Bacteria – Friend or Foe?

By Rachel L. Dittmar & Rosa M. Santana Carrero
rldittmar@mdanderson.org, rsantana@mdanderson.org
April 2020

Danger! Sick! Gross! Vaccine!

Disease! Medicine!

Dirty! MRSA! Eww! *E. coli!*

What is the first thing that comes to mind when you hear "bacteria"?

Science!

Microscope! MRSA! *Salmonella*!

Hospital! Germs!

Staph! Small! Food!

Introduction to Bacteria

Bacterial nomenclature

- Bacteria are referred to by their **genus** and **species**, with genus coming first and species coming last:

Escherichia coli

Escherichia: genus

Species: coli

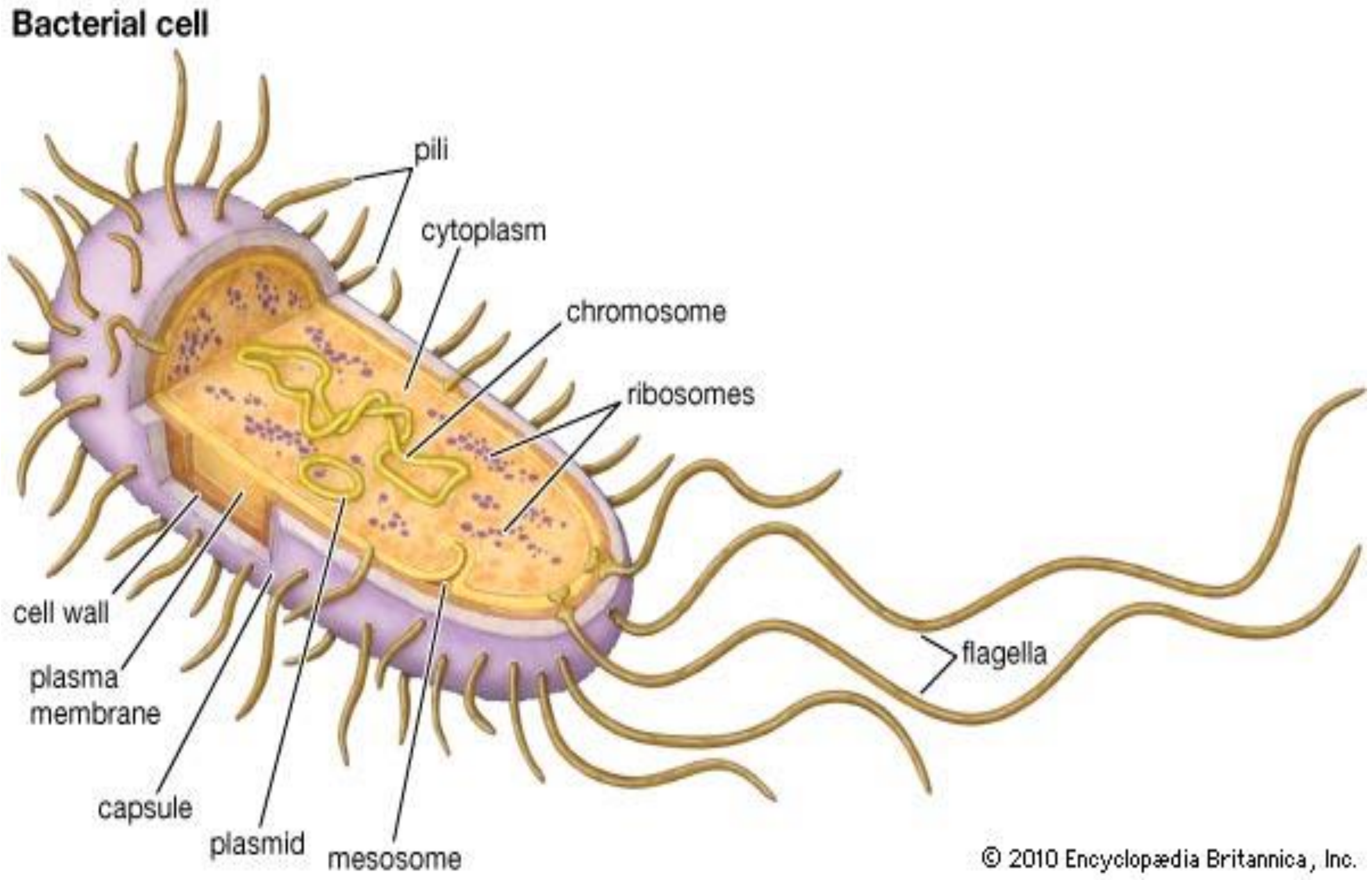
Bacteria names are ALWAYS italicized.

Genus names are capitalized and species names are not.

Sometimes, the genus is abbreviated by its first initial: *E. coli*

Bacteria are prokaryotes.

What are prokaryotes?



- Plasma membrane separates the cell from its surrounding environment
- Cytoplasm contains organelles
- Contain DNA consisting of a single large, circular chromosome
- Ribosomes make proteins

Prokaryotes v. Eukaryotes

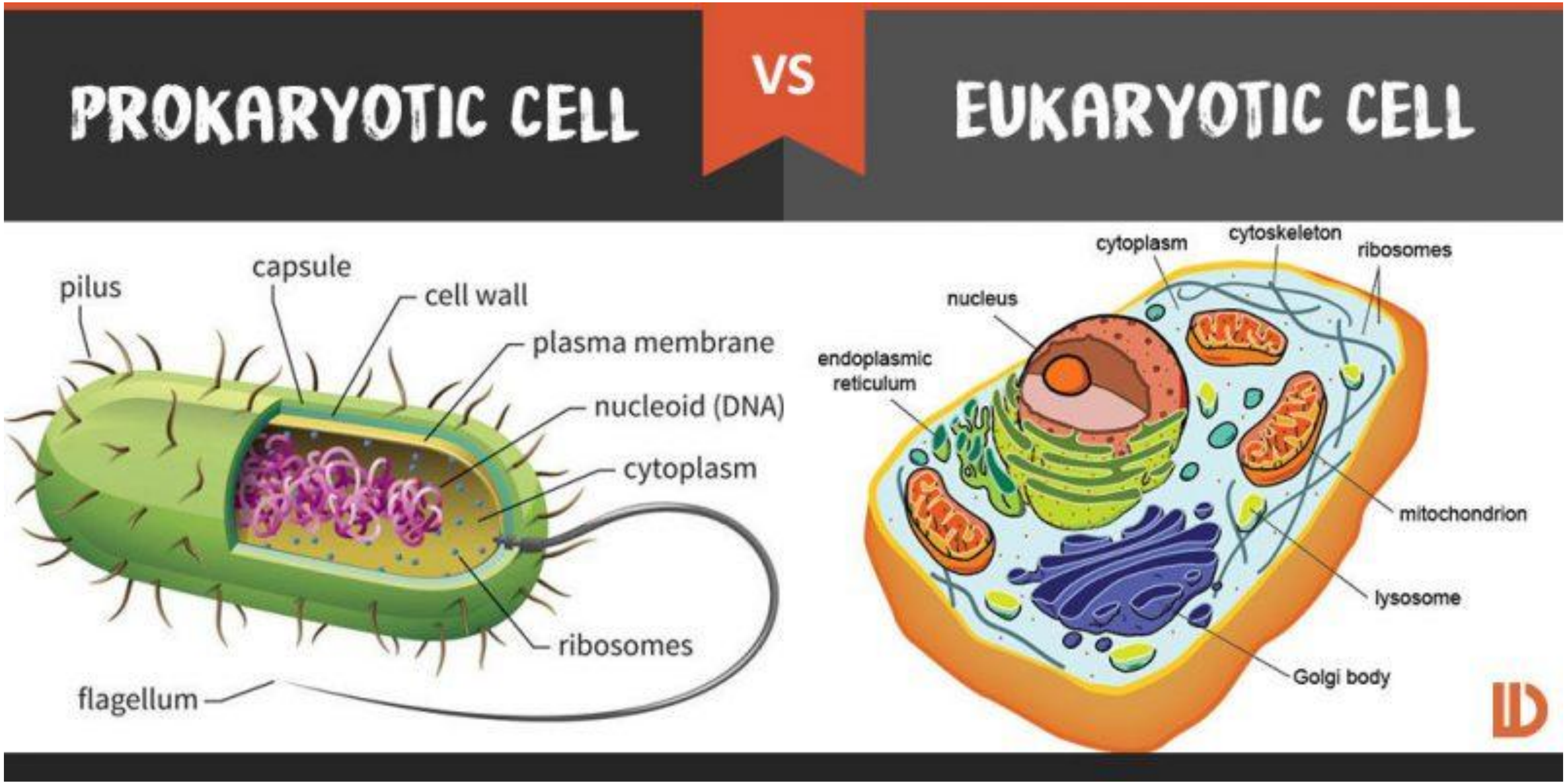


Image from: https://www.difference.wiki/prokaryotic-cell-vs-eukaryotic-cell/

How do these organisms differ?

Prokaryotes

- circular DNA
- no nucleus
- no membrane bound organelles
- small- less than 10μm
- unicellular

Eukaryotes

- linear DNA (found in nucleus)
- nucleus
- membrane bound organelles
- larger than 10μm
- can be unicellular and multicellular

Bacteria are very small.

How big are bacteria?

Bacteria are very small:
0.1 – 5.0 **micrometers**.

A micrometer (µm) is 0.000001 meters or 0.001 millimeters (mm)

For comparison, a human hair is 30 – 100 µm

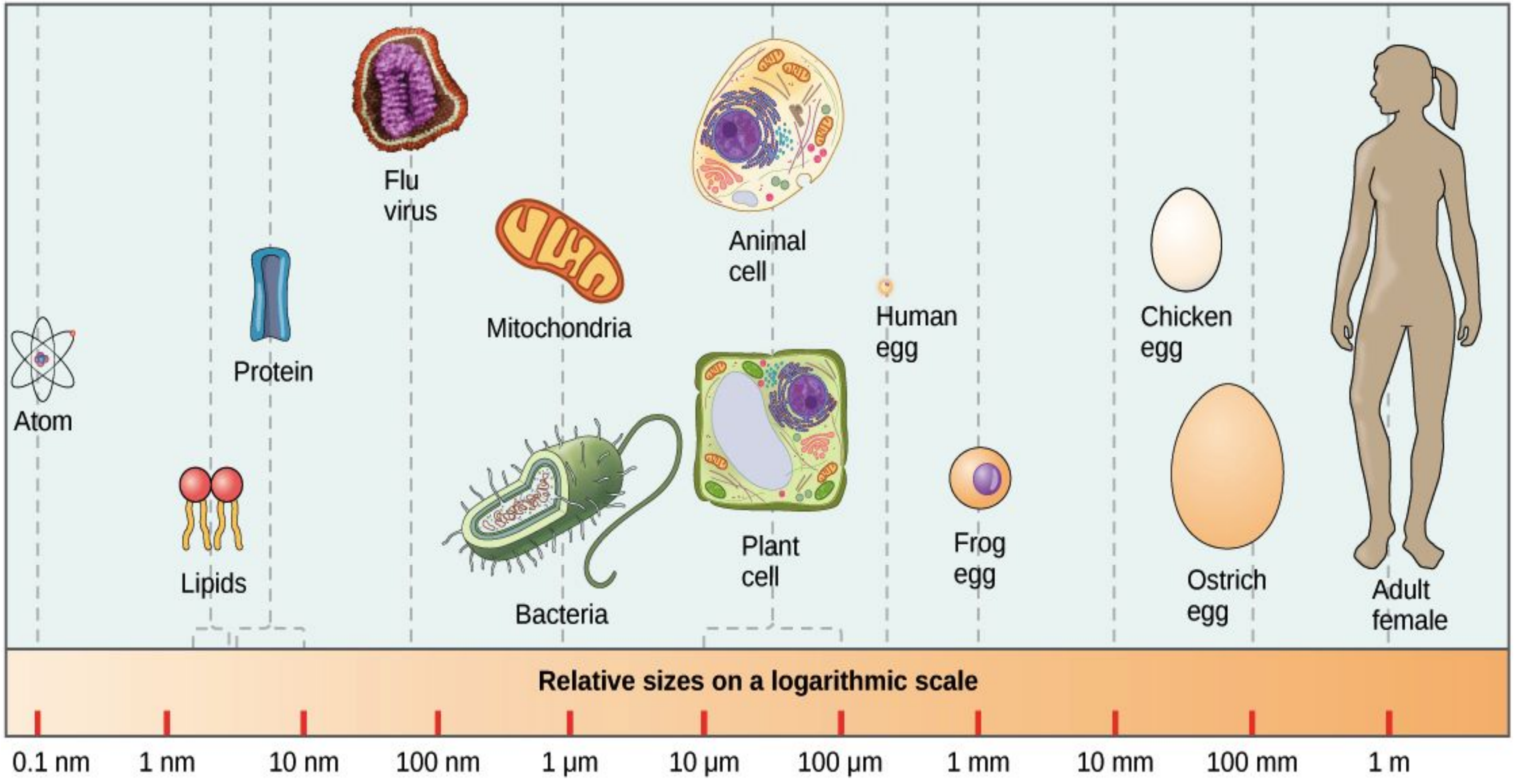


Image from: https://www.khanacademy.org/science/high-school-biology/hs-cells/hs-prokaryotes-and-eukaryotes/a/prokaryotic-cells

Bacteria are classified by phenotype or genotype.

How are bacteria classified?

