

# Teaching History of Pharmacy According to the AIHP Guidelines:

## E. Growth of the Pharmaceutical Industry

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# Italy

- Earliest European development of chemical industry
  - 1294 – Venice
  - Venetian treacle was an important export
  - Monasteries got involved in industrial pharmaceutical activity (Florence)
    - Distilled waters
    - Cosmetics



# 17<sup>th</sup> and 18<sup>th</sup> Century

- The first pharmaceutical manufacturing in England began with The Society of the Art and Mystery of the Apothecaries of the City of London
  - In 1623, the Society established a cooperative of apothecaries who agreed to produce Galenicals and chemicals on a large scale



# 17<sup>th</sup> and 18<sup>th</sup> Century

- Robert Boyle (father of modern chemistry) and Ambrosius Gotfried Hanckwitz (Godfrey)
  - Built chemist's shop with laboratory in London
  - Godfrey later transformed shop into world's leading producer of phosphorus
  - Also prepared several chemicals and Galenicals



# 17<sup>th</sup> and 18<sup>th</sup> Century

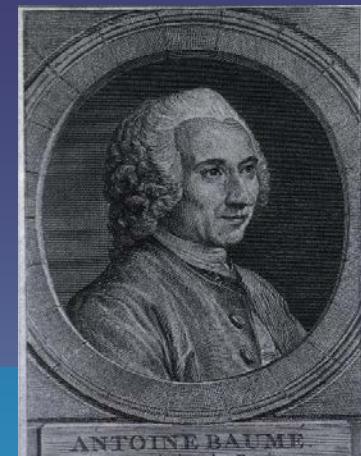


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# 17<sup>th</sup> and 18<sup>th</sup> Century

- Antoine Baume
  - 1728-1804
  - French chemist and pharmacist
    - One of first in France to manufacture chemicals and Galenicals in large scale
    - Transformed his shop into a manufacturing plant
    - Inventor of a number of technical improvements to laboratory equipment
    - Over 2400 products on his 1775 price list





# 17<sup>th</sup> and 18<sup>th</sup> Century

- 1698: first drug patent
  - Epsom salts (magnesium sulfate heptahydrate)

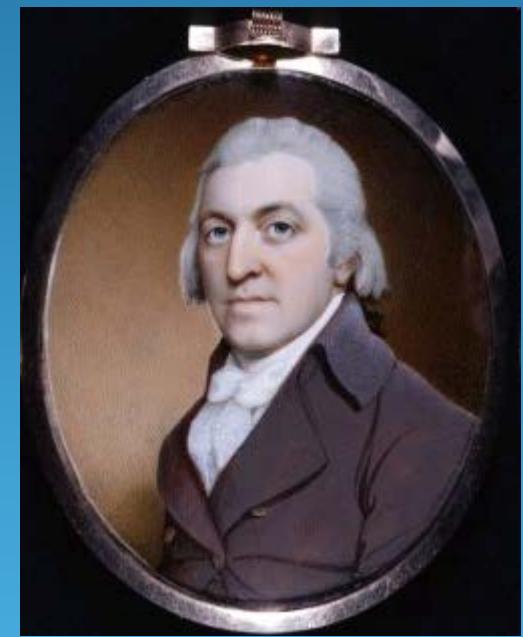


# Revolutionary War Era

- Continental Congress resolution (1775)
  - Established an Army Hospital
  - Staff included:
    - Director-general and chief physician
    - 4 surgeons
    - 1 apothecary
    - 20 mates
- Resolution reorganizing the medical department (1777)
  - Apothecaries roles restricted to pharmaceutical ones

# Andrew Craigie

- 1754-1819
- Appointed Apothecary General of all US military districts during American Revolution
  - Rank of Lieutenant Colonel
  - Accompanied physicians to battle
  - Apothecary job description separate and distinct from physician





# Andrew Craigie

- Role as Apothecary General:
  - Receive, prepare and deliver drugs (and instruments and shop furniture) to the army
  - Created and supervised large-scale compounding / chemical warehouse, the Elaboratory, to fill and deliver medicine chests to military hospitals and battlefields
- Sets precedent for pharmacists to gain professional recognition
- After war, became Apothecary General of the US

# Andrew Craigie 1<sup>st</sup> Apothecary General (1775-1783) at the Battle of Bunker Hill





# Revolutionary War Era

- Main concerns with military drug supply
  - Drug shortages
  - Market speculations
  - Uncertain transport



# Methods of Treatment and Drugs Used During the Revolution

- **Antiseptic:** Mercury (metals and salts)
- **Pain:** Laudanum (a tincture of opium, saffron & Canary wine)
- **Laxative:** Mercurous chloride (calomel), Glauber's salt (sodium sulfate)
- **Syphilis:** Larger doses of mercurous chloride
- **Malaria:** Jesuits Bark (cinchona contains quinine)
- **Heart conditions:** Digitalis
- **Bloodletting:** Still used from Hippocratic times
- **Purging:** Botanicals, emetics, jalap, ipecac, rhubarb
- **Amputation** – 70% were fatal

**There were no thermometers, stethoscopes, hypodermic syringes**



# Drugs in the Medicine Chests

- Calomel
- Epsom salts
- Peruvian bark (cinchona)
- Tartar emetic
- Opium or Paregoric Elixir
- Jalap
- Rhubarb
- Glauber's Salts
- European and Local Herbs

# Medicine Chest early 1800's





# Where did the drugs come from?

- Bought drugs from apothecaries
  - Not enough for the growing military need
  - British blockade, prices skyrocketed
  - Marshall Apothecary\*, Andrew Craigie's warehouse
    - Shipped chests of drugs to various army districts



# Where did the drugs come from?

- Loyalists indifferent to the cause
  - Patriot pharmacies loyal to the cause faced losing everything
- Loyalist Brits and their physicians poisoned supplies left behind as Continental Army moved in to Boston
  - Mixed in arsenic



# Where did the drugs come from?

- Privateers captures British ships and drugs (best source)
  - Captured over 1000 ships – prices went higher
- Jamaica and Bermuda, brought drugs to Philadelphia
  - Quality was scanty, other countries were unreliable
  - Eventually supplied on a regular basis



# Christopher Marshall and the Marshall Apothecary

- 1709-1707
- Irish immigrant; trained in England
- Opened apothecary shop in Philadelphia in 1729
  - Remained open until 1825
- Highly respected; apprentices wanted to train with him



# Christopher Marshall and the Marshall Apothecary

- Sons Christopher Jr. (1740-1806) and Charles (1744-1825) were partners in the business
  - Charles became first president of Philadelphia College of Pharmacy; his granddaughter Elizabeth became the first US female pharmacist



# Christopher Marshall and the Marshall Apothecary

- Key role in the American Revolution
  - Supplied medicine to George Washington's troops
  - Manufactured chemicals and medicine chests
- Advertised with sign:
  - “We fill prescriptions according to the wishes of your physician”

