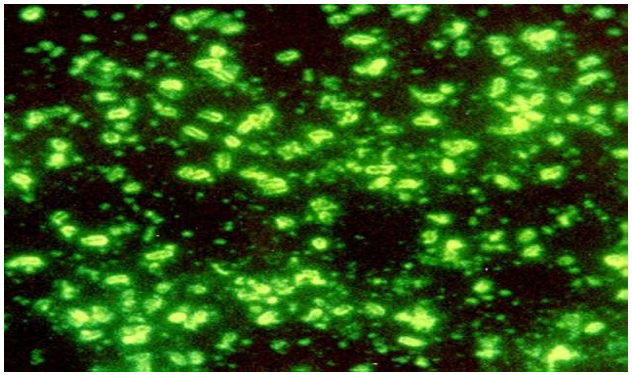
- Fever
- Headache
- Vomiting Blood

Diagnostic Tests

- Take smear from blood or feces for bubonic plague



Can also use FA (fluorescent-antibody) test
All plague bacilli have unique diagnostic envelope glycoprotein called the Fraction 1 (F1) antigen



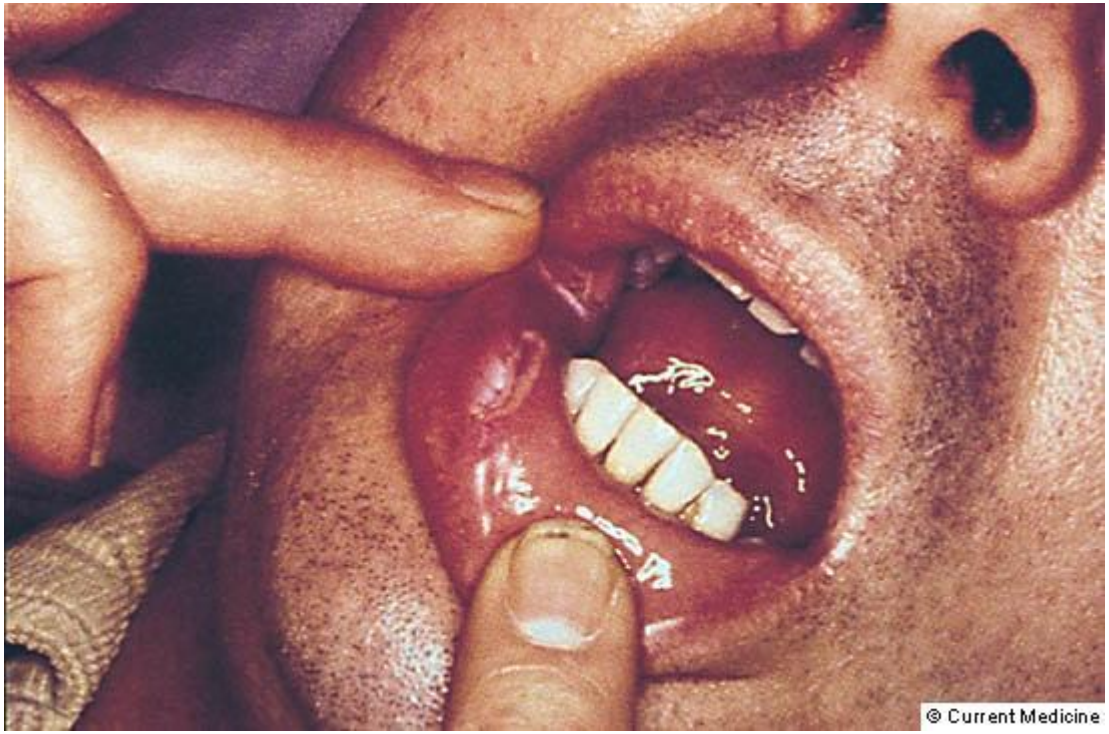
SYPHILIS
INTRODUCTION

- **Caused by *Treponema pallidum*.**
- **Transmission: sexual; maternal-fetal, and rarely by other means.**
- **Primary and secondary syphilis in the US dropped by ~ 90 %t from 1990 to 2000, the number of cases have gone up since then.**
- **A dramatic increase in cases in men from 2000 to 2002 reflected syphilis in MSM.**
- **Syphilis increases the risk of both transmitting and getting infected with HIV**

