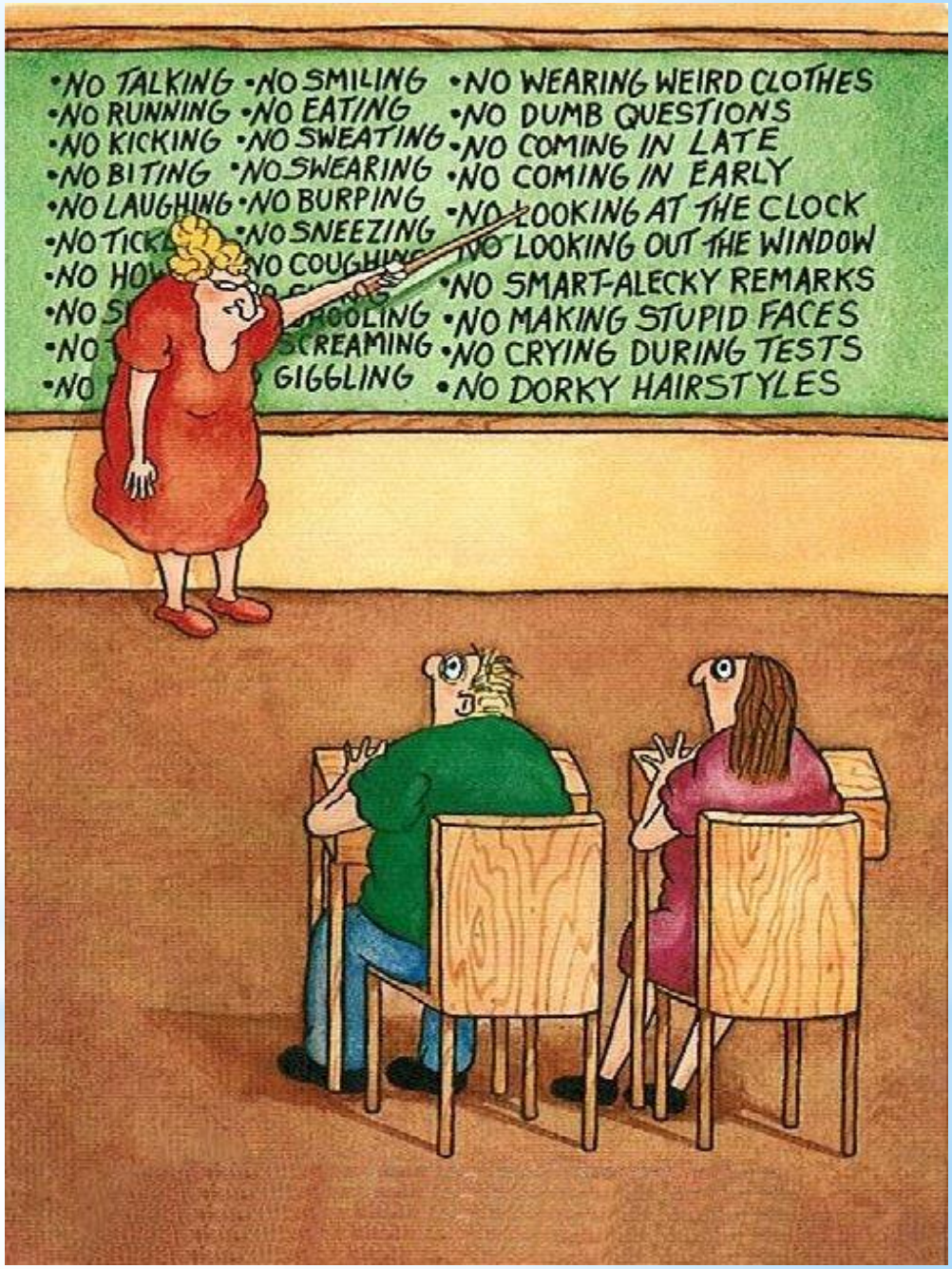

Good Afternoon!

Some Housekeeping Rules Before We Begin



The Good

The Bad

The Ugly

Olli Spring 2020 Semester

January 28 to March 17

Néstor A. Ramírez, MD, MPH, FAAP

Hope You Get a Charge From Today's Session!

February 11, 2020

Rivalries Between Scientists

Session 3

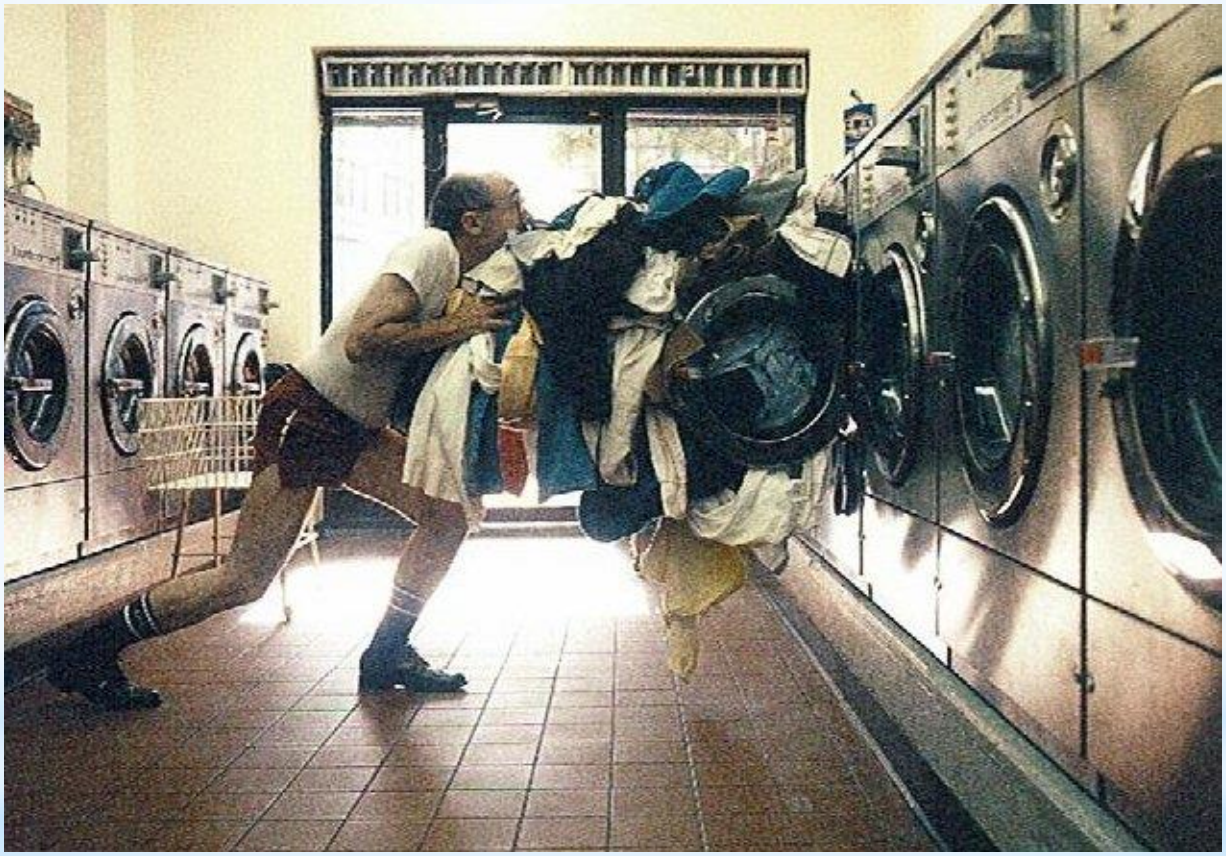
February 11, 2020

Two sides of an Issue

Of Inventors and Discoverers

In Medicine and Science, credit is given to the one who perfects an idea and tells others about it, not to the one who has the idea first.

J. H. Tiner 1999



Timeline of Great Inventions

1811: Friedrich Koenig invents the first powered printing press.

1816: Francis Ronalds builds the first electric telegraph.

1822: Nicéphore Niépcethe invents first photographic process.

1837: Samuel Morse invents Morse code.

1841: Alexander Bain devises a printing telegraph.

1864: Louis Pasteur invents the pasteurization process.

1867: Alfred Nobel invents Dynamite.

1876: Alexander Graham Bell patents the telephone.

1879 :Thomas Edison patents a functional light bulb.

1903: Orville and Wilbur Wright invent fixed wing motorized aircraft.

Haeckel, Remak and Virchow

Cells and Evolution

Ernst Heinrich Haeckel(1834-1919)

German evolutionist, morphologist, and developmental biologist.

Argued that "**ontogeny recapitulates phylogeny**" (later proved wrong).

The development of an organism (*ontogeny*) expresses all the intermediate forms of its ancestors throughout evolution (*phylogeny*).

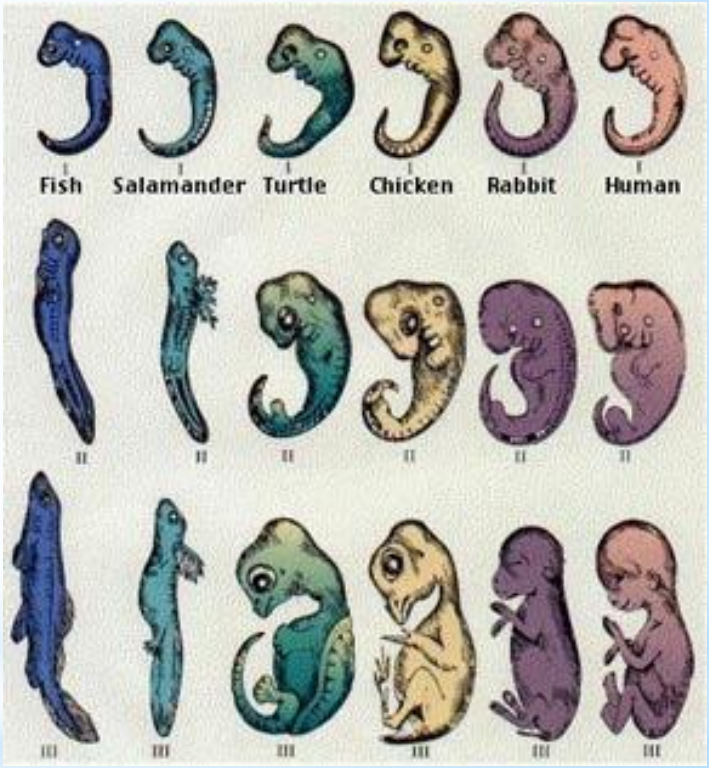
The 1st exponent of Lamarckian evolution in the German-speaking world.

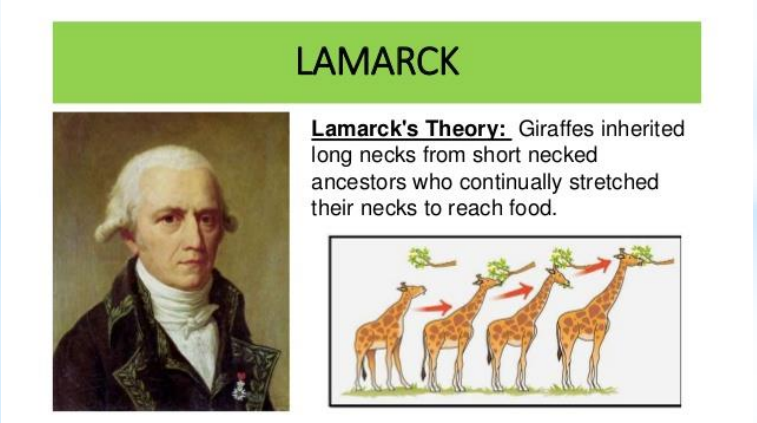
Decades-long conflict with Virchow, the anti-evolutionary Prussian anthropologist and pathologist.

His attempt to describe human evolution in racial terms later became a part of the pseudo-scientific basis for Nazism.

Haeckel's Ontogeny Theory

* Theory of recapitulation, "biogenetic law" or "embryological parallelism."
* *Ontogeny* is primarily concerned with the change in shape of the embryo.
* *Phylogeny* is the evolutionary history of a species and applies to entire populations
* Supported Lamarckian evolution.





Robert Remak (1815-1865) (1)

Jewish-Polish-German embryologist, physiologist, & neurologist from Prussia.

Discovered that the origin of cells was by the division of pre-existing cells.

Proved Pasteur's principles that spontaneous generation does not exist.

Due to his Jewish faith, he was denied full professor status.

Later in life appointed assistant professor: 1st Jew teacher in Berlin U.

He was never fully recognized for his discoveries.

Robert Remak (2)

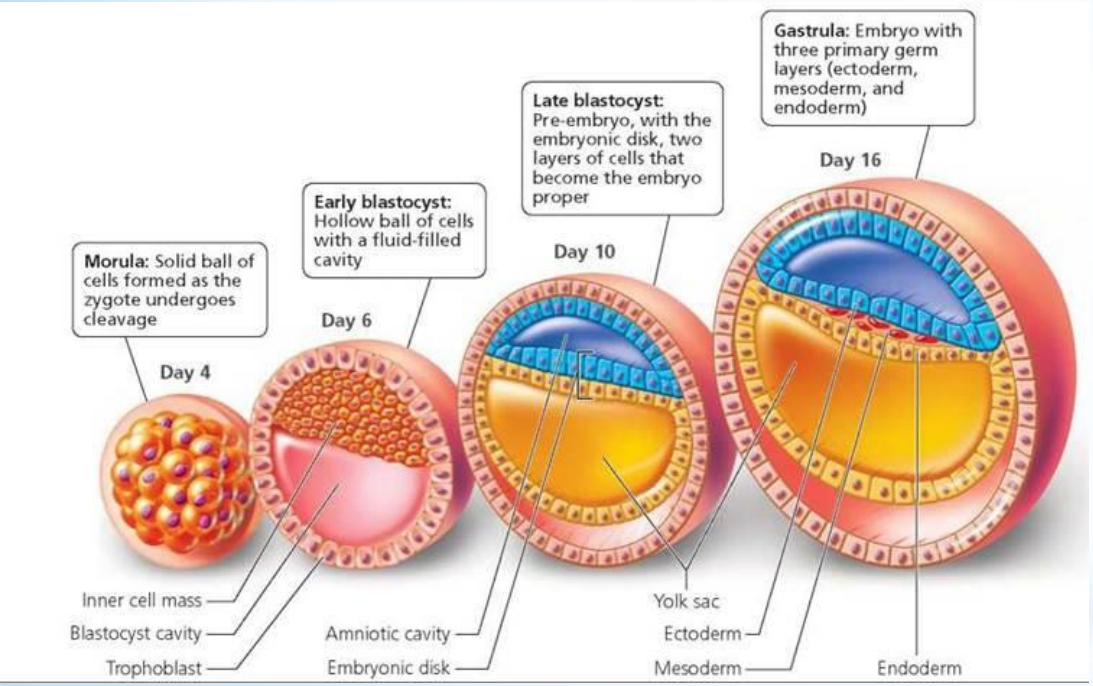
* Wrote on cell division, claimed Schleiden and Schawnn were incorrect about generation schemes. (1852)

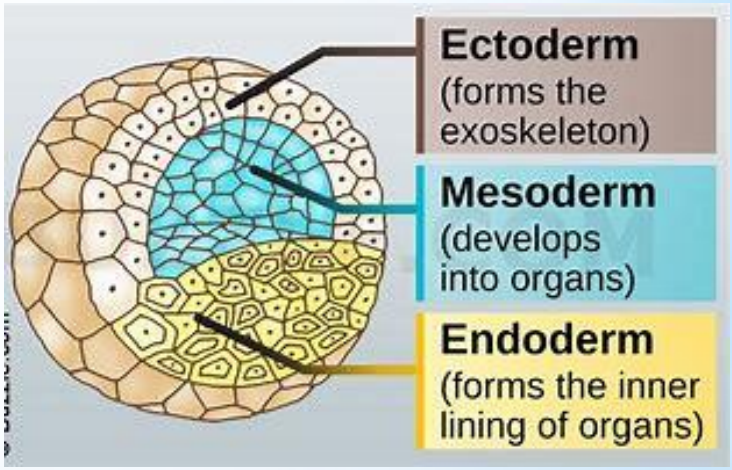
* Said that "binary fission", first introduced by Dumortier, was how reproduction of new animal cells were made.

* Many scientists did not agree with him.

* Remak was later plagiarized by Rudolf Virchow who published Remak's findings as his own in 1855.

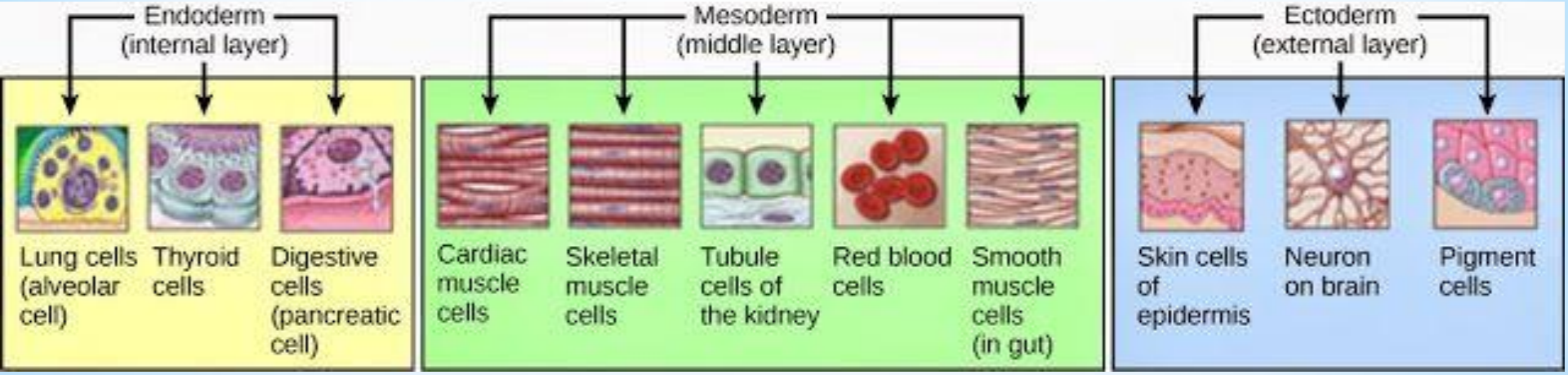
Remak and Germ Cell Layers





Remak's Germ Cell Layers

Reduced Karl Ernst von Baer's four germ layers to three.



Knowledge About Cell Division

Barthelemy Dumortier, a botanist, was 1st scientist to see cell division in plants, called it *binary fission*. (1832).

Matthias Schleiden, botanist, said plant tissues were made up of cells and that a new plant arose from one cell. (1838)

Theodor Schwann, biologist, said that animal tissue was composed of cells. (1839)

Robert Remak, embryologist, confirmed Dumortier's cell division findings in animal cells. (1844)

Rudolf Virchow, physiologist, added a 3rd part to cell theory, plagiarized Remak, published as his own findings.(1855)

Additions and Contradictions to contemporaneous research.

Rudolf Ludwig Carl Virchow
(1821-1902)

* Critical of "Nordic mysticism" regarding the Aryan race.
* Called Darwin an "ignoramus" and Ernst Haeckel a "fool".
* Said Neanderthal man was nothing but a deformed human.
* Proposed the third of 3 basic dictums of modern cell theory:
  * All living organisms are composed of one or more cells.
  * Cell is basic unit of structure and organization in organisms.
  * All cells arise from pre-existing cells. (*omnis cellula e cellula*).

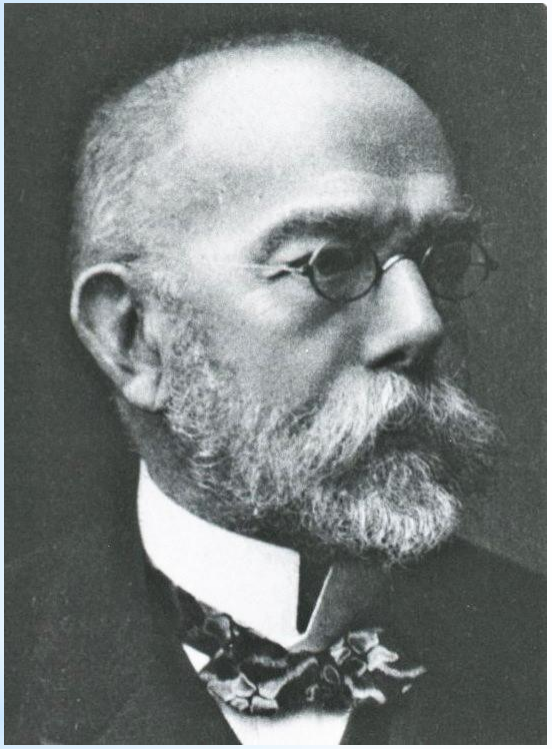
Virchow and Remak

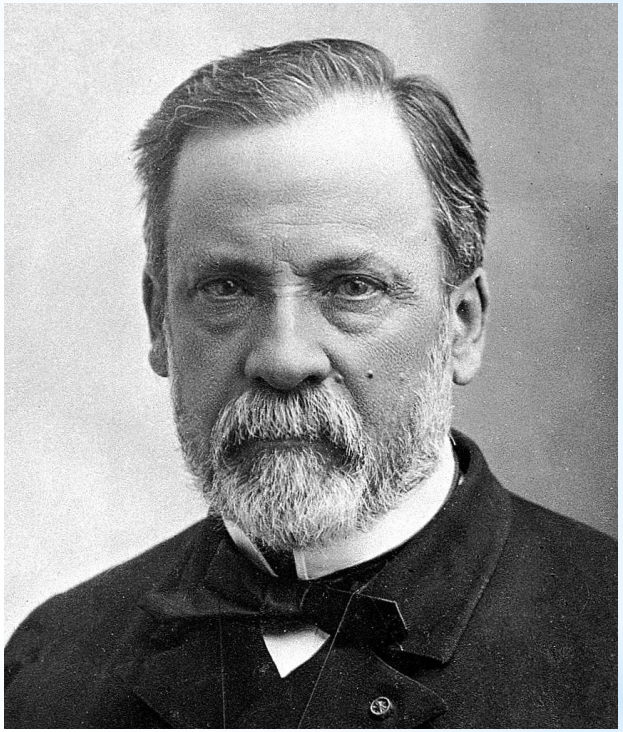
* Idea that all cells come from pre-existing cells was proposed by Robert Remak (1815-1865).

* Virchow realized that Remak was right, so he published Remak's work as his own in 1855, causing a falling-out between them.

* Virchow plagiarized Remak and did not give him credit.

* Remak had sought the position of prosector at LaCharité in Berlin but it was given to Virchow.





Koch and Pasteur

Giants of Microbiology

Pasteur and Koch(2)

Louis Pasteur

* Made vaccines for fowl cholera, anthrax and rabies.
* Found cause of silkworm disease.
* Found reason for wine spoilage.
* Identified the microbes for swine erysipelas, childbirth fever and pneumonia.
* Used attenuated agents to protect.
* Invented Pasteurization.
* Died in 1895 before Nobel started.
* Arrogant, defensive, scornful, cocky, critical, irritable, impatient.

Robert Koch

* Proved that germs cause disease.
* Discovered the germ for TB and cholera.
* Isolated the anthrax bacillus and proved it formed long-lived spores.
* Produced tuberculin as therapy.
* Introduced pure cultures.
* Staining and solid culture plates.
* 4 Postulates of Infection.
* One germ = One disease
* 1905 Nobel for microbiology.
* Methodical, scientific, persistent, aggressive, Germanic

Koch's Postulates

* A specific microorganism must be found in all creatures with the disease, but should not be found in healthy ones.

* The microorganism must be isolated from a diseased organism and grown in pure culture.

* The cultured microorganism should cause the specific disease when introduced into a healthy host.

* The microorganism retrieved from the inoculated, experimental host must be identical to the original specific causative agent.

Pasteur (1822-1895)

- Development of the germ theory of disease
- Use of vaccines to prevent animal diseases.
- Studied contamination of wine and beer by airborne yeast.
- On Pasteur's advice, Lister began to systematically sterilize his instruments, bandages and sprayed phenol solutions in his OR's .
- Pasteur told physicians that avoidance of microbes is avoidance of infection.

Pasteur

* Pasteur refused to patent his findings.
* Believed they should be for the benefit of all mankind.
* Created the Pasteur Institute for that purpose.
* "Each of my efforts until my last day will carry an epigraph: Hatred of Prussia, Vengeance, Vengeance!"

Pasteur

- Colorful, flamboyant and somewhat eccentric.
- Knack for public relations and "unbecoming showmanship".
- Practiced deception to defeat his rivals.
- Modified and even falsified results after the fact.

- Awarded Medical degree by Bonn University (1868)
- Returned it with an insulting letter to Dean (1871)
- Lied about some of his methods.
- Many of his "discoveries" were the work of others.

Pasteur

* Joseph Meister, the first person to receive the rabies vaccine, served at the Pasteur Institute as a Gatekeeper.

* In 1940, 45 years after his treatment, he was ordered by the German occupiers of Paris to open Pasteur's crypt.

* Rather than comply, Joseph Meister committed suicide!

Koch on Pasteur

Koch thinks Pasteur went much too fast and too far.

Said the discovery and development of protective inoculation was absolutely valueless.

Pasteur's methods and results were unreliable due to:

- Absence of proper microscopical research.
- Inoculation of mixed, not pure, substances.
- Selection of unsuitable animals for the experiments.

Said Pasteur's false methods of investigation inevitably led to false conclusions.

Pasteur had mistaken interpretations of pathological processes and symptoms of disease.

Pasteur vs Koch(1)

The dispute was tinged with acrimony due to the difference in nationalities, language incompatibility and the difference in ages.

Franco-Prussian War led French to bitterness, hatred and demand for revenge. → Pasteur lived and taught in German-annexed Alsace. → Rivalry extended from national to personal. → Pasteur was chemist and microbiologist before becoming a doctor.

Pasteur and Koch

* German Robert Koch and French Louis Pasteur, got into a duel with national rivalry and language barrier as their weapons.

* Both geniuses clashed when they started working on the same disease: Anthrax.

* Things started heating up when they met at a Medical Congress in London in 1881.

* Later, the game of one-upmanship continued, but in the end the rivalry benefited mankind.

Pasteur vs Koch

Both had a profound reciprocal misjudgment of their work.

Pasteur didn't read German, Koch understood French poorly.

In Geneva, Pasteur listed and commented appropriately and properly on the work of Koch.

Pasteur referred to the *German Collected works* (*Recueil allemand*).

Koch mistook the word ***recueil*** (collection) for ***orgueil*** (pride).

Felt his self-respect deeply wounded and heard *German pride* as a grave insult.

Koch angrily interrupted Pasteur to protest the disrespectful terms.

Koch (1843-1910)

- Occasional aggressive tone and criticizing attitude.
- Exhibited the failings he reproved in Pasteur, when he announced tuberculin as a cure for TB:
  - Rush to proclaim definitive results on work in progress.
  - Fondness for publicity and self-promotion.
  - Desire to impose his authority.
  - Opposition to any opinion contrary to his work.
- Profound disdain towards Frenchmen, especially Pasteur.
- Often disparaged and discredited Pasteur's findings.
- Patented several findings and sold them for millions of marks.

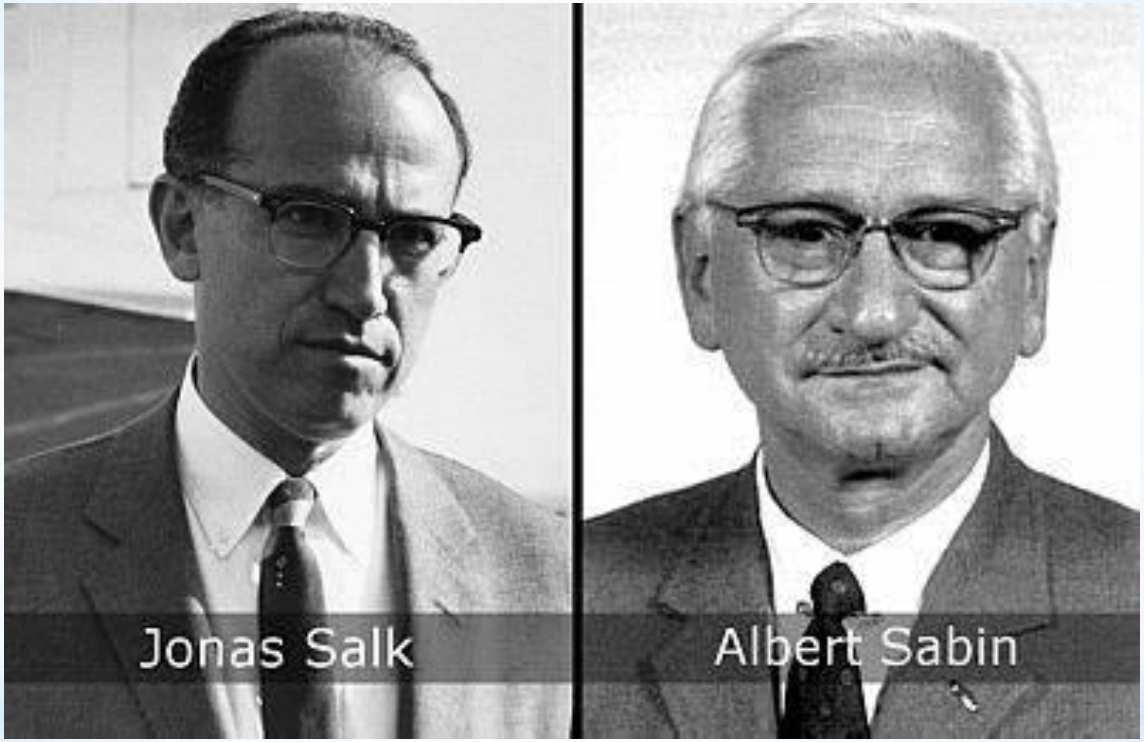
Koch on Pasteur

* Preventive inoculation with modified virus should not be established until protective inoculation for bacterial diseases of mankind was done.

* Pasteur should not make a secret of his processes and methods.

* Pasteur should have more regard for truth and scientific accuracy in his statements.

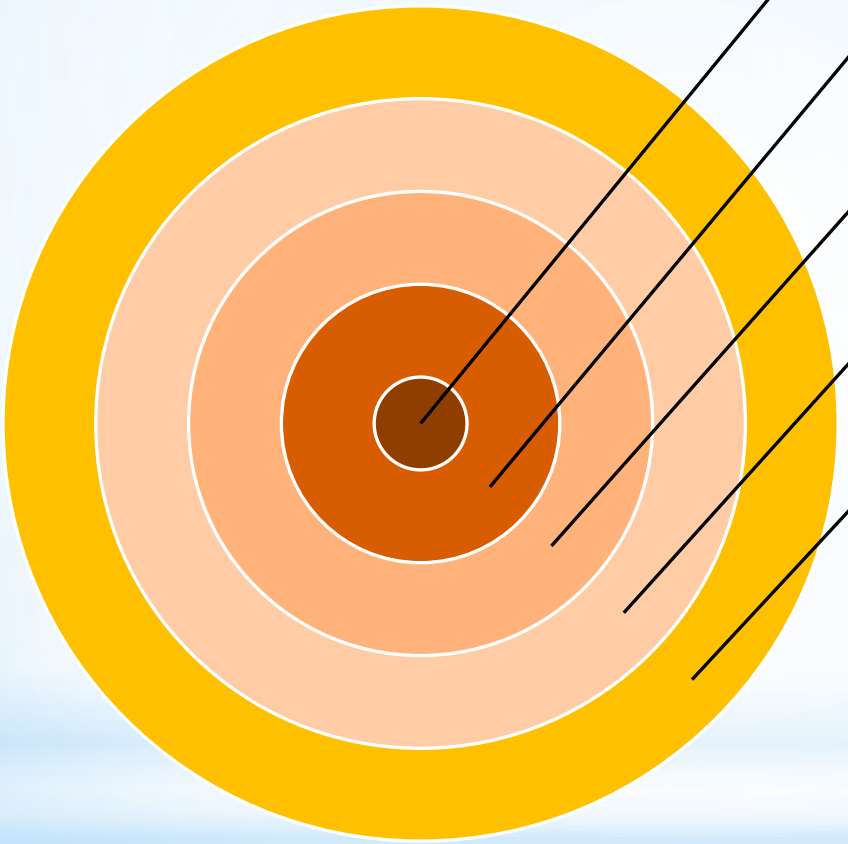
* All future workers in his department should proceed with greater "objectiveness," and with a more conscientious self-criticism.



Salk and Sabin

The Polio Vaccine Battle

Polio in US



In 1916, a summer outbreak of polio started in NYC.

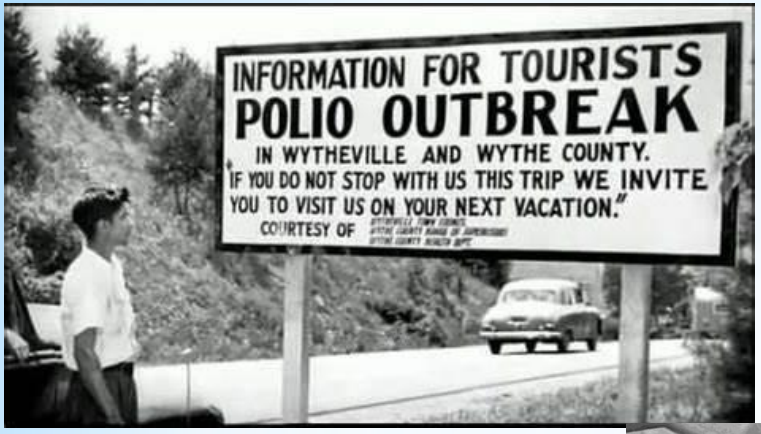
Epidemic lasted through October.

6,000 Americans lost their lives.

NYC had 8,900 cases, with 2,400 deaths.

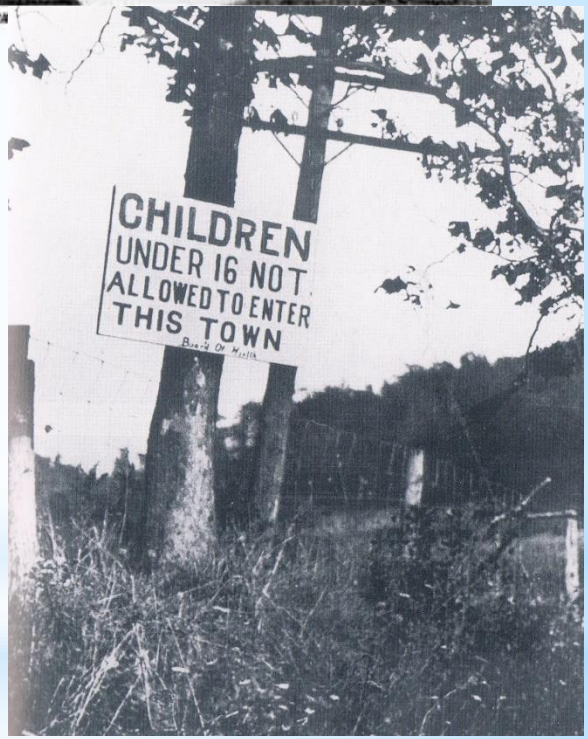
80% of deaths were children under five.

In 1921, at the age of 39, FDR got polio while on vacation in Canada.


INFORMATION FOR TOURISTS
POLIO OUTBREAK
IN WYTHEVILLE AND WYTHE COUNTY.
IF YOU DO NOT STOP WITH US THIS TRIP WE INVITE
YOU TO VISIT US ON YOUR NEXT VACATION."
COURTESY OF


UNIVERSITY OF ILLINOIS


NOTICE
THIS HOUSE IS UNDER
QUARANTINE
No person shall enter or leave this house nor remove any person or thing from it without the permission of the Local Health Officer.
Any person removing or interfering with this card without authority, is liable to a fine of Fifty Dollars.
Per Order, LOCAL HEALTH OFFICER.


CHILDREN
UNDER 16 NOT
ALLOWED TO ENTER
THIS TOWN

Polio facts

Between 1940's and 1950's:

- 10X more children killed in accidents.
- 3X more killed by cancer.

NF turned a horrific but relatively uncommon disease into the most feared affliction of its time.

Disease of white middle-class children, Blacks not as succeptible.

Not caused by filth, squalor or poverty.

The National Foundation March of Dimes (1)

Roosevelt bought the Georgia Warm Springs resort and created the GWS Foundation in 12926.

Built a “little White House” where he died in 1945.

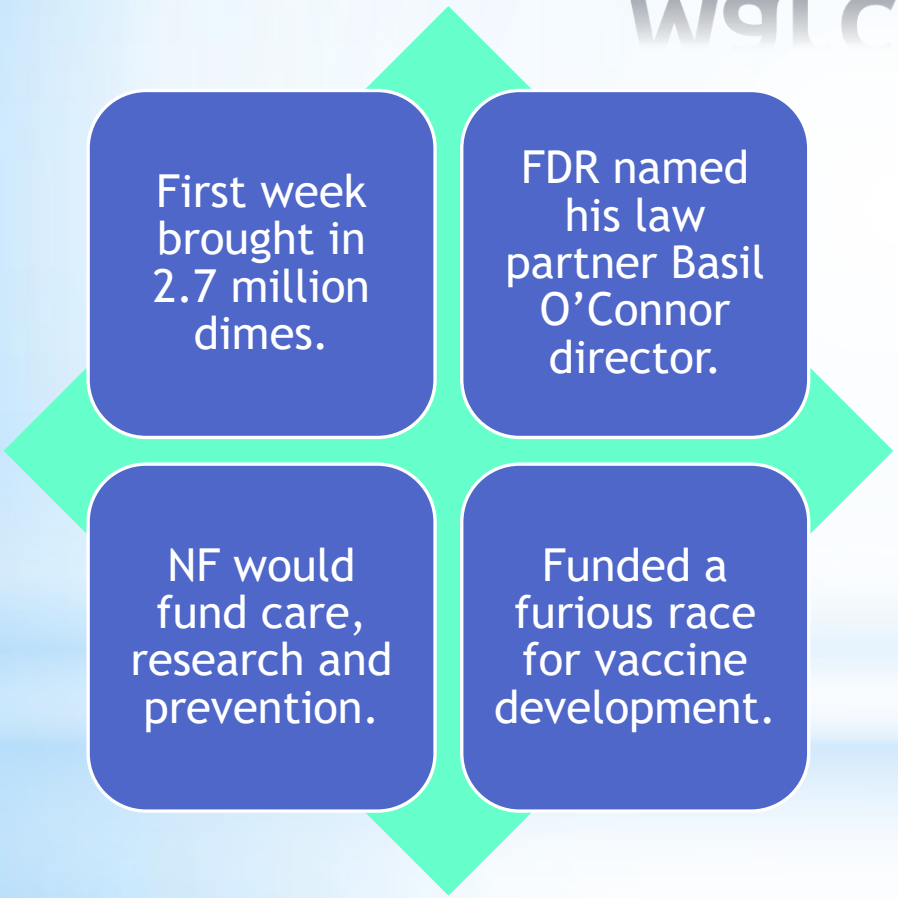
GWSF became “The National Foundation for Infantile Paralysis” in 1938.

Fund-raising efforts were massive and nation-wide.

Eddie Cantor suggested the slogan “March of Dimes”.

The dime became the emblem of the fight against polio.

The National Foundation March of Dimes (2)



Made polio seem more ominous, frequent and curable than other diseases.

History of Polio Vaccines

* Two separate teams, led by John Kolmer and Maurice Brodie developed polio vaccines.

* Reported their results at the annual meeting of the American Public Health Association in November **1935.**

* Both efforts were cancelled due to the angry reaction from other researchers, because vaccinated children had died in both studies.

* No researchers dared attempt a polio vaccine for another 20 years!!!

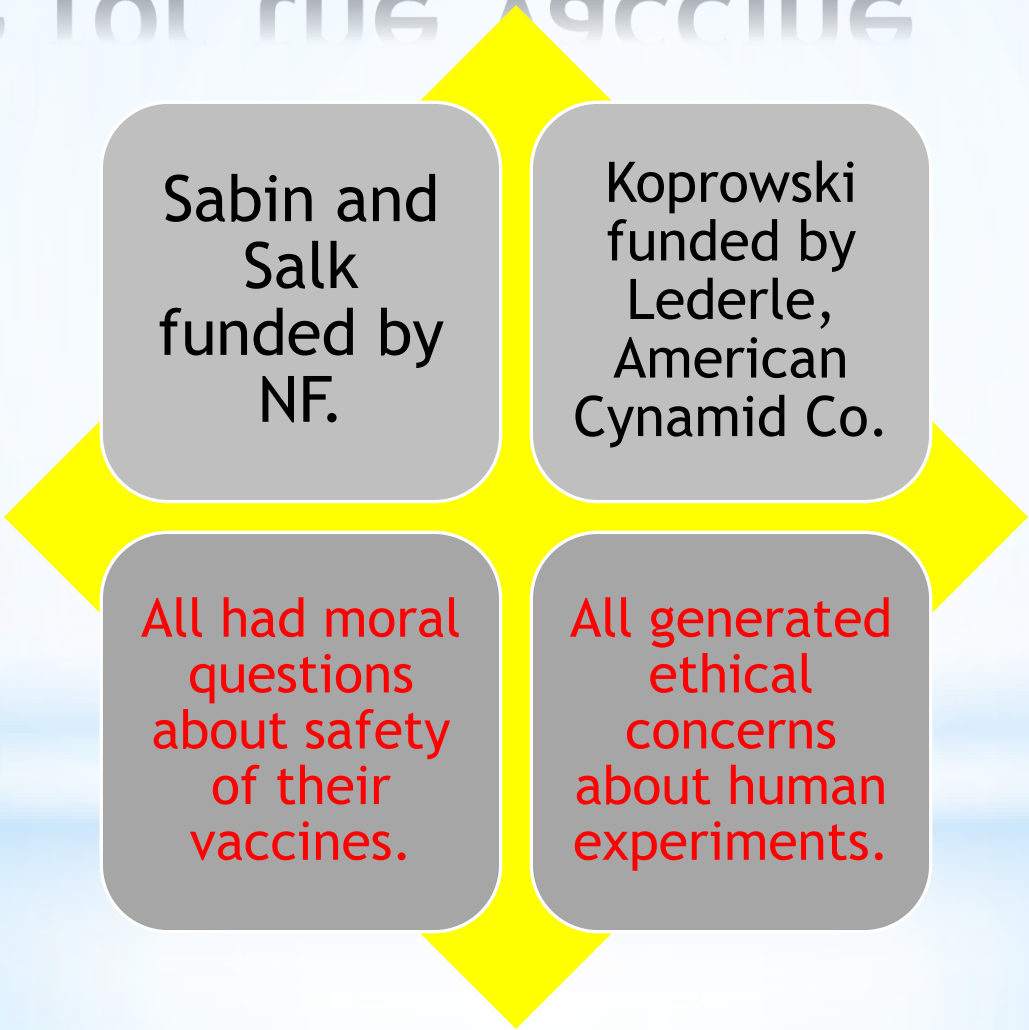
Hilary Koprowski (1916-2013)

* **Koprowski**, Polish virologist inventor of the world's first effective live polio vaccine.
* Tried it on himself in 1948, and on February 27, 1950 gave it to 20 children at Letchworth Village, a home for disabled persons in Rockland County, New York. (Consent???)
* None developed any complications.
* Target of accusations in the "OPV AIDS hypothesis“ that his Africa polio-vaccine trials introduced the HIV-1 virus to humans.

Race for the Vaccine (1)

Three main contestants in the race:	Albert Sabin, University of Cincinnati.	Hilary Koprowski, Lederle Laboratories.	Jonas Salk, University of Pittsburgh.
Sabin & Koprowski championed a live-virus vaccine.	Triggers a natural infection.	Infection too weak to vcause serious disease.	Generates long-lasting antibodies.
Salk favored a killed-virus version.	Stimulates immune system.	Produces antibodies w/o disease.	

Race for the Vaccine



National Foundation

* Favored simpler killed virus vaccine (Salk).
* Thought it had fewer risks for the public.
* Believed it could be marketed more quickly.
* Without government oversight, conducted the largest medical experiment in US history (Salk Field Test, 1954).
* 2 million school children throughout the country.

Salk Vaccine Results

* Six companies started producing and selling vaccine in US.
* Lobbied intensely in Washington to prevent government manufacture and distribution.
* A batch from Cutter labs was contaminated with live virus and caused 260 cases with 192 paralyzed children.
* Salk lost prestige, Sabin publicly accused him and blamed him.
* Government agencies and corporations had come to dominate medical science, so vaccine development had become a very different game.

JONAS EDWARD SALK 1914-1995

Other polio researchers found this kind of grandstanding intolerable.

Never forgave Salk for the TIME cover, for the photo spreads in Life, and for letting himself be Basil O'Connor's poster boy.

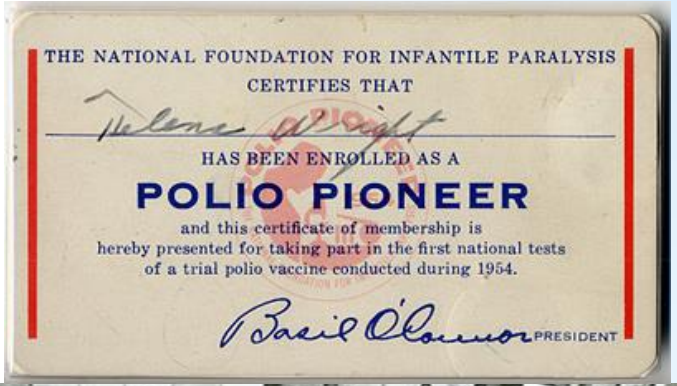
They accused him of allowing "outsiders" to dictate the pace and direction of his work.

Many MD's thought free, massive vaccination of children was "perilous socialized medicine".

Congressional Gold Medal in 1955 and in 1977 the Presidential Medal of Freedom.

1977.

Never was admitted to the National Academy of Sciences.


THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS
CERTIFIES THAT

Helene Wright

HAS BEEN ENROLLED AS A

POLIO PIONEER

and this certificate of membership is
hereby presented for taking part in the first national tests
of a trial polio vaccine conducted during 1954.

Basil O'Connor PRESIDENT

Sabin

* After harshly criticizing Koprowski, Sabin attempted to do research on mentally “defective children”.
* He did 30 prisoners in Chillicothe, OH in 1954-1955.
* He went to the Soviet Union, and vaccinated 10 million children.
* Reportedly campaign was so successful, Soviet government. decided to vaccinate everyone under age 20 (70M).
* In Russia: no control groups, no placebo, no exclusions.

Jonas Salk

"It was pure kitchen chemistry, Salk didn't discover anything."(Sabin)

Sabin said Salk just refined an old idea: kill viruses with formaldehyde to turn them into a vaccine.

Ed Murrow asked Salk, "Who owns the patent on this vaccine?" He replied: "Well, the people. There is no patent. Could you patent the sun?"

Nothing to patent: researchers are not allowed rights and royalties for discoveries made with NF money…

Salk and Sabin Vaccines

Comparison of poliovirus vaccines

Characteristic	IPV / inactivated Salk	OPV / attenuated Sabin
Prevents disease	Yes	Yes
Induces humoral IgG	Yes	Yes
Induces intestinal sIgA	No	Yes
Prevents intestinal colonization	No	Yes
Secondary (herd) protection by spread to others	No	Yes
Reverts to virulence	No	Yes, very rarely
May cause disease in immuno-compromised	No	Yes

vaccines might cause the disease

IPV (Salk)

* 90% or more of individuals develop protective antibodies to all 3 serotypes of polio virus after 2 doses, and at least **99%** are immune to polio virus following 3 doses.

* The duration of immunity induced by IPV is not known with certainty.

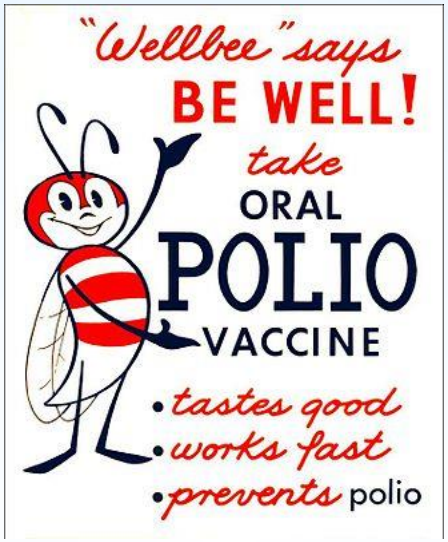
* A complete series is thought to provide protection for many years.

OPV (Sabin)

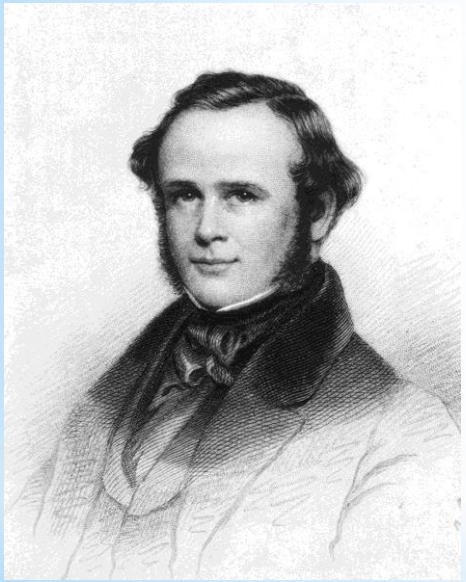
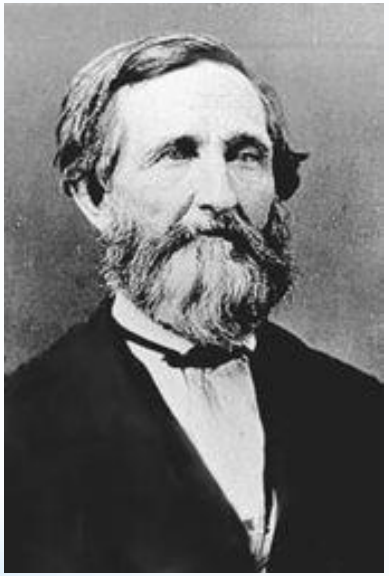
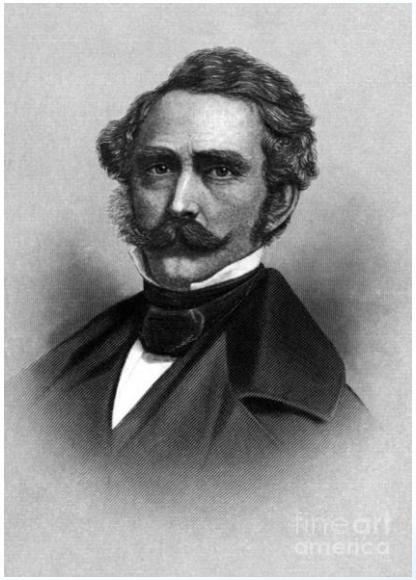
* One dose of OPV produces immunity to all three poliovirus serotypes in 50% of recipients.

* Three doses of OPV produce protective antibodies to all 3 poliovirus types in more than 95% of recipients.

* The live virus used in the vaccine can *rarely* shed in the stool and can *rarely* spread to others within a community.


"Wellbee" says
BE WELL!
take
ORAL
POLIO
VACCINE
• tastes good
• works fast
• prevents polio


END
POLIO
NOW
ROTARY
INTERNATIONAL
WORLD
POLIO
DAY
OCTOBER 24TH
Rotary
"Rotary in particular has inspired my own personal commitment to get deeply involved in achieving eradication." Bill Gates

Wells, Long,Morton, Jackson

Anesthesia

The *Painful* History of Anesthesia (1)

* Through History, mankind has used different means to alleviate pain in injuries and procedures, for example:
  * Heavy bleeding until patient lost consciousness!
  * Alcohol
  * Mandragora, henbane, coca, opiates
  * Inhaled gases: Chloroform, nitrous oxide, ether
  * Physical restraints.

* Invention plagued by greed for fame, glory and **patents.**

The *Painful* History of Anesthesia (2)

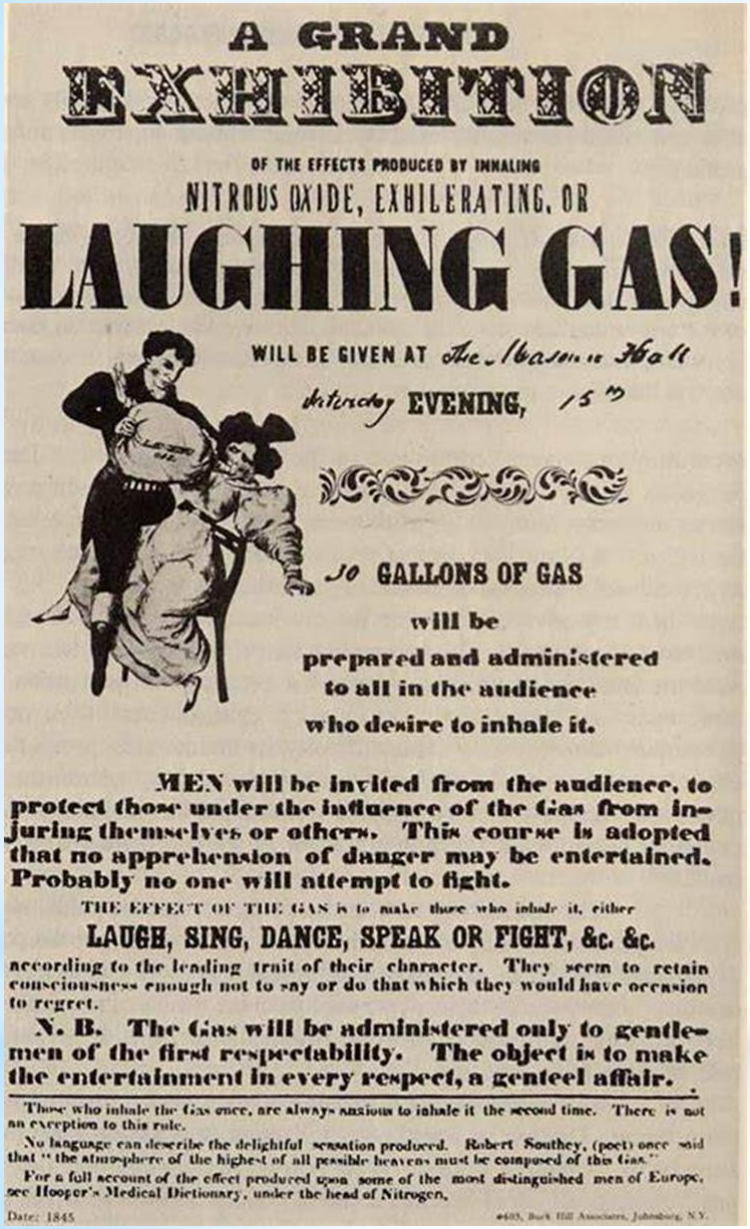
* 13th Century Ramon Llull, Spanish alchemist mixed vitriol with alcohol and distilled it to get "*sweet vitriol*".

* Attributed to Valerius Cordus, German botanist in 16th century.

* Used by doctors for other things, but it took 600 years before they learned that inhaling this achieves profound anesthesia.

* In 1700's Joseph Priestley described nitrous oxide for painful oral conditions and its use in ***laughing parties***.

* He used it, but did not pursue the pain dulling idea!



A GRAND

EXHIBITION

OF THE EFFECTS PRODUCED BY INHALING

NITROUS OXIDE, EXHILERATING, OR

LAUGHING GAS!

WILL BE GIVEN AT The Masonic Hall

Saturday EVENING, 15th

10 GALLONS OF GAS

will be

prepared and administered

to all in the audience

who desire to inhale it.

MEN will be invited from the audience, to protect those under the influence of the Gas from injuring themselves or others. This course is adopted that no apprehension of danger may be entertained. Probably no one will attempt to fight.

THE EFFECT OF THE GAS is to make those who inhale it, either

LAUGH, SING, DANCE, SPEAK OR FIGHT, &c. &c.

according to the leading trait of their character. They seem to retain consciousness enough not to say or do that which they would have occasion to regret.

N. B. The Gas will be administered only to gentlemen of the first respectability. The object is to make the entertainment in every respect, a genteel affair.

Those who inhale the Gas once, are always anxious to inhale it the second time. There is not an exception to this rule.

No language can describe the delightful sensation produced. Robert Southey, (poet) once said that "the atmosphere of the highest of all possible heavens must be composed of this Gas."

For a full account of the effect produced upon some of the most distinguished men of Europe, see Hooper's Medical Dictionary, under the head of Nitrogen.

Date: 1845

The *Painful* History of Anesthesia (3)

- Horace Wells, dentist, thought nitrous would be useful for tooth extractions.
- In 1845, he tried it on himself, arranged public demo at Mass General with Dr. John C. Warren.
- Laughter, derision, mockery and cries of "***Humbug***" followed.
- He ended up a broken man, addicted to narcotics and chloroform.
- Jailed for throwing vitriol at a prostitute, committed suicide in prison.


Press to open
F. S. N. 6505-153-8225
0804G ¼ LB. (113.4 Gm.)
Mallinckrodt
ETHER
FOR
ANESTHESIA
PRODUCED AND TESTED SPECIFICALLY FOR ANESTHETIC USE
This highly purified ether conforms to all U.S.P. requirements and contains the ideal amount of alcohol. To preserve its original purity and to provide maximum storage stability, Mallinckrodt Ether for Anesthesia is sold only in chemically treated containers.
CAUTION: Federal law prohibits dispensing without prescription.
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ETHER
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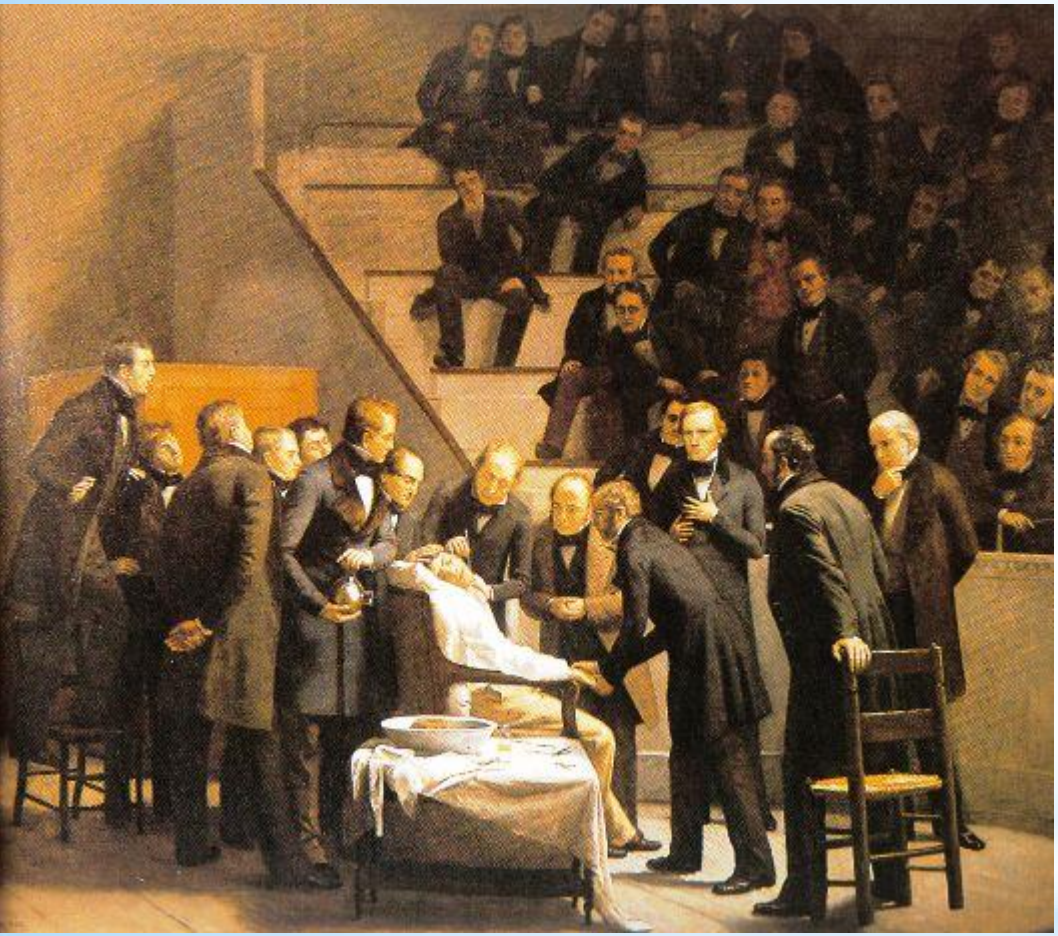
The *Painful* History of Anesthesia (4)

On 16 October 1846, John C. Warren performed surgery with ether anesthesia by William T. Morton.

The Operation theater at Mass General is known today as the Ether Dome.

Warren reportedly said: "Gentlemen, this is no humbug."

Morton published his experience as "the first public use of ether soon after.

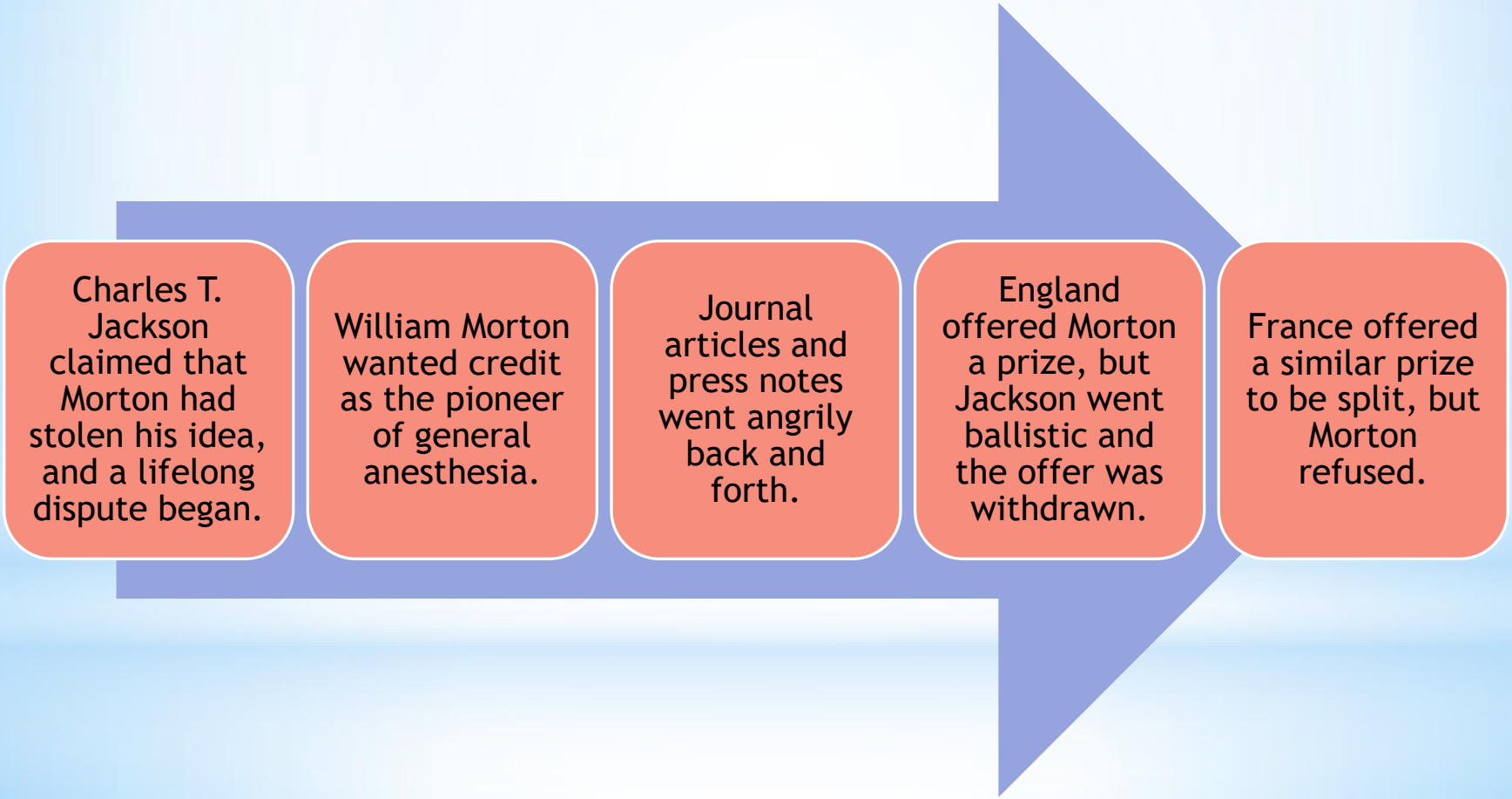


October 14, 1846 Mass General

Replica of Morton's ether ball.

Trilene and ether inhalation set.

Morton vs Jackson



Morton vs Long (1)

* Crawford W. Long started using ether in 1842, published in1849.
* Morton's demonstration occurred 4 years after Long's first use.
* Long asked William C. Dawson, Senator from Georgia to support his claim on the floor of the United States Senate.
* US Congress was dragged into the fight; Senate was split.
* Congress never ruled on one or the other.

Morton vs Long (2)

* Sir William Osler was on Morton's side.
* American College of Surgeons was on Long's side.
* Mass General Hospital commission ruled for Morton.
* Morton descended to imposture and quackery.
  * Used dyes and aromatic oils to disguise the odor of ether.
  * Tried patenting it with the name of "Letheon".
* Dr. Warren forced him to withdraw patent application.

Morton and Jackson, R.I.P.

* In July 1868, while riding in a carriage in NYC, William Morton saw a newspaper account favorable to Jackson.

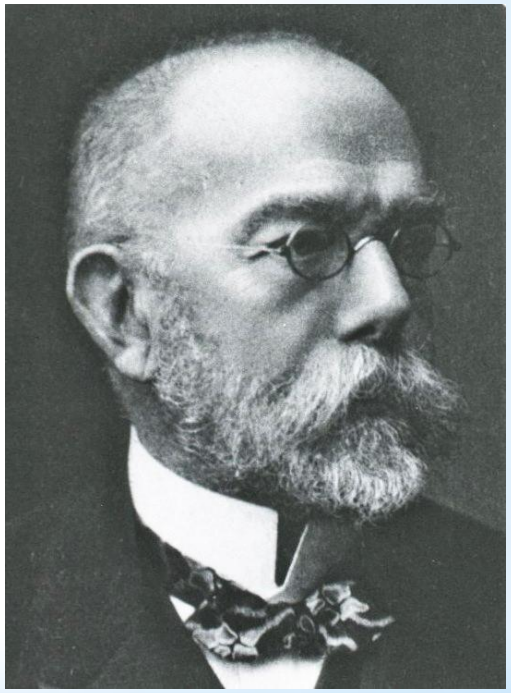
* His anger caused a stroke and he died a few days later.

* In 1873, Jackson, walking through a Boston cemetery saw Morton's tombstone calling him "Inventor of anesthetic inhalation".

* His anger and savage jealousy caused him to go totally mad.

* Found raving by the tombstone, he was taken to the McLean asylum where he died in 1880.

Ross Grassi Koch



Malaria Research

Giovanni Battista Grassi (1854-1925)

* Italian physician and zoologist, well known for his pioneering work on parasitology and malariology.
* Professor of Comparative Zoology and Anatomy at the Universities of Catania and Rome.
* First to describe and establish the life cycle of the human malaria parasite, *Plasmodium falciparum*.
* Discovered that only female anopheles mosquitoes can transmit the disease.

Giovanni Battista Grassi (2)

Not strong, abominable eyesight.

Full of argumentative petulance.

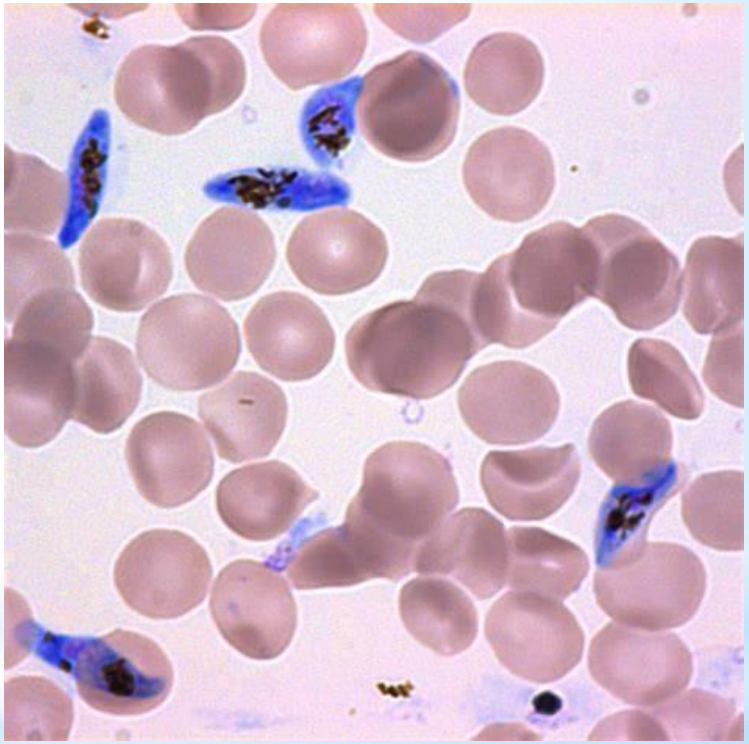
Modest but desirous of credit for all he did.

Persistent, hard worker.

Wanted Malaria research glory for Italy.

Anopheles claviger

Malaria parasite and RBC's



Ronald Ross (1857-1932) (1)

* Major in British Medical Corps in India and Burma.
* Initially started with no knowledge.
* Ross was original and energetic and wanted to find it HIS way.
* Ross was sublimely ignorant, but it was best, since he had nothing to unlearn.

Ronald Ross (2)

* Could not find malaria germ described by French doctor Laveran in 1880, thought it didn't exist.

* Met Patrick Manson, eminent English doctor.

* Manson proved that mosquitoes suck worms from Chinamen's blood, and that they developed in mosquito stomachs.

* Manson showed Ross the malaria parasite, and told him his theory.

* When he found the answer, he called Manson's theory "Nonsense!"

Grassi vs Ross (Nobel) (1)

* British army surgeon Ronald Ross, who discovered the transmission of malaria in **birds** was given the 1902 Nobel Medicine.

* Grassi's research:
  * Demonstrated complete route of transmission of **human** *Plasmodium*.
  * Correctly identified the types of malarial parasites.
  * Proved the mosquito vector, *Anopheles claviger*.

* Grassi was denied the Nobel.

Grassi Vs Ross (Nobel) (2)

* Grassi's Law: "There is no malaria without *Anopheles*" (or Infected man + anopheles mosquitoes = Malaria).

* Nobel nomination in 1902 began a fiery polemic over priority between him and Ross.

* Initial opinion of the Nobel Committee was that the prize should be shared between Ross and Grassi.

* Ross made a defamatory campaign accusing Grassi of deliberate fraud.

Koch and Malaria

* Grassi admired Koch, and was awed by him.
* Koch visited Grassi in Italy but denigrated his work.
* Koch thought malaria went from man to man!
* Koch thought baby mosquitoes inherited malaria from mothers!

Grassi vs Koch

* Koch laughed publicly at Grassi's ideas about mosquitoes.
* Grassi thought Koch in his later years had been fumbling and muddling about malaria.
* Grassi later pointed out flaws in Koch's methodology on malaria research.

Grassi vs Ross (Nobel) (3)
Koch's Involvement

* Ross said that Grassi was a charlatan, a thief, and had contributed almost nothing to mosquito research.

* Grassi had set out to demolish Koch on malaria.

* Nobel Prize situation was worsened with the involvement of Robert Koch.

* Koch was appointed as a "neutral arbitrator" but "[He] threw the full weight of his considerable authority in insisting that Grassi did not deserve the honor".

Ross's Lab in Calcutta

SCD carriers Protected from Malaria?

* Despite SCD's lethal symptoms, it protects the carrier from malaria.
* Sickle cell trait is thought to have evolved because it provides vital protection from malaria.
* The mutation of the hemoglobin affects the parasite.
* With sickling, CO2 is produced which kills the parasites.

Watson, Crick and Franklin

Structure of DNA

DNA History (1)

* Discovered in 1869 by Swiss chemist Friedrich Miescher.

* Russian biochemist Phoebus Levene 1905 studied *nuclein:*
  * *DNA: 4 bases*— Adenine(A), Guanine(G), Cytosine(C), Thymine(T).
  * Also a sugar called *deoxyribose* and a phosphate group.

* Austro-Hungarian biochemist Erwin Chargaff discovered the two basic rules of structure (Chargaff ratios).
  * Amount of Guanine (G) equals amount of Cytosine (C)
  * Amount of Adenine (A) equals amount of Thymine (T)

* Erwin Schrödinger suggested an irregular crystal with no repetitions.

DNA History (2)

* 1950 New Zealand physicist Maurice Wilkins made pictures of ram DNA and thought structure was a double helix.

* Chemist Rosalind Franklin came in 1951 as a researcher in crystallography.

* Wilkins thought she was hired as his assistant.

* She continued to work and took a picture called ***Photo 51***.

* It showed the ribose and phosphate on the outside with the 4 paired bases inside!

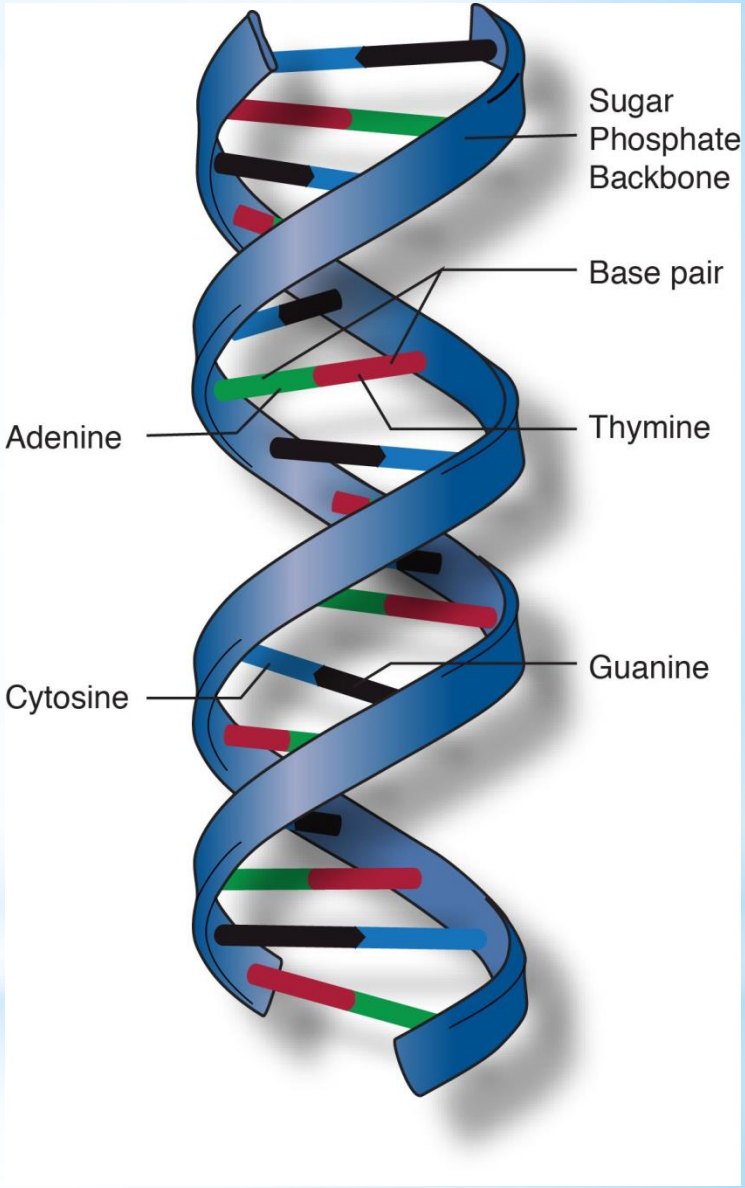
DNA History (3)

* Watson and Crick in Cambridge were working an the structure of DNA.
* Franklin told them that their 1952 model was wrong, it was inside-out!
* In early 1953, Maurice Wilkins showed Crick & Watson a copy of photo 51 **without** Franklin's permission.
* In March 1953 Crick & Watson produced the now-famous model for the DNA double-helix.
* All 4 agreed that C & W would take credit for the model, with Wilkins and Franklin credited with the background research.

DNA Double Helix

Amount of Guanine (G) equals amount of Cytosine (C)

Amount of Adenine (A) equals amount of Thymine (T)



DNA History (4)

* In 1962, Francis Crick, James Watson and Maurice Wilkins were jointly awarded the Nobel Price for their first accurate description of the double-helix.

* Rosalind Franklin had died of cancer in 1958.

* NB: The Nobel is not awarded to more than 3 researchers, and it is never given posthumously!