# Marshall Apothecary 1729-1825

Christopher Marshall with sons, Christopher Jr. and Charles





# Revolutionary War Era

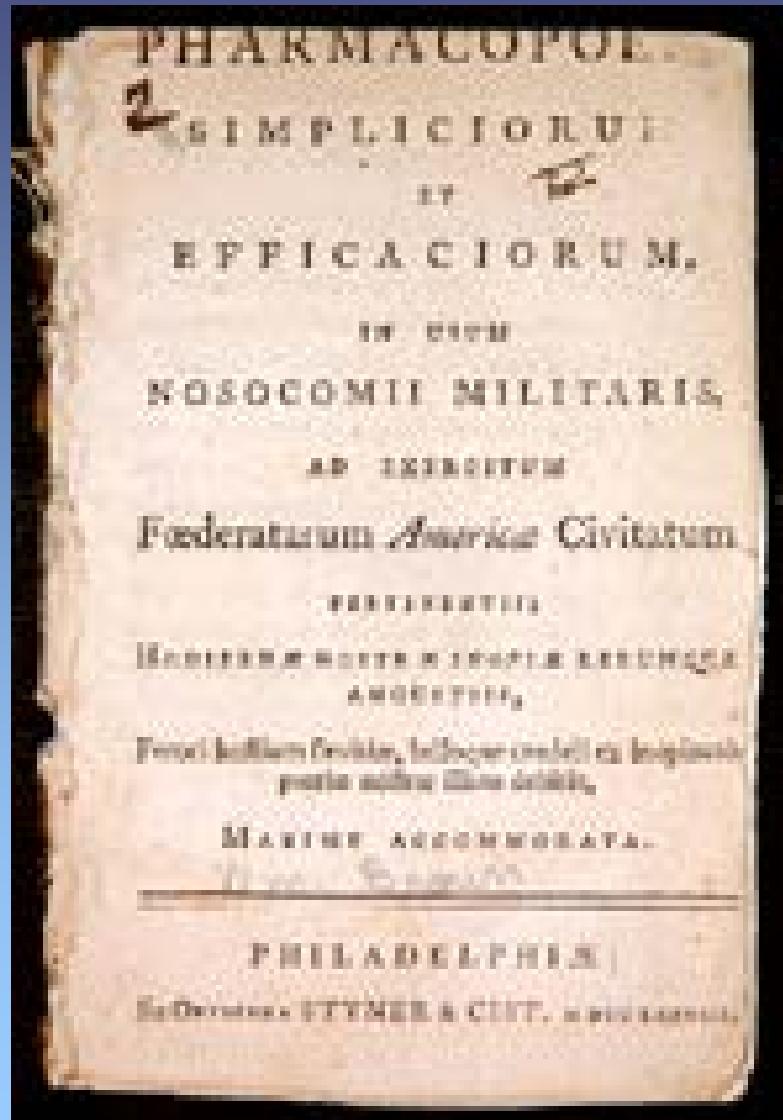
- Lititz Pharmacopoeia
  - Military formulary of 1778
  - Small booklet
  - Contained simple yet efficacious remedies
  - Illustrates:
    - Choice of items based on medical knowledge of the time (esp. British knowledge)
    - Results of the American experience
    - Difficulties arising from being a nation at war



# Revolutionary War Era

- Lititz Pharmacopoeia
  - Because of the drug shortage
    - Permitted official substitution of therapeutically equivalent substances for drugs in uncertain supply

# Lititz Pharmacopoeia





# Revolutionary War Era

- Coste's Compendium
  - Compiled for French medical hospitals in America
  - Jean-Francois Coste
    - Chief physician to the French Army serving with the colonists



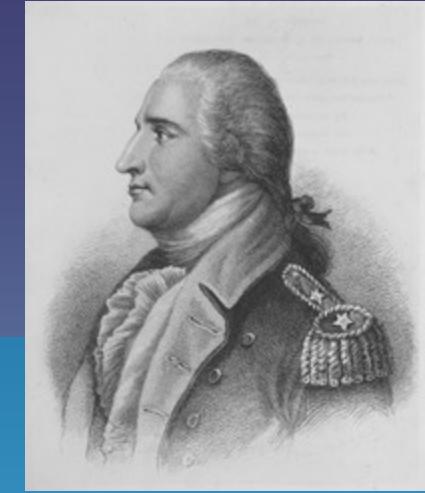
# Revolutionary War Era

## Importance of Revolution to Pharmacy

1. 8 years of separate but equal status as a profession apart from medicine
2. First known large-scale manufacture of pharmaceuticals on American soil
3. First practical attempt at a uniform formulary as a basis for satisfactory and reliable work



# Benedict Arnold



- c. 1741 – 1801
- General during the American Revolution
  - First for the American Continental Army
  - Defected to the British after plot to surrender West Point exposed
  - Name largely synonymous with treason in the United States



# Benedict Arnold

- But before all that...
  - 1762: pharmacist and bookseller in New Haven, CT
  - Began trading in the West Indies
    - Sister Hannah managed the apothecary in his absence
    - Became smuggler by default by ignoring the Stamp Act



# 19<sup>th</sup> Century

- Industrial Revolution accentuated diminution of the age old paradigm of the apothecary compounding individual prescriptions by hand



# 19<sup>th</sup> Century

- Era of alkaloids and phytochemistry
  - Roots of modern pharmaceutical chemistry
  - Discovery of alkaloids such as morphine and quinine catalyzed the need for large scale production

# 19<sup>th</sup> Century



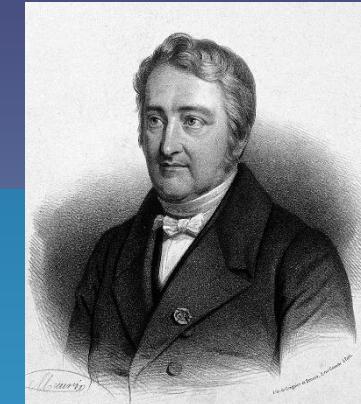
- Friedrich Wilhelm Adam Sertürner
  - 1783-1841
  - German pharmacist
  - First to isolate morphine from opium (1804)
    - Published paper on its isolation, crystallization, crystal structure, and pharmacological properties (in stray dogs, then self-experiments)





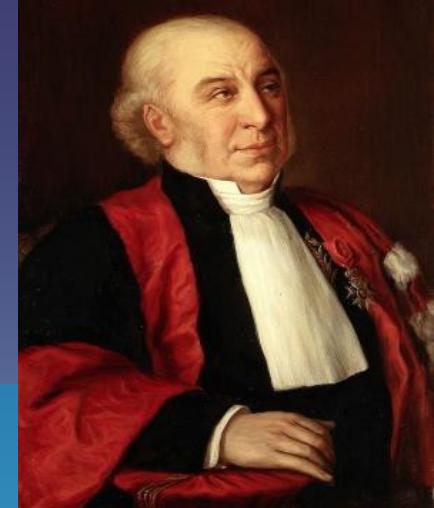
# 19<sup>th</sup> Century

- 1822: Pierre-Joseph Pelletier opened an industrial plant for quinine manufacturing in France
- 1823: Rosengarten & Sons produced and sold quinine in Philadelphia



# 19<sup>th</sup> Century

- Joseph Bienaimé Caventou
  - 1795-1877
  - French pharmacist and professor
  - Collaborated with Pelletier
  - Pioneer in the use of mild solvents to isolate a number of active ingredients from plants, particularly alkaloids



# Most Modern Pharmaceutical Companies Have Roots in the 19<sup>th</sup> Century

Pharmaceutical Company	Year of Foundation
H.E. Merck, Germany	1827
Pfizer	1849
E.R. Squibb & Sons, US	1858
Wyeth, US	1860
Bayer AG, Germany	1863
Burroughs, Wellcome & Company, England	1880
Eli Lily, US	1876
Johnson & Johnson, US	1885
Bristol-Myers, US	1887
Abbott Laboratories, US	1888
Merck & Companies, US	1891
F. Hoffmann-La Roche AG, Switzerland	1896