STAGES OF SYPHILIS

1. **Primary**
2. **Secondary**
3. **Latent**
    - **Early latent**
    - **Late latent**
4. **Late or tertiary**
    - **May involve any organ, but main parts are:**
        - **Neurosyphilis**
        - **Cardiovascular syphilis**
        - **Late benign (gumma)**

Oral chancres in primary syphilis



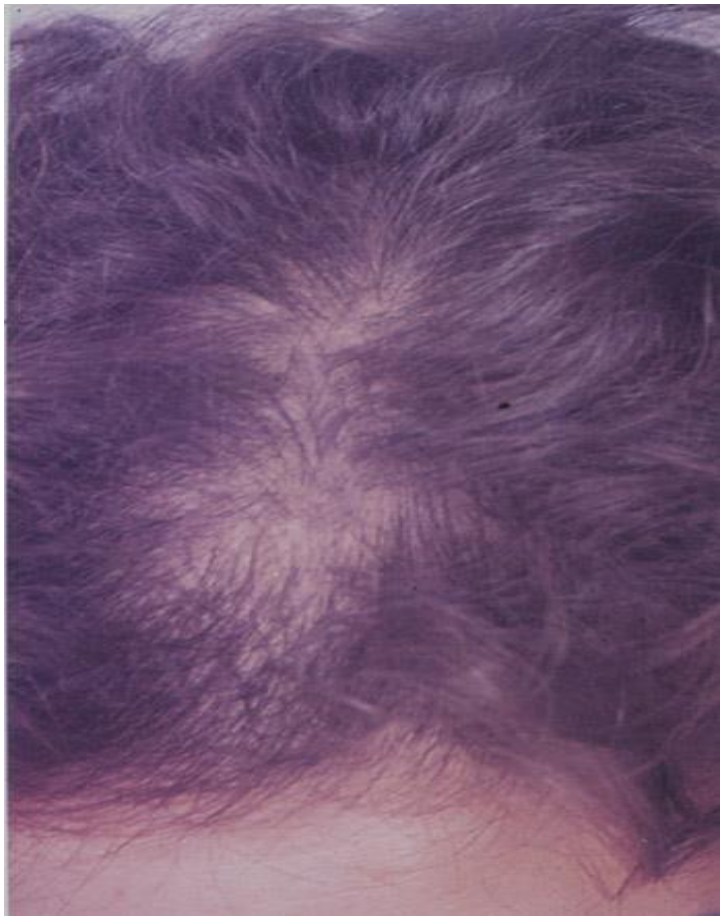
SECONDARY SYPHILIS (Cont.)

- **The skin rash:**
  - Diffuse,
  - often with a superficial scale (papulosquamous).
  - May leave residual pigmentation or depigmentation.

- **Mucosal lesions:**

  ~ 30% of secondary syphilis patients develop mucous patch (slightly raised, oval area covered by a grayish white membrane, with a pink base that does not bleed).
  - Highly infectious

