THE HISTORY OF MICROBIOLOGY

Microbiology - CCV
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Antoni van Leeuwenhoek (1623-1723)

- The first man to discover the bacterial world
- Dutch tailor, merchant, lens grinder
- Microscope maker
- Didn't like to share his secrets—set us back by 100 years after his death
- "animalcules"--description
- Life in a drop of water
- Discovered previously unknown microbial world: fungi, protozoa, bacteria, algae

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The Golden Age of Microbiology
(late 1800's and early 1900's)

- 50 year span
- The field of microbiology was driven by the search for answers to 4 questions:

1) Is spontaneous generation of microbial life possible?
2) What causes fermentation?
3) What causes disease?
4) How can we prevent infection & disease?

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Is Spontaneous Generation of Microbial Life Possible?

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Spontaneous Generation (abiogenesis)

Defined:

The theory that living organisms can arise from nonliving matter

- Theory proposed by Aristotle (384-322 B.C.)
- Widely accepted for over 2000 years because it seemed to explain a variety of commonly observed phenomena (i.e. maggots on spoiling meat)
- Came under challenge in the 17th century

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Redi's Experiments—questioning spontaneous generation

- Late 1600's
- Francesco Redi (an Italian physician) did a series of experiments involving spoiling meat
- Maggots never developed on meat that was isolated from exposure to flies
- Scientists began to doubt Aristotle's theory and began to adopt the view that animals come only from other animals

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Needham's Experiments

- Rekindling of spontaneous generation debate with Leeuwenhoek's discovery of microbes in freshly collected rainwater
- Needham (1713-1781) boiled beef gravy and infusions of plant material in vials, which were then sealed tightly with corks
- Infusions became cloudy
- His conclusion: there is a *life force* which causes inanimate matter to spontaneously come to life
- Basis: the vials were heated sufficiently to kill everything

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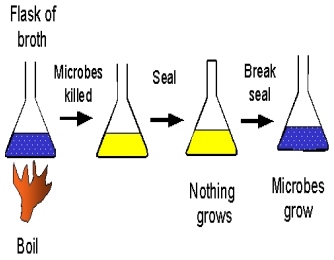
Spallanzani's Experiments (1729-1799)

- Repeated the infusion boiling experiments with slender necks which he melted shut
- His infusions remained clear unless the seal was broken and exposed to air



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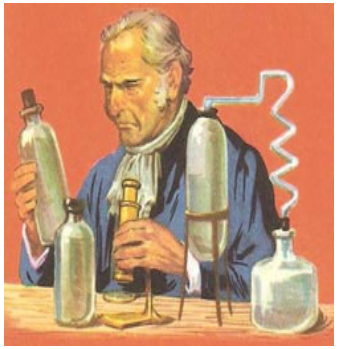
Spallanzani's Conclusions

- Needham either had failed to heat his vials suffienciently to kill all microbes or had not sealed them tightly enough
- Microorganisms exist in the air and can contaminate experiments
- Spontaneous generation of microorganisms does not occur; all living things arise from other living things



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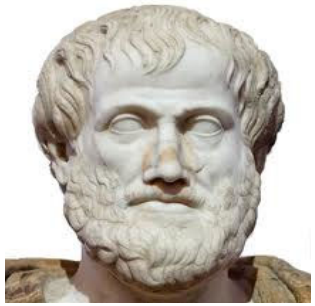
Old Theories Die Hard…though…

- Despite the conclusions of Spallanzani's experiments, it proved difficult to dethrone a theory that existed for 2000 years
- Spallanzani's work was critiqued heavily and questioned
- The spontaneous generation theory was not laid to rest until the work of Louis Pasteur in the 1800's…



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Louis Pasteur(1822-1895) ends the debate…

- Boiled the infusions
- Used unsealed S-shaped flasks for the broth
- The S-shaped flask allowed air to enter but prevented the introduction of dust and microbes into the broth
- Swan-necked flasks remained free of microbes
- "Never will spontaneous generation recover from the mortal blow of this simple experiment."

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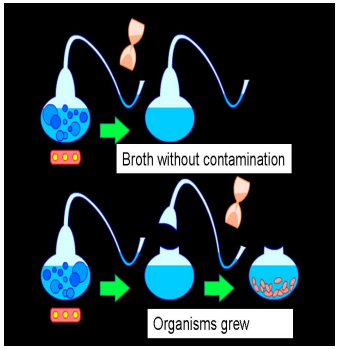
Pasteur's conclusion

- Followed swan-neck experiments with further demonstrations
- Broke the necks off some flasks, exposing the liquid directly to the air, carefully tilted other bottles to allow dust from the necks to reach the broth…both yielded cloudy broths the next day
- Conclusion: microbes in liquid were the progeny of microbes that had been on dust particles in the air



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What Causes Fermentation?

- Pasteur conducted a series of investigations to answer this question
- Wine industry in France was being threatened by contaminated wine
- Pasteur was asked to investigate this
- Pasteur's accomplishments in this experimentation led many to refer to him as **The Father of Microbiology**

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Wine Studies by Pasteur

Conclusions:

- Yeast cells grow and bud in grape juice; yeast cells only arise from yeast cells
- Yeast live with or without exposure to oxygen (yeasts = facultative anaerobes)
- Bacteria ferment grape juice to produce acids
- Yeast cells ferment grape juice to produce alcohol
- Anaerobic bacteria fermented grade juice into acids—method to prevent wine spoilage—add oxygen in the production process

http://www.youtube.com/watch?v=0OmWbRKW4K8

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Pasteurization

= the use of heat to kill pathogens and reduce the number of spoilage microorganisms in food and beverages

This practice began being used in winemaking at that time—grape juice was heated just long enough to kill most contaminating bacteria without changing the juice's basic qualities so that it could then be inoculated with yeast to ensure that alcohol fermentation occurred.

Pasteur thus began the field of **INDUSTRIAL MICROBIOLOGY (biotechnology) =** microbes are intentionally used to manufacture products

Pasteurization is routinely used for milk, juices, and other beverages in the present day to safeguard against the contamination by certain microbial pathogens

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Buchner's Studies on Fermentation

- Studies on fermentation began with the idea that fermentation reactions were strictly chemical and did not involve living organisms.
- This idea was supplanted by Pasteur's work showing that fermentation proceeded only when living cells were present that that different types of microoganisms growing under varied conditions produced different end products
- In 1897, Eduard Buchner resurrected the chemical explanation by showing that fermentation does not require living cells
- His experiments demonstrated that fermentation does not require living cells but that enzymes can also promote the process (= cell-produced proteins that promote chemical reactions)

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What Causes Disease?

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Early Thoughts About Disease

Prior to the 1800's, disease was attributed to various factors:

- Evil spirits
- Astrological signs
- Imbalances in body fluids
- Foul vapors

Girolamo Fracastoro (1878-1553)—Italian philosopher

- Conjectured in 1546 that "germs of contagion" cause disease
- The idea that germs might be invisible living organisms awaited Leeuwenhoek's investigations 130 years later

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Germ Theory of Disease

- Pasteur's discovery that bacteria are responsible for spoiling wine led naturally to his hypothesis in 1857 that microorganisms are also responsible for diseases
- This idea came to be known as the **Germ Theory of Disease**

- **Pathogen** = a microorganism capable of causing a disease

Today we understand:

- Germ theory applies only to *infectious diseases*
- Some diseases are genetic
- Allergic reactions and environmental toxins cause other diseases

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Robert Koch's Experiments

- German physician
- Considered to be the Founder of Modern Bacteriology
- Started with studies on Anthrax
- Moved on to studying other diseases
- Took smears from ill victims and allowed them to colonize on a potato or gelatin medium
- Isolated them and injected them into lab animals to investigate the organism's potential to cause disease

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Koch's Contributions to Advances in Lab Microbiology

- Isolation today is on agar plates vs. the gelatinous or potato slice medium, but current technique borrows on Koch's model of isolating organisms
- Simple staining techniques for bacterial cells and flagella
- First photomicrograph of bacteria in diseased tissue
- Techniques for estimating the number of bacteria in a solution based on the number of colonies that form after inoculation onto a solid surface
- Use of steam to sterilize growth media
- Lab techniques such as transferring bacteria between media using a metal wire that has been heat-sterilized in a flame
- Elucidation of bacteria as distinct species

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Koch's Postulates

- After discovering the anthrax bacterium, Koch continued to search for disease agents.
- He eventually discovered *Mycobacterium tuberculosis* as the cause of tuberculosis
- Through his work with TB, he outlined a series of steps called Koch's Postulates that must be taken to prove the cause of any infectious disease
- We use the term *suspected causative agent* until the postulates have been fulfilled

Koch's Postulates:

1. The suspected causative agent must be found in every case of the disease and be absent from healthy hosts
2. The agent must be isolated & grown outside the host
3. When the agent is introduced to a healthy, susceptible host, the host must get the disease
4. The same agent must be found in the diseased experimental host

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TABLE 1.2 Other Notable Scientists of the "Golden Age of Microbiology" and the Agents of Disease They Discovered

Scientist	Year	Disease	Agent
Albert Neisser	1879	Gonorrhea	*Neisseria gonorrhoeae* (bacterium)
Charles Laveran	1880	Malaria	*Plasmodium* species (protozoa)
Carl Eberth	1880	Typhoid fever	*Salmonella enterica* serotype Typhi (bacterium)
Edwin Klebs	1883	Diphtheria	*Corynebacterium diphtheriae* (bacterium)
Theodore Escherich	1884	Traveler's diarrhea Bladder infection	*Escherichia coli* (bacterium)
Albert Fraenkel	1884	Pneumonia	*Streptococcus pneumoniae* (bacterium)
David Bruce	1887	Undulant fever (brucellosis)	*Brucella melitensis* (bacterium)
Anton Weichselbaum	1887	Meningococcal meningitis	*Neisseria meningitidis* (bacterium)
A. A. Gartner	1888	Salmonellosis (form of food poisoning)	*Salmonella* species (bacterium)
Shibasaburo Kitasato	1889	Tetanus	*Clostridium tetani* (bacterium)
Dmitri Ivanowski and Martinus Beijerinck	1892 1898	Tobacco mosaic disease	*Tobamovirus tobacco mosaic virus*
William Welch and George Nuttall	1892	Gas gangrene	*Clostridium perfringens* (bacterium)
Alexandre Yersin and Shibasaburo Kitasato	1894	Bubonic plague	*Yersinia pestis* (bacterium)
Kiyoshi Shiga	1898	Shigellosis (a type of severe diarrhea)	*Shigella dysenteriae* (bacterium)
Walter Reed	1900	Yellow fever	*Flavivirus yellow fever virus*
Robert Forde and Joseph Dutton	1902	African sleeping sickness	*Trypanosoma brucei gambiense* (protozoan)

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Gram's Stain

- Because most microbes are colorless and difficult to see, scientists began to use dyes to stain them and make them more visible under the microscope
- Hans Christian Gram developed a staining technique that we still use today (Gram Stain)
- This is one of the first steps in identifying bacteria today
- Gram's staining technique has allowed us to separate bacteria into two large groups
  - Gram positive (stain purple)
  - Gram negative (stain pink)

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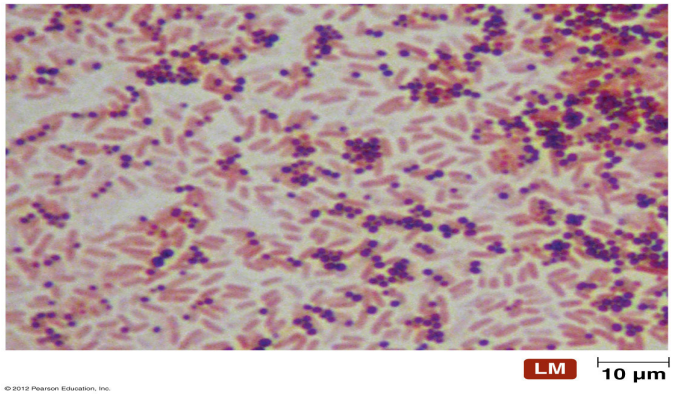
Gram Stain



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How Can We Prevent Infection & Disease?

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Microbe Dangers in Environmental and Healthcare Settings

- In the mid-1800's, modern principles of hygiene, such as those involving sewage and water treatment, personal cleanliness, & pest control were not widely practiced.
- Typically, Medical personnel and health care facilities lacked adequate cleanliness.
- *Nosocomial infections*—infections that are acquired in a health care setting—were rampant
- Common: gangrene following surgical procedures or when under a doctor's care, women giving birth in hospitals often died from puerperal fever
- Six health care practitioners were instrumental in changing health care delivery: Semmelweis, Lister, Nightingale, Snow, Jenner, & Ehrlich

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Pioneering Ideas for Disease Prevention

- Semmelweis and handwashing
- Lister's antiseptic technique
- Nightingale and nursing
- Snow – infection control and epidemiology
- Jenner's vaccine – field of immunology
- Ehrlich's "magic bullets" – field of chemotherapy

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Semmelweis & Lister—Antiseptic Technique

http://www.youtube.com/watch?v=T73PYNyyeiI&feature=related

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Florence Nightingale (1820-1910)

- Nurse; introduced cleanliness & other antiseptic techniques into nursing practice
- Instrumental in setting standards of hygiene that saved innumerable lives during the Crimean War of 1854-1856
- Ordered 200 scrubbing brushes into the hospital wards
- Dirty clothes and surgical dressings were removed from patient care sites
- Documented statistical comparisons to show that poor food and unsanitary conditions in the hospitals were responsible for the deaths of many soldiers
- After the war, she returned to England was active in applying political pressure for hospital and public health policy reform & changed nursing education permanently

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Snow & Epidemiology

- English Physician John Snow (1813-1858) played a key role in setting standards for good public hygeine to prevent the spread of infectious diseases
- Snow had been studying the propogation of cholera and suspected that the disease was spread by a contaminating agent in water.
- In 1854, epidemic cholera was mapped and found to center around a public water supply on Broad Street in London
- Snow's careful documentation of the epidemic highlighted the critical need for adequate sewage treatment and a pure water supply
- His study was the foundation of 2 branches of microbiology: **infection control** & **epidemiology**
- **Epidemiology =** the study of the occurrence, distribution, and spread of disease in humans

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Jenner's Vaccine--Smallpox

- In 1796, English Physician Edward Jenner tested the hypothesis that a mild disease called cowpox provided protection against potentially fatal smallpox
- Intentional inoculation of a boy with pus colleted from a milkmaid's cowpox lesion→boy developed cowpox and survived→Jenner then injected the boy with smallpox pus→boy had become immune to smallpox→disease never developed (note: MAJOR ETHICAL VIOLATIONS HAPPENING HERE!)
- *Vaccinia virus* causes cowpox→name vaccination was given
- Pasteur capitalized on Jenner's work by producing weakened strains of various pathogens for use in preventing the serious diseases they cause (fowl cholera, anthrax, rabies)
- ***Vaccine*—**reference to all weakened, protective strains of pathogens.

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Variolation-Lady Mary Wortley Montagu

- Lady Mary Wortley Montagu (1689-1762) introduced inoculation against smallpox to Europe
- She had learned in her travels that it was possible to provide some protection against deadly forms of the disease by inoculating children with pus from an individual with a milder form.
- She had her daughter inoculated in 1721, which was the first time this practice was introduced in England.
- The process was promoted in England and called "variolation."

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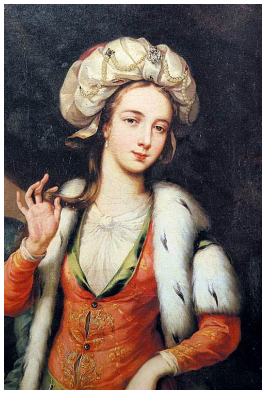
"Variolation"



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Ehrlich's "Magic Bullets"

- Gram's discovery that stained bacteria could be differentiated into two types suggested to German microbiologist Paul Ehrlich (1845-1915) that chemicals could be used to kill microorganisms differentially.
- He undertook a survey of chemicals to find the "magic bullet" that would destroy pathogens while remaining nontoxic to humans.
- By 1908, he had discovered a chemical active against the causative agent of syphilis, though the arsenic-based drug was also toxic to humans.
- His discoveries began the branch of medical microbiology known as **chemotherapy**
- Chemotherapy = a branch of medical microbiology in which chemicals are studied for their potential to destroy pathogenic organisms

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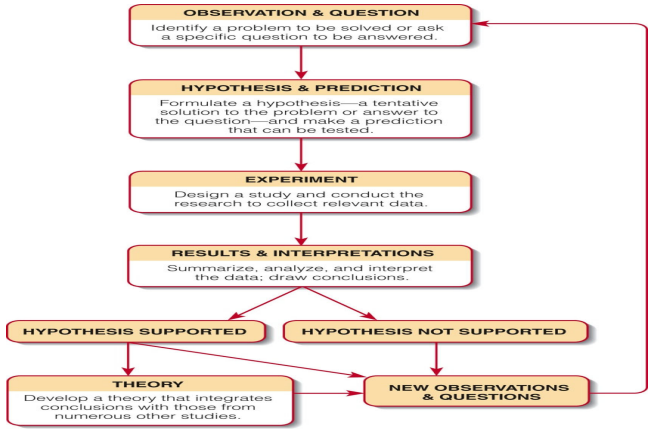
Scientific Method



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