24

Microbiology

Doctor 2018 | Medicine | JU

◉ Sheet ○ Slides

Done By

Ameen Alsaras

Contributed in the Scientific Correction

Sarah K. Al-Qudah

Contributed in the Grammatical Correction

Sarah K. Al-Qudah

Doctor

Anas Abu-Humeidan

*We'll talk today about some pathogens that have many things in common. Most of them are gram-negatives, somewhat **curved**, and cause GI problems.*

* These pathogens seems similar to the spirochete phylum morphologically although they differ in structure; spirochetes' axial filaments(flagella) run lengthwise between the bacterial inner & outer membrane giving the spirochete a helical(spiral) shape & twisting motion. On the other hand; those pathogens express the classic form of flagella.

* Remember: viral gastroenteritis can be cased by Norovirus, rotavirus & less commonly by adenovirus.

1-Campylobacter

❖ General Features:

- They are small gram-negative rods, motile and **curved.**

- In some regions, campylobacter is the most common cause of bacterial gastroenteritis, they're responsible for most infections with Campylobacter jejuni that causes histologic damage to the **mucosal surfaces of the jejunum** as well as other parts of the intestine.

-They are **oxidase-positive** and **catalase-positive.** This can help in the identification of these organisms.

-These organisms are killed when exposed to gastric acids, so conditions that decrease or neutralize gastric acid secretion favor disease

❖ Growth:

-The growth conditions of these bacteria are said to be fastidious as they need specific microaerophilic conditions. **(Microaerophilic means that these bacteria need lower concentrations of oxygen than aerobes do).** These organisms grow best in an atmosphere of reduced oxygen (5% to 7%) and increased carbon dioxide (5% to .10%). Finally, C. jejuni grows better at 42° C rather than at 37° C.

*This figure shows different types of oxygen requirements for different bacteria. **Remember, C. jejuni is microaerophilic→E.**

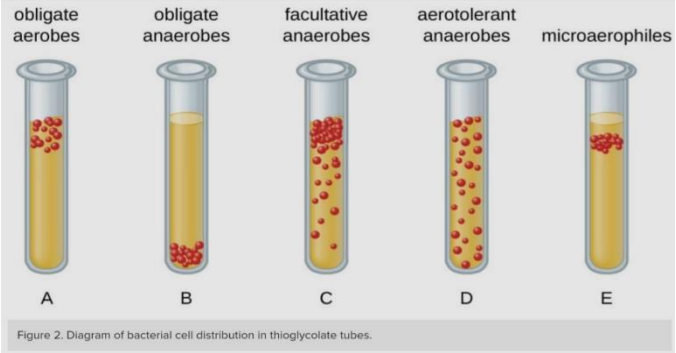


Figure 2. Diagram of bacterial cell distribution in thioglycolate tubes.

❖ Virulence and Pathogenesis:

-Express lipooligosaccharides (LOSs lack O-antigen in LPS)

-Campylobacter infections are zoonotic, with a variety of animals serving as reservoirs, especially contaminated poultry.

-It is uncommon for the disease to be transmitted by food-handlers.

-It can cause acute enteritis with bloody diarrhea, fever, vomiting and severe abdominal pain.

-**Guillain-Barré syndrome** and **reactive arthritis** are well-recognized complications of Campylobacter infections (although uncommon). Probably through molecular mimicry.

Remember:
Molecular mimicry happens when antigens on a certain pathogen that you have faced before are similar to antigens you have in your body. So, immune cells that were formed against that pathogen attack you.

Guillain-Barre syndrome is associated with neuronal antigens; thus causing descending paralysis.

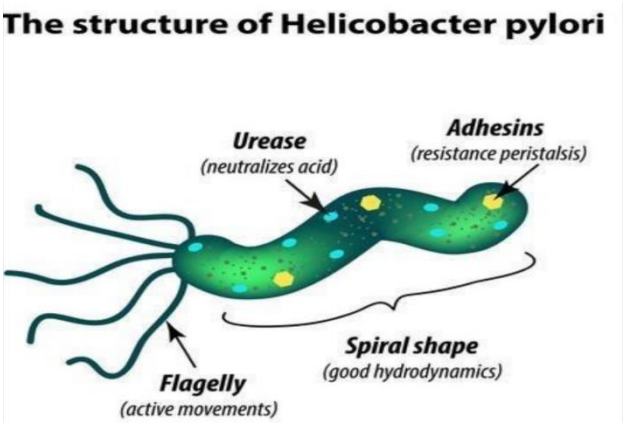
Extra clinical notes

-THE CONTINUOUS DAMAGE CAUSED BY SEVERE WATERY DIARRHEA CAN TURN INTO BLOODY DIARRHEA.

