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- The SPO Virtual Classrooms offer many educational resources, including practice test questions, review questions, lecture PowerPoints, video tutorials, sample assignments and course syllabi. New materials are continually being developed, so check back frequently, or follow us on Facebook (Science Prof Online) or Twitter (ScienceProfSPO) for updates.
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# History of Microbiology



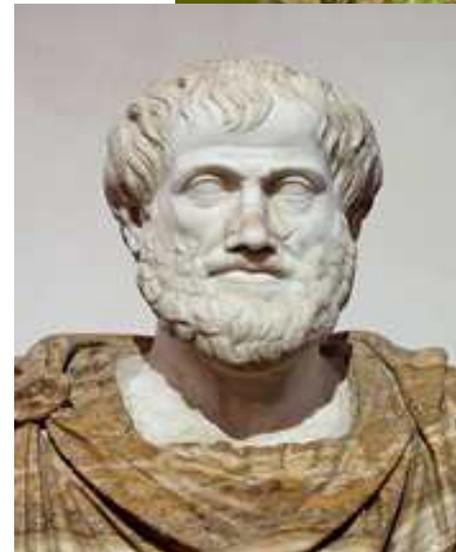
Image:

[Drawing of Death Bringing Cholera in](#)

From the [Virtual Microbiology Classroom](#) on [ScienceProfOnline.com](#)

# Spontaneous Generation Debate

- The belief in the spontaneous generation of life from nonliving matter was introduced by **Aristotle**, who lived around 350 BC.
- According to Aristotle, it was:  
*"readily observable that aphids arise from the dew which falls on plants, fleas from putrid matter, mice from dirty hay."*
- This belief remained unchallenged for more than 2000 years.
- Until...



Aristotle: 384 - 322 B.C.

# Spontaneous Generation Debate

## Francesco Redi - Experiments on Flies

First to formally challenge the accepted belief of spontaneous generation.

**Redi's Question:** Where do maggots come from?

**Hypothesis:** Maggots come from flies.

**Experiment:** Redi put meat into three separate jars.

### Jar-1

- Left open
- Maggots developed
- Flies were observed laying eggs on the meat in the open jar

### Jar-2

- Covered with netting
- Maggots appeared on the netting
- Flies were observed laying eggs on the netting

### Jar-3

- Sealed
- No maggots developed



Francesco Redi, Italian physician, naturalist & poet, 1626 - 1697.

# Spontaneous Generation Debate

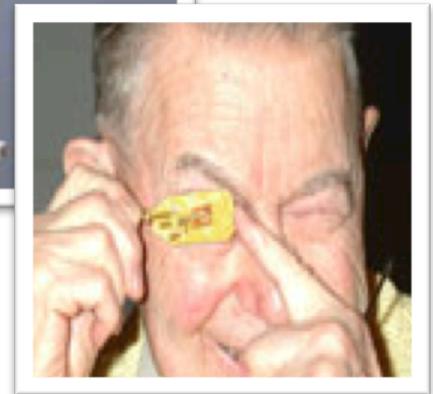
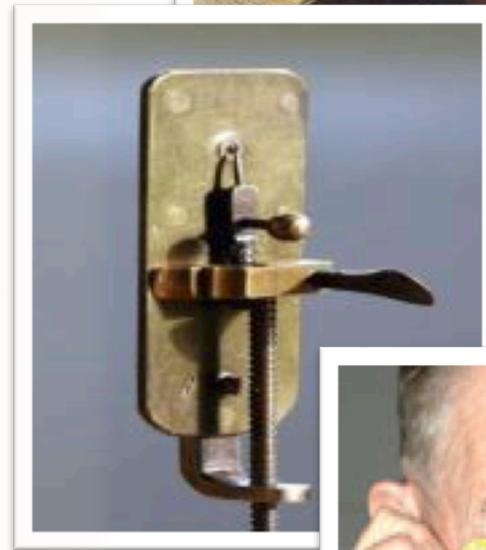
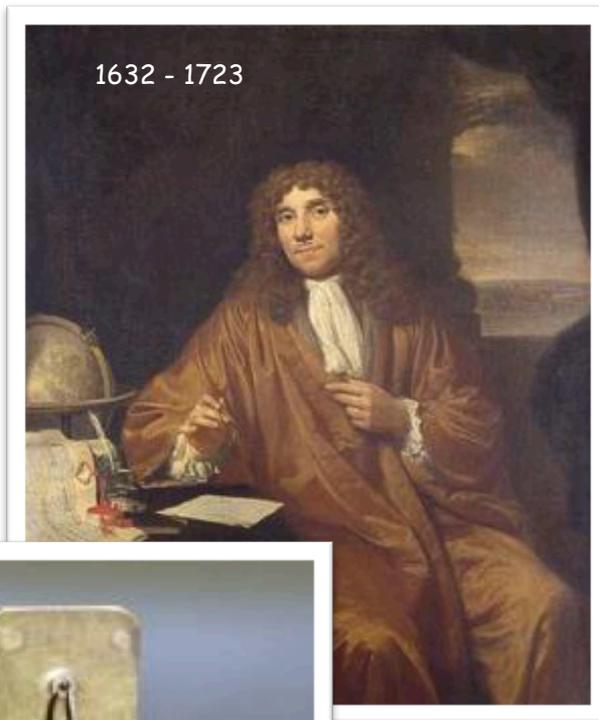
## Anton van Leeuwenhoek's "Animalcules"

(Pronounced Lay-ven-hook)

- As a *draper* (merchant who sells cloth and dry goods), he used lenses to examine cloth. This probably led to his interest in lens making.
- He assembled hundreds of microscopes, some of which magnified objects 270 times.
- As he looked at things with his microscopes, he discovered "micro" organisms - organisms so tiny that they were invisible to the naked eye.
- He called these tiny living organisms "animalcules". He first described bacteria, protozoans and many cells of the human body.

**LISTEN** to the Radiolab episode "Sperm" to learn how Anton let his **freak flag fly!**

♪ **Sing It SUPER FREAK!!** ♪



# Anton van Leeuwenhoek: “Animalcules”

(Pronounced Lay-when-hook)

Below is a poem about Van Leeuwenhoek by Maxine Kumin, from the fantastic book of science-related poetry [The Tree That Time Built](#).

## The Microscope

Anton Leeuwenhoek was Dutch. He sold pincushions, cloth, and such.  
The waiting townfolk fumed and fussed, as Anton's dry goods gathered dust.

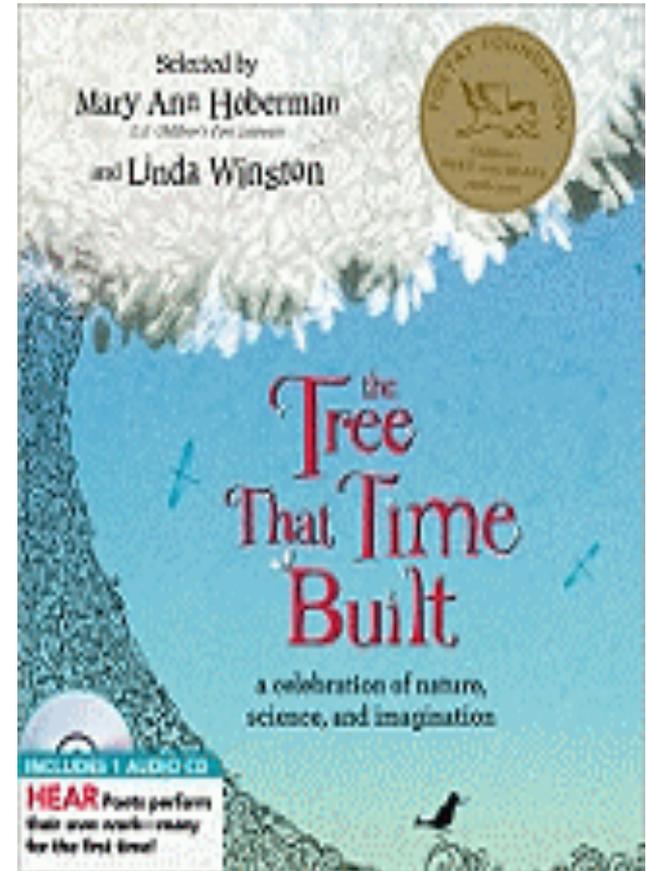
He worked, instead of tending store,  
At grinding special lenses for  
A microscope. Some of the things  
He looked at were: mosquitoes' wings,  
the hairs of sheep, the legs of lice,  
the skin of people, dogs, and mice;  
ox eyes, spiders' spinning gear,  
fishes' scales, a little smear  
of his own blood, and best of all,  
the unknown, busy, very small  
bugs that swim and bump and hop  
inside a simple water drop.