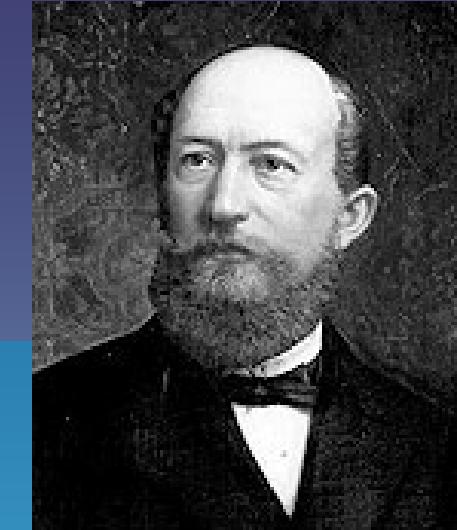
# 19<sup>th</sup> Century

- HE Merck
  - 1827
  - Began manufacturing and selling various alkaloids in Germany
  - Later opened a pharmaceutical plant in the US in 1891



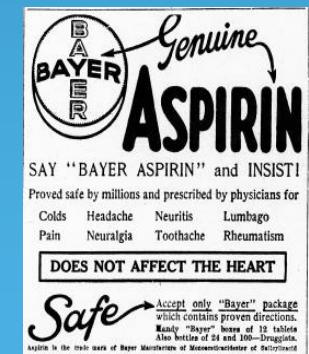
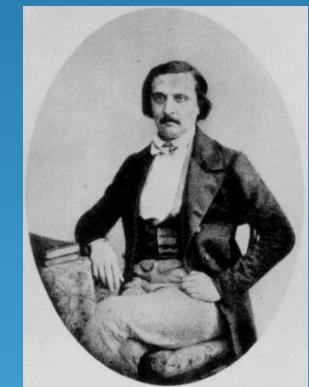
# 19<sup>th</sup> Century

- Friedrich Bayer
  - 1825-1880
  - 1863: Founded Bayer AG in Germany
    - Began as a dyestuff factory



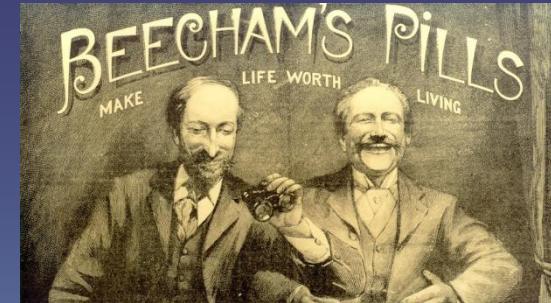
# 19<sup>th</sup> Century

- 1897: Bayer chemists synthesized pure acetyl salicylic acid
  - Had previously been synthesized in an impure form by French chemist Frédéric Gerhardt (1816-1856)
- 1899: filed aspirin trademark worldwide





# 19<sup>th</sup> Century



- Thomas Beecham
  - 1820-1907
  - 1842: marketed Beecham's Pills (laxative)
    - Contained aloe, ginger and soap with some minor ingredients
  - 1859: Beecham's opened first factory for rapid production in Lancashire, England
    - Mergers → SmithKline Beecham → GlaxoSmithKline



# Philadelphia: Birthplace of American Pharmaceutical Industry

- 1823: Rosengarten & Sons produced and sold quinine in Philadelphia
  - Also produced morphine salts and other alkaloids
- 1826: Samuel Wetherill began manufacturing various chemicals and alkaloids





# Philadelphia: Birthplace of American Pharmaceutical Industry

- 1841: John K. Smith established a pharmaceutical factory with his accountant, Mahlon Kline
- 1856: William Warner invented and began manufacturing the sugar-coated pill





# Philadelphia: Birthplace of American Pharmaceutical Industry

- 1860: John (1834–1907) and Frank Wyeth found Wyeth and Brother
  - 1872: Henry Bowers developed first rotary compressed tablet machine in US
  - Name changes over time:  
American Home Products → Wyeth  
→ acquired by Pfizer in 2009





# Expansion of US Pharmaceutical Industry in the 19<sup>th</sup> Century

- 1849: Pfizer founded in New York City
  - Charles Pfizer and Charles F. Erhart
  - First product: palatable form of santonin (antiparasitic)



# Expansion of US Pharmaceutical Industry in the 19<sup>th</sup> Century

- 1855: Frederick Stearns and Company established in Detroit
  - Specialized in fluid extracts
  - Stated listing the names of the ingredients in the preparations before it was required by the Pure Food and Drug Act of 1906



# The Role of War on the Pharmaceutical Industry

- Accentuated need for mass production of good-quality pharmaceuticals
- 1846-1848: Mexican American War
  - Resulted in significantly higher casualties off the battlefield
    - In part caused by import of fake or adulterated drugs
    - Led to passage of first pharmaceutical regulation, the 1848 Drug Import Law



# Expansion of US Pharmaceutical Industry in the 19<sup>th</sup> Century

- 1858: Squibb founded in Brooklyn, NY by Edward R. Squibb
  - Enlisted as a navy doctor during the Mexican American War
  - Frustrated by poor drug quality and spent career working to combat adulteration





# The Age of Quackery

## Compounded products you won't see prescribed today

- Blue mass pills
  - Staple in 1850's for melancholy
  - Contained:
    - Mercury (375 mcg)
      - Safe daily dose = 21 mcg
    - Honey
    - Rose water
    - Licorice root
    - Rose petals



# The Age of Quackery

## Compounded products you won't see prescribed today

- Blue mass pills
  - Known to be taken by Abraham Lincoln
  - Probably explain outbursts of rage and bizarre behavior
    - Lincoln-Douglas debate, 1858
    - Shook Orlando Ficklin and lifted him out of his seat
    - Realized it was the pills; never took them again



# Age of Quackery

## Patent Medicines

- Age of quackery
  - 1880s:
    - Very popular sales items
    - Ingredients kept secret until 1906 Federal legislation
    - Few were actually patented
    - Claims were often sensational and exaggerated
    - Sometimes effective, but often dangerous



# Age of Quackery Patent Medicines

- Many of these drugs developed out of the custom of pharmacists producing and marketing their own remedies
  - Largely vegetable drugs

A wonderful Medicine.

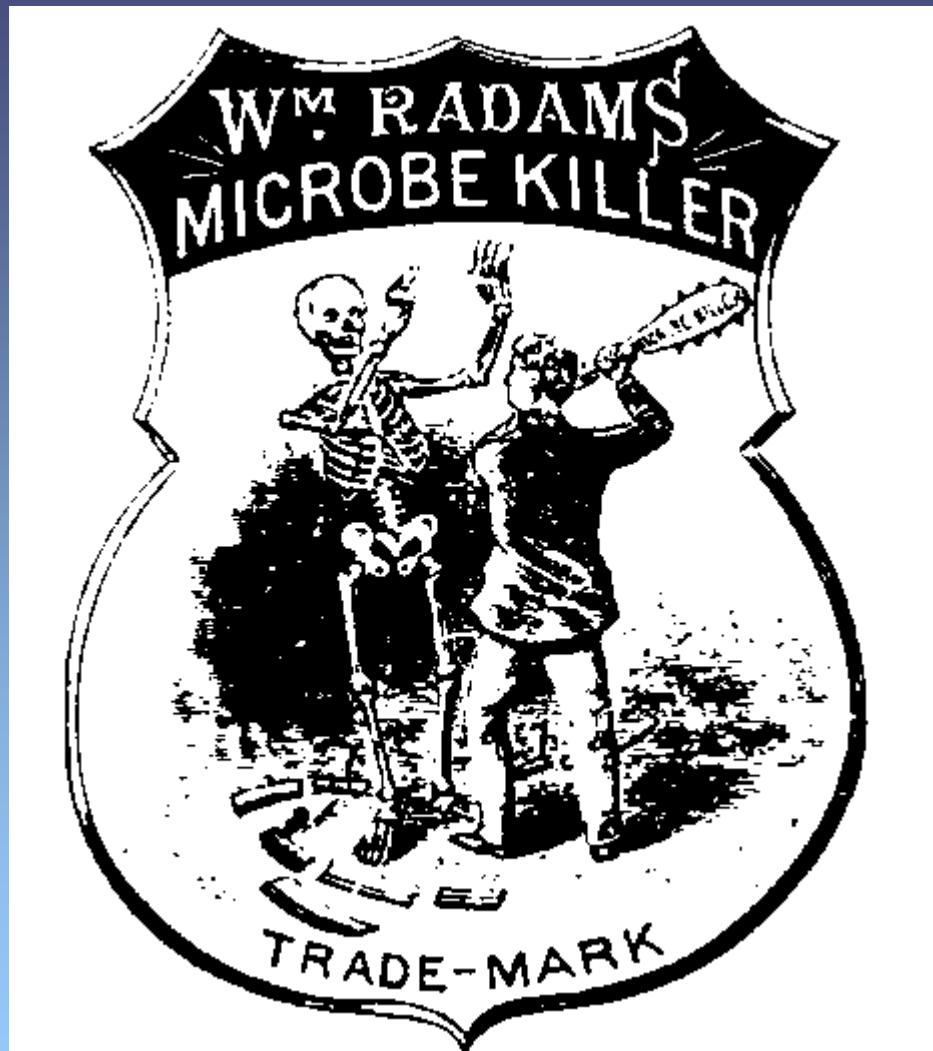
# BEECHAM'S PILLS

For Bilious and Nervous Disorders, such as Wind and Pain in the Stomach, SICK Headache, Giddiness, Fulness and Swelling after meals, Distress and Drowsiness, Cold Chills, Flushings of Heat, Loss of Appetite, Shortness of Breath, Convulsions, Blotches on the Skin, Disturbed Sleep, Frightful Dreams, and all Nervous and Trembling Sensations, &c. The first Dose will cure ~~any~~ <sup>most</sup> in twenty minutes. This is no fiction. Every sufferer is earnestly invited to try one Box of these Pills, and they will be acknowledged to be "WORTH A GUINEA A BOX."

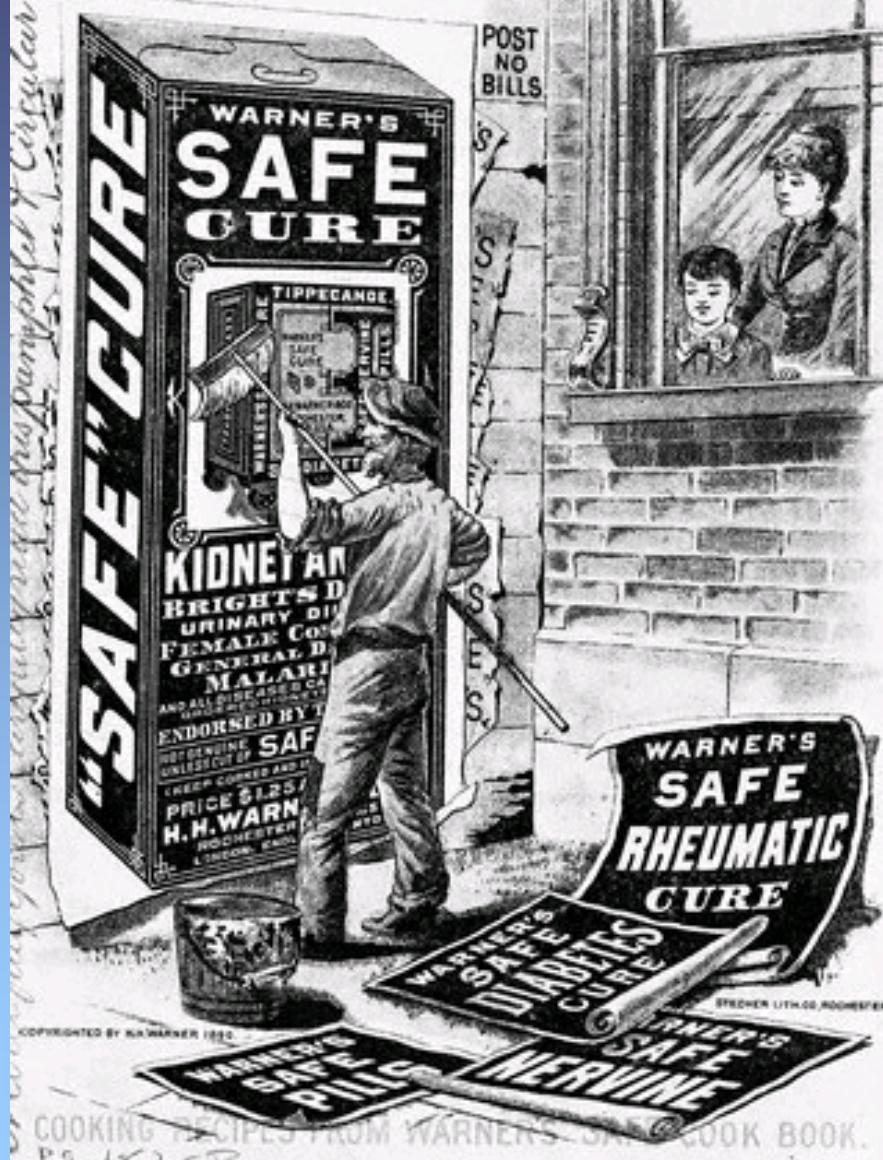
BEECHAM'S PILLS, taken as directed, will quickly restore females to complete health. They promptly remove any obstruction or irregularity of the system. For a

**Weak Stomach; Impaired Digestion; Disordered Liver;**  
they act like magic — a few doses will work wonders upon the Vital Organs; Strengthening the muscular System; restoring the long-lost-Compliances; bringing back the lost signs of youth, and arresting with the Reservoir of Health the whole natural course of the human frame. These are "herbs" admitted by thousands, in all classes of society, and one of the best guarantees to the Nervous and Delirious, is that *Beecham's Pills have the longest list of any Patent Medicine in the world.* Full directions with each box.

Prepared only by THOMAS BEECHAM, St. Helens, Lancashire, England.  
Send every place, in Boxes £. 1*1/2* and 2*1/2* each.



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*SAFE CURE ALMANAC*  
FOR 1890.



# Miraculous Cure

Richard D. Creech, of 1062 Second St., Appleton, Wis., says:

"Our son Willard was absolutely helpless. His lower limbs were paralyzed, and when we used electricity he could not feel it below his hips. Finally my mother, who lives in Canada, wrote advising the use of Dr. Williams' Pink Pills for Pale People and I bought some. This was when our boy had been on the stretcher for an entire year and helpless for nine months. In six weeks after taking the pills we noted signs of vitality in his legs, and in four months he was able to go to school. It was nothing else in the world that saved the boy than Dr. Williams' Pink Pills for Pale People.—*From the Crescent, Appleton, Wis.*

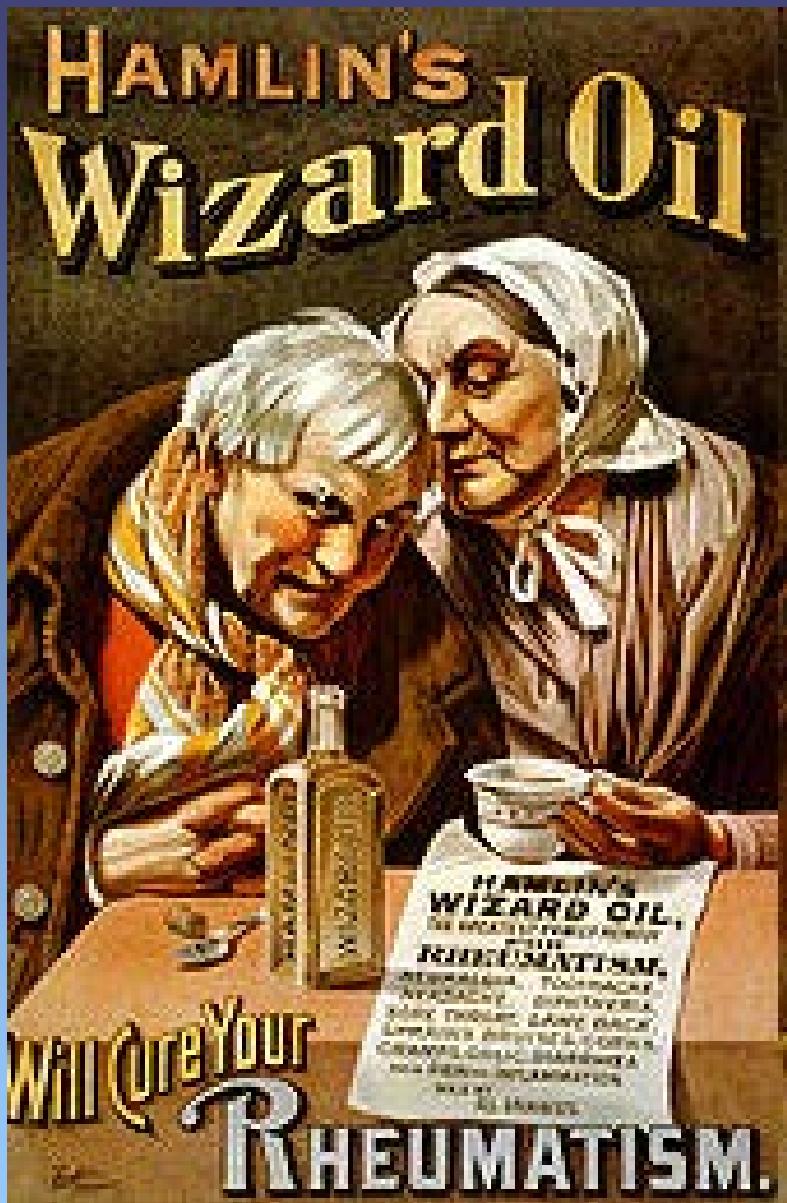
## Dr. Williams' Pink Pills for Pale People

are sold by all druggists or direct from Dr. Williams' Medicine Co., Schenectady, N.Y., postpaid on receipt of price, 80c. per box; six boxes, \$2.50.

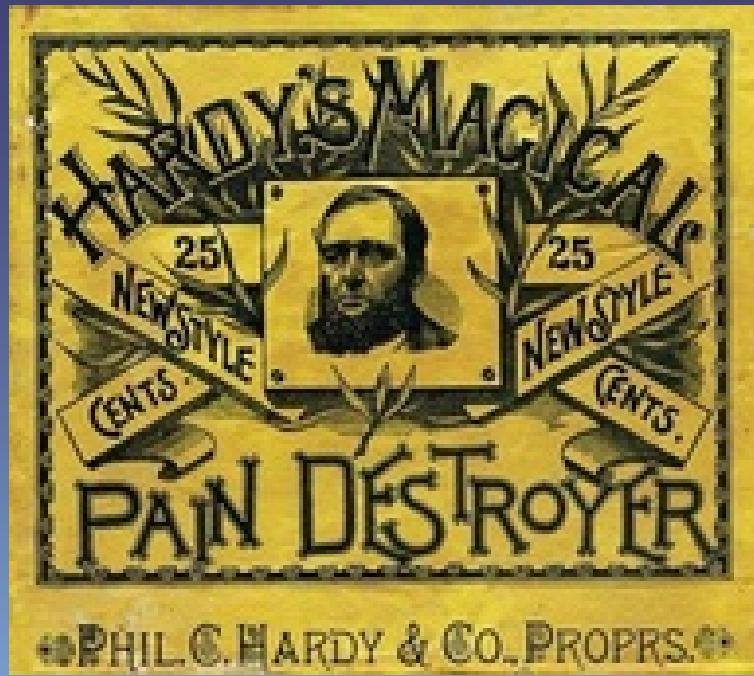
- Contained iron oxide and magnesium sulfate

- Mostly laudanum





- Liniment for rheumatic pain
- Also advertised for:
  - pneumonia, cancer, diphtheria, earache, toothache, headache and hydrophobia
- Contained:
  - 50-70% alcohol
  - Camphor
  - Ammonia
  - Chloroform
  - Sassafras
  - Cloves
  - Turpentine
- Could taken internally or used topically



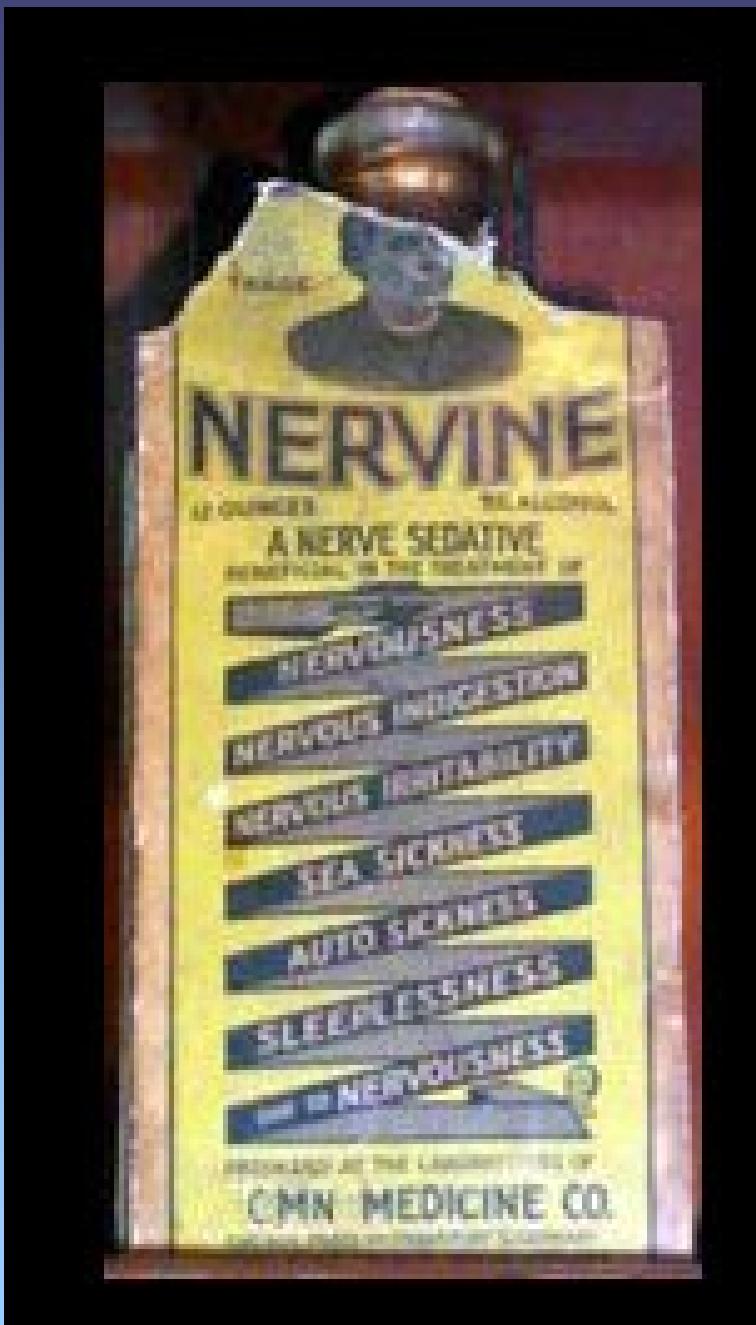
•PHIL. C. HARDY & CO. PROPS.•

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CANDY. Avoid worthless imitations.