- Cell wall make up:
  - Gram positive – thick peptidoglycan* layer in cell wall
  - Gram negative – thin lipopolysaccharide layer in cell wall

The technique used here is called Gram staining

*Peptidoglycan or murein- polymer consisting of sugars and amino acids that forms a mesh-like layer outside the plasma membrane

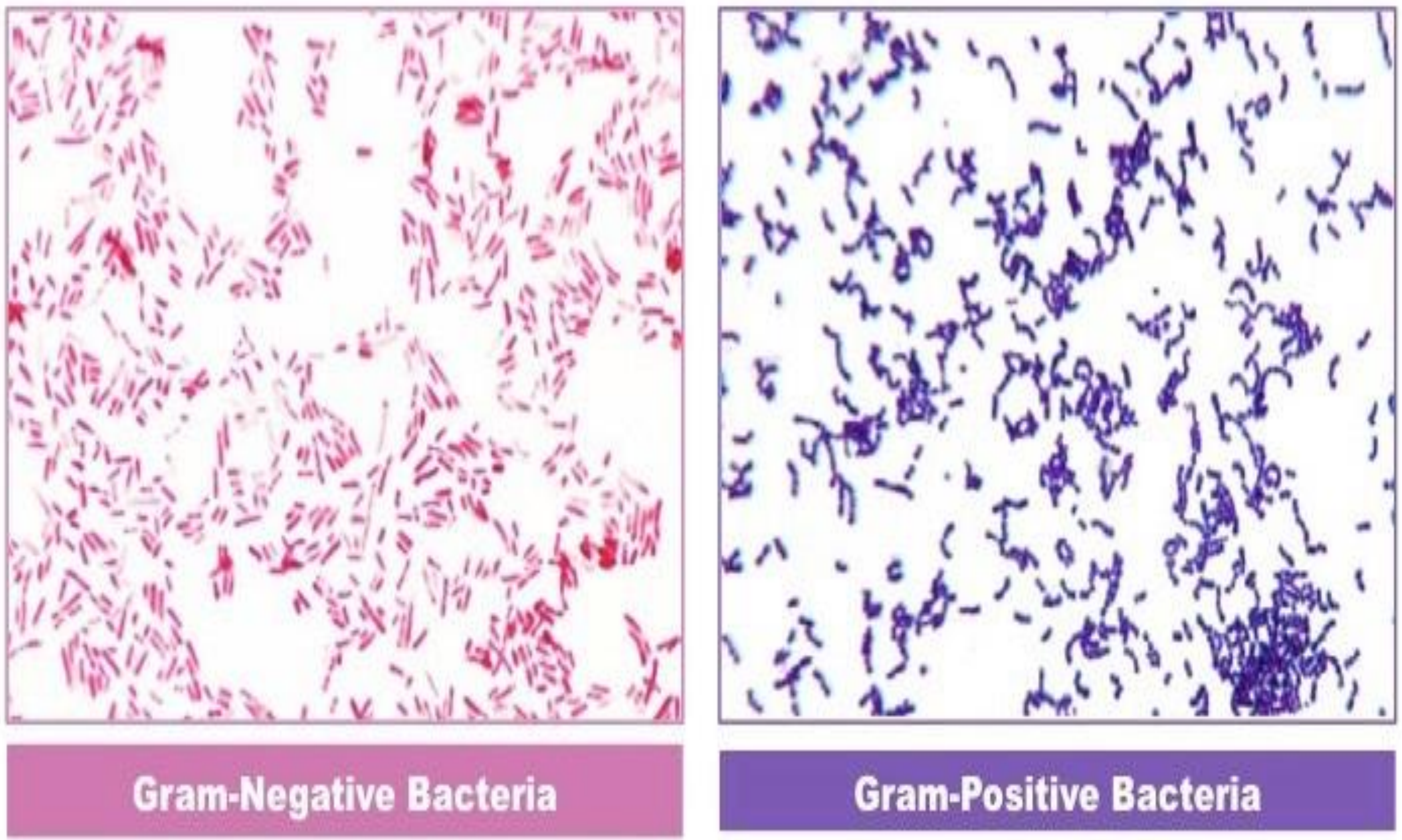
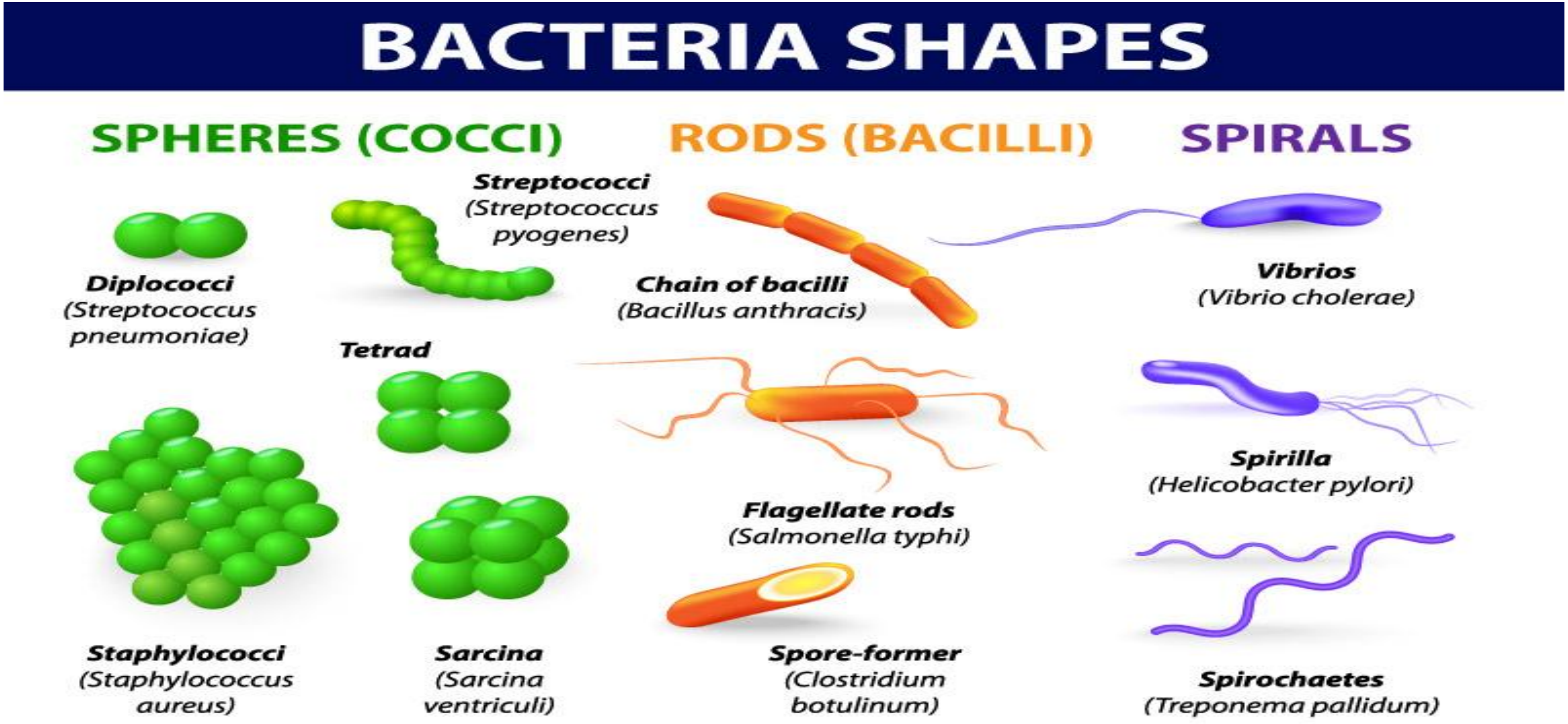


Image from: http://ib.bioninja.com.au/options/untitled/b1-microbiology-organisms/gram-staining.html

How are bacteria classified?



https://laboratoryinfo.com/various-shapes-and-arrangements-of-bacterial-cells/

How are bacteria classified?

Classification	Oxygen Requirements
Obligate aerobes	Required to survive
Microaerophiles	Require low levels of oxygen (lower than found in the atmosphere)
Facultative anaerobes	Survive in presence and in absence of oxygen
Aerotolerant anaerobes	Oxygen can be tolerated, but not used
Obligate anaerobes	Die in presence of oxygen

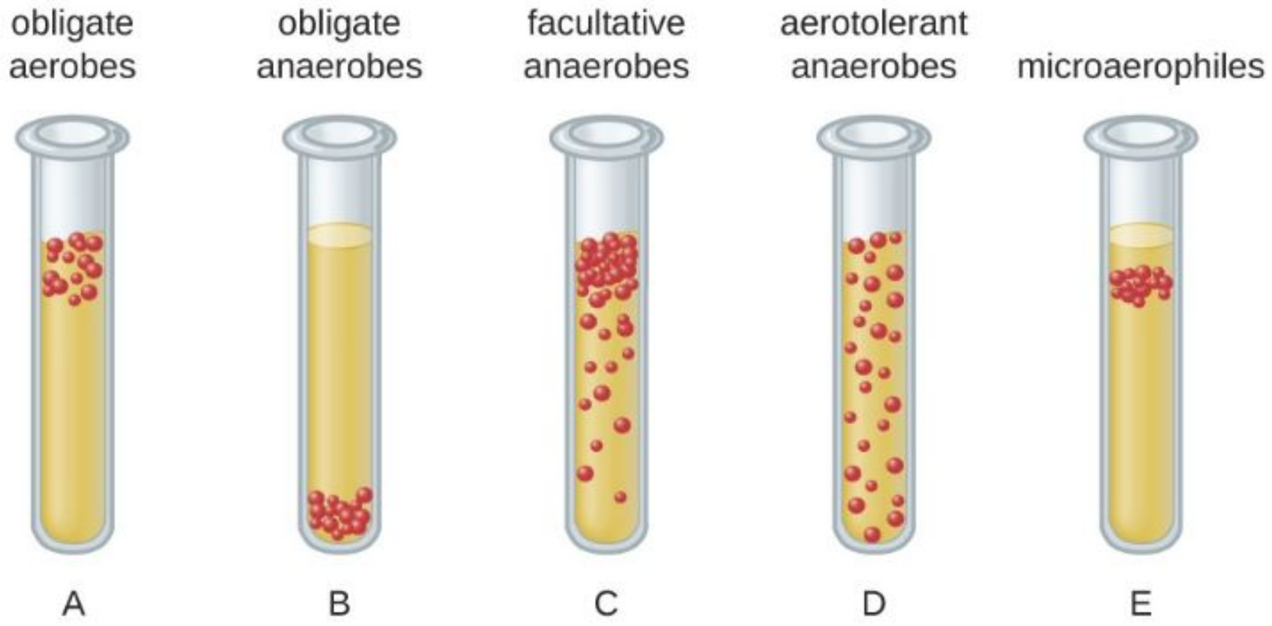


Image and information from: https://courses.lumenlearning.com/microbiology/chapter/oxygen-requirements-for-microbial-growth/

How are bacteria classified?

- Biochemical Reactions
  - Hydrogen sulfide production
  - Indole test
  - Oxidase test
  - Oxidative fermentation
  - Phenylalanine deaminase test
  - Antibiotic susceptibility tests

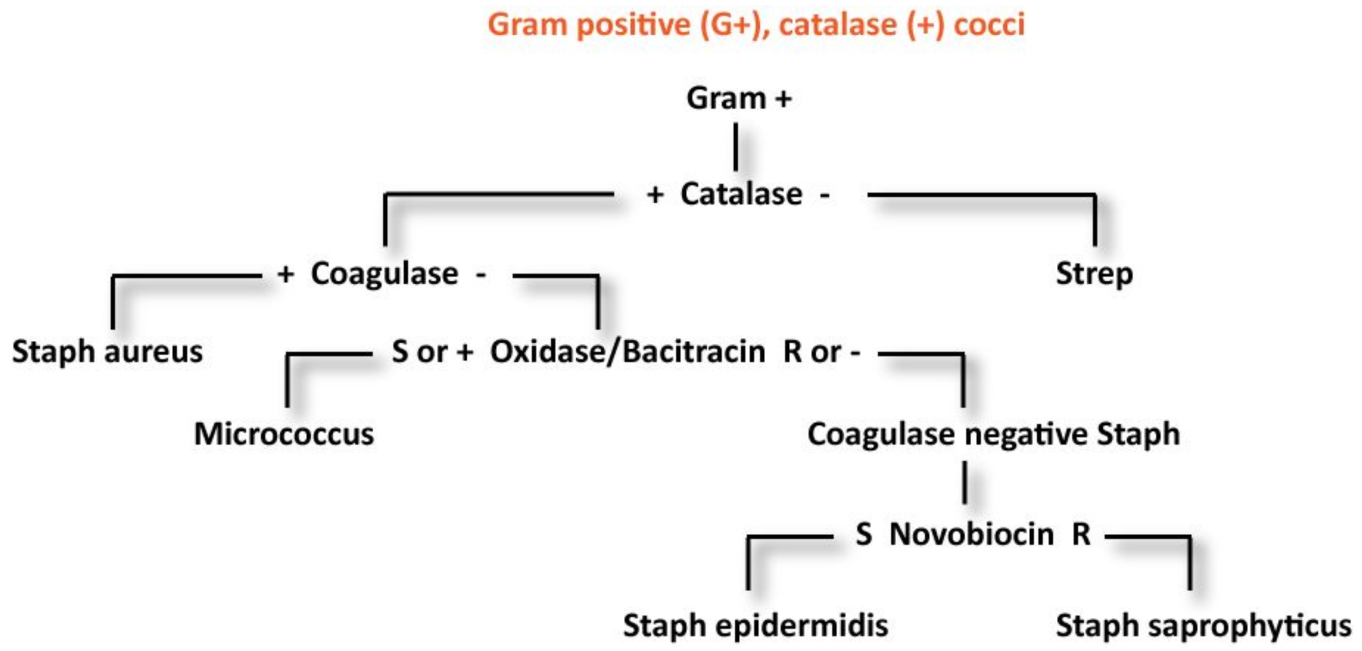


Image from: https://clsresource.com/index.php/microbiology-gram-positive-catalase-positive-cocci/

How are bacteria classified?

- Phylogenetic analysis: the study of the evolutionary past of an organism

- We study gene sequences from genetic material, like DNA and RNA, to understand when organisms started to diverge and differentiate from their ancestors

- Pictured here is a phylogenetic tree of life

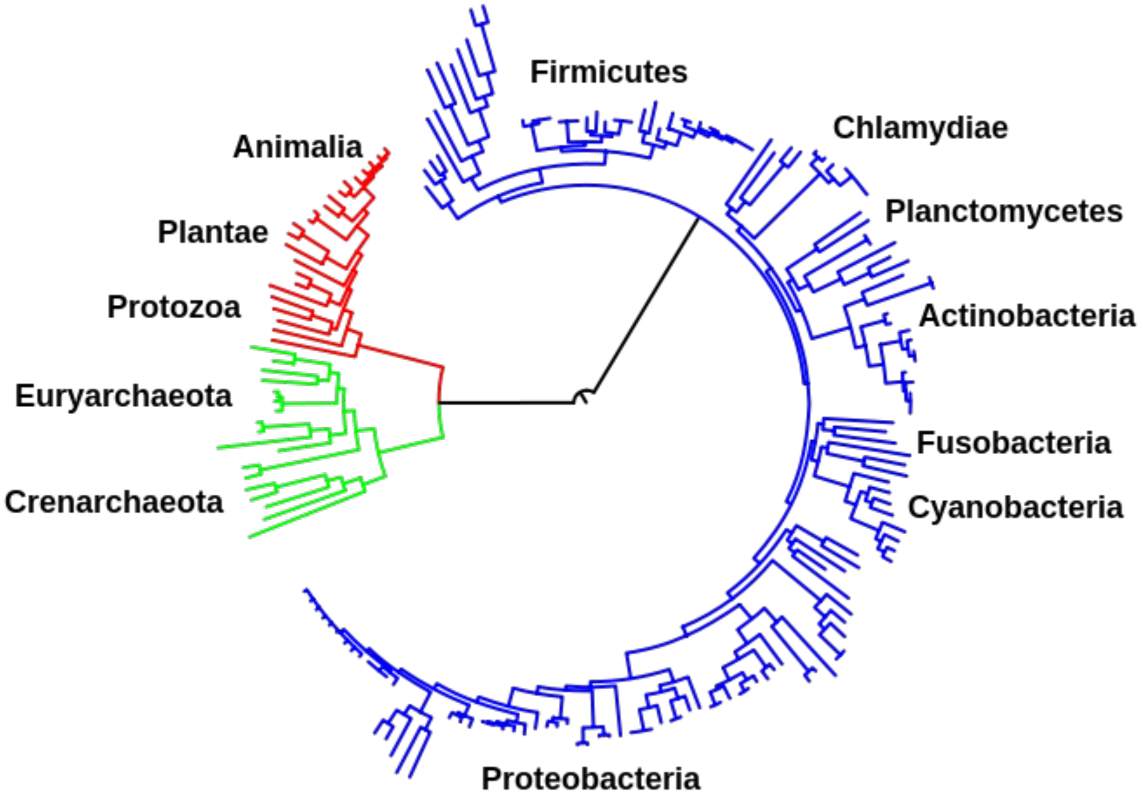


Image from https://courses.lumenlearning.com/boundless-microbiology/chapter/methods-of-classifying-and-identifying-microorganisms/

For more information on phylogenetic trees visit:
https://www.khanacademy.org/science/high-school-biology/hs-evolution/hs-phylogeny/a/phylogenetic-trees

Bacteria live everywhere.

Where do bacteria live?

- Everywhere!
  - High temperatures
  - Low temperatures
  - Alkaline environments
  - Acidic environment
  - High pressure
  - High salinity environments
  - Desiccant environments
  - Soil
  - Water
  - Air
  - Other living creatures

Image from: https://www.yellowstonepark.com/things-to-do/grand-prismatic-midway-geyser-basin

Why should I care about bacteria?

- Some bacteria can make you sick: **<u>pathogenic</u>** bacteria
- Some bacteria neither help nor harm humans: **<u>commensal</u>** bacteria
- Some bacteria are an integral part of our health: **<u>symbiotic</u>** bacteria
- Bacteria are important for:
  - Human health
  - Food production
  - Medication development
  - Environmental clean up
  - Fuel production
  - Science

Summary of Characteristics of Bacteria

- Bacteria are **prokaryotes**.
  - Prokaryotes are single celled organisms that lack a nucleus and membrane-bound organelles.
- Bacteria are very small: 0.1 – 5.0 **micrometers**.
  - A micrometer (µm) is 0.000001 meters or 0.001 millimeters (mm)
  - For comparison, a human hair is 30 – 100 µm
- Bacteria are classified by their **phenotype** or **genotype**.
  - Phenotype: Observable characteristics of an individual resulting from the interaction of its genetic make-up with the environment.
  - Genotype: The genetic make-up of an organism.
- Bacteria are found everywhere!
  - Soil, air, water, animals, even extreme environments. **Extremophiles** live in extreme environments
- Some bacteria are **symbiotic**, some are **commensal** while others are **pathogenic**
  - Symbiotic bacteria get something from us and help us in return
  - Commensal bacteria neither hurt nor harm healthy people
  - Pathogenic bacteria make you sick – "germs"!

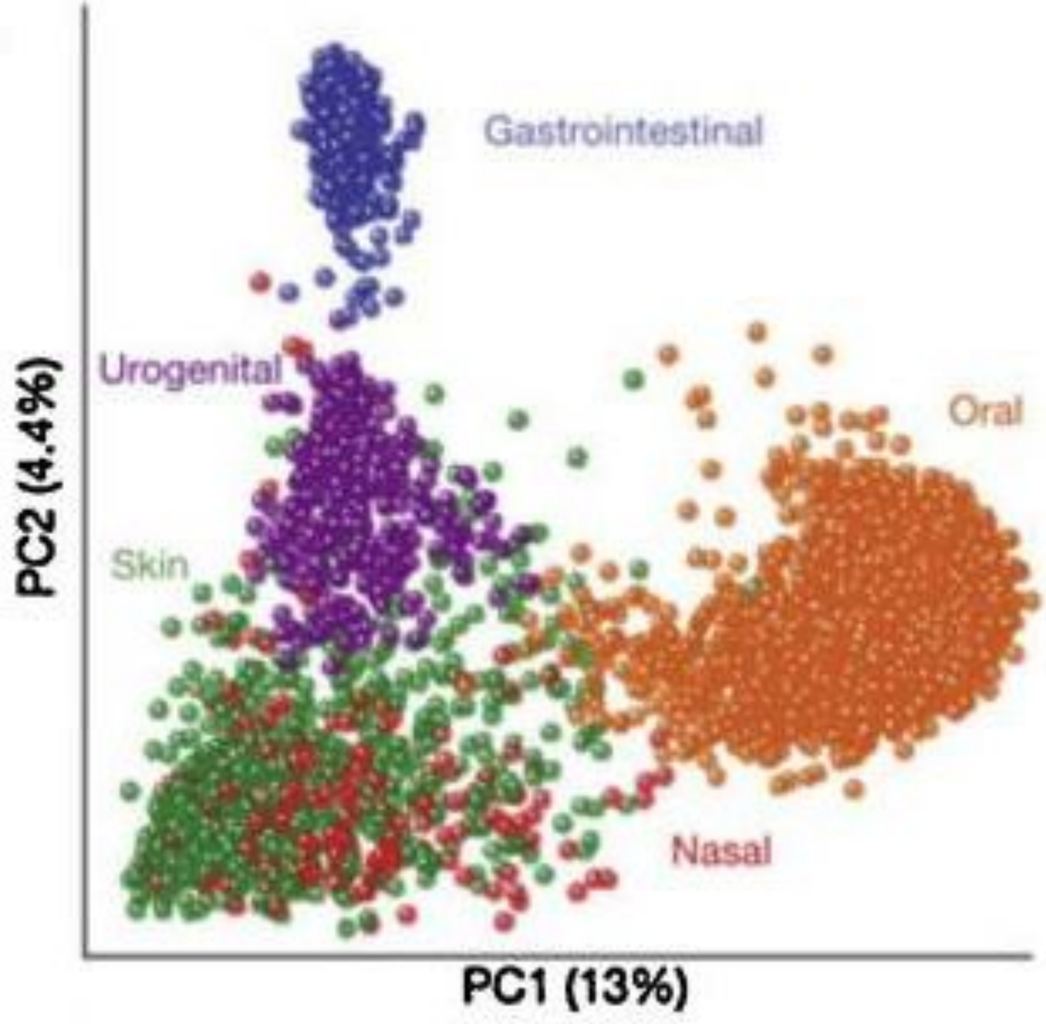
The Good Guys

Image from: https://experiencelife.com/article/good-bacteria-welcome/

Microbiome

Microbiome

- **Microbiota or Microbiome**: the population of symbiotic, commensal, and pathogenic microorganisms (often called "**flora**") of the human body.
- Members of our microbiota include:
  - Bacteria
  - Fungi
  - Protists
  - Viruses



Images from: Sanford and Gallo 2014

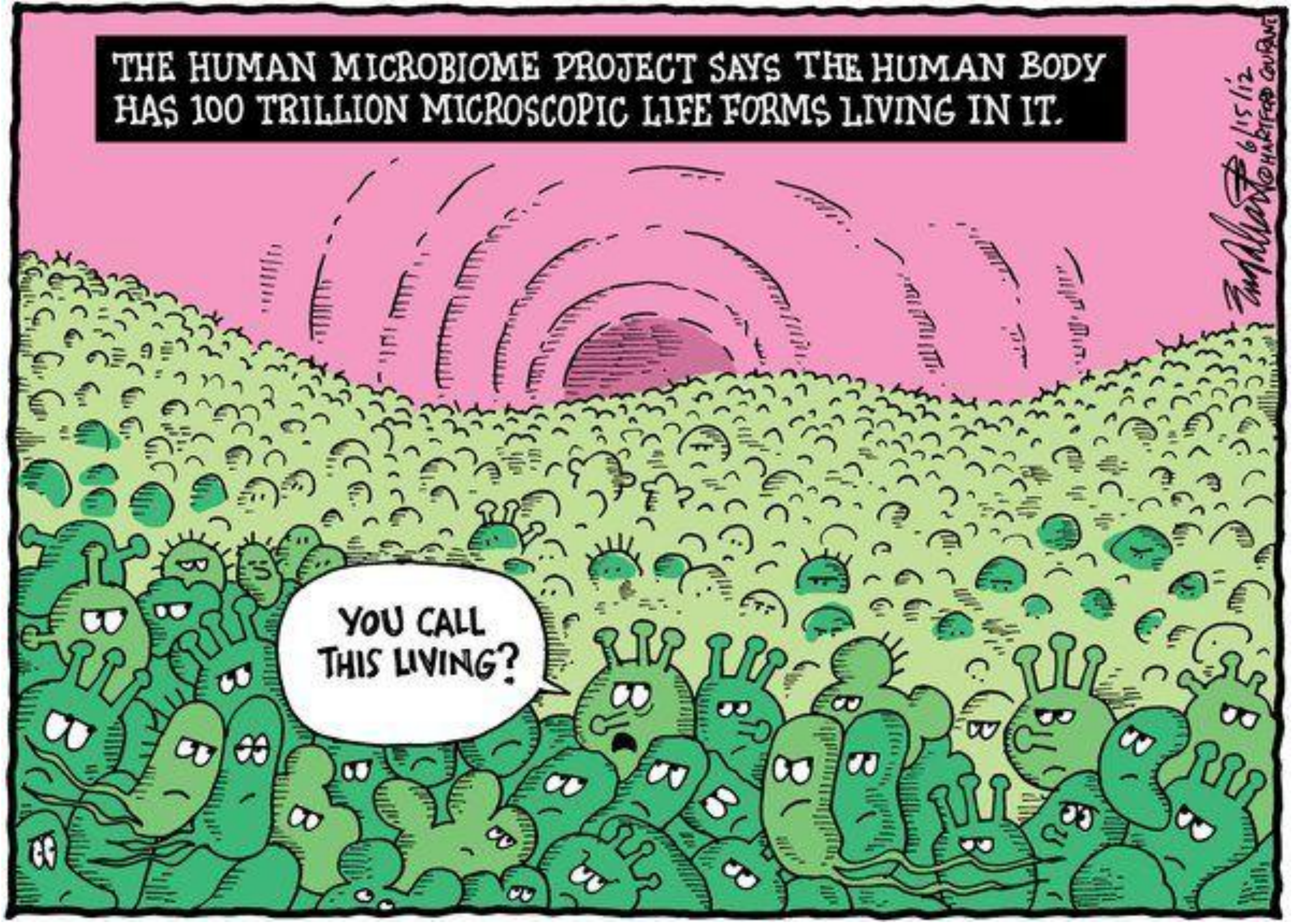
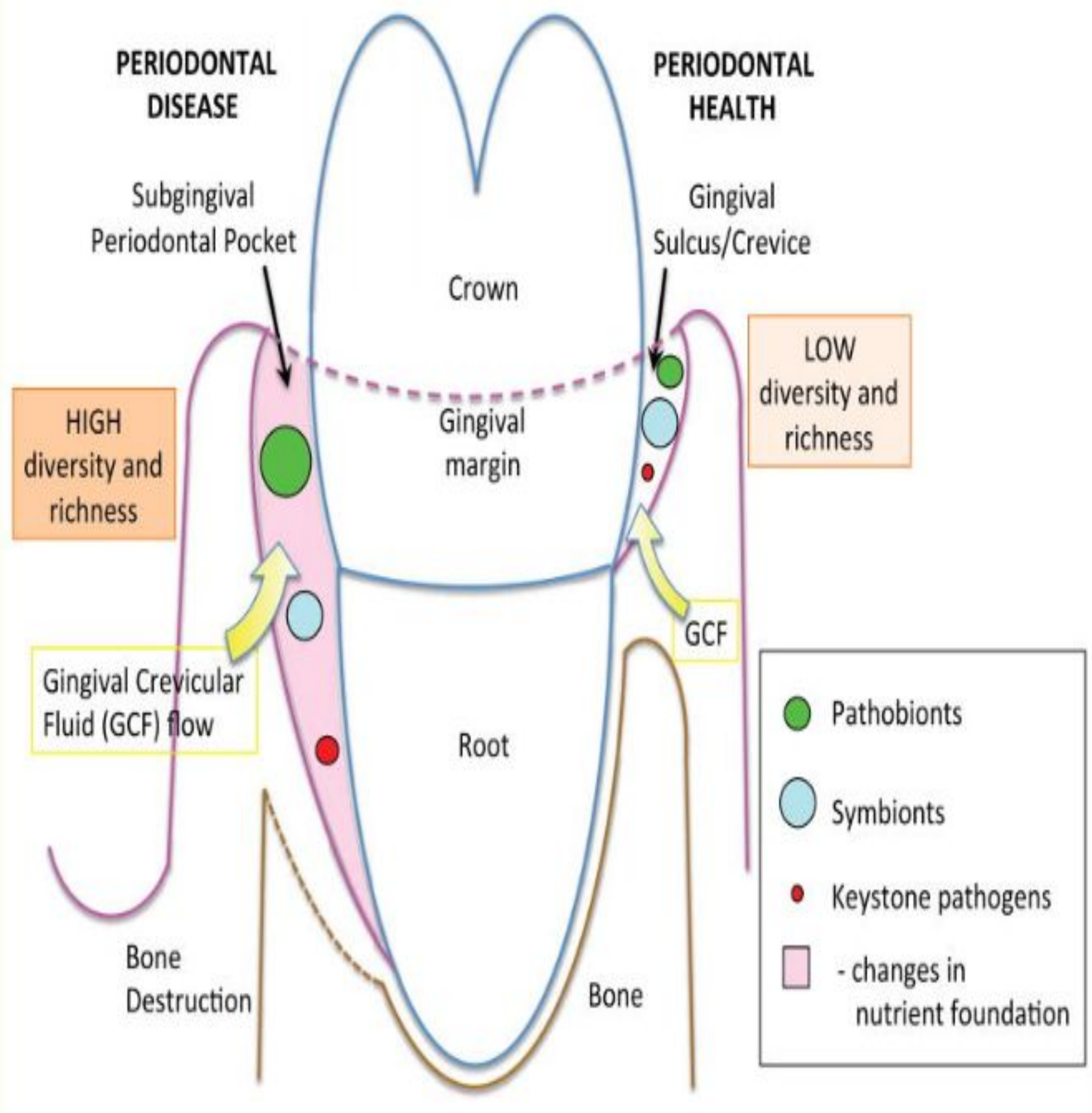