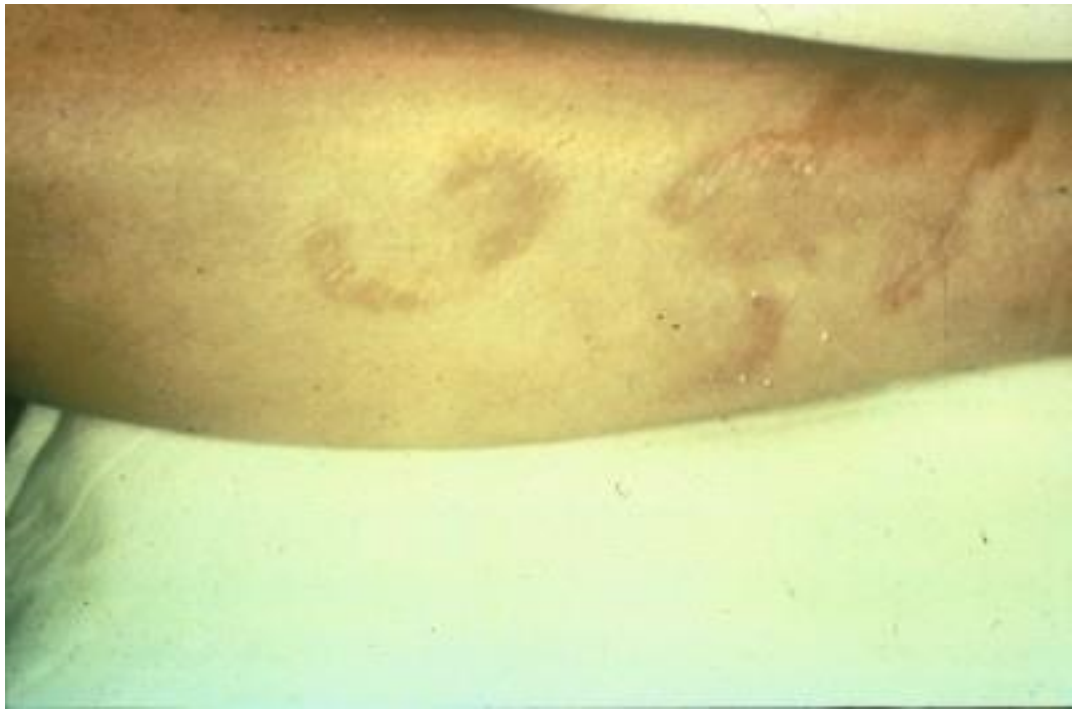
Alopecia area



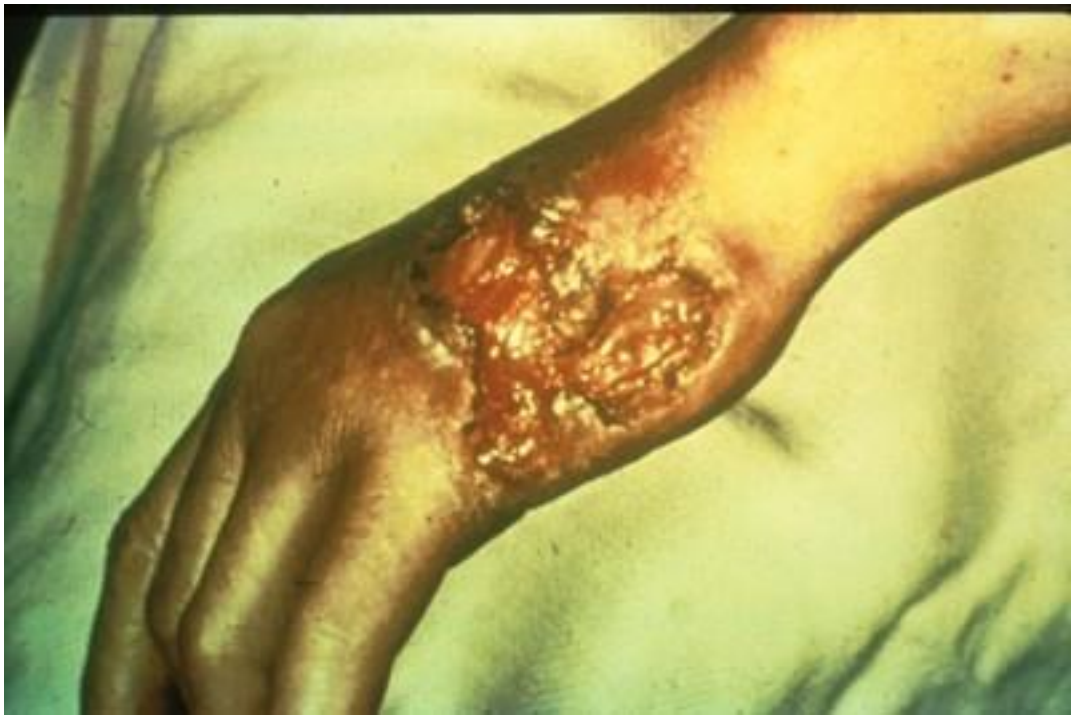
LATENT SYPHILIS (cont.)

1. **Early latent:**
   - **The first year after the resolution of primary or secondary lesions, or**
   - **A reactive serologic test for syphilis in an asymptomatic individual who has had a negative serologic test within the preceding year.**
   - **Infectious.**
2. **Late latent:**
   - **Usually not infectious, *except for the pregnant woman, who may transmit infection to her fetus.***

