

R E G I S T E R N O W !

1,000,000,000 CHF investment

7,000,874 hours of work

6,587 experiments

423 researchers

1 medicine



THE MAKING OF AN INNOVATIVE MEDICINE

*Introductory workshops on translational biomedical research,
drug discovery and development*

**BIO-698 resumes Thursday September 11. 2025
4:15 PM @ CM013**



Judge Prof Dr med Olaia Naveiras



Sciences de la Vie -SV



With Justine Epiney MD PhD cand Mehdi AliGadiri MD PhD cand

Prof Roger G. Clerc

The Making Of An Innovative Medicine – class schedule

Thursday's @ 4-6 PM except 04.12/11.12.25 @2-6 PM



Session 1: **Scope of the course _ general organization _ case study**

11.09.25 *Embracing a career at the heart of biomedical research !?*

CM012

Session 2: **Historical perspective: the modern pharmacy**

18.09.25 *Advent of modern medicines - placebo controlled drug development*

CM012

Session 3: **Introduction to translational research: crossing the bridge**

25.09.25 *A chasm has opened wide between biomedical research and patients in need*

CM013

Sessions 4-5: **Therapeutic target identification I & II**

02-09.10.25 *"me too" vs a wealth of innovative targets _ small MW cpds vs biologicals*

CM013

Early front loading of biomarker identification for cohort stratification

Session 6: **Structure based drug design _ medicinal chemistry_low/high throughput**

16.10.25 **screening assays_ multiple parallel optimization_ML-powered screens**

CM013

Setting up screening assays, the robotics, the million cpds libraries

Session 7: **Therapeutic modalities peptides and biologicals: today's -**

30.10.25 **tomorrow's pharmacy NBEs**

CM013

Challenges (cost of goods - healthcare payers) and opportunities

Flipping the class : how to encourage doctoral trainees to speak up ?



Presentations

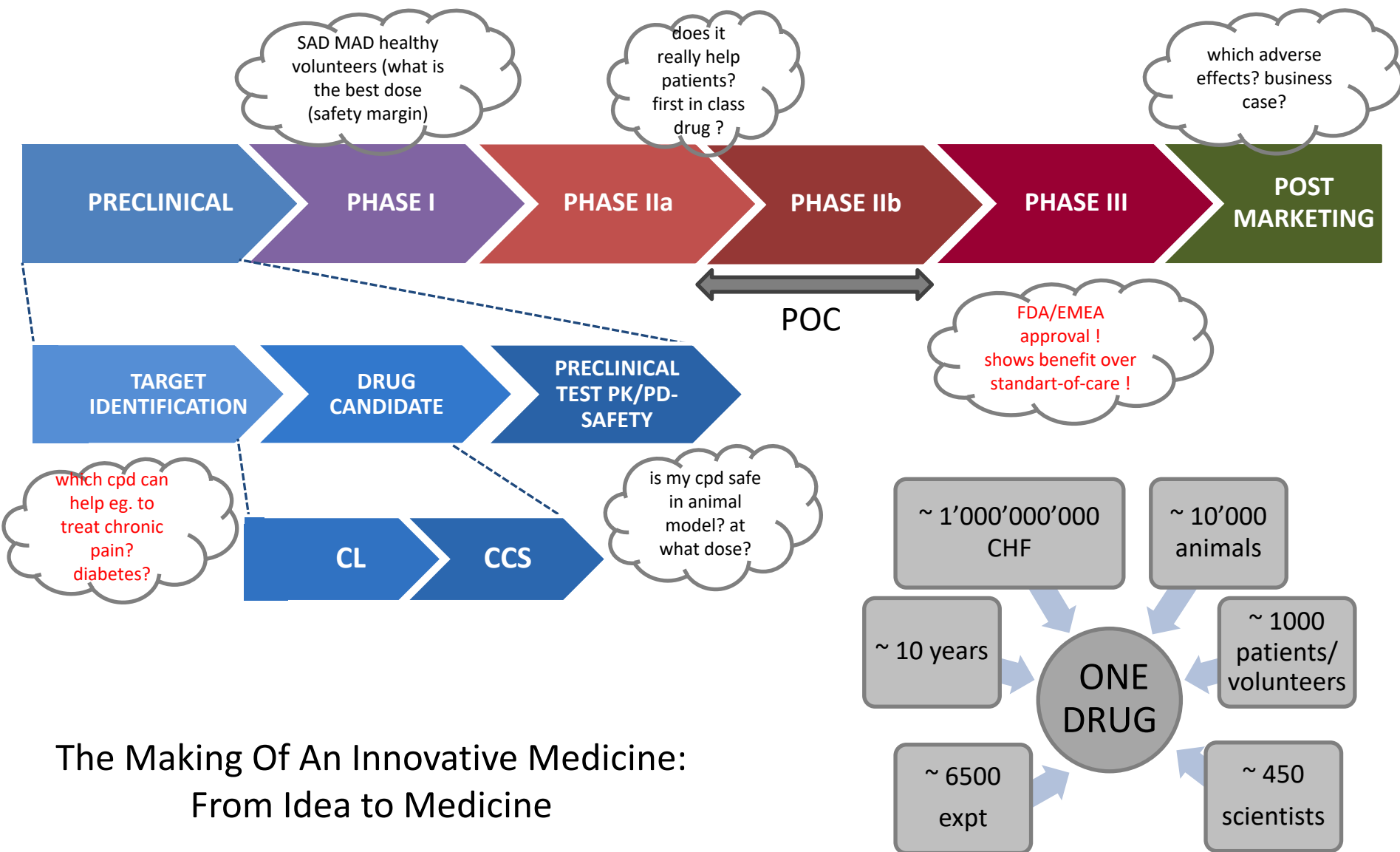
Briefly introduce yourself to your neighbor, sharing **one question** you have for this afternoon.