Image from: http://articles.courant.com/2012-06-14/news/hc-human-microbiome-project-20120614_1_human-body-microbes-human-genome-project

Mouth Microbiota

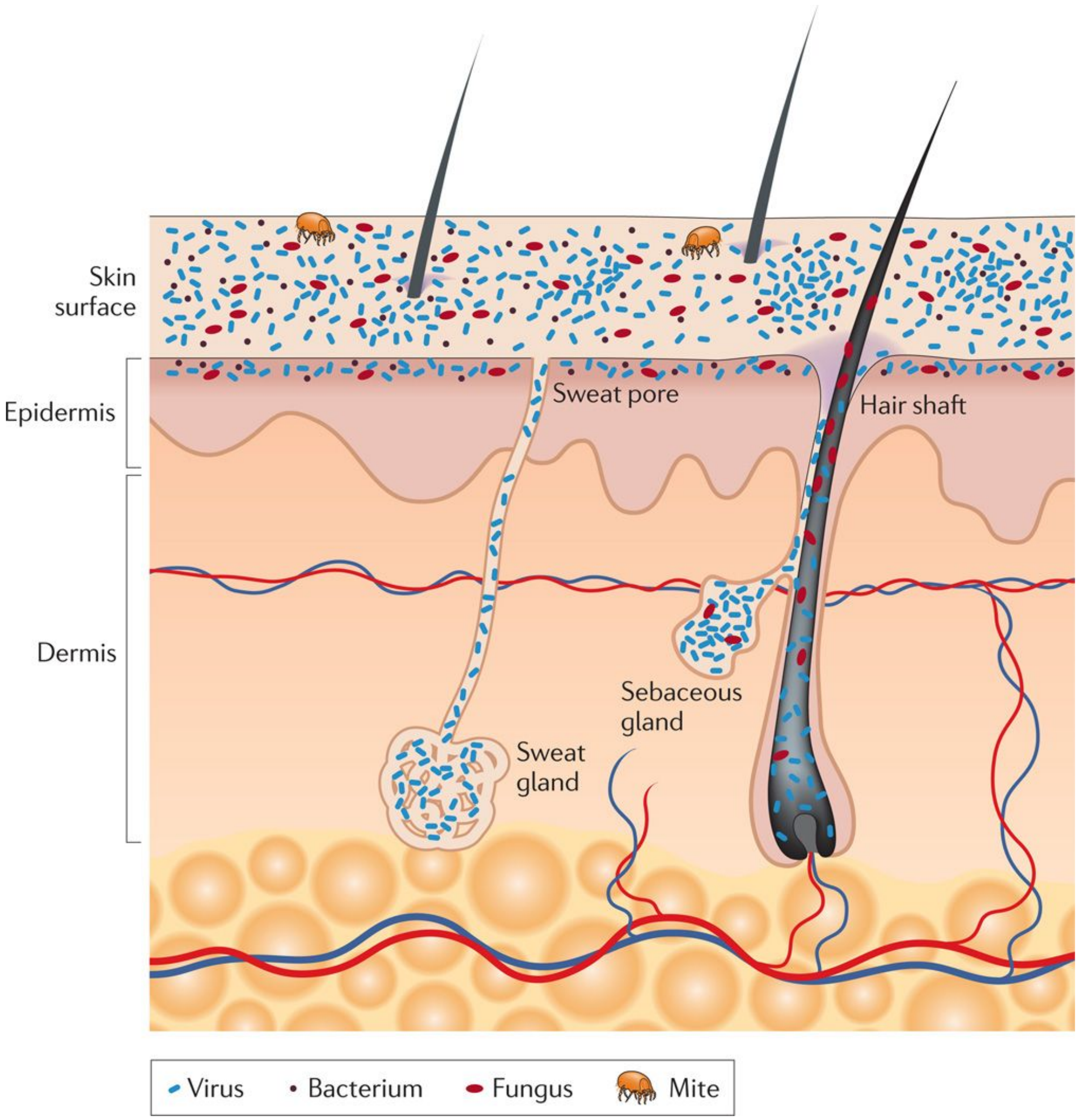
- Refers to all the microorganisms that reside in the human oral cavity
- 2nd largest community of microorganisms in human body
- Around 700 species of prokaryotes have been identified
- The bacteria found in the mouth form a biofilm (a layer of bacteria) that covers teeth
- The oral microbiome is important to protect teeth against periodontal disease



Images from: Costalonga et Herzberg 2014. Information from: Deo PN, Deshmukh R. Oral microbiome: Unveiling the fundamentals. *J Oral Maxillofac Pathol*. 2019;23(1):122–128.

Skin Microbiota

- The skin is the largest organ of the human body
- The skin microbiome includes bacteria, fungi, viruses and even mites
- The skin microbiome protects us by producing molecules that inhibit the colonization of other microorganisms or alter their behavior
- It also helps to educate the adaptive and innate immune system



Images from: Grice EA, Segre JA. The skin microbiome [published correction appears in Nat Rev Microbiol. 2011 Aug;9(8):626]. *Nat Rev Microbiol*. 2011;9(4):244–253.

Gut Microbiota

- More than 100 trillion microbes live in the human gut
- Most gut microbes are strict anaerobes
- Most microbes are from the phyla Bacteroidetes & Firmicutes
- The gut microbiome plays important roles in many processes including digestion, protection of the host and interacting with cells of the immune system

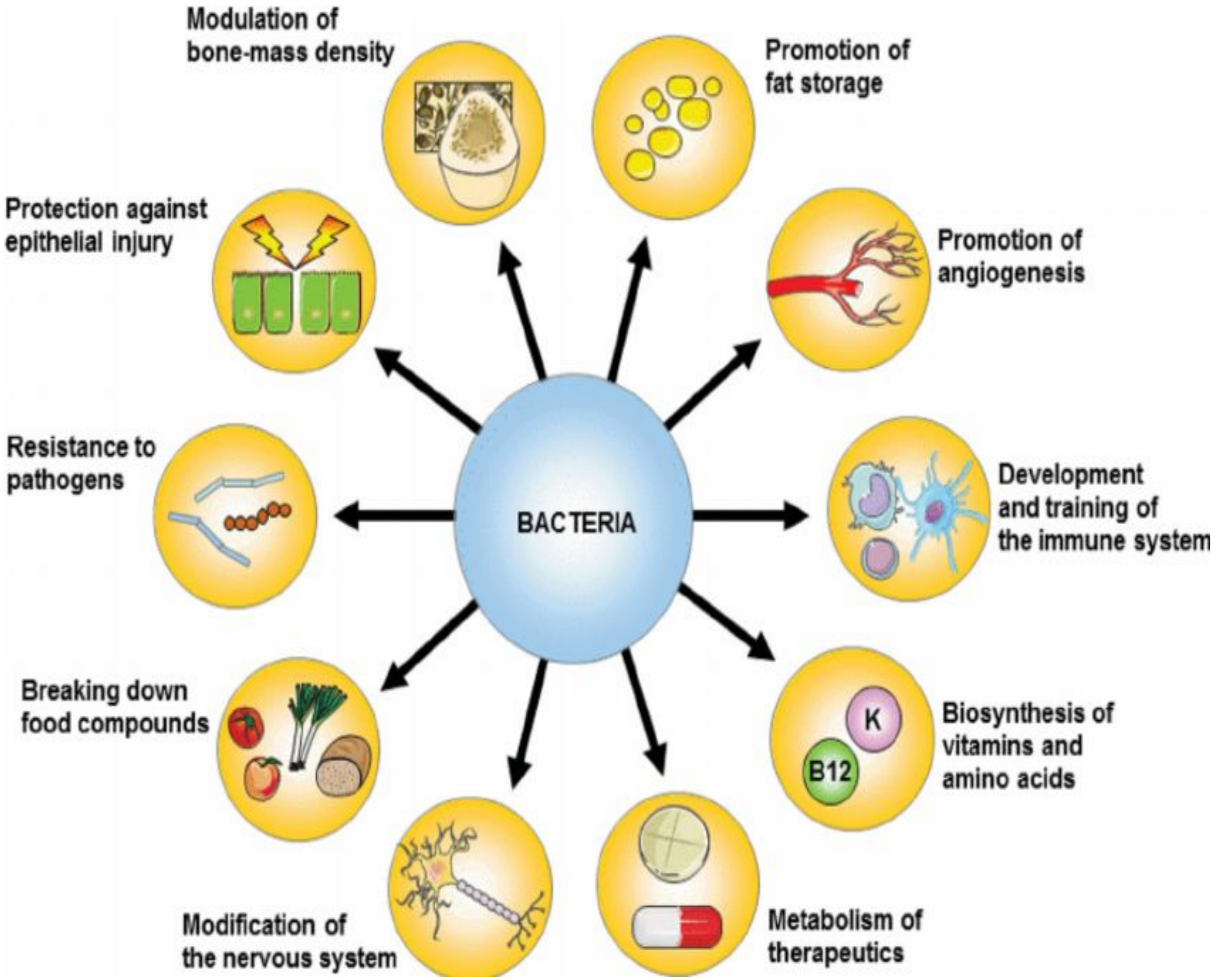


Image from: Laukens et al. 2015

Gut Metabolism

- Produce vitamin K and various members of the vitamin B family
  - I.e. *Escherichia coli*
- Synthesize essential and nonessential amino acids
  - I.e. *Clostridia, Proteobacteria, and Bacillus-Lactobacillus-Streptococcus* group
- Produce secondary bile acids
  - I.e. *Clostridia*
- Breakdown otherwise nondigestible carbohydrates, including starches, cellulose, hemicellulose, pectins, and gums
  - I.e. *Bacteroides thetaiotaomicron*

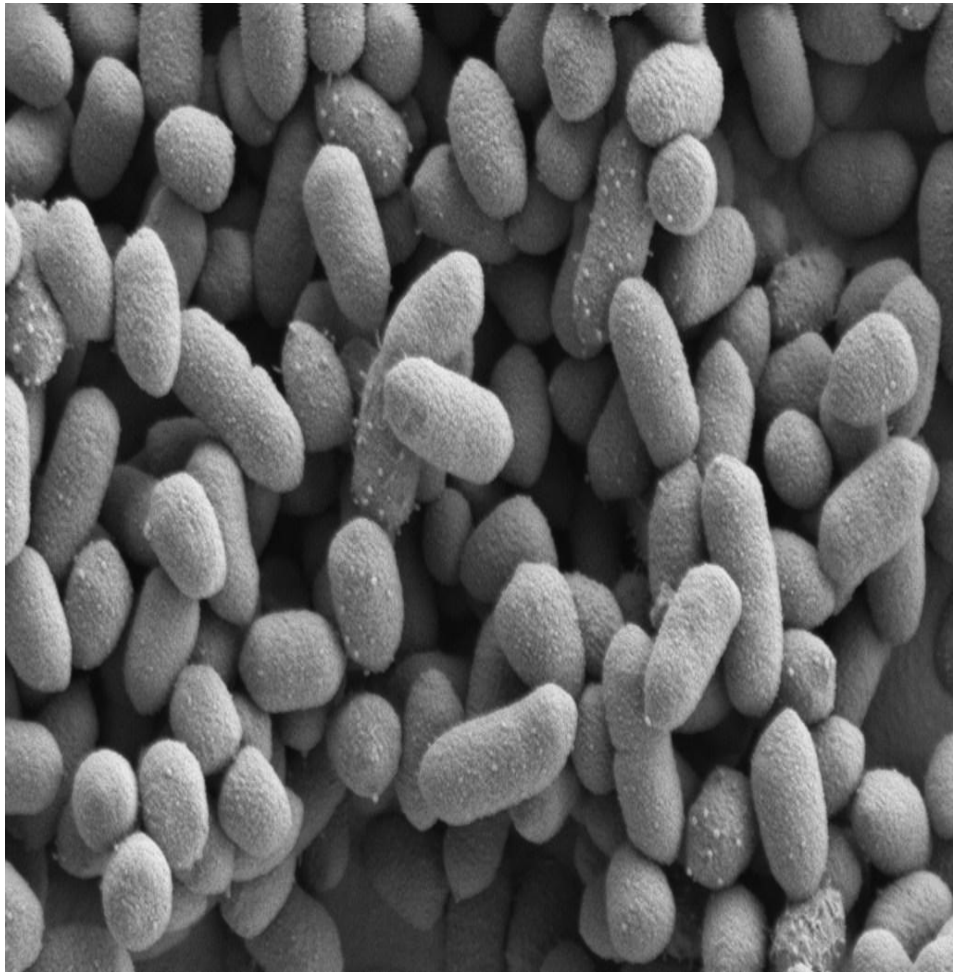


Image from: https://biotechin.asia/2015/02/15/how-does-gut-bacteria-maintain-its-stability-during-inflammation

Host Protection & Immune-system Development

- Produce antimicrobial agents (bacteriocins) to prevent colonization of pathogens
  - I.e. *Lactobacillus*
- Compete with pathogens for nutrients, preventing colonization by pathogens: barrier or competitive-exclusion effect
- Modulate the gut-mucosal immune system
- Prevention of allergies

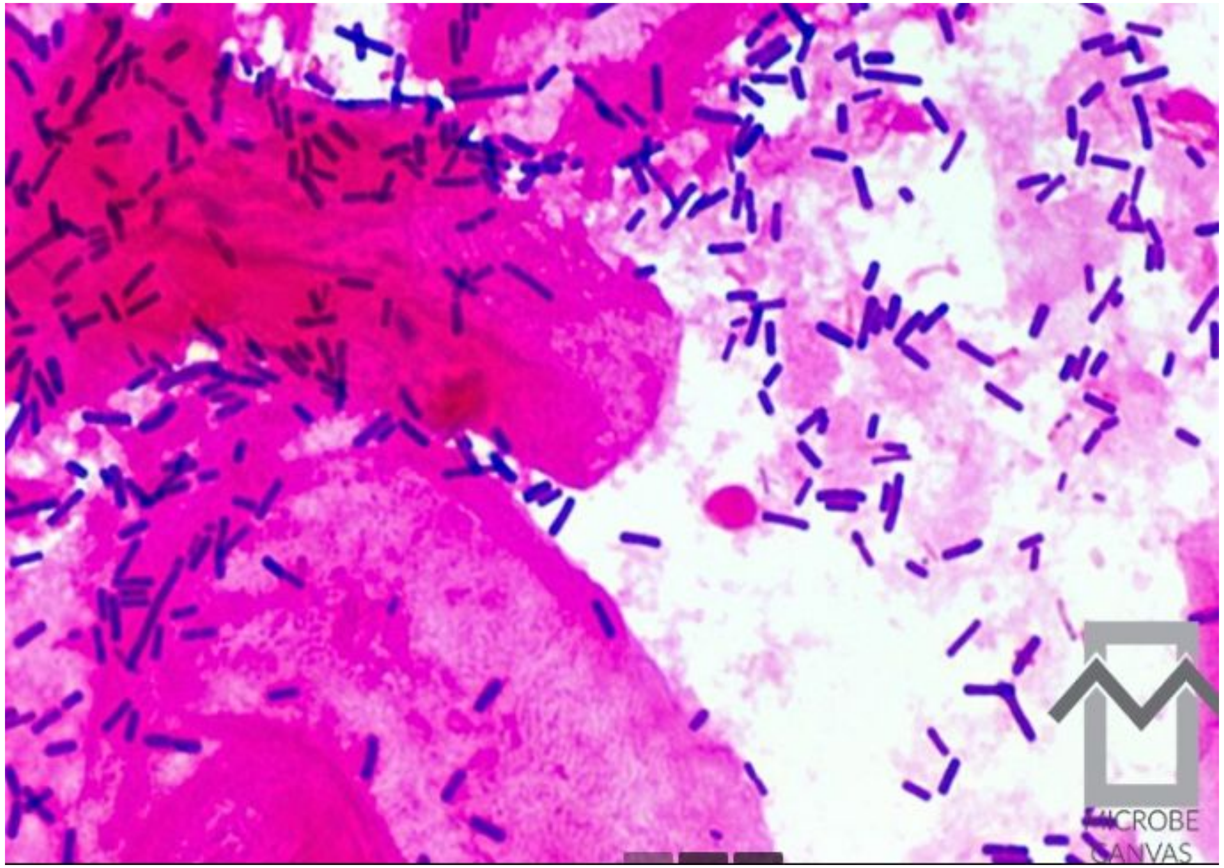


Image from: http://microbe-canvas.com/Bacteria.php?p=1250

Gut-Brain Axis

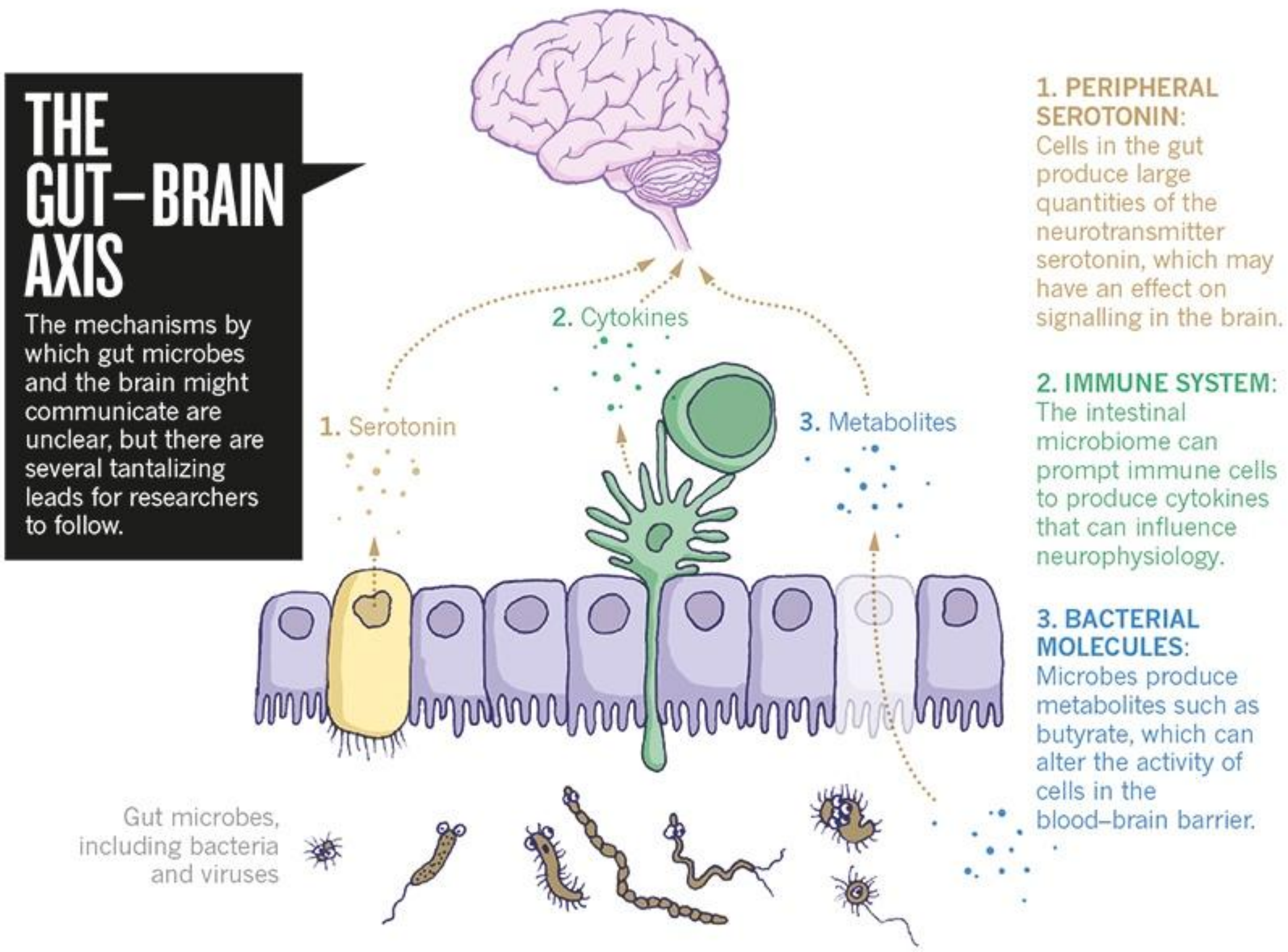


Image from: https://www.selfhacked.com/wp-content/uploads/2018/02/Gut-Brain-axis.jpg

Health

Probiotics

- **Probiotics** are live "micro-organisms that, ...when administered in adequate amounts, confer a health benefit on the host"
- Probiotics can be in the form of food (often yogurt), dietary supplements, and topical creams
- Probiotics may be helpful in preventing diarrhea caused by infections and antibiotic uses, as well as for mitigation of irritable bowel symptoms
- *Lactobacillus* and *Bifidobacterium* are two common genera found in probiotics

https://www.bbcgoodfood.com/howto/guide/what-are-probiotics-and-what-do-they-do

Fecal Transplant

- **<u>Fecal transplant</u>**: A method to restore the normal gut flora by introducing healthy bacteria through transplant of stool by colonoscopy, enema, or mouth via capsules from a healthy donor.
- Used as a treatment for recurrent, antibiotic resistant *Clostridium difficile.*

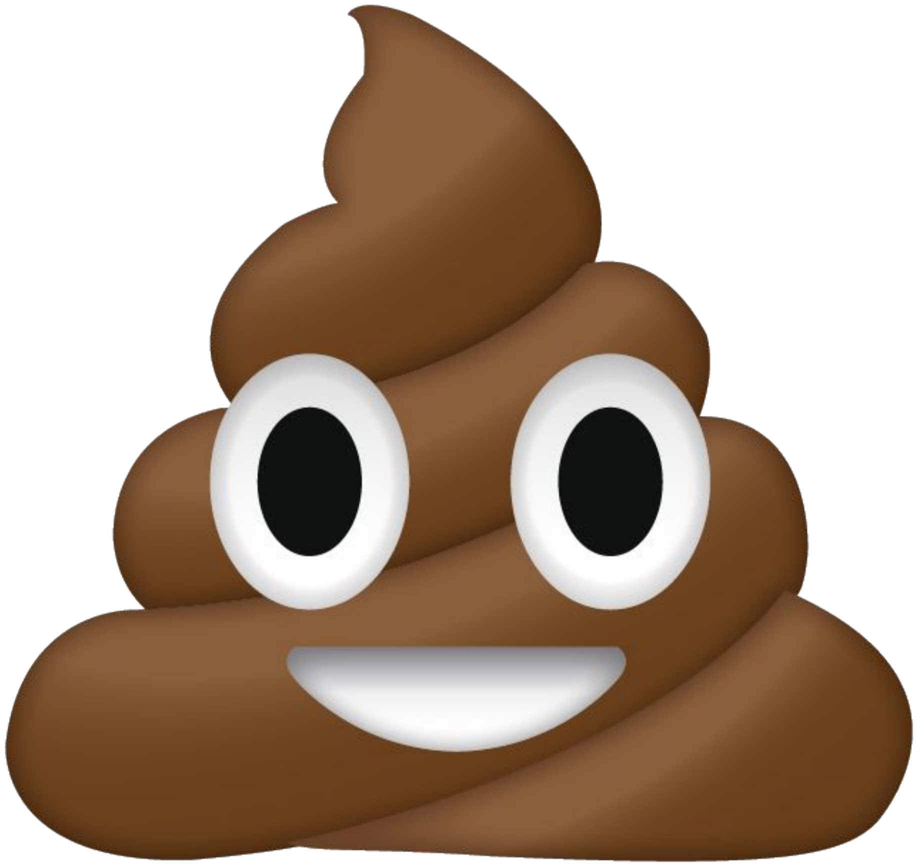


Image from: https://emojiisland.com/products/poop-emoji-icon

Botox

- Botox comes from the deadliest toxin known to man: botulinum toxin
- *Clostridium botulinum* (and a few related species) produce this toxin
- Botulinum toxin prevents the release of a neurotransmitter, acetylcholine, from axon ends at neuromuscular junctions, causing paralysis
- Botox is used for removing wrinkles, but also for taming muscle spasms and chronic migraines

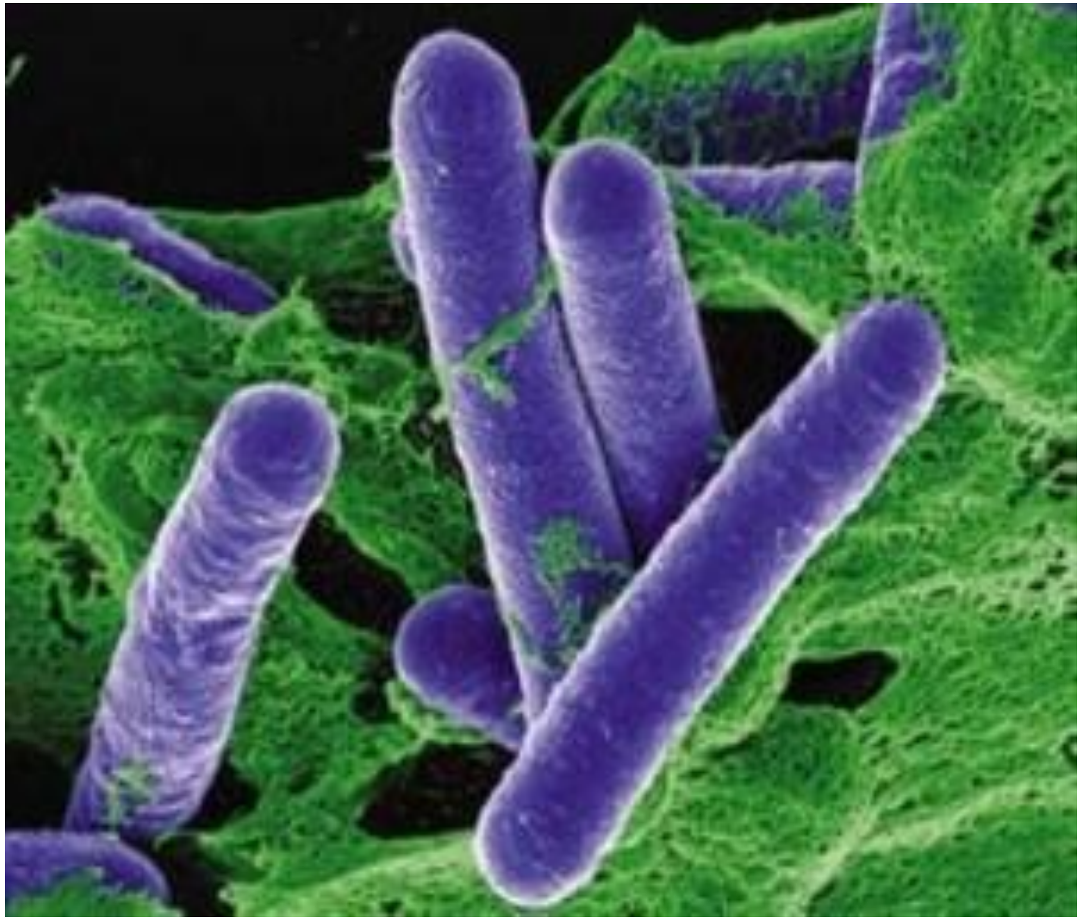
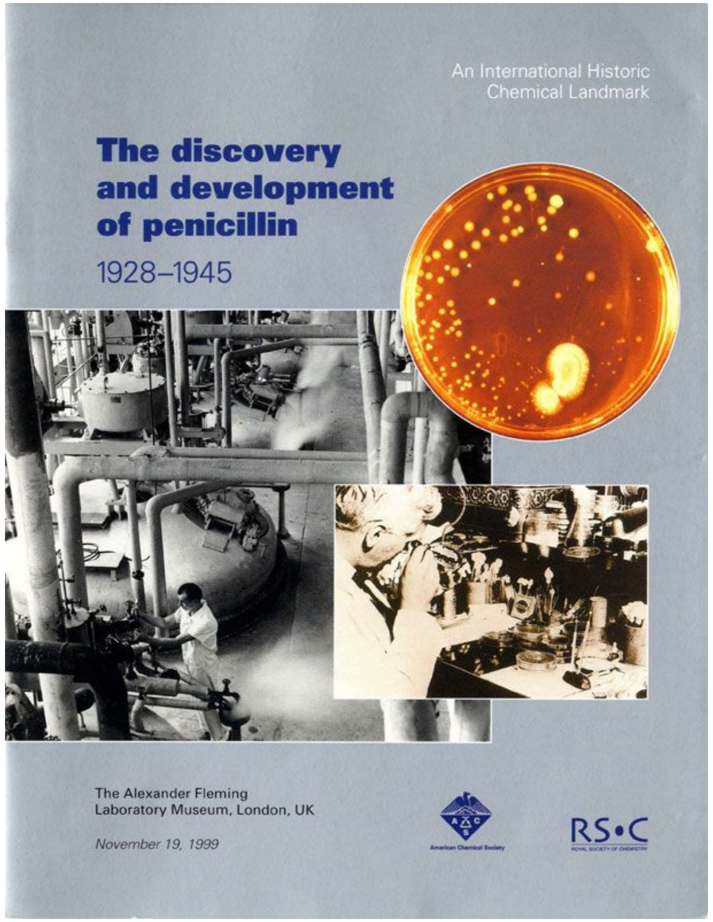


Image from: https://www.medical-actu.com/en/lesson/bacteriology/clostridium-botulinum/

What are antibiotics?