-RAPID GASTROENTERITIS THAT FOLLOWS A MEAL INDICATES INTOXICATION; A PREVIOUS TOXIN WAS FORMED BY AN UNKNOWN BACTERIA= NO ANTIBIOTIC DESCRIBED; THE FOOD WAS MOST LIKELY HEATED, MEANING THAT THE PRESENCE OF A PREFORMED TOXIN ISN'T OBLIGATING THE PRESENCE OF THE BACTERIA.

-IN A STAGE 2 DEVELOPING OF GASTROENTERITIS IF A DIARRHEA WAS HAPPENING, WE SUSPECT AN INFECTION; THE PATIENT HAS TO DO A STOOL TEST TO INDICATE THE PATHOGEN SO WE CAN GIVE THE ACCURATE SPECIFIC TREATMENT. ANTIMOTILES AREN'T PREFERRED; WE NEED THE INTESTINES TO MAKE THEIR JOB.

2-Helicobacter



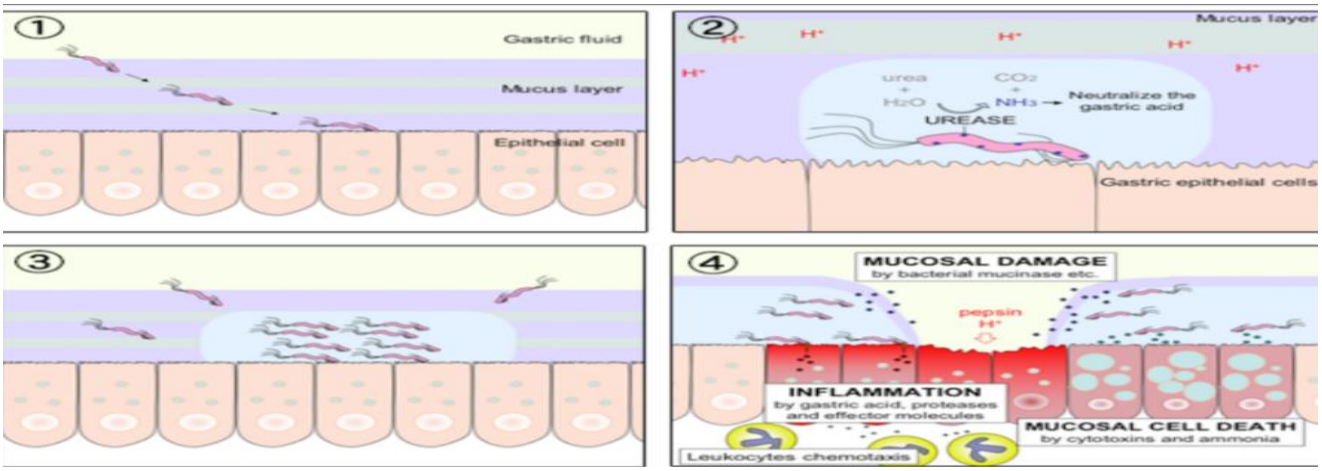
❖ General Features:

- These species are spiral gram-negative rods resembling campylobacters. All gastric helicobacters, including H. pylori, are **microaerophilic**, highly **motile** (corkscrew motility) and strong producers of **urease**. Additionally, they are **catalase-positive** and **oxidase-positive**. Note that some infections are not necessarily caused due to toxins of bacteria.