Impossible! Most Dutchmen said.  
This Anton's crazy in the head!  
We ought to ship him off to Spain!  
He says he's seen a housefly's brain!  
He says the water that we drink  
Is full of bugs! He's mad, we think!

They called him dumkopf, which means dope.

That's how we got the microscope.

**Watch Video:**  
[“Pond Life Under the  
Microscope”](#)



# The Controversy Over Spontaneous Generation

John Needham & Lazzaro Spallanzani

## The Question:

What causes tiny living things to appear in decaying broth?

*Needham's Hypothesis:* Spontaneous generation.

*Spallazani's Hypothesis:* Microbes come from the air. Boiling will kill them.



French  
chemist  
Louis  
Pasteur's

design of this  
experiment settled  
the argument.

Needham >



1713 - 1781

Spallazani >



1729 - 1799

# The Controversy Over Spontaneous Generation

## Louis Pasteur & Industrial Microbiology



### Pasteur's Observations:

1. Blobs were alive because they divide and make more of themselves.
2. Put grape juice + yeast in open and in air-tight containers. Fermentation occurred in both. This means that yeast are **facultative anaerobes**.
3. Took two flasks of sterile grape juice and introduced bacteria into one and yeast into another.



- **Q: What is fermentation?**

- What causes fermentation?

*Some scientists thought that air caused fermentation*

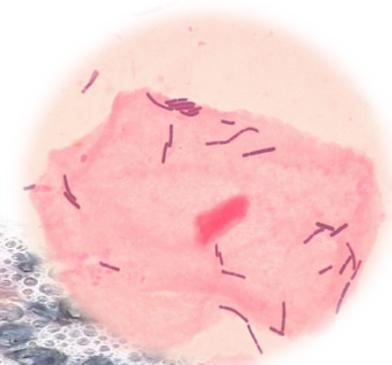
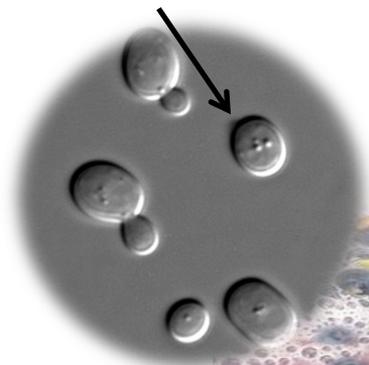
*Others thought that microbes caused fermentation.*

- **Q: What is pasteurization?**

Are these non-living blobs or living microbes?

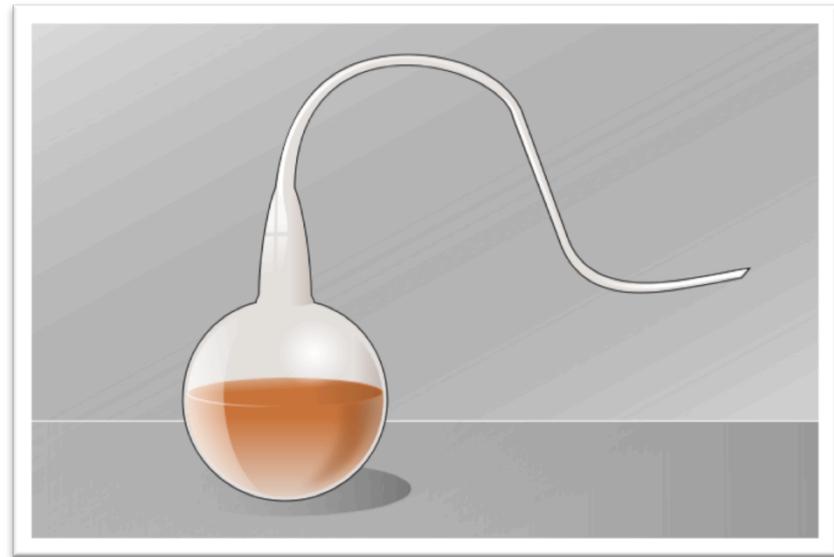
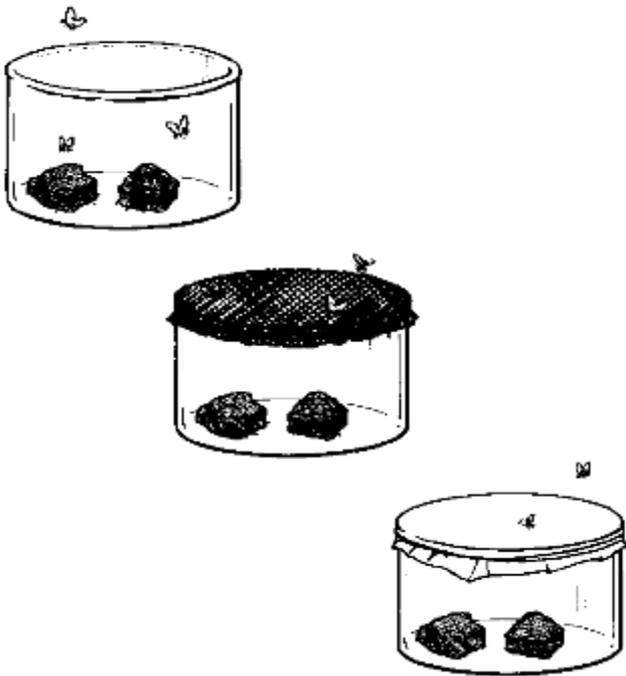
< yeast + grapes = yummy wine 😊 (ethanol)

bacteria + grapes = spoiled wine 😞 (lactic acid) >



# REVIEW!

## Animated lesson of experiments testing Spontaneous Generation



# The Germ Theory of Disease

## Sherlock This...

- Oliver Wendell Holmes Sr. & Ignaz Semmelweis - physicians practicing in different parts of the world.

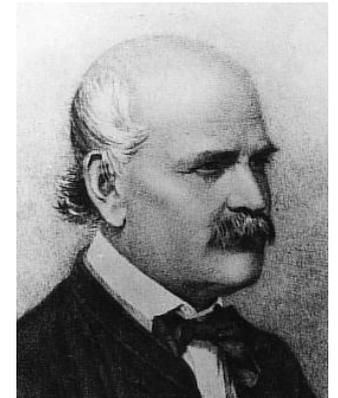
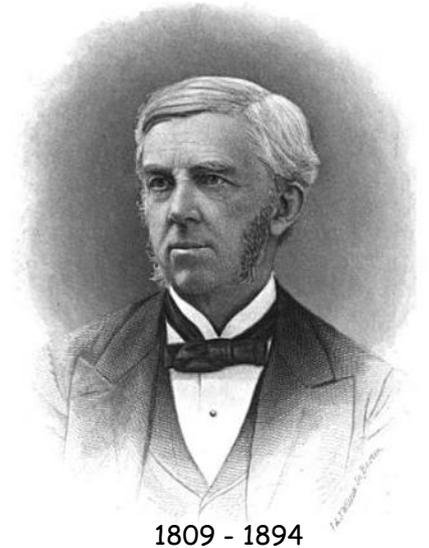
### ➤ Holmes (US)

Believed death following childbirth (puerperal fever) often caused by the material on hands of midwives or attending physicians.

### ➤ Semmelweis (Austria)

Noticed death rates higher in maternity wards staffed by medical students than in those attended by midwives. Death rates decreased in summer.

**Q:** Why?





# The Germ Theory of Disease

## Importance of Hand Washing



 Most frequently missed

 Frequently missed

 Less frequently missed

Sung to tune of "Row, row, row your boat."

Wash, wash, wash your hands,

Play our handy game.

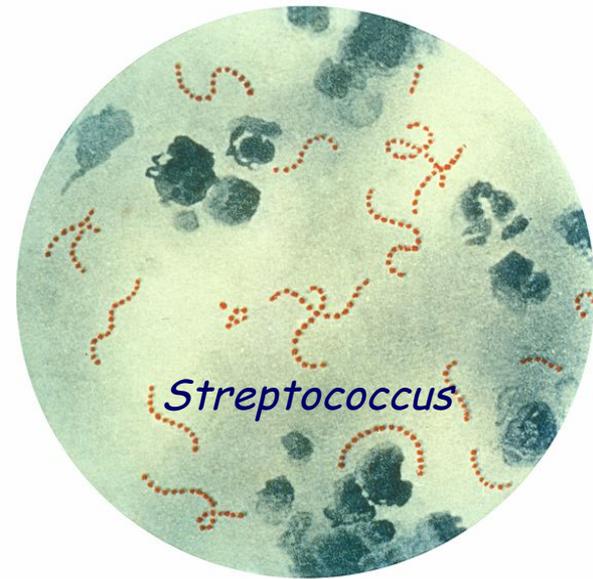
Rub and scrub, scrub and rub,

Germs go down the drain.