Antibiotics

- Any substance that can **specifically** kill or inhibit the growth of **bacteria**
- Naturally produced by bacteria and fungi to protect against other organisms
- Used commonly to treat bacterial infections
- Broad spectrum antibiotics are compounds that are effective against multiple types of bacteria



The first antibiotic, penicillin, was discovered by Alexander Fleming in the late 1920's. It was produced by the mold *Penicillium notatum*.

Image and information from https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/flemingpenicillin.html

Antibiotics & Antimycotics*

Antibiotic	Producer organism	Activity	Site or mode of action
Bacitracin	*Bacillus subtilis*	Gram-positive bacteria	Wall synthesis
Polymyxin B	*Bacillus polymyxa*	Gram-negative bacteria	Cell membrane
Amphotericin B	*Streptomyces nodosus*	Fungi	Cell membrane
Erythromycin	*Streptomyces erythreus*	Gram-positive bacteria	Protein synthesis
Neomycin	*Streptomyces fradiae*	Broad spectrum	Protein synthesis
Streptomycin	*Streptomyces griseus*	Gram-negative bacteria	Protein synthesis
Tetracycline	*Streptomyces rimosus*	Broad spectrum	Protein synthesis
Vancomycin	*Streptomyces orientalis*	Gram-positive bacteria	Protein synthesis
Gentamicin	*Micromonospora purpurea*	Broad spectrum	Protein synthesis
Rifamycin	*Streptomyces mediterranei*	Tuberculosis	Protein synthesis

* Antimycotics- substances that kill or inhibit the growth of fungi

Information from: http://archive.bio.ed.ac.uk/jdeacon/microbes/penicill.htm

Science

Bacteria Produce Insulin for Diabetic Patients

The first example of this occurred in 1978 when Herbert Boyer, took a version of the human insulin gene and inserted it into the bacterium *Escherichia coli* to produce synthetic "human" insulin.

Four years later, it was approved by the U.S. Food and Drug Administration.

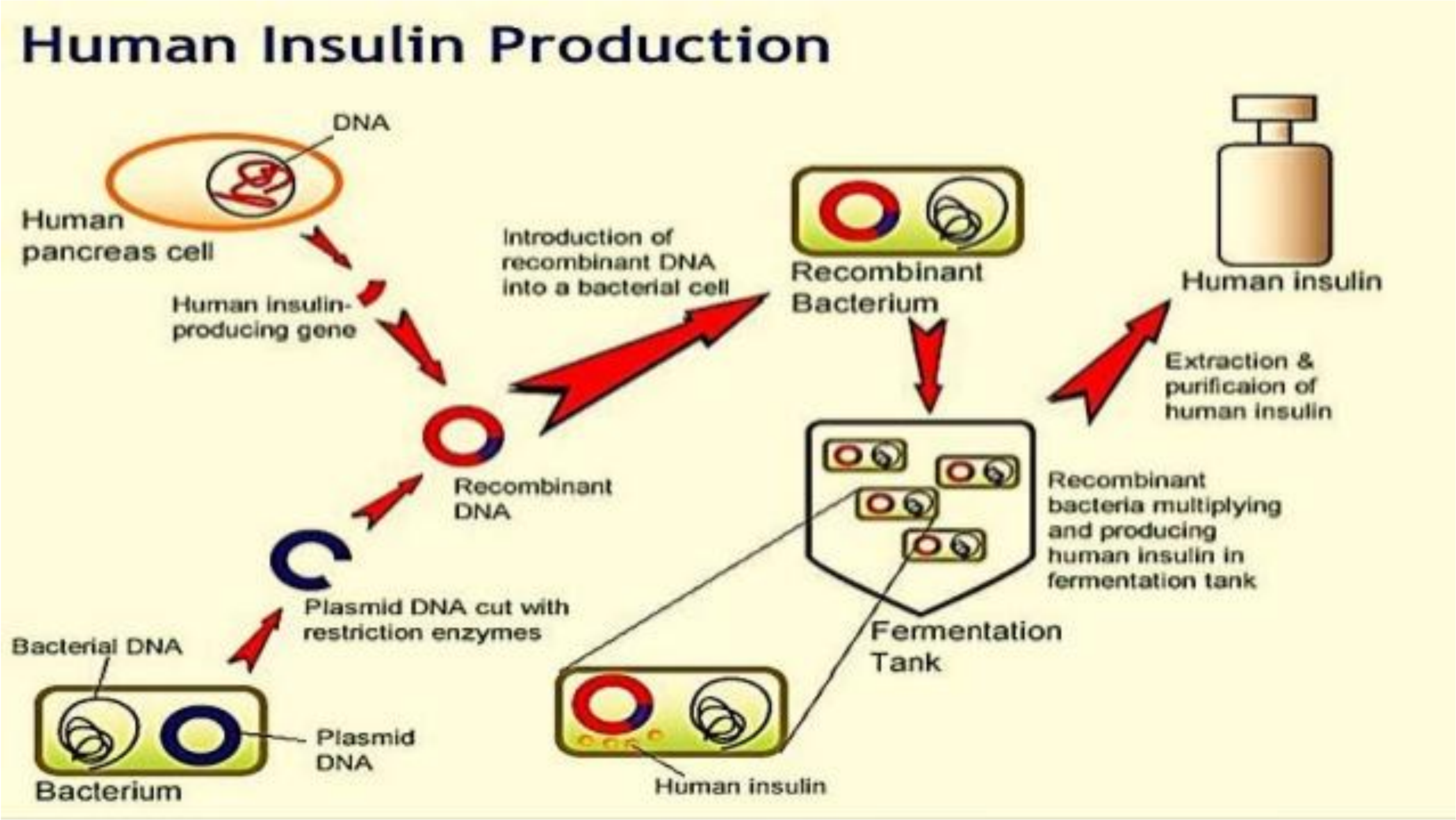


Image from: https://www.slideshare.net/MohamedElasalyPTCKTP/insulin-production-and-synthesis

Gene editing by CRISPR/Cas9

For more information on CRISPR/Cas9 visit:
https://www.brainfacts.org/in-the-lab/tools-and-techniques/2019/crispr-explained-071519

- Based on a defense mechanism used by some bacteria against viruses
- CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)- DNA sequences found in prokaryotes that are derived from viral DNA
- Cas9- enzyme that recognizes the CRISPR repeats and can break apart the viral DNA
- We can now use this system to edit genes in bacteria, plants, animals and even as potential therapies for diseases

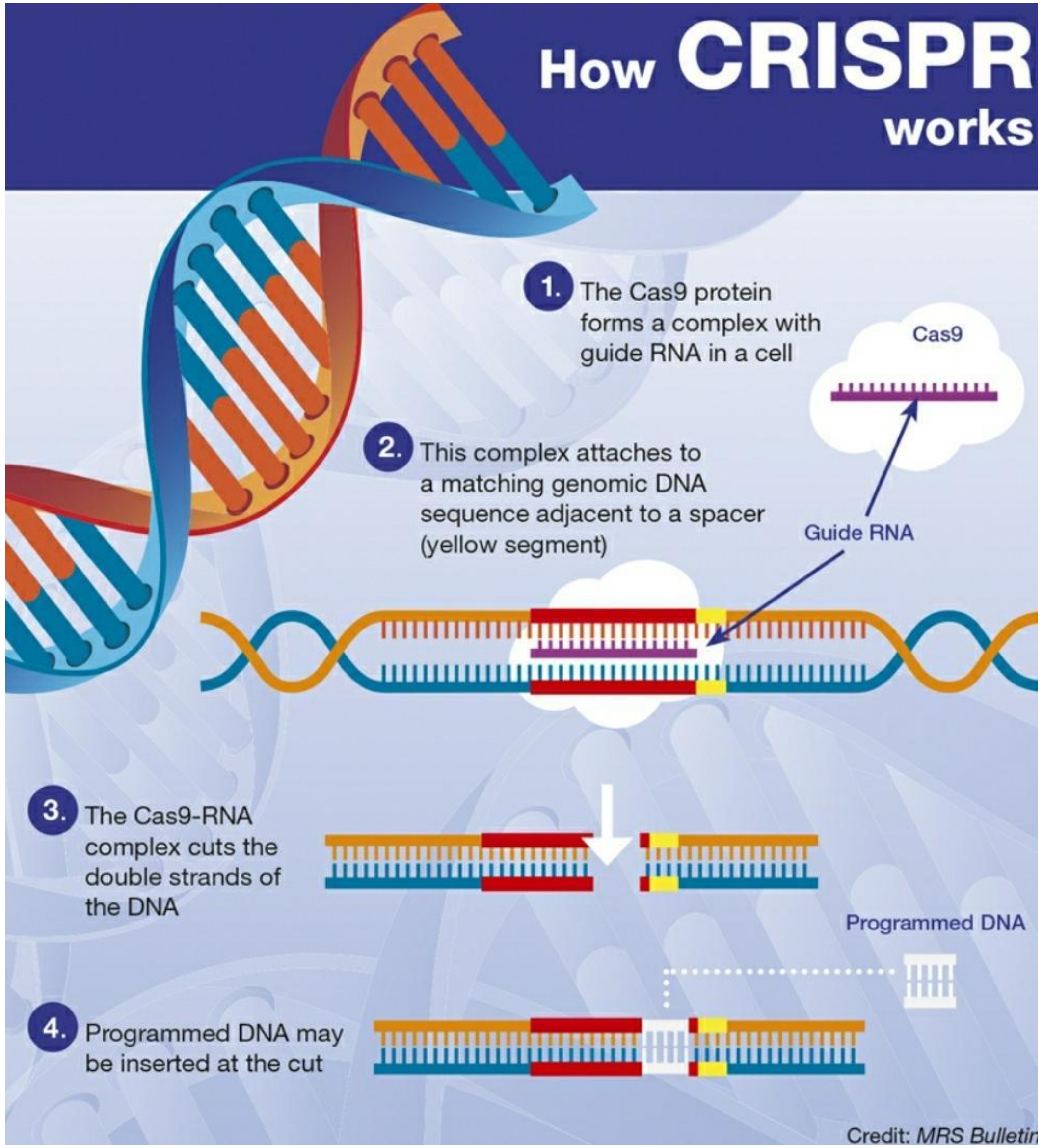


Image from: https://www.cambridge.org/core/services/aop-file-manager/file/582df76221b559de0536a2c2

Environment

Plastic Clean Up

- *Ideonella sakaiensis* were identified by Japanese scientists outside of a plastic bottle recycling plant
- Bacteria secrete PETase to break down Polyethylene terephthalate (PET), polymers that made up plastic, by cleaving ester bonds
- Scientists are working to use PETase from bacteria in reactors to recycle plastics and clean up the environment

Image from: https://metro.co.uk/2018/02/06/how-to-reduce-plastic-waste-10-simple-changes-you-can-make-today-7291656/

Food

Can you think of any foods that bacteria help us make?