Epilogue

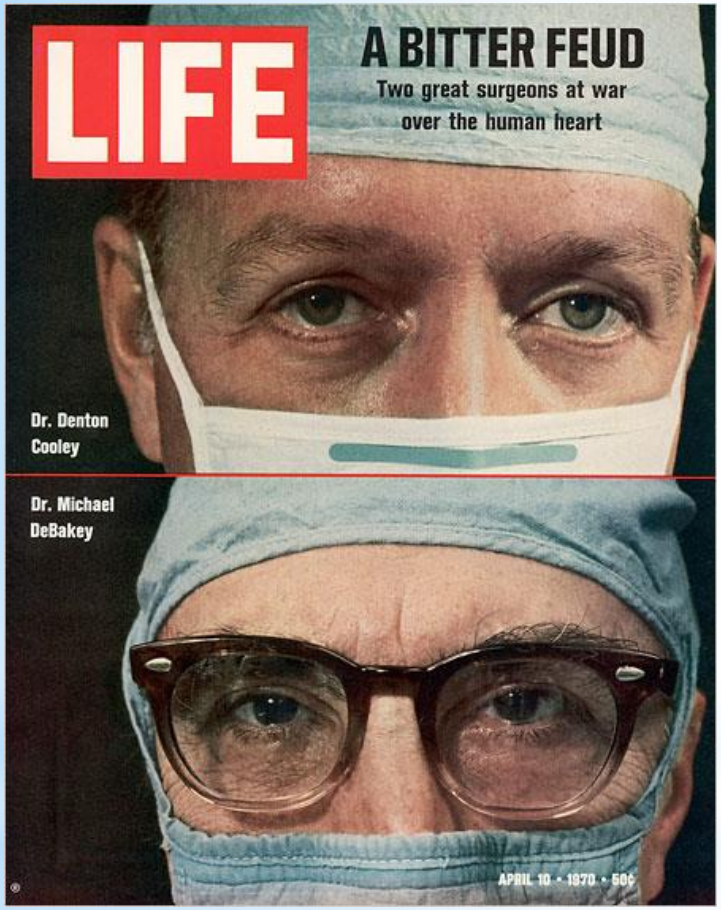
* Watson wrote *The Double Helix*, about the discovery of DNA.

* Harvard University Press refused to publish it because Crick, Wilkins and Pauling objected to the "immaturity and bad taste of the author".

* Watson described Franklin as:

  "Rosy, the termagant who hoarded data she couldn't comprehend, treated men like little boys and wore dresses even dowdier than those of the average Englishwoman."

* Rosalind Franklin's mother Muriel said: "I would rather she be forgotten than remembered in this way".



Cooley and Debakey

Feuding Hearts

Denton Cooley (1920-2016) (1)

- Performed the first implantation of a total artificial heart.
- In the 1950s, Cooley began working with Michael DeBakey.
- Developed a new method of removing aortic aneurysms.
- In 1960, moved to St. Luke's Episcopal Hospital while continuing to teach at Baylor.
- In 1969, following a dispute with DeBakey, he resigned his position at Baylor.
- More than 900 cardiac surgeons from 50 countries are members of the Denton A. Cooley Cardiovascular Society.

Denton Cooley (2)

* When a lawyer during a trial asked him if he considered himself to be the best heart surgeon in the world, he said “YES”.

* “Don't you think that's being rather immodest?” the lawyer replied.

* "Perhaps," Cooley responded. "But remember I'm under oath.“

Cooley and Debakey (1)

* Cooley and heart surgeon Michael E. DeBakey had a professional rivalry that lasted more than 40 years.
* They made amends in a public resumption of cordial relations on November 7, 2007.
* DeBakey was 99 years old and Cooley was 87.
* Cooley died on November 18, 2016, at the age of 96.

Michael E. DeBakey (1908-2008) (1)

- Surgical innovations included coronary bypass operations, carotid endarterectomy, and ventricular assist devices.
- Used Dacron grafts to replace or repair blood vessels.
- Pioneered surgical repairs of aortic aneurysms, an operation he, himself, had at the age of 97.
- Operation lasted 7 hours with a complicated post-op course of 8 months with a hospital cost over $1M.
- He was released in September 2006 and returned to good health.

Michael E. DeBakey (2)

* Dr. Domingo Liotta, from Argentina came to work with Debakey.
* DeBakey put him to work on LV Assist Devices, instead of artificial heart.
* Liotta took his artificial heart to Cooley at the Texas Heart Institute in 1968.
* Implanted it in 1969, never felt DeBakey's permission needed.
* Reaction from DeBakey and federal government was swift.
* DeBakey accused Cooley of stealing the heart, tried to get the medical profession to chastise Cooley.

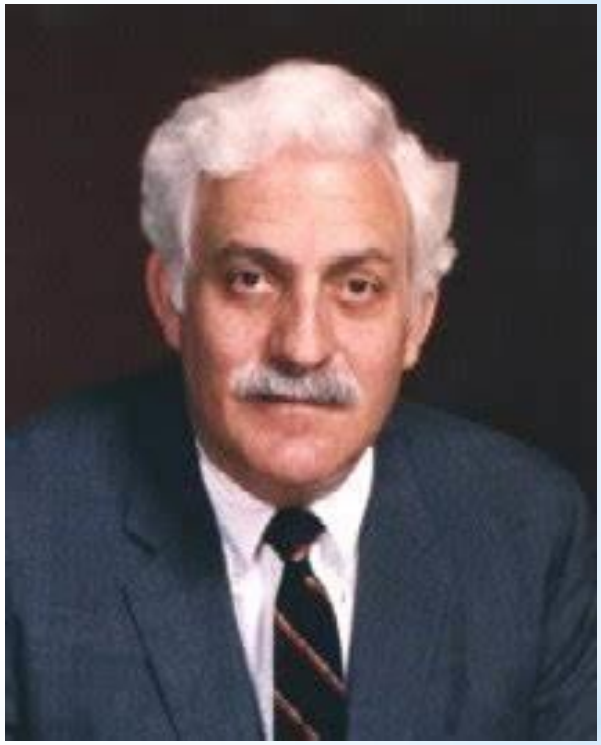
Michael E. DeBakey (3)

* Received a National Heart Institute grant for artificial heart research in 1964.

* National Institutes of Health started a program to put a man-made heart in a human by 1969.

* Race for first human implantation was large part of riff.

* Cooley and DeBakey reconciled in 2007.



Lauterbur and Damanian

Invention of the MRI

Paul Christian Lauterbur (1929 -2007) (1)

* In 1971, Lauterbur had the idea that information from NMR signals could be made into images from a living subject.

* He developed the idea despite widespread skepticism and criticism.

* He used related work by other scientists:
  * Robert Gabillard, gradients in the magnetic field.
  * Peter Mansfield (Lauterbur's Nobel co-recipient).
  * Raymond Damadian (feuded with Lauterbur over credit for the ideas behind MRI, was denied the Nobel).
  * Bloch and Purcell, NMR, 1952 Nobel

Paul Christian Lauterbur (2)

* In 1973, paper sent to *Nature*, but it was rejected because the pictures were too fuzzy.
* He called the process zeugmatography.
* Resubmitted it and then was accepted.
* Received joint Nobel with Mansfield in 2003.

Raymond Damanian

* Raymond Damadian, a New York MD did earlier work using NMR to analyze malignant tissues, first whole body NMR scan in 1977.

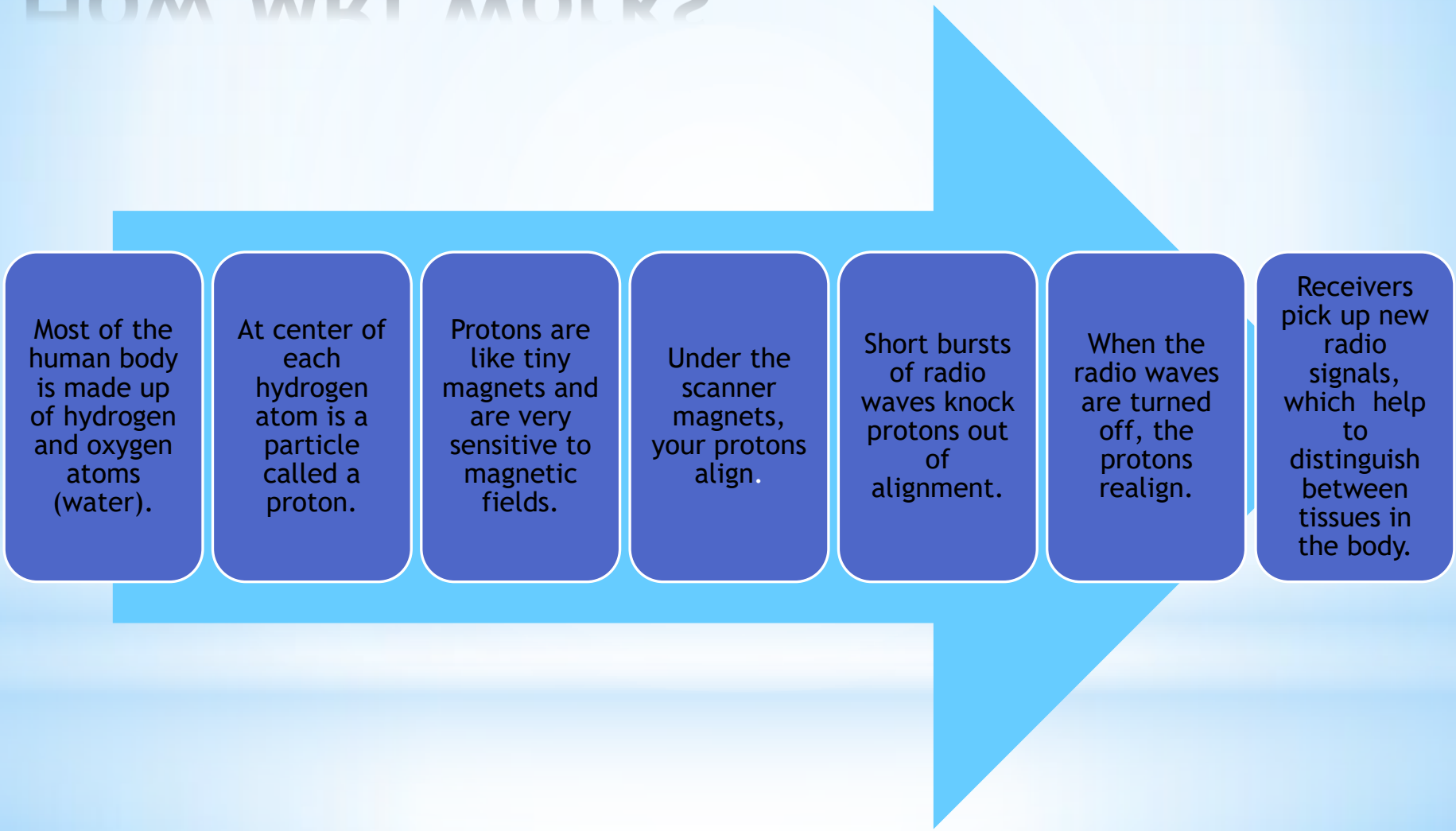
* Damadian & Lauterbur received the Medal of Technology from President Reagan in 1988.

* He was inducted into the National Inventors Hall of Fame in 1989.

* **Patented** NMR for cancer detection in 1974.

* His name was not included in the 2003 Nobel.

How MRI Works



Recap Session 3

* Rivalries, competition and antagonism frequent in science.

* Race to be first at a discovery:
  * Personal reputation and grants, benefits, publicity.
  * National Pride.
  * Gender discrimination.

* Personal antipathy, sexism(?)

* Reluctance to accept own mistakes.

Questions?


Gracias!!