# Civilian Pharmacy during the Civil War Period

- Most crude drugs were imported
  - Sold to wholesalers or large drug companies
  - Finished medicines were distributed to retail pharmacists and physicians for sale to the public



# Civilian Pharmacy during the Civil War Period

- Challenges:
  - Volatile prices due to speculators
  - Drug adulteration
  - Lack of formal pharmacy education
  - Most crude drug was imported to the Northern states – problem for those living in the Confederacy



# Military Pharmacy during the Civil War Period

- 4 major stages of drug supply during the war, all of which involved pharmacists:
  1. Acquisition of materials
  2. Inspection and preparation of finished medicines
  3. Distribution to depots and hospitals
  4. Dispensing to patients



# Military Pharmacy during the Civil War Period

- Pre-war:
  - US Army bought medicine on the open market
  - Distributed through a large depot in New York, plus some smaller depots



# Military Pharmacy during the Civil War Period

- During war (in the North):
  - Expanded to 30 depots
    - Major centers in New York and Philadelphia
    - Relied heavily on handful of domestic drug companies for stable inventories and prices
  - In field, medical purveyors:
    - Requisitioned medicines
    - Distributed to units



# Military Pharmacy during the Civil War Period

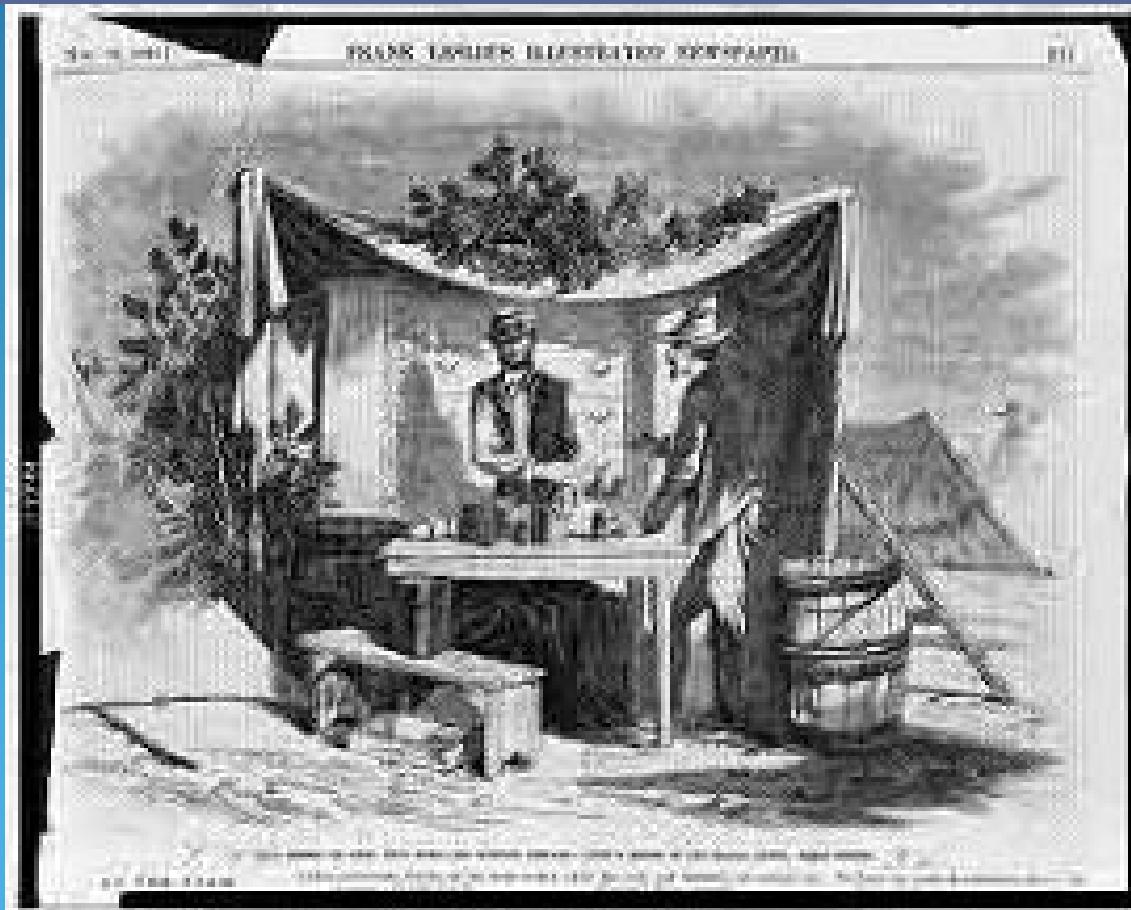
- During war (in the South):
  - Acquisition hampered by blockade
  - Southern drugstore stock was quickly used up
  - What to do?
    - Blockade running
    - Smuggling through enemy lines
    - Capture of Union supplies
    - Use of native plants and remedies



# Military Pharmacy during the Civil War Period

- Both sides established laboratories to:
  - Inspect raw drug material
  - Prepare finished medicines
  - Union labs:
    - Philadelphia, Long Island, Brooklyn, St. Louis
  - Confederate labs:
    - Richmond, plus labs in Alabama, Georgia, North and South Carolina, Arkansas, and Texas

# Battlefield Drugstore



[http://www.drugstoremuseum.com/images/level\\_imgs/65498419851.jpg](http://www.drugstoremuseum.com/images/level_imgs/65498419851.jpg)



# Need for Standards

Patent medicines and adulterated drugs during the Civil War contributed greatly to the need for standards



# Charles Rice

- 1841-1901
  - Received compounding training in the Navy
  - Subsequently began work at Bellevue Hospital in NYC
    - Lived there most of his life
  - Outspoken about need for compounding and dispensing standards
    - Creator of modern day pharmacopeia
    - Also instrumental in creating National Formulary
    - USP/NF (unified in 1975) is the official compendium of drug standards in the US



# United States Pharmacopeia

- Designed to bring uniformity to the *materia medica* and pharmacy preparations of the day
  - First published in 1820
  - Initial work (first and second revisions) was done by physicians
  - USP Convention in 1840 involved pharmacists as well
  - Physicians lost interest by 1870



# United States Pharmacopeia

- First Edition – what sort of formulas did it contain?

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## TOBACCO LINIMENT.

*Take of Tobacco, cut fine, one ounce.  
Hog's lard, one pound.*

*Simmer the tobacco in the lard over a gentle fire until it becomes crisp, and strain.*

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## DECOCTION OF SQUILL.

Take of Squill, three drachms.

Juniper, four ounces.

Seneca snakeroot, three ounces.

Water, four pints.

Boil to the consumption of one half the liquor; then strain and add,

Spirit of nitrous ether, four fluidounces.

---

—  
WINE OF OPIUM.

*CALLED SYDENHAM'S LAUDANUM.*

Take of Opium, two ounces.

Cinnamon, bruised ;

Cloves bruised, each one drachm.

Wine, one pint.

Macerate for ten days, and strain.

—

—  
WINE OF TOBACCO.

Take of Tobacco, one ounce.

Wine, one pint.

Macerate for ten days, and filter.

—

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## TROCHES OF LIQUORICE AND OPIUM.

Take of Opium, two drachms.

Tincture of tolu, half a fluidounce.

Simple syrup, eight fluidounces.