(Sing 2x = about 20 seconds.)

# Meet the Microbe

Organism: *Streptococcus pyogenes*



## Streptococcal Infections

Streptococcus is a **Gram +** cocci-shaped genus of bacteria, which produce toxins that contributes to its pathogenesis.



Some diseases caused by this bacterium include:

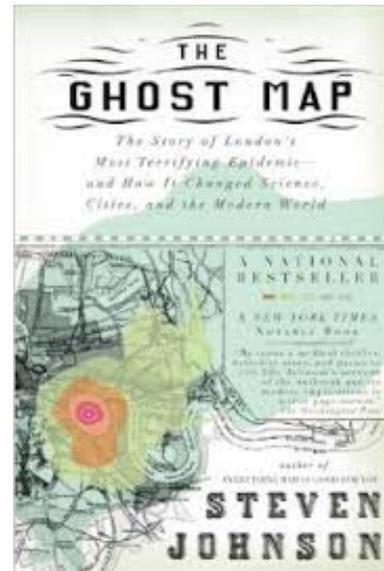
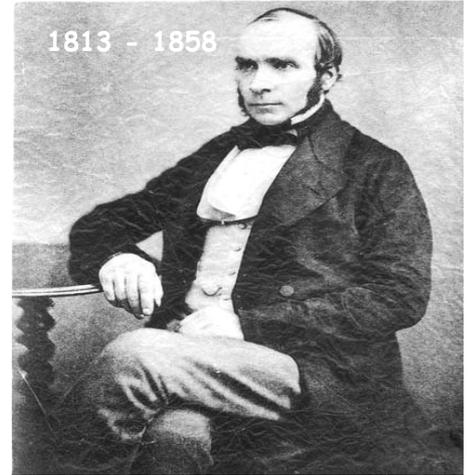
- Puerperal fever
- Strep Throat
- Streptococcal Pneumonia
- Scarlet fever
- Necrotizing fasciitis (flesh-eating bacteria)



# Germ Theory of Disease

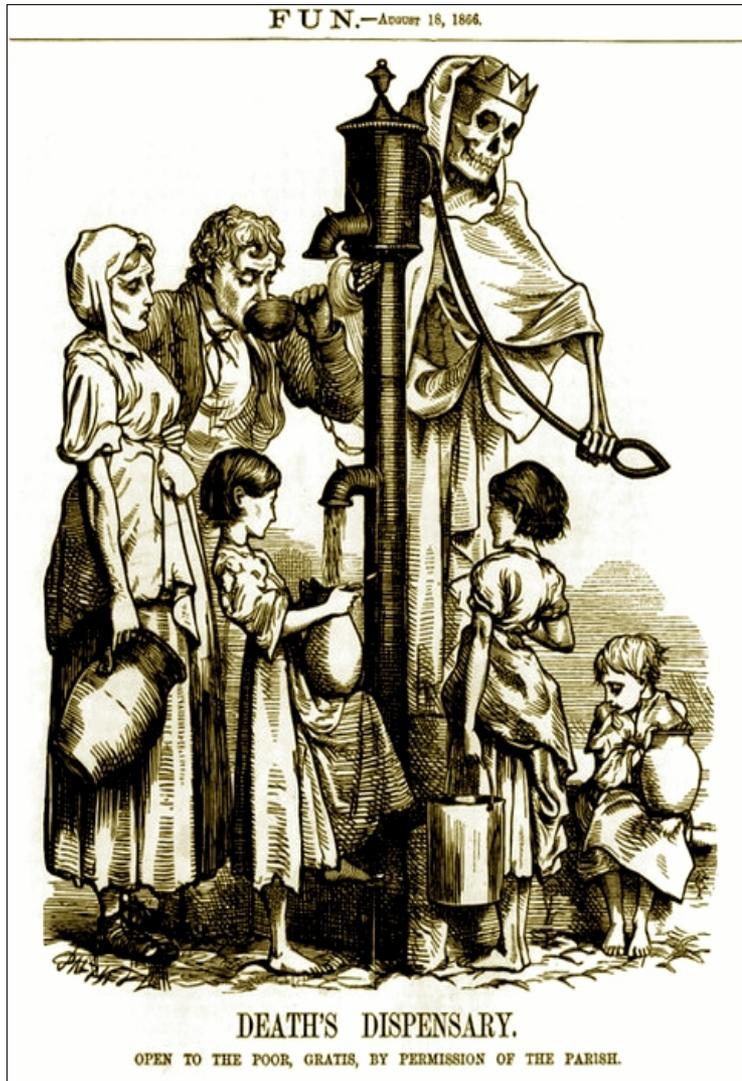
## Dr. John Snow & the Investigation of Cholera

- Played key role in setting standards for good public hygiene and preventing spread of infectious disease.
- Snow skeptic of the then-dominant "miasma theory" (disease caused by bad air).
- Believed cholera transmitted by water contaminated with waste of other cholera sufferers.
- Mapped occurrence of cholera cases during epidemic in London and found cases centered around a specific public water supply.
- Asked city of London to dismantle the pump.
- **Q:** *What do you think happened once water pump was dismantled?*



# Disease, Please!

# Cholera



- Infectious gastroenteritis caused by the **Gram -** bacterium *Vibrio cholerae*.

- Transmission occurs through ingesting contaminated water or food.

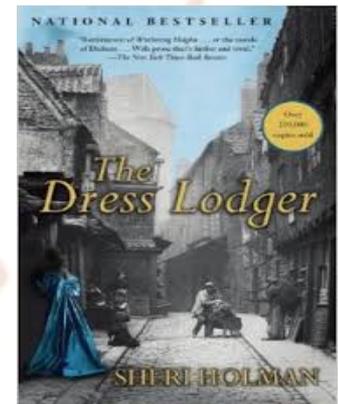
- Action on mucosal epithelium lining of the small intestine responsible for the characteristic massive diarrhea.

- One of the most rapidly fatal illnesses known.

- Can progress from first liquid stool to shock in 4 to 12 hours, with death quickly following without rehydration treatment.

- **Read excerpt from**

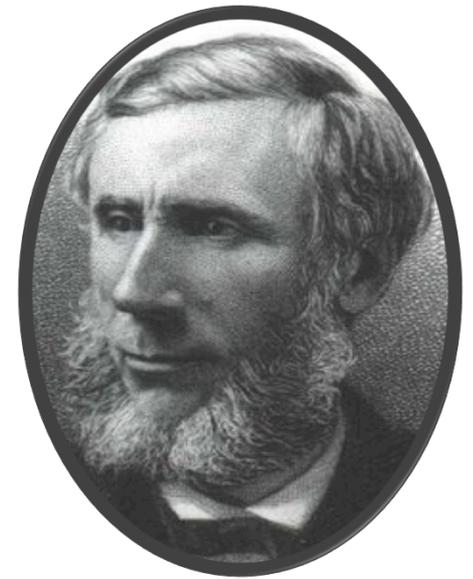
- **"The Dress Lodger" p.114**



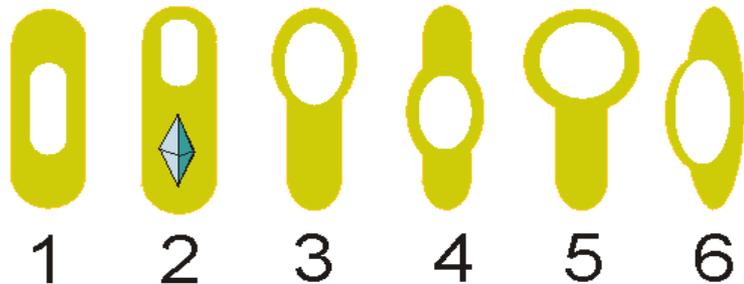
# Germ Theory of Disease

## John Tyndall and the Discovery of Endospores

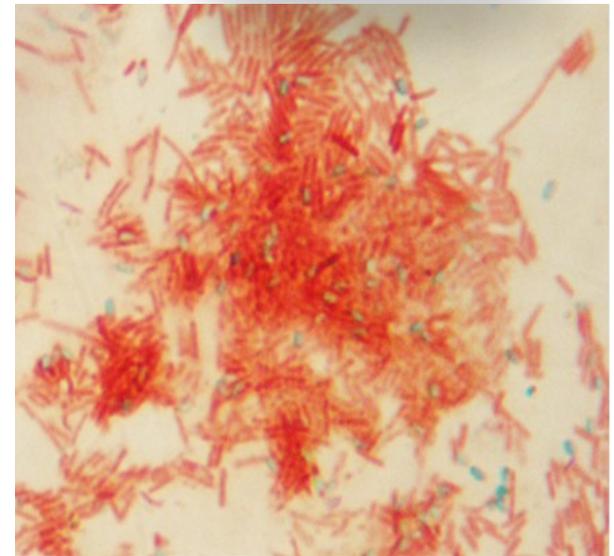
- Discovered that some bacteria existed in two forms:
  1. heat-stable form (endospore)
  2. heat-sensitive form (vegetative cell)
- Need prolonged or intermittent heating to destroy the heat-stable endospores.
- His research resulted in a method of sterilizing liquid by heating it to boiling point on successive days, referred to as Tyndallization.
- Tyndallization is useful for sterilization of growth media in science classes and other situations where autoclaves not available for pressure sterilization.