Bacteria are used to Ripen Cheese

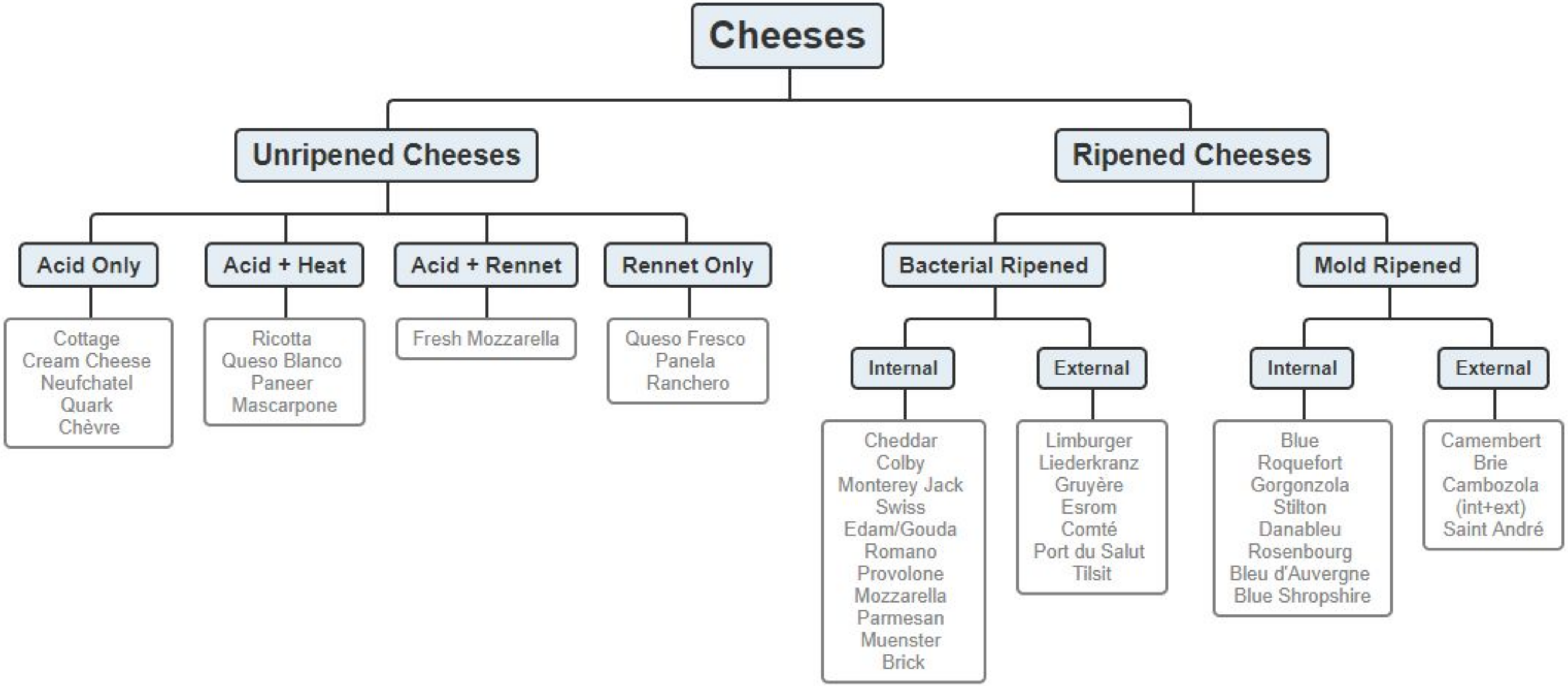


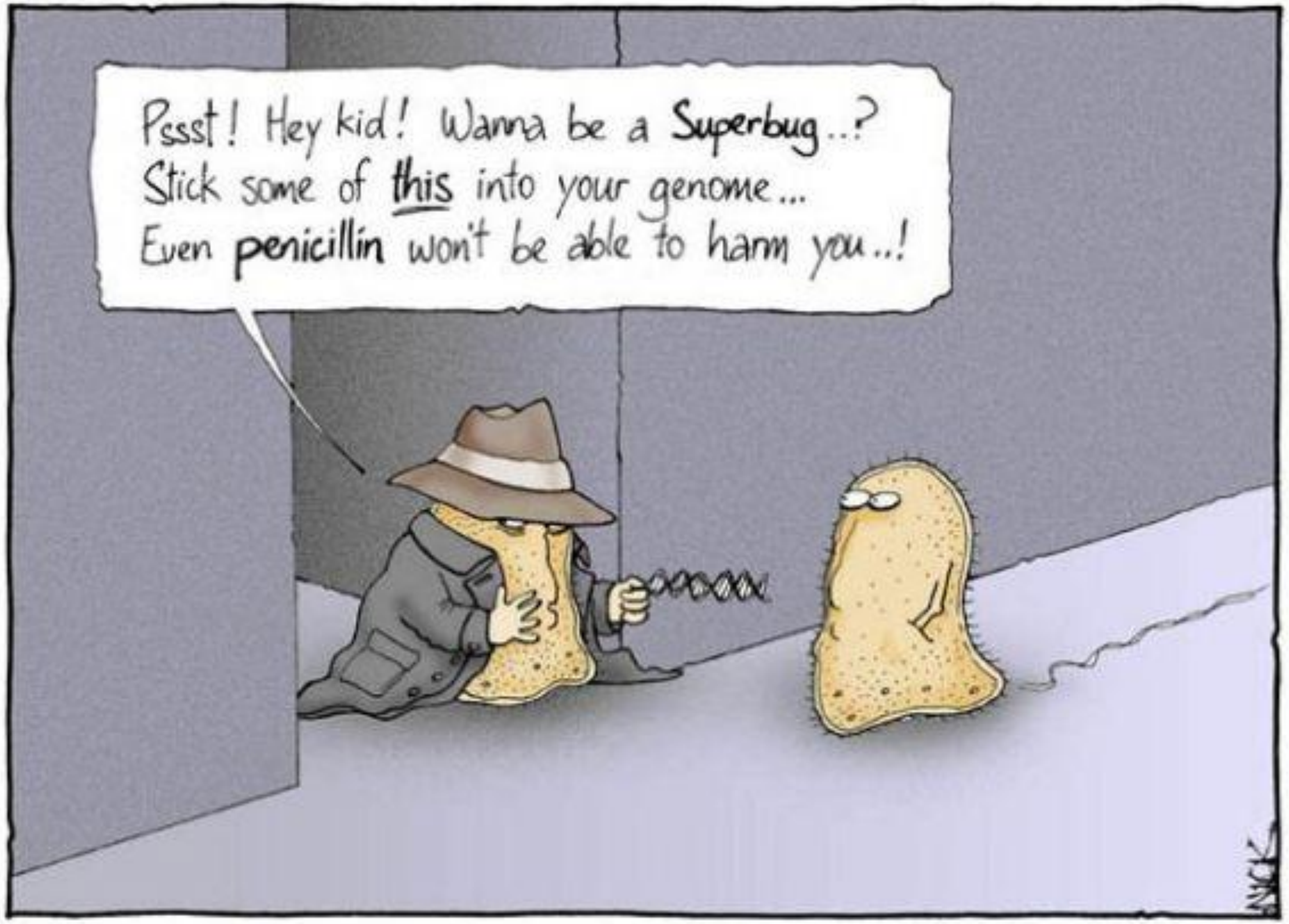
Image and information on how cheese is produced from: https://www.cheesescience.org/cheese_types/

Bacteria are important in other foods too

Conclusion

- Bacteria are GOOD for many reasons:
  - Microbiome
  - Health
  - Science
  - Environment
  - And many other reasons we didn’t have time to cover!

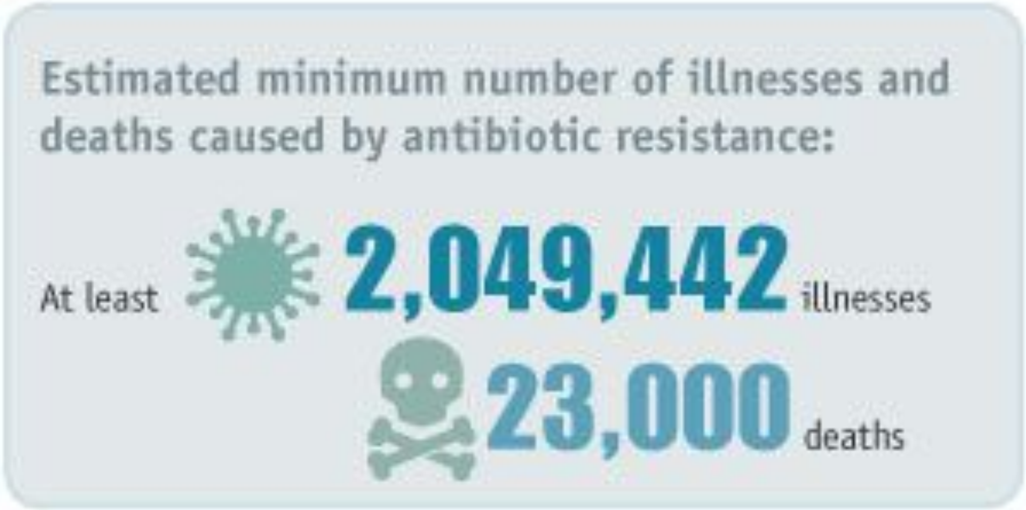
The Bad Guys

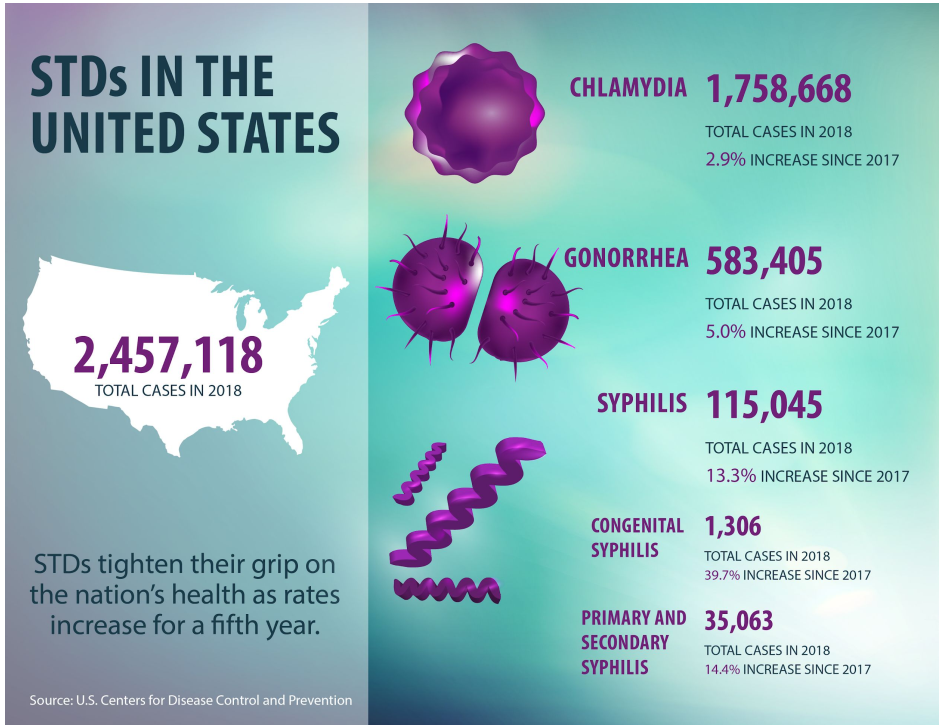


It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Image from: https://www.tujawellness.com/antibiotic-resistance-armageddon/

The Bad





Images from : top left- https://blogs.cdc.gov/safehealthcare/files/2015/02/Estimated-Illness_AR.jpg, top right- https://www.cdc.gov/nchhstp/newsroom/images/multimedia/std/stds-us-2018_higRes.jpg, bottom center-https://www.cdc.gov/foodsafety/images/food-Safety-symptoms-500px.png

Food Poisoning

Organisms: *Salmonella* & *Escherichia coli*

Two of the most common causes of food poisoning

Sources: Contaminated eggs, poultry, meat, unpasteurized milk or juice, cheese, contaminated raw fruits and vegetables

Symptoms:

- Diarrhea, fever, abdominal cramps, vomiting

Images from: top-https://www.cdc.gov/media/releases/2014/images/p0326-salmonella-data.jpg
bottom- https://www.giantmicrobes.com/us/media/catalog/product/cache/2/small_image/9df78eab33525d08d6e5fb8d27136e95/e/c/ecoli_2.jpg,

Tetanus

Organism: *Clostridium tetani*

Source: soil, saliva, dust and manure

Enters through a puncture or skin cut

Symptoms:

- Begins with jaw muscle spasms and could lead to spasms of many body muscles

Mechanism: Tetanus toxin initially binds to peripheral nerve terminals

Image from: https://phil.cdc.gov//PHIL_Images/20041014/19f02a819c8f4352804bc5abbdd820c0/6374_lores.jpg

Botulism

Organism: *Clostridium botulinum*

Botulinum toxin- blocks nerve function, causing nerve paralysis

Bacterial spores found in soil and water, low acid foods improperly stored (including pickled things and honey)

Infant botulism- floppy infant syndrome (acute muscular hypotonia)

Symptoms:

- Muscle weakness typically occurs starting with cranial nerves

Image from: http://casemed.case.edu/clerkships/neurology/NeurLrngObjectives/floppy.jpg

Anthrax

Organism: *Bacillus anthracis*

Spreads through contact with bacterial spores either breathing, eating or through open skin

Affects skin, lungs and gastrointestinal tract

Symptoms:

- Can lead to inflammation of the mediastinum and pneumonia that can lead to shock and sudden death

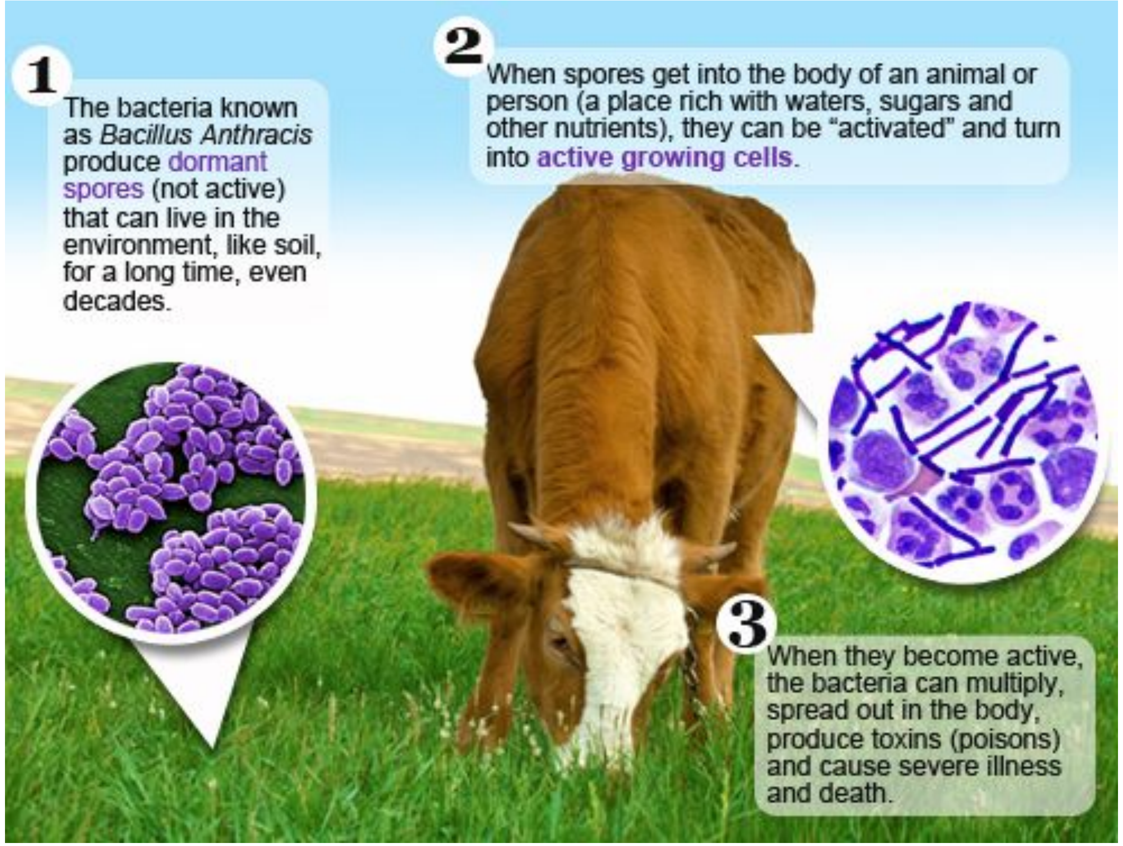


Image from: https://www.cdc.gov/anthrax/images/illustrations/anthrax-life-cycle.jpg

Sexually Transmitted Diseases (STDs)