Extract of liquorice softened in hot water

Acacia gum in powder, each five ounces.

First rub the opium thoroughly with the tincture, then by degrees add the syrup and extract; after which, gradually sprinkle in the powdered gum, finally dry the mass, and form into troches, each weighing ten grains.

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## SYRUP OF RHUBARB WITH SENNA.

Take of Rhubarb, bruised ;

    Senna, each one ounce and a half.

    Cardamom, three drachms.

    Boiling water, one pint.

    Digest for twenty-four hours, and evaporate with a gentle heat till the liquor is reduced to half a pint ; then strain and add one pound of sugar ; lastly boil to form a syrup.

## OPIATED TINCTURE OF CAMPHOR.

Take of Opium ;

Benzoic acid ;

Oil of anise, each one drachm.

Liquorice, half an ounce.

Clarified honey, two ounces.

Camphor, two scruples.

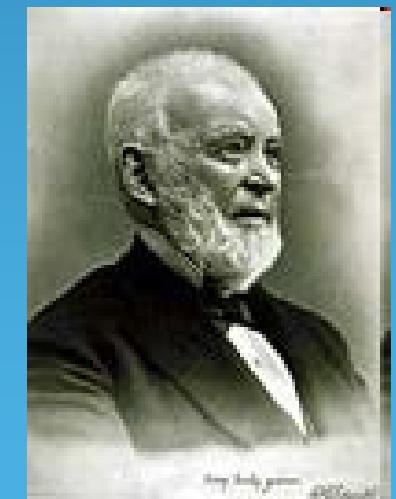
Diluted alcohol, two pints.

Digest for ten days, and filter.



# Edward Robinson Squibb

- 1819-1900
  - Advocate of product standards
    - Quality more important than lowest price
    - Ether – steam process of production led to more standardized, efficacious product
      - Refused to patent process
      - Published for others to use





# Edward Robinson Squibb

- Went on to form pharmaceutical company in 1858
  - Initial lab was destroyed by fire when a lab assistant dropped a bottle of ether
  - Rebuilt; lab assistant was retained (and promoted!)
  - Saw tremendous growth
    - Sold ether with excellent reputation for quality
    - Civil War increased demand for products



# Edward Robinson Squibb

- Post-war: increased attention on substandard and adulterated medicines
- 1876 APhA meeting: led debate on the future of the USP
  - Need for more frequent revision
  - Increased discussion of monographs
  - Correction of errors
- 1877 APhA meeting:
  - Formed Committee on Revision
  - Charles Rice named as chair



# Charles Rice

- 1841-1901
  - Creator of the modern pharmacopeia
    - 6<sup>th</sup> Revision was very different from previous editions
    - Provided a useful tool for pharmacists who were abandoning in-store manufacturing and focusing on quality and standards
  - Father of the National Formulary



# United States Pharmacopeia

- Changes implemented with Rice at helm:
  - List of guiding principles - 1880
    - Use of English weights and measures (rather than English and Latin)
    - Parts by weight
    - Use of a single alphabetic list
    - Chemical formulas, specific gravities, and atomic weights were to be added
    - USP VI was to “address the needs of professional practice, mass manufacturing, and developing regulations against drug adulteration”



# National Formulary

- Pharmacists were becoming concerned with rapid growth of manufacturers in the mid-1880s
  - Didn't want to merely "count and pour"
  - Wanted lists of formulas that physicians could prescribe and pharmacists could compound
- Rice served as chair of Committee on Unofficial Formulas of the APhA
  - New York and Brooklyn Formulary was starting point
  - Eventually resulted in NF
  - Only involved in first edition



# The Era of Biologicals

- 1866: Parke Davis and Company established in Detroit
  - Standardized botanical extracts
  - First to establish its research institute in 1902



# The Era of Biologicals

- 1876: Eli Lilly & Company established in Indianapolis
  - Eli Lilly was a Union artillery colonel
  - Produced standardized botanical extracts
  - Began commercial manufacture of insulin worldwide in 20<sup>th</sup> century



# The Era of Biologicals

- 1894: HK Mulford Company established in Philadelphia
  - Produced anti-toxins
  - By 1900: produced dozens, including rabies, tetanus, anti-streptococcus
  - Along with Parke Davis, received first licenses to produce





# The Era of Biologicals

- 1901: 13 children in St. Louis die of tetanus following administration of contaminated diphtheria anti-toxin
  - Leads to Biologics Control Act of 1902, designed to regulate serums and vaccines





# War Changes Everything

- Prior to World War I (1914-1918), the US pharmaceutical industry relied heavily on German scientific research
  - Most of the German pharmaceuticals sold in the US were manufactured in American plants under licensing agreements and protected by US patents



# War Changes Everything

- Bayer's US assets were seized during WWI
  - 1918: Sterling Products, Inc. acquired Bayer Company Incorporated of New York for \$5.5 million
    - Sales of Bayer's aspirin in US was \$600 million in 1970 alone
    - Bayer reacquired rights for aspirin in 1994 for \$1 billion



# War Changes Everything

- Merck and Co. was confiscated following WWI
  - Set up as an independent company in the US
- Many US pharmaceutical companies set up their own research at this point



# The Era of Insulin and Penicillin

- 1921: insulin discovered by Frederick Banting and Charles Best (Univ. Toronto)
- 1922: Eli Lilly and Univ. Toronto researchers worked together to develop large scale production of insulin
- 1923: Lilly begins selling Iletin® (insulin), first commercially available insulin for treatment of diabetes



# The Era of Insulin and Penicillin

- 1928: penicillin discovered by Alexander Fleming
- WWII: War Production Board oversees mass production of penicillin by numerous companies: Merck, Pfizer, Abbott, Squibb, Lilly, Parke Davis, Upjohn, Lederle, Reichel Laboratories, and Heyden Chemical
  - Paradigm shift in capabilities of US pharmaceutical industry



# The Rise of the Pharmaceutical Industry Post-WWII

- US pharmaceutical industry flourished after WWII
  - Knowledge of large scale penicillin production catalyzed further discovery of antibiotics
    - 1945: Streptomycin (Merck)
    - 1948: Chlortetracycline (Lederle)
    - 1949: Chloramphenicol (Parke Davis)
    - 1950: Oxytetracycline (Pfizer)
    - 1952: Erythromycin (Lilly)



# The Rise of the Pharmaceutical Industry Post-WWII

- Other therapeutic areas
  - Antihistamines (Benadryl, Parke Davis, 1946)
  - Tranquilizers
  - Antidepressants
  - Proton pump inhibitors
  - Anti-hypertensives
  - Anti-hyperlipidemics



# The Era of Block Buster Drugs

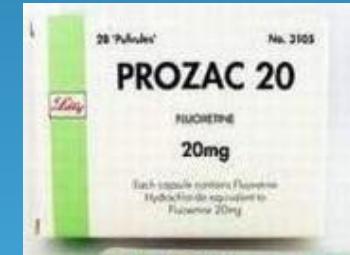
- 1977: Tagamet (cimetidine)
  - Smith, Kline and French
  - Anti-ulcer medication
  - First ever “block buster” drug
  - Earning > \$1 billion per year
  - Nobel Prize: Sir James Black





# The Era of Block Buster Drugs

- Competition to develop next “block buster”
  - 1987: Prozac (fluoxetine)
    - Eli Lilly
    - First SSRI
    - Revolutionized mental health field
  - 1987: Mevacor (lovastatin)
    - Merck
    - First statin (HMG CoA reductase inhibitor)





# Lipitor®: the best selling drug in the history of pharmaceuticals

- 1985: atorvastatin first synthesized
  - Team led by Bruce Roth at Warner-Lambert's Parke Davis research facility
    - Roth fought to get drug into trials, were it outperformed simvastatin on safety/efficacy
    - 1996: Warner-Lambert and Pfizer entered into co-marketing agreement
    - 2000: Pfizer acquired Warner-Lambert
    - Flagship drug for years; > US\$125 billion in sales over ~14.5 years

# The Era of Mergers and Acquisitions

Consolidation has been a continuing process

1980

Merck	Hoffmann	Hoechst Roussel	Squibb	Sandoz	Glaxo	Pfizer
Schering-Plough	Roche	Marion	Meyers	Geigy	Wellcome	Parke-Davis
Organon	Genentech	Merrill Dow	Bristol	Ciba	French	Warner Lambert
		RhonePoulenc	DuPont Pharma		Kline	Monsanto
		Sanofi			Smith	Upjohn
		Synthelabo			Beecham PLC	Pharmacia
						A.H. Robbins
						Amer. Cyanamid
						AHP

34 Companies

LaRoche	Hoechst	Squibb	Sandoz	French	Pfizer
Syntex	Sanofi-Synthelabo	Bristol-Meyers	Ciba-Geigy	Beecham PLC	Warner Lambert
Genentech	RhonePoulenc & Fissons	DuPont Pharma		SmithKline	Monsanto
	Marien Merrill Dow				Pharmacia Upjohn

Hoechst	Bristol-Myers	Squibb	Beecham PLC	Pfizer
Roussel			GlaxoWellcome	Pharmacia
	RhonePoulenc & Fissons		SmithKlineFrench	AHP (Wyeth)
	Sanofi-Synthelabo			

Merck	Hoffmann	Aventis	GlaxoWellcome	Wyeth
Schering-Plough	LaRoche	Sanofi-Synthelabo	SmithKline	Pfizer
	Genentech		Beecham	

7 Companies

2010



# The Rise of the Generic Drug Industry

## Drug Price Competition Act of 1984

### AKA Hatch-Waxman Act

- Amended the Federal Food, Drug and Cosmetic Act (FDCA) and the Patent Act
- Established an abbreviated new drug application (ANDA) process requiring only bioequivalence studies
  - Provided for filing of generic drug applications 60 days later





# Drug Price Competition Act of 1984

## AKA Hatch-Waxman Act

- Created modern US generic drug industry
  - Generic drugs now account for a major portion of the prescriptions in the US
  - Worldwide sales of generic drugs is > \$80 billion



# The Era of Biologics

## Biotech Industry

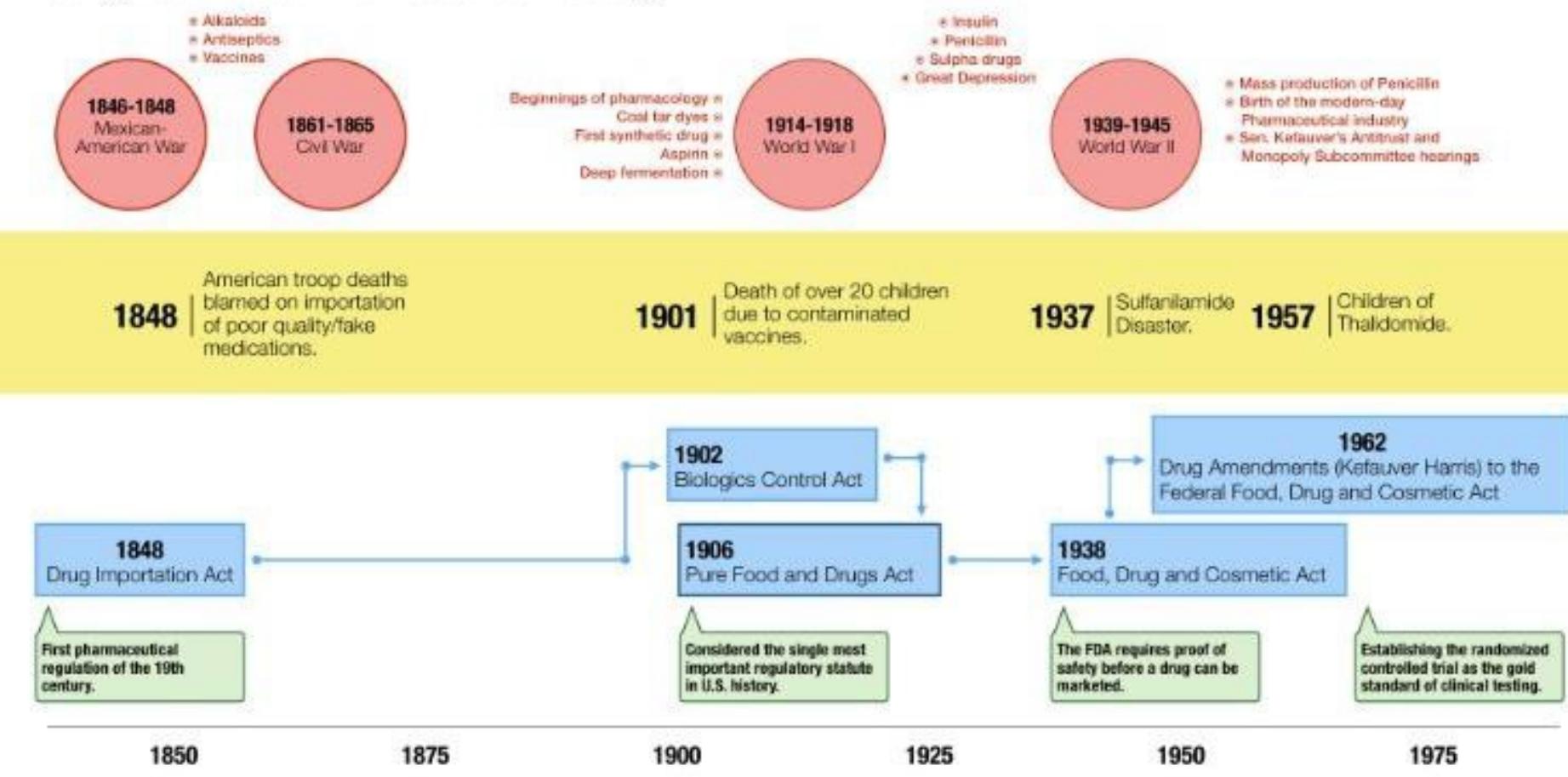
- Many biotech companies were founded in late 20<sup>th</sup> Century that focused on development of biotechnology based medicine
  - 1976: Genentech
  - 1978: Biogen
  - 1980: Amgen
  - 1981: Immunex

# The Era of Biologics

## First five biologics approved in major categories.

Monoclonal antibody	Receptor modulator	Enzyme modulator
Muromonab CD3 (Ortho, 1982)	rhInsulin (Eli Lilly, 1982)	Dornase alfa Genentech (1993)
Abciximab (Centocor, 1993)	Interferon alpha-2a (Roche, 1986)	Pegaspargase (Enzon, 1994)
Rituximab IDEC (1997)	Epoetin alfa (Amgen, 1989)	Imiglucerase (Genzyme, 1994)
Basiliximab (Novartis, 1998)	Filgrastim (Amgen, 1991)	Alteplase (Genentech, 1996)
Palivizumab (MedImmune, 1998)	Sagramostim (Immunex, 1991)	Reteplase (Boehringer-Mannheim, 1996)

## The origins of the US Pharmaceutical Industry



<https://www.linkedin.com/pulse/creation-crisis-consequence-brief-history-early-us-industry-rahman>

# Pioneering Pharmaceuticals

The origins of the US Pharmaceutical Industry