- Humans are the primary reservoir for H. pylori, and colonization is believed to persist for life unless the host is specifically treated. **Transmission is most likely via the fecal-oral route (contaminated food or water).**

❖ Virulence and Pathogenesis:

- Helicobacter is special in a form that they can colonize the stomach and evade the gastric acids by their fast motility & chemotaxis reaching the mucous that lines the gastric epithelium, then using their adhesion tools they bind to this gastric epithelium. Helicobacter produce an enzyme called urease that breaks down the urea to give ammonia & CO2, creating a basic microenvironment that helps bacteria resist the acidity of the stomach. Helicobacter multiplies and forms a population, establishing the infection by releasing many enzymes such as **mucinase** (that breaks down mucous which is part of the innate immunity) and phospholipases. Making the epithelium vulnerable and damaged by stomach's acidity. Moreover, toxins such as **vacuolating cytotoxin A (VacA)** and **cytotoxin-associated gene (cagA)** destroy the gastric epithelium. Leukocytes would come just to make everything worse and induce inflammation=**Gastritis**.



*Vacuolating cytotoxin A (VacA) damages the cells by producing vacuoles while cytotoxin-associated gene (cagA) interferes with the normal cytoskeletal structure of the epithelial cells damaging them.

- The **acute phase of gastritis** is characterized by a feeling of fullness, nausea, vomiting, and hypochlorhydria. If it persists, it can evolve to **chronic gastritis,** with disease confined to the gastric antrum or involve the entire stomach. Chronic gastritis will progress to develop **peptic ulcers.** The ulcers develop at the sites of intense inflammation, commonly involving the junction between the corpus and antrum **(gastric ulcer)** or the proximal duodenum **(duodenal ulcer).** If the damages reaches blood vessels this will cause bleeding ulcer.

- H. pylori is responsible for 85% of the gastric ulcers and 95% of the duodenal ulcers.

- Chronic gastritis increases the risk of gastric cancer and MALT lymphoma (mucosa-associated lymphoid tissue B-cell lymphomas).

❖ Detection:

Since H. pylori adheresto gastric mucosa , H. pylori can be detected by histologic examination of gastric biopsy specimens, but identification is usually done by non-invasive methods. A number of polyclonal and monoclonal immunoassays for H. pylori antigens excreted in stool have been developed and demonstrated to have sensitivities and specificities exceeding 95%. You can also look for certain antibodies in the blood sample. However, **Urea Breat Test** is the best and most convenient method. Patients ingest urea that has labeled carbon atoms. Then, they breath in a bag and the labeled carbon is searched for in the CO2 exhaled by pateints. **Remember, urea is broken down by urease into ammonia and CO2. Urea broken down → Urease is there → Helicobater pylori is there.**


THE LANCET

Volume 321, Issue 8336, 4 June 1983, Pages 1273-1275

Letters to the Editor

UNIDENTIFIED CURVED BACILLI ON GASTRIC EPITHELIUM IN ACTIVE CHRONIC GASTRITIS

J Robin Warren [a], Barry Marshall [b]

→ History: In 2005, the Karolinska Institute in Stockholm awarded the Nobel Prize in Physiology or Medicine to Marshall and Robin Warren, his long-time collaborator, "for their discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease"

3-Vibrio

❖ General Features:

-Facultatively anaerobic, fermentative, oxidase-positive, gram-negative curved rods with polar flagellum (on one side) for motility.

❖ Growth:

-Vibrio species can grow on a variety of simple media within a broad temperature range (from 14° C to 40° C). And tolerate a wide range of pH (e.g., pH of 6.5 to 9.0) but are susceptible to stomach acids.

-Most species are halophilic ("salt-loving"). Requiring sodium chloride (NaCl) for growth.

-Vibrio species, including V. cholerae, grow naturally in estuarine and marine environments worldwide.

-Pathogenic vibrios can also flourish in waters with chitinous shellfish.

❖ Epidimiology:

-V. cholera is spread by **contaminated water and food** rather than direct person-to-person spread, because a **high inoculum** (e.g., $>10^8$ organisms) is required to establish infection in a person with normal gastric acidity. So, if you ever got these bacteria from another person, your acidic stomach will destroy them, no infection occurs.

-Cholera is usually seen in communities with poor sanitation, like in India and Africa where people get water from anywhere. It is estimated that 3 to 5 million cases of cholera and 120,000 deaths occur worldwide each year. Seven major pandemics of cholera have occurred since 1817, resulting in thousands of deaths and major socioeconomic changes and the most recent outbreak was in Yemen due to war and poor sanitation.

❖ Virulence and Pathogenesis:

-V. cholerae is subdivided, using serotyping (O polysaccharide), to V. cholerae O1 and O139 which make cholera toxin & cause cholera epidemics. Other strains of V. cholerae are not toxin producing and epidemic causing – however, they may cause non-epidemic infections.