Organisms: *Chlamydia trachomatis, Neisseria gonorrhoeae, Treponema Pallidum*

Diseases: Chlamydia, Gonorrhea, Syphilis

Transmitted from one person to another during vaginal, anal, and oral sex

Prevented by avoiding unprotected sex

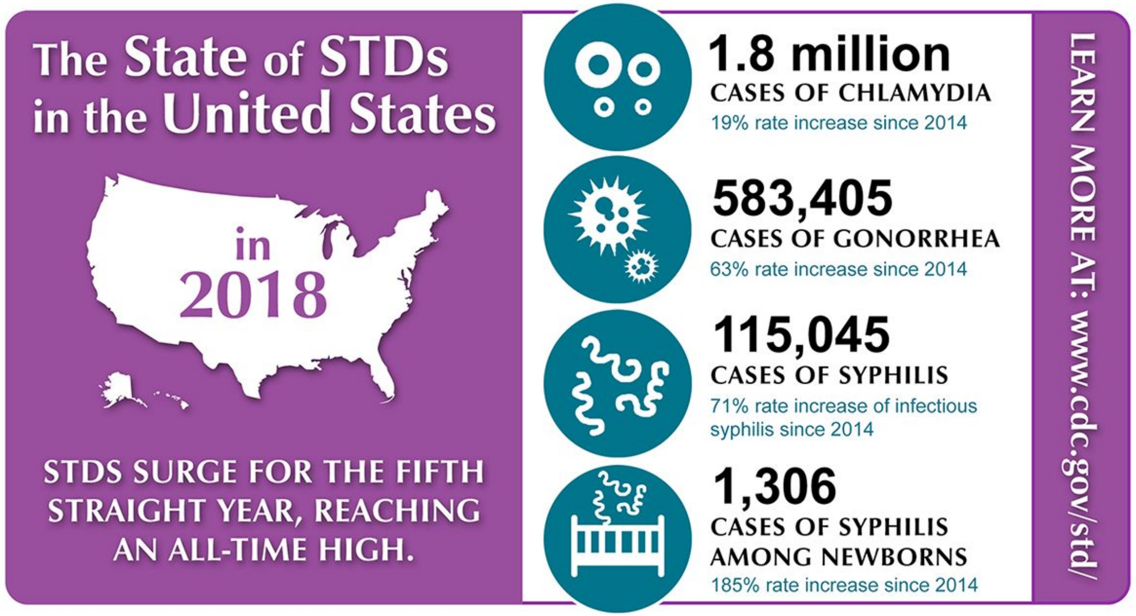


Image from: https://www.cdc.gov/std/stats18/images/infotweet-1-2018.png

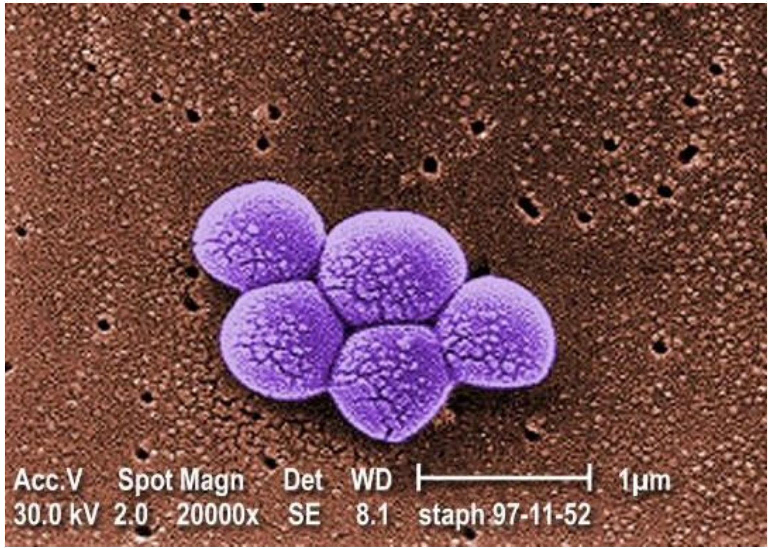
Antimicrobial Resistance

- Occurs when bacteria and fungi become resistant to antibiotics and antimycotics and can no longer be killed by them

- It is considered one of the greatest public health threats of our time

Image from: https://www.cdc.gov/antibiotic-use/community/images/AR-Burden-Numbers-2019.png

Methicillin-Resistant *Staphylococcus aureus* (MRSA)



Common in hospitals, prisons and nursing homes

Presents as red bumps in the skin, fever and rash. As time passes the bumps become painful and filled with pus

Began as a hospital acquired infection

Resistant to broad spectrum antibiotics

Images from: top- https://www.cdc.gov/mrsa/images/mrsa_magn_lg.jpg, bottom- https://www.cdc.gov/mrsa/images/MRSA_abscess_Moran2.jpg

Cholera

Organism: *Vibrio cholerae*

Cholera toxin- activates the enzyme adenylate cyclase that produce cAMP. High levels of cAMP leads to secretion of chloride ions that promote the accumulation of fluid in the gut

Spreads through contaminated water and food

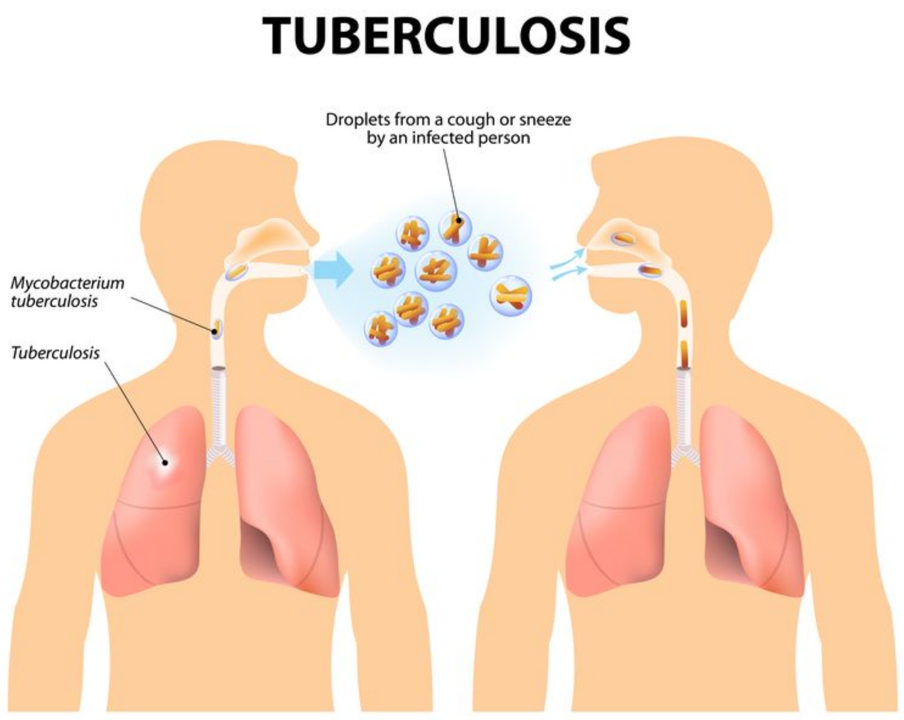
Only affects humans

Symptoms:

- Watery diarrhea, severe dehydration, vomiting, muscle cramps

Image from: https://www.cdc.gov/cholera/images/cholera-banner.jpg

Tuberculosis



Organism: *Mycobacterium tuberculosis*

Spreads through the air.

Affects lungs and sometimes brain

10% of infections progress to active disease

Symptoms:

- Cough with bloody sputum, fever, night sweats and weight loss

Image from: https://www.health.harvard.edu/media/content/images/medical-illustrations/tuberculosis-dreamstime_s_47704368.jpg

Bubonic Plague

Organism: *Yersinia pestis*

Also known as Black Death- acral necrosis (gangrene)

Spread by fleas from small animals (i.e. rats)

Symptoms:

- *Chills, fever, infected and enlarged lymph nodes (buboes), seizures, vomiting blood*

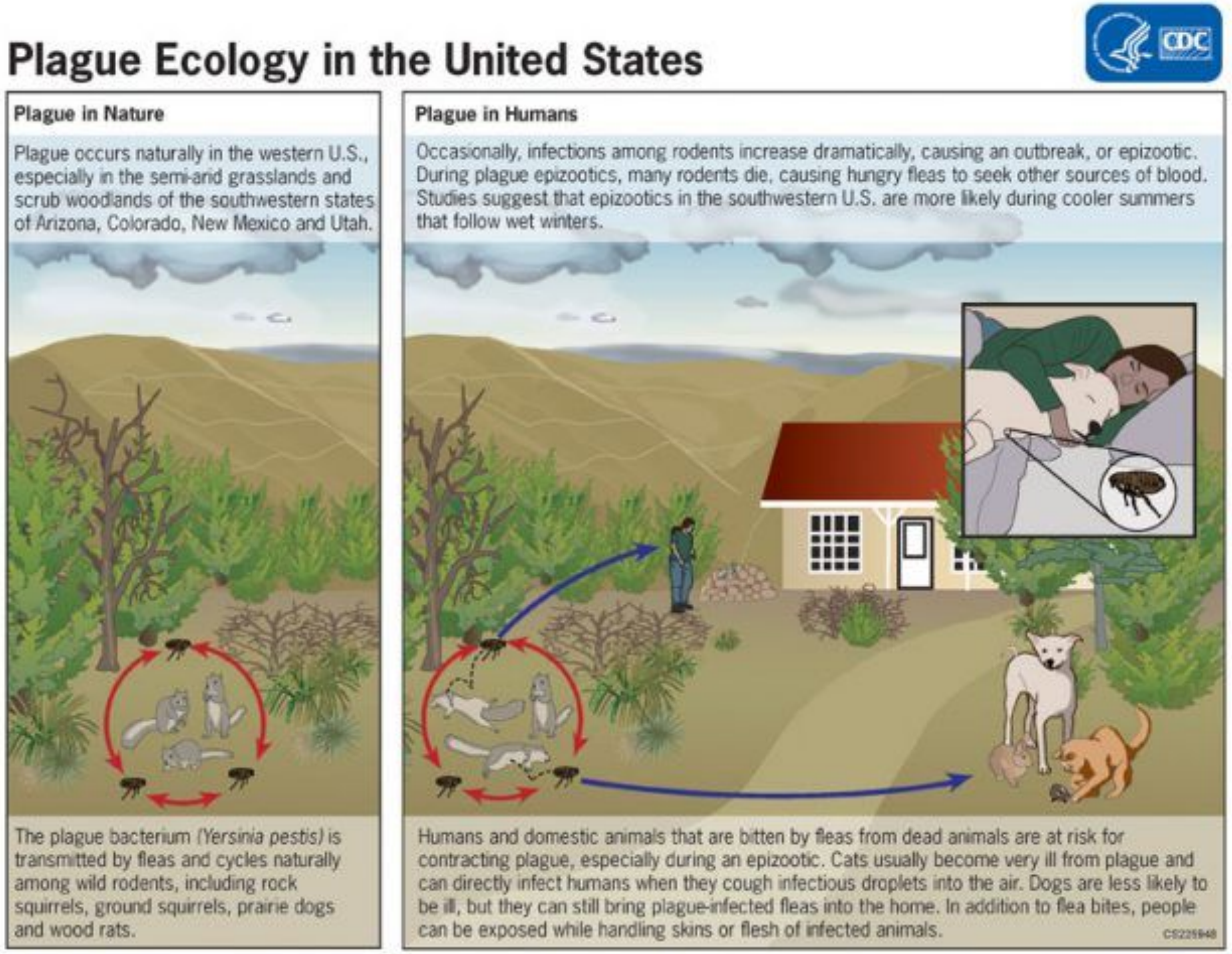


Image from: https://www.cdc.gov/plague/images/PlagueEcologyUS-medium.jpg

Hansen's Disease

Organism: *Mycobacterium leprae*

May spread through coughing or contact with fluids of infected person, however **prolonged (over many months) close contact** with **someone untreated** for Hansen's disease would be **required** to get the disease

Not very contagious

Usually infections remain without symptoms for 5-20 years

Symptoms:

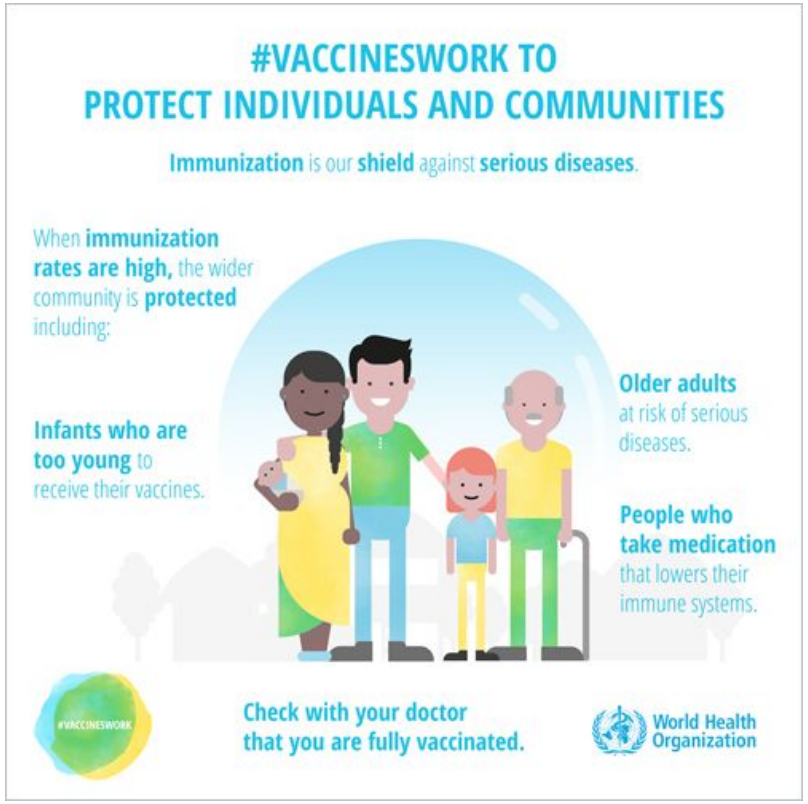
- Pinkish patches of skin that become insensitive to pain or temperature, numbness in hands and feet, secondary infections can lead to tissue loss

Image from: https://www.cdc.gov/leprosy/images/health-care-workers/healthcare-1.jpg

What can we do to protect ourselves?

- For more information about vaccines visit: https://www.cdc.gov/vaccines/vac-gen/default.htm

- For more information about antimicrobial resistance visit: https://www.cdc.gov/drugresistance/about.html



Images from: left- http://www9.who.int/entity/campaigns/immunization-week/2017/infographic-protect-individuals-500.jpg,
right- https://www.cdc.gov/ncezid/images/partners/stop-it-UN-AR.png