Late syphilis - serpiginous gummata of forearm



Late syphilis - ulcerating gumma



Primary, Secondary, Early Latent Syphilis

Recommended regimen

-Benzathine Penicillin G, 2.4 million units IM

Penicillin Allergy*

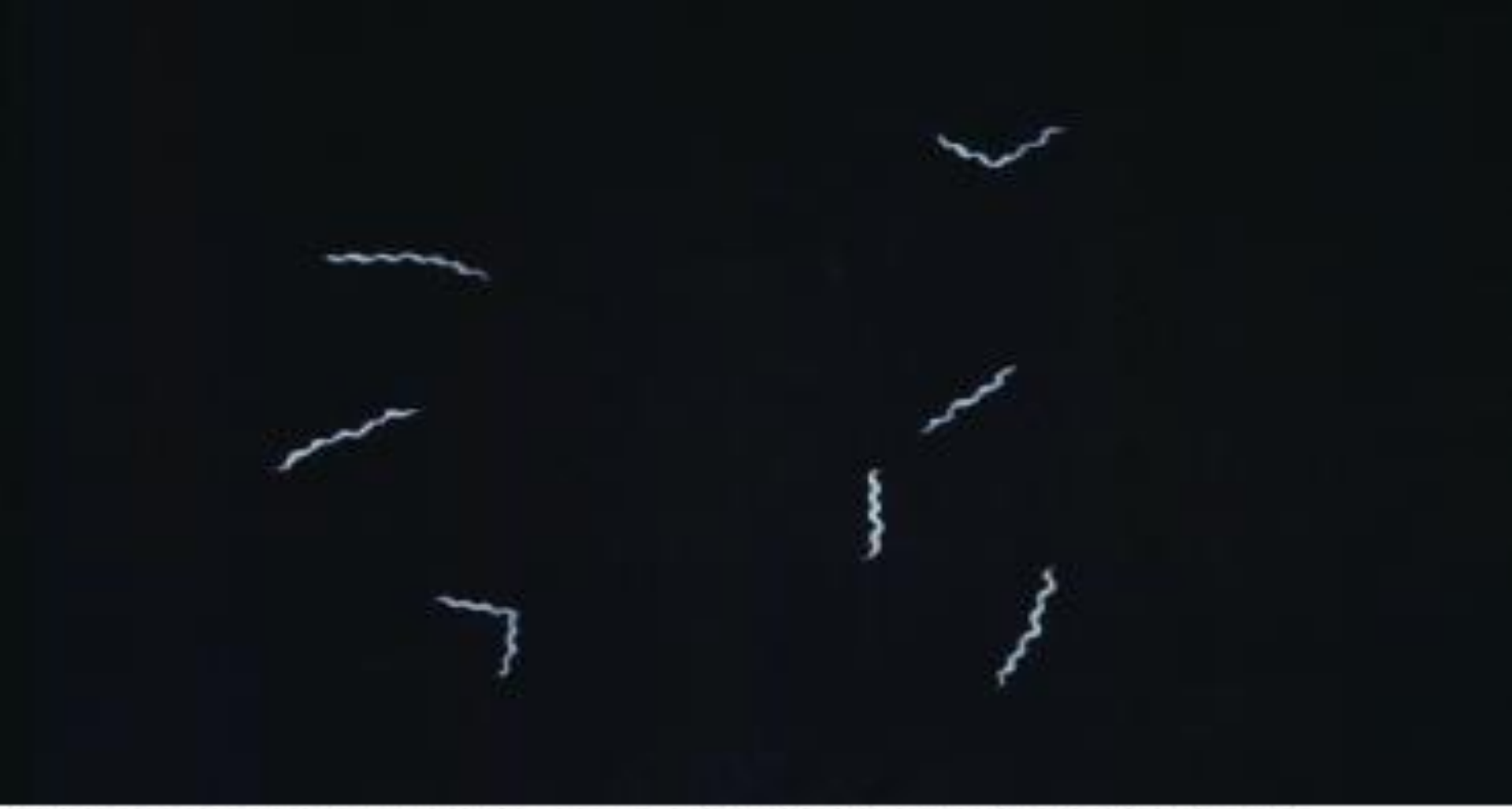
-Doxycycline 100 mg twice daily x 14 days

or

-Ceftriaxone 1 gm IM/IV daily x 8-10 days (limited studies) or

-Azithromycin 2 gm single oral dose

- **Congenital syphilis is transmitted in utero after the first 16 weeks of pregnancy, therefore it is usually not a cause of abortion during the first trimester.**
- **The infected child born later in a family usually has less severe syphilis.**



Treponema pallidum Dark field examination of exudate from a penile ulcer (x1000) in a patient with syphilis. The spirochete Treponema pallidum, which is too small to be seen using ordinary microscopy, appears as a delicate spiral rod when dark field illumination is employed. Courtesy of Harriet Provine.