1820 - 1893



Variations in endospore morphology:  
(1, 4) central endospore;  
(2, 3, 5) terminal endospore;  
(6) lateral endospore



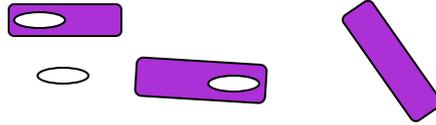
Images: [John Tyndall](#), H.B. Hall N.Y. 1878; Endospore stain T. Port

# Bacterial Genus : Clostridium

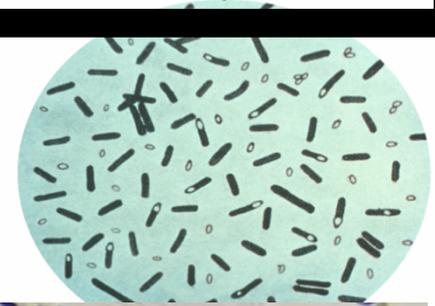
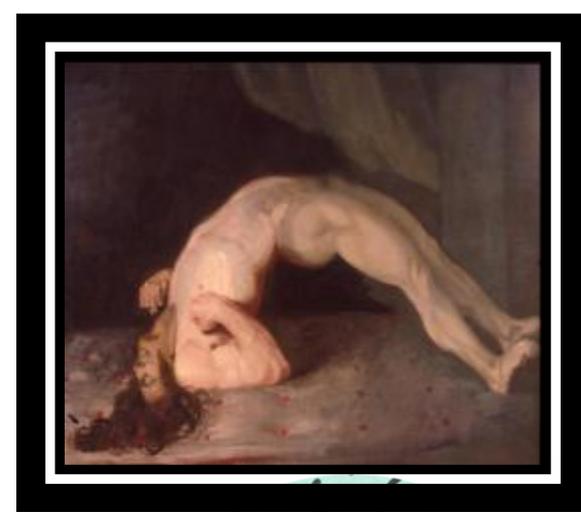
## GRAM-POSITIVE

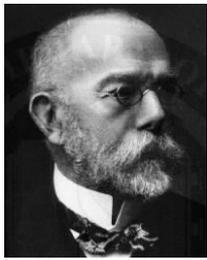
### Obligate anaerobes

bacillus-shaped  
endospore producer



- The members of this genus have a couple of bacterial "superpowers" that make them particularly tough pathogens.
- All have a strictly **fermentative** mode of metabolism (Don't use oxygen).
- Vegetative cells are **obligate anaerobes** killed by exposure to O<sub>2</sub>, but their **endospores** are able to survive long periods of exposure to air.
- Known to produce a variety of toxins, some of which are fatal.
  - *Clostridium tetani* = agent of tetanus
  - *C. botulinum* = agent of botulism
  - *C. perfringens* = one of the agents of gas gangrene
  - *C. difficile* = part of natural intestinal flora, but resistant strains can proliferate and cause pseudomembranous colitis.



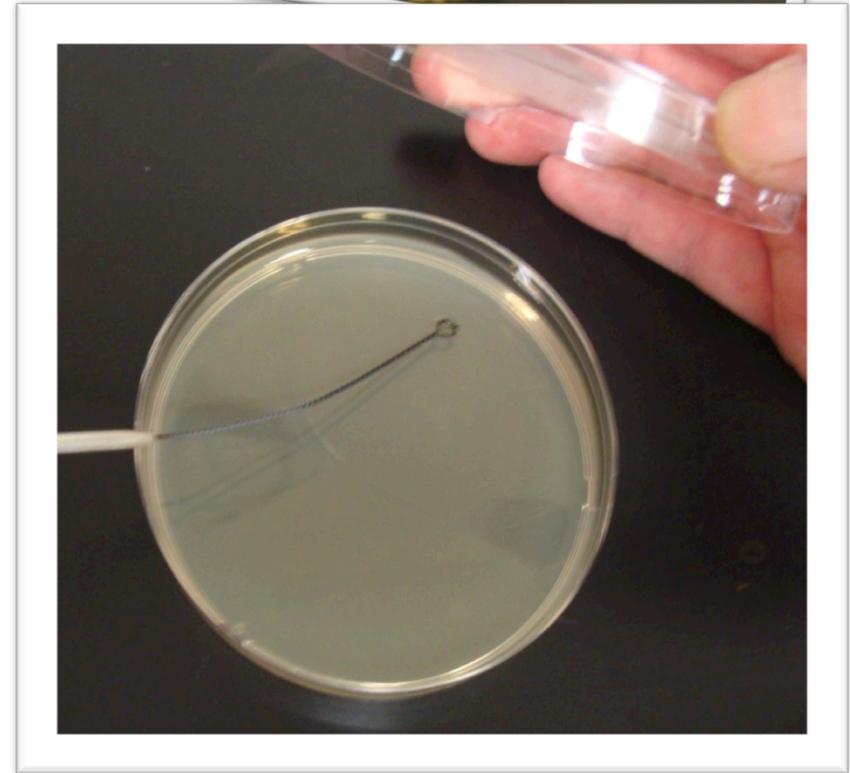


1843 - 1910

# Germ Theory of Disease

## Robert Koch

- Experimented with **medium** to grow bacteria on.
- He tried **gelatin**, but it did not work.
- Wife of colleague recommended **agar** (a gelatin-like product derived from seaweed).
- Didn't melt, and bacteria couldn't digest it.
- He could also add various **nutrients** necessary to grow certain organisms.
- Koch (*pronounced Coke*) originated use of a two part dish for growing bacteria (**Petri dish** named after Julius Petri, a German bacteriologist), and a technique for isolating pure **bacterial colonies**.



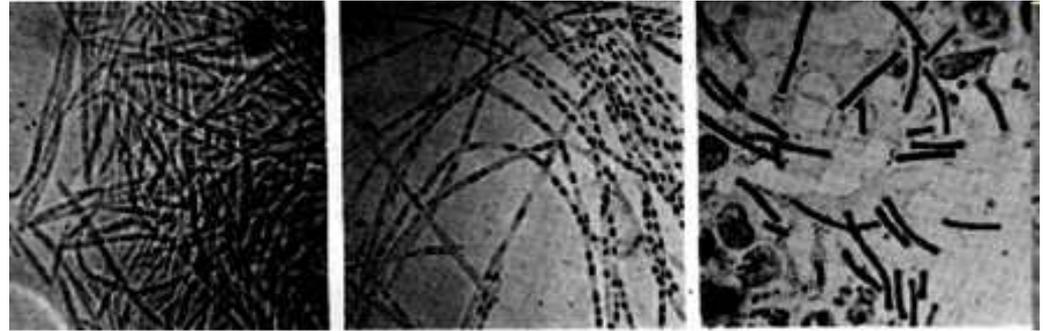
Images. *Micrococcus luteus* colonies, T. Port; [Robert Koch portrait](#), 1843-1910, NIH; MAC differential media, T. Port

# Disease, Please!



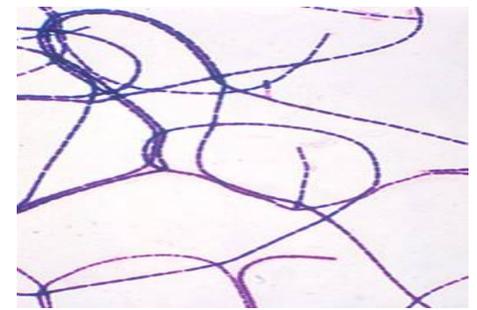
## Anthrax

Gram + bacteria  
*Bacillus anthracis*



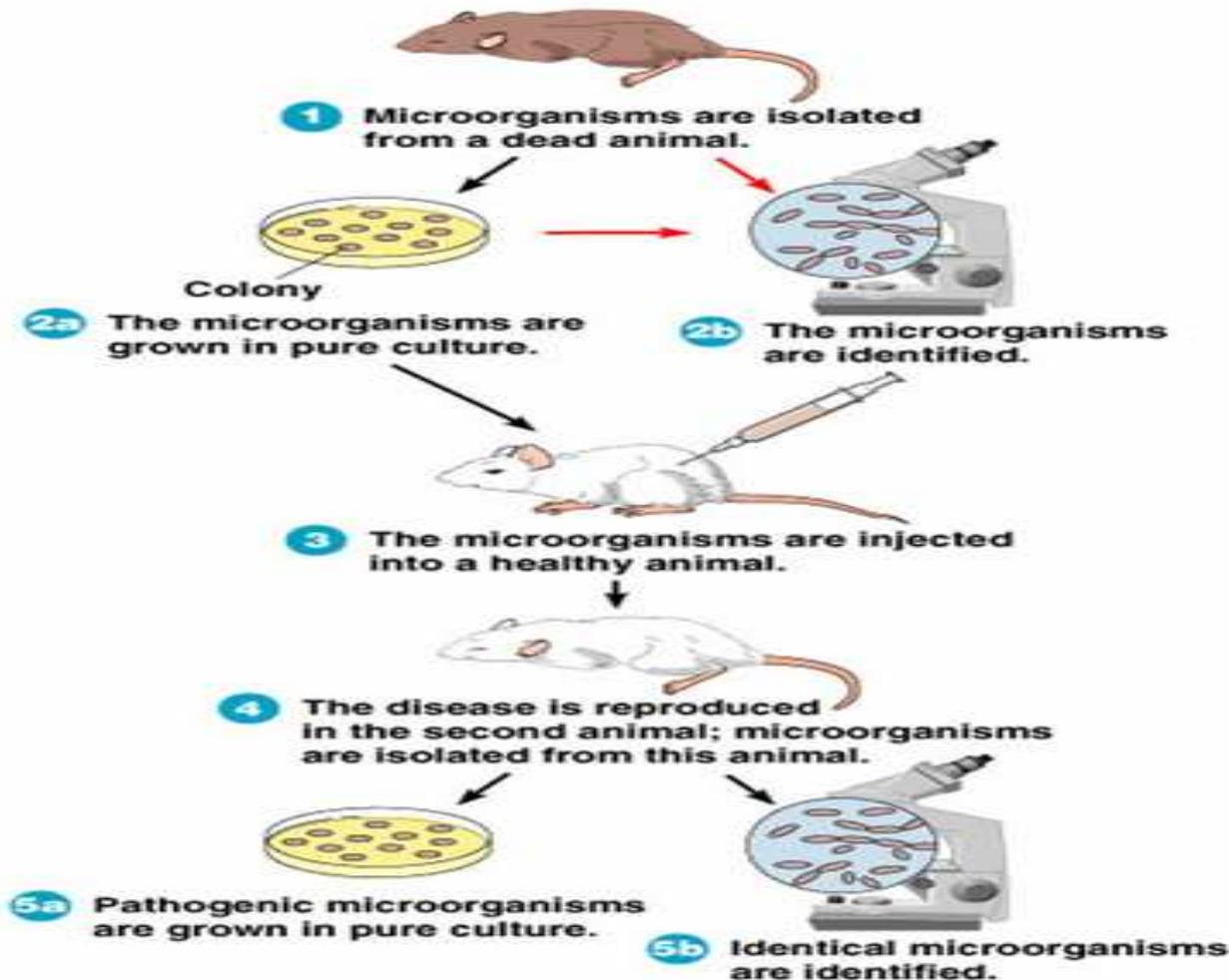
Robert Koch's original micrographs of the anthrax bacillus.

- An endospore-producing bacterium. (Genera *Bacillus* & *Clostridium* examples of endospore producing bacteria.)
- *Bacillus anthracis* first bacterium proven to be the cause of a disease.
- Anthrax was a disease killing European livestock. Farm animals, apparently healthy in the morning, might die by the end of the day, **blood turned black**.
- Humans interacting with the animals were also at risk of becoming ill.
- In 1877, Robert Koch grew *Bacillus anthracis* in pure culture, demonstrated its ability to form endospores, and produced experimental anthrax by injecting it into animals.
- These experiments resulted in Koch formulating guidelines, called Koch's Postulates, for linking specific organisms with specific diseases.



# Germ Theory of Disease

## Koch's Postulates



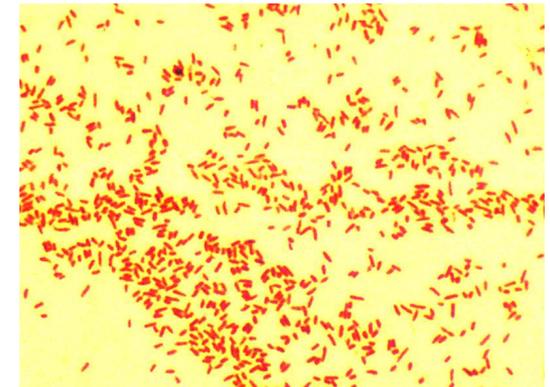
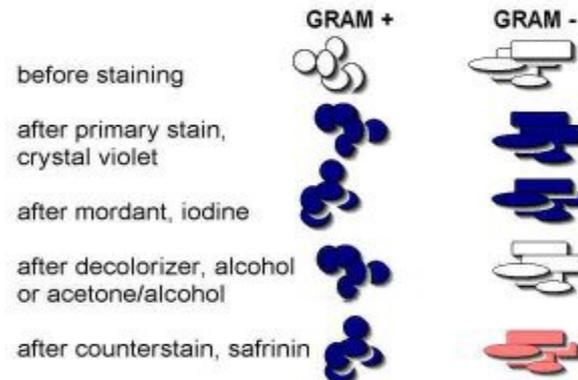
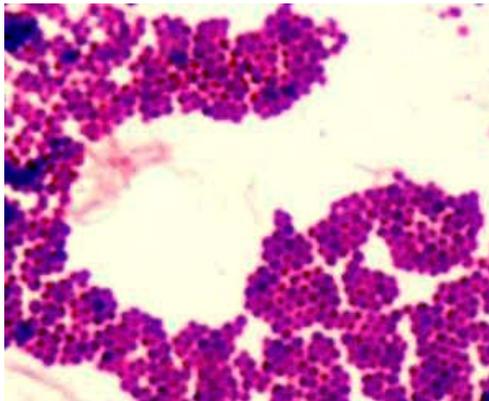
**REVIEW!**

Click through [animated lesson on Koch's Postulates](#) connecting *Bacillus anthracis* with the disease anthrax.

# Germ Theory of Disease

## Gram Stain

- First of [Koch's postulates](#) demands that the suspected agent must be found in **every case** of a given disease.
- That means the tiny microbes must be seen and identified. However, in most cases, microbes are colorless and difficult to see.
- Christian Gram (1850-1938) developed a technique, the [Gram stain](#), that is still widely used today.
- [Differential stain](#) that involves the application of a series of dyes.
- Leaves some microbes purple and others pink.
- Microbes that stain purple, [Gram-positive](#), and those that stain pink, [Gram-negative](#).



# The Germ Theory of Disease

Dr. Joseph Lister - Father of Modern Antisepsis



1827 - 1912

Prevailing belief = Wound infection due to exposed to stinking "miasma" in air.

Lister had read a paper by Pasteur showing that rotting could occur without oxygen if microorganisms present.

Maybe microorganisms were causing gangrene?

Pasteur suggested three methods to get rid of microorganisms:

1. \_\_\_\_\_
2. \_\_\_\_\_
3. \_\_\_\_\_



The first two inappropriate for use in human wounds, so Lister experimented with the third.

**Carbolic acid** was used for deodorizing sewage, so Lister tried spraying instruments, surgical incisions, wounds and dressings with solution.

It markedly reduced the incidence of gangrene.

As germ theory became more widely accepted, understood infection best avoided by **preventing bacteria from getting into wounds in the first place**. This led to the rise of sterile surgery.

# The Germ Theory of Disease

## Florence Nightingale and Nursing



1820 - 1910

- English nurse who was a proponent of cleanliness and antiseptic techniques to the field of nursing.
- She came to prominence for her pioneering work in nursing during the Crimean War (say cry-me-in), where she tended to wounded soldiers.
- She was meticulous about collecting and analyzing data on her practices, to provide proof of their efficacy.
- Founded the Nightingale School for Nurses, the first nursing school in the world.

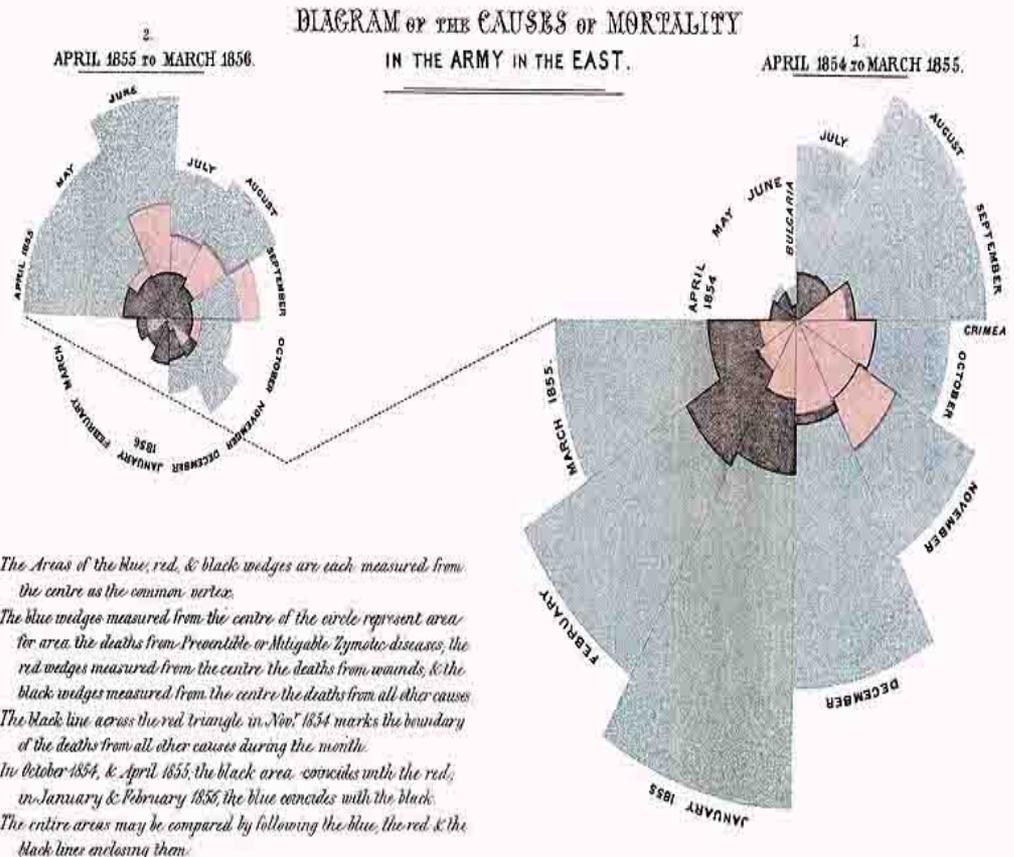
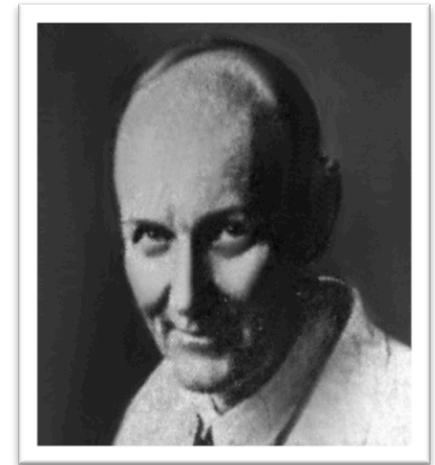


Image: [Florence Nightingale](#) from Carte de Visite, circa 1850; [Polar area diagram by Florence Nightingale](#) 1858.

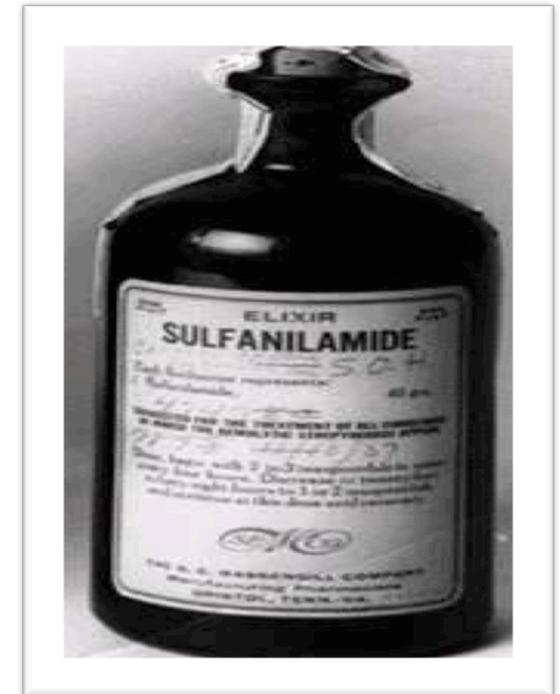
# Discovery of Antimicrobial Agents

## Sulfa Drugs (Sulfonamides)

- **Dr. Gerhard Domagk** (*say Doe-mock*), a German chemist, discovered that the dye Prontosil was effective against a wide range of bacteria.
- Sulfanilamide portion of the Prontosil molecule is responsible for its antibacterial effect. Inhibits essential enzyme activity in effected bacteria.
- Won the 1939, Nobel Prize in Medicine.



1895 - 1964

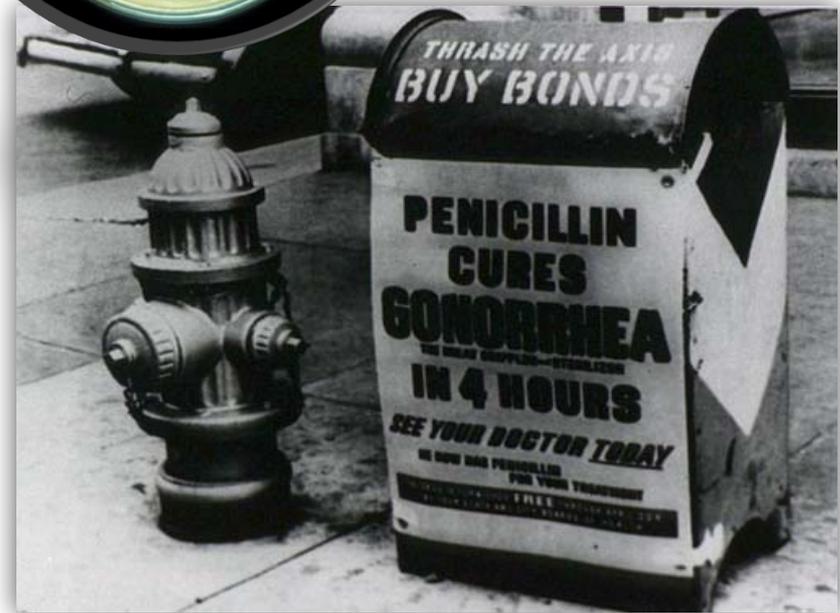
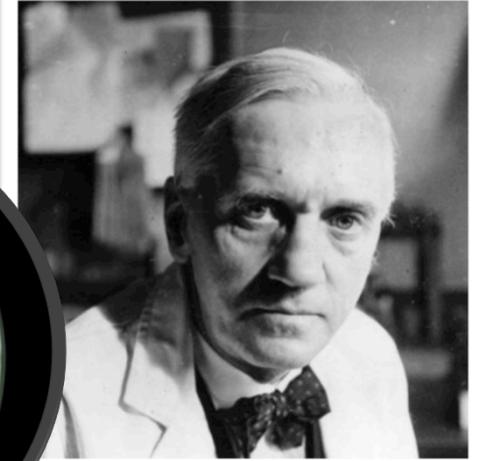
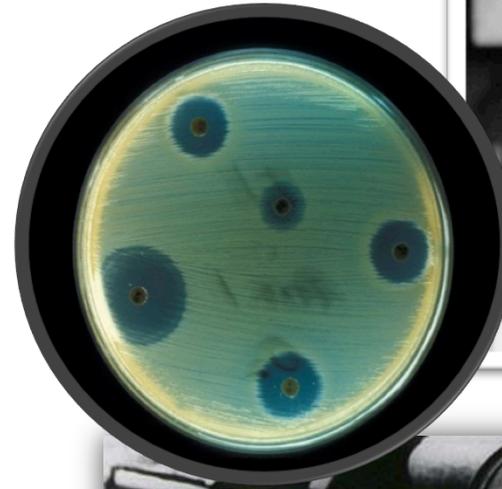


Images: [Dr. Gerhard Domagk](#), 1964, Wiki, Sulfanilamide elixir, Source

# Discovery of Antimicrobial Agents

## Penicillin

- **Alexander Fleming** (1881 - 1955), a Scottish biologist and pharmacologist, observed bacterial staphylococci colonies disappearing on plates contaminated with mold.
- Fleming extracted the compound from the mold responsible for destruction of the bacterial colonies.
- The product of the mold was named penicillin, after the *Penicillium* mold from which it was derived.
- Nobel Prize in Physiology of Medicine in 1945.



Images: *Penicillium* mold, [PHIL #8396](#);  
*Staphylococcus aureus* on antibiotic test plate, [PHIL #2641](#);  
Poster attached to a mailbox offering advice to [World War II](#)  
[servicemen](#), 1944, NIH

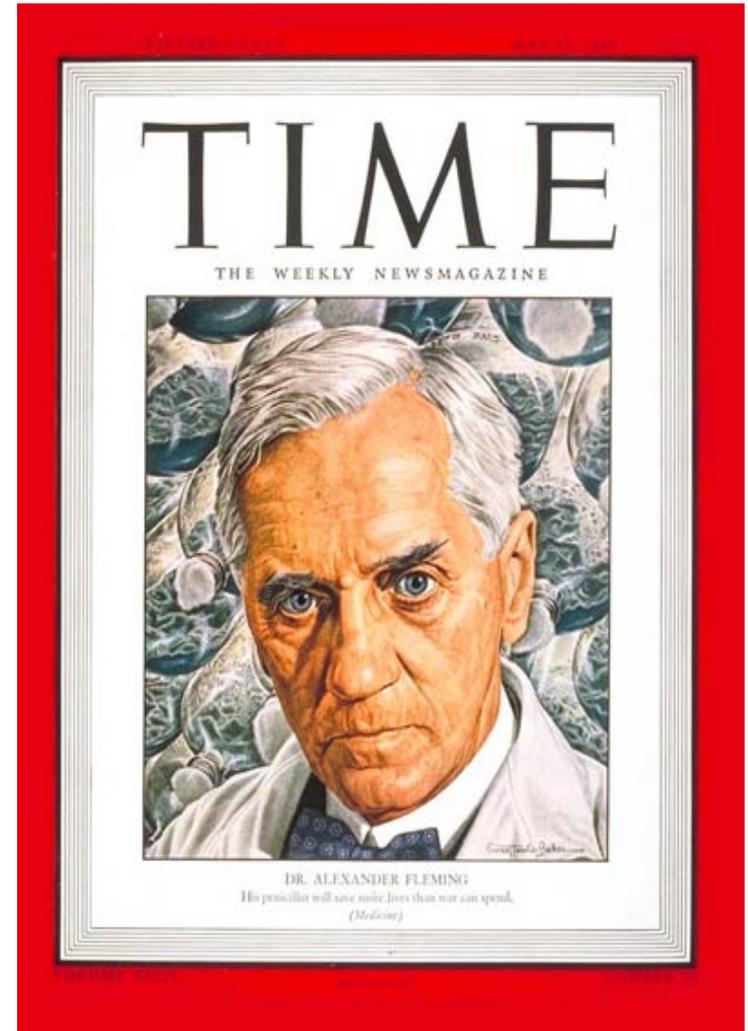
# Discovery of Antimicrobial Agents

## Antibiotic resistance

- In 1944, height of WWII, Alexander Fleming was featured on the cover of Time magazine, with the subtitle:

***"His penicillin will save more lives than war can spend."***

- About the same time that Fleming's face appears on Time magazine, a Stanford researcher publishes that he has found 5 different strains of *Staph* that do not respond to penicillin...The first sign that the *Staph* population has responded to penicillin, by developing resistance.
- This began the "arms race" of development of new antibiotics in response to antibiotic resistance. A few examples:
  - Streptomycin 1943 (resistance 1948)
  - Methicillin 1960 (resistance 1961)
  - Clindamycin 1969 (resistance 1970)
  - Ampicillin 1961 (resistance 1973)
  - Carbenicillin 1964 (resistance 1970)
  - Piperacillin 1980 (resistance 1981)
  - Linezolid 2000 (resistance 2002)



Listen to Radiolab episode  
["Staph Retreat"](#).

# REVIEW!

See brief *SPO Class Notes* articles:

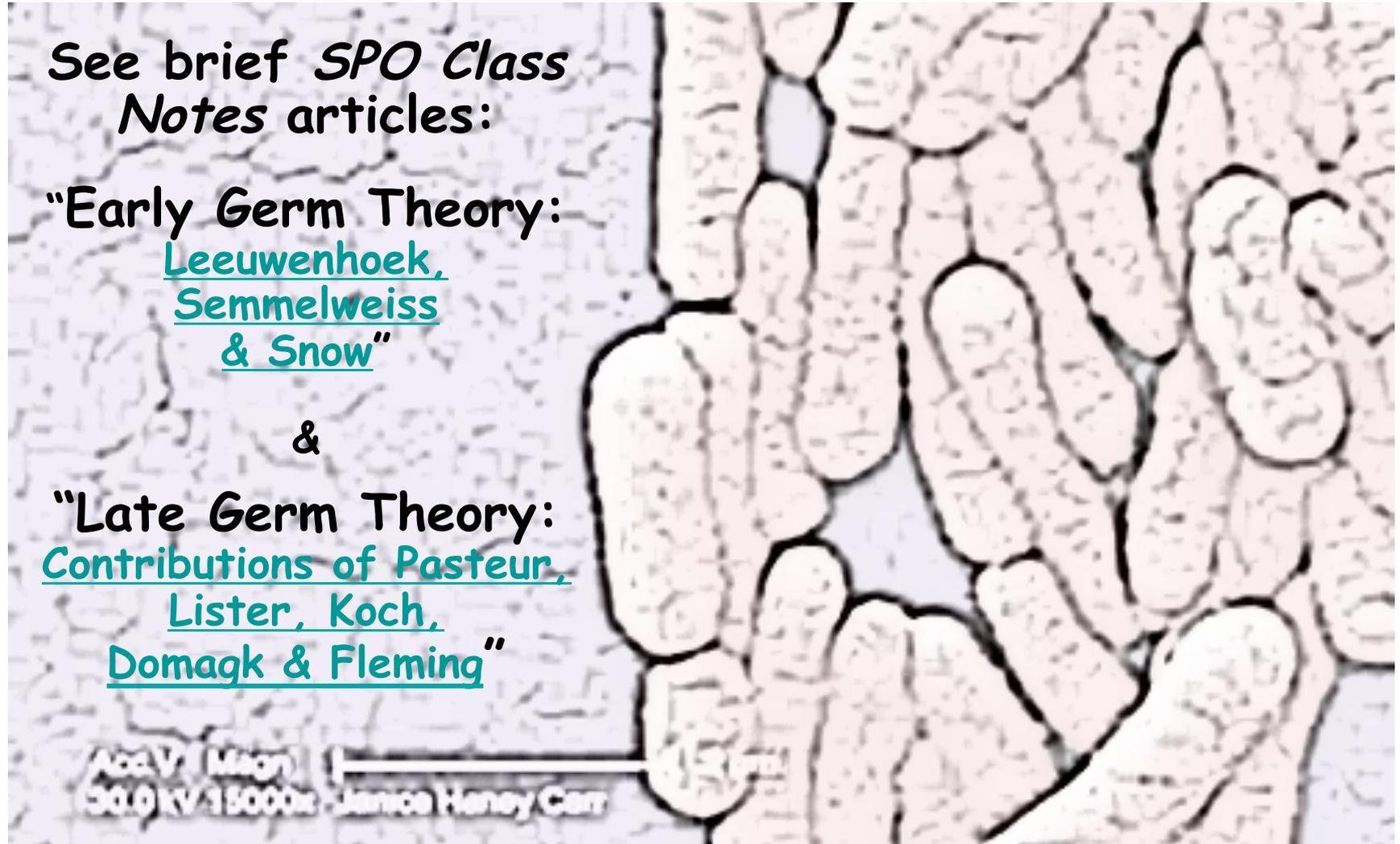
“Early Germ Theory:

Leeuwenhoek,  
Semmelweiss  
& Snow”

&

“Late Germ Theory:

Contributions of Pasteur,  
Lister, Koch,  
Domagk & Fleming”

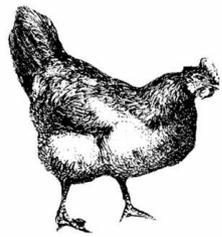


# Early History of Immunology

## Dr. Edward Jenner and the First Vaccine

- Rural physician aware of farm workers' belief that if you had cowpox in past, you wouldn't get smallpox.
- **Cowpox** caused mild discomfort, aching, a few pustules, some swelling...symptoms that disappeared in a few days.
- In contrast, **smallpox** caused massive disfigurement, sometimes blindness, and often death.
- Jenner, in the late 1700s, made small incisions or punctures with cowpox material in arms of human subjects in order to prevent smallpox.
- At first his peers doubted the safety and efficacy of his treatment, but eventually the value of the cowpox inoculum was recognized.
- Jenner's works are said to have saved more lives than the efforts of any other person in history.

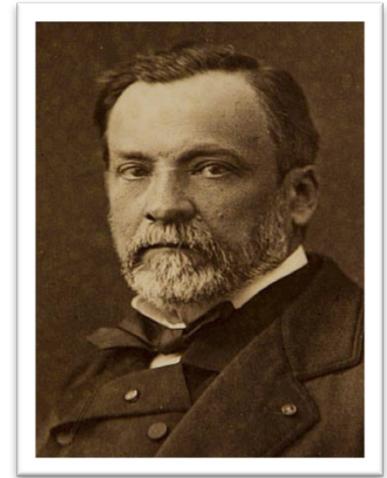




# Early History of Immunology

## Pasteur's Attenuated Vaccines

- Individuals who recover from an infectious disease sometimes immune from future attack.
- Prompted Pasteur to try to find a way to prevent fowl cholera in chickens.
- Colleague of Pasteur's postponed inoculations of cholera into a group of chickens, a remarkable discovery resulted.
- Inoculation with these neglected cultures made the chickens immune to fowl cholera.
- The microbes had been **weakened or attenuated**.
- Pasteur also modified other organisms (anthrax and the virus causing rabies).
- Ultimately created inoculation procedures ... **vaccinations**.
- **REVIEW!** See brief *SPO Class Notes* article: "[Early History of Immunology: Edward Jenner & Louis Pasteur](#)"



1822 - 1895

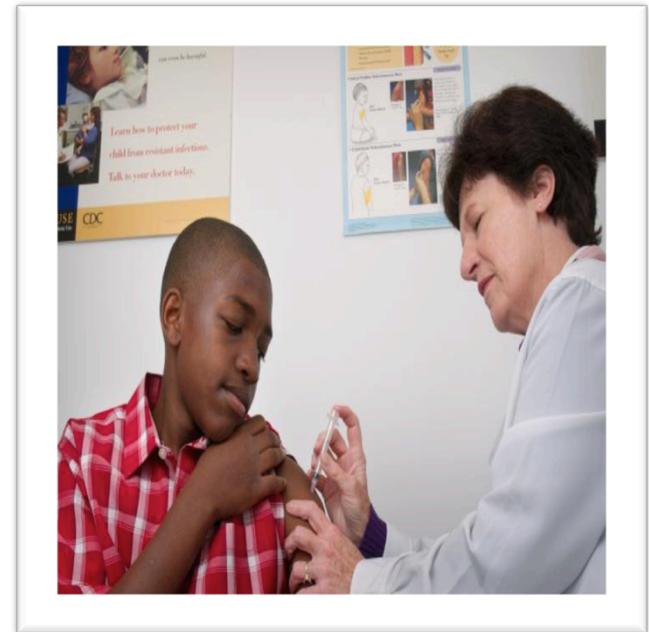
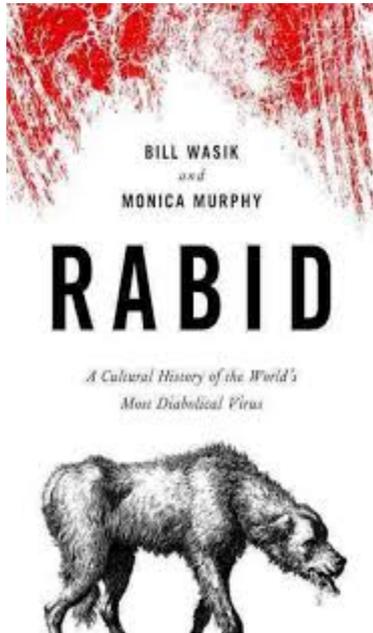


Image: [Louis Pasteur](#), Pierre Lamy Petit, French circa 1866, Boy being vaccinated, [PHIL](#) #9364.

# Disease, Please! Rabies

- Rabies is an infectious disease caused by a **virus**.
- Mortality rate of nearly 100%.
- Description of rabies, from RadioLab "[Rodney vs. Death](#)" Podcast, from WNYC Public Radio (segment time 8:00 to 11:06). See [Virtual Microbiology Classroom Main Page](#) for homework assignment on this podcast.
- [Video of rabies in humans.](#)



- Pasteur developed his rabies vaccine by growing the virus in rabbits, then drying the infected nerve tissue to weaken (attenuate) the virus.
- On July 6, 1885, the vaccine was administered to a 9-year-old boy who had been attacked by a rabid dog. The boy did not develop symptoms of rabies and survived.
- Most rabies cases reported to the CDC each year occur in wild animals like raccoons, skunks, bats, and foxes.



Rabies virus looks like little tiny bullets!

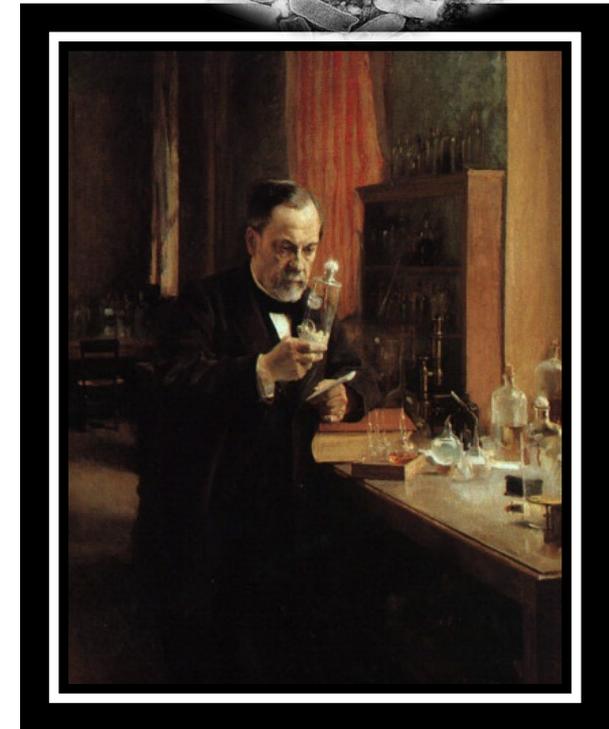


Image: Cover of book [Rabid](#), Rabies virus as seen through electron microscope, [PHIL](#), image #5611; [Portrait of Louis Pasteur in his lab 1885](#), by Albert Edelfelt

# Confused?

Here are links to fun resources that further explain aerobic respiration:



- [History Microbiology Main Page](#) on the Virtual Microbiology Classroom of [Science Prof Online](#).
- ["Got the Time"](#) music video by Anthrax.
- [Experiments Testing Spontaneous Generation](#), animation and quiz.
- [The Dress Lodger](#), a historical novel about cholera, prostitution and body snatching set in Sunderland England 1831.
- [Brief History of Microbiology](#) online flashcards from Quizlet.
- [Microbe Hunters](#), a classic book by Paul De Kruif Harvest Books.
- Play ["Fling The Teacher"](#), an interactive "Medicine: Infectious Disease" Quiz in which you get to build a teacher (victim), then fling them with a trebuchet if you correctly answer the quiz questions.
- [History of Microbiology](#) interactive timeline from Microbe World.
- Play [Disease Defenders](#) educational video game, Rice University.

*(You must be in PPT slideshow view to click on links.)*

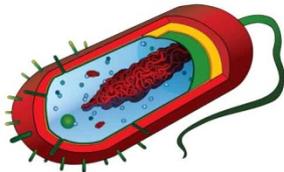


# Are microbes intimidating you?

*Do yourself a favor. Use the...*

## Virtual Microbiology Classroom (VMC) !

The VMC is full of resources to help you succeed,  
including:



- practice test questions
- review questions
- study guides and learning objectives

You can access the VMC by going to the Science Prof Online website  
[www.ScienceProfOnline.com](http://www.ScienceProfOnline.com)