-Cholera toxin:

Once V. cholerae is ingested, it releases its toxin into the intestine. This toxin is a classic **A-B toxin**. B subunit helps in binding the **ganglioside receptor** while the A subunit is internalized causing increased adenylyl cyclase activity which leads to increased amounts of cAMP. Increased [cAMP] contributes in the massive secretion of water and electrolytes, like: Na^+, Cl^-, K^+ and HCO_3^- from the epithelium into the lumen.

-Toxin co-regulated pilus (TCP):

Their role isn't only for adhering the bacteria to the intestinal cells. They contribute in transforming the non-toxigenic V. cholerae to toxigenic, and this happen as follows:

1-Non-toxigenic V. Cholerae expresses TCP on Vibrio pathogenicity Island (VPI).
2-It's infected by a phage.
3- The phage gets its genome incorporated with the non-toxigenic V. Cholerae making it toxigenic.

*Other virulence factors are discussed in this table, but keep in mind that those mentioned above are the most important ones. →

Species	Virulence Factor	Biological Effect
V. cholerae	Cholera toxin	Hypersecretion of electrolytes and water
	Toxin co-regulated pilus	Surface binding site receptor for bacteriophage CTXΦ; mediates bacterial adherence to intestinal mucosal cells
	Chemotaxis protein	Adhesin factor
	Accessory cholera enterotoxin	Increases intestinal fluid secretion
	Zonula occludens toxin	Increases intestinal permeability
	Neuraminidase	Modifies cell surface to increase GM_1 binding sites for cholera toxin

❖ Clinical Manifestations and Treatment:

-It starts showing symptoms at an average of 2 to 3 days after ingestion of the bacteria (can be <12 hours).

***Characterized by:**

1- abrupt onset vomiting and sever watery diarrhea (as much as 1L/hr) and within few days the person is dehydrated (the diarrhea is in the form of rice-water stool which indicates that it has no color and no smell).

2-Painful muscle cramps.

3-Metabolic acidosis, due to bicarbonate ($HCO3^-$) loss.

4-Hypokalemia with hypovolemic shock (K^+ loss) and renal failure.

5-Cardiac arrhythmia (since the heart depends on certain electrolytes).

*It's treated by **rehydration** and IV replacement of the lost electrolytes (this has decreased the mortality from 70% to less than 1%).

4-Mycoplasma

❖ General Features:

-Mycoplasma and Ureaplasma organisms are the smallest free-living bacteria. They are unique among bacteria because they do not have a cell wall and their cell membrane contains sterols.

-The mycoplasmas form **pleomorphic** shapes varying from coccoid forms to rods (There is no cell wall so no definitive shape).

❖ Pathogenesis:

Organism	Site	Human Disease
Mycoplasma pneumoniae	Respiratory tract	Tracheobronchitis, pharyngitis, pneumonia, secondary complications (neurologic, pericarditis, hemolytic anemia, arthritis, mucocutaneous lesions)
Mycoplasma genitalium	Genitourinary tract	Nongonococcal urethritis, pelvic inflammatory disease

-Exposure to M. pneumoniae typically results in asymptomatic carriage.

❖ Detection and Treatment:

-Microscopy is of no diagnostic value because mycoplasmas poorly stain with the Gram stain (No cell wall). So, we use molecular techniques such as **PCR** looking for genetic material.

-Absence of the cell wall renders the mycoplasmas resistant to **penicillins, cephalosporins, vancomycin**, and other antibiotics that interfere with synthesis of the cell wall.

5-Aggregatibacter

-Two members of this genus are important human pathogens:
A.actinomycetemcomitans and A.aphrophilus.

-A. actinomycetemcomitans is a Gram-negative, facultative anaerobe, non-motile bacterium that is often found in association with localized aggressive periodontitis.

-it contributes to the gum damage which results from the long-lasting plaques on the patient teeth's, resulting in recession of the gum increasing the space between it & the teeth.

-Both species colonize the human mouth and can spread from the mouth into the blood by scratching the gum in brushing or dental surgeries, normally it doesn't cause sepsis but it will stick to a previously damaged heart valve or artificial valve if existed, leading to the development of endocarditis or cardiac myositis.

Good Luck!!