Drug Discovery : The Value Chain



«the discovery of a new medicine is a very difficult task»



The Making Of An Innovative Medicine:
From Idea to Medicine

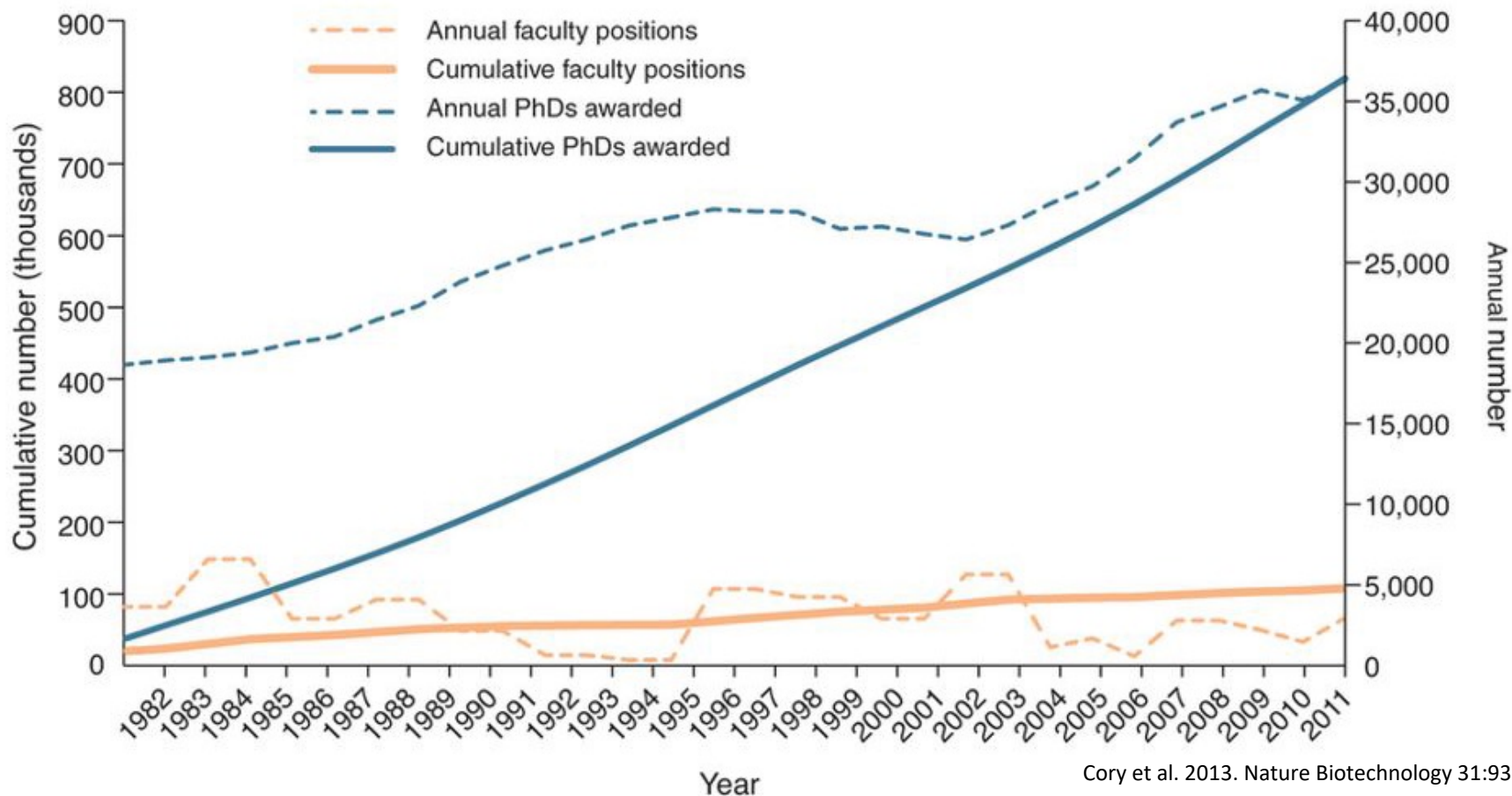
The professional future of PhDs competing with the global job market

Embracing a career at the heart of biomedical research ?



From: *The missing piece to changing the university culture*

MAKE YOUR OWN PLANS, REGARDLESS !



Cory et al. 2013. Nature Biotechnology 31:938-942

*Changing the university /academic career culture
academia vs industry ?*

WORKSHOP LISTING - THE MAKING OF AN INNOVATIVE MEDICINE BIO 698-HS2025 in CM013

! NON EXHAUSTIVE LISTING - SUGGESTIONS WELCOME !

| sessions | workshops | speaker/s |
|-----------------------------------|--|-----------|
| S02 (18-09-25) | | |
| historical medicines | penicilin: impact, whose invention ? | |
| hopping on giant shoulders | prozac at the core of psychiatry | |
| | vaccine discovery:smallpoxJennerTodaymRNAvaccine | Eugenio |
| | artemisinin and malaria | |
| | insulin-Banting Best et al. beagle dog | |
| | slide51-X-ray image DNA--Rosalind Franklin | |
| | cyclosporin from soil sample to life saver | |
| S03 (25-09-25) | | |
| translational research | expanding scope of translational therapies | |
| from bench to bedside and back | chronotherapy,circadian clock,sex,longevity | |
| | CAR-T, TCR-T cell therapies in "cold" tumors | |
| | Y chrom loss in immune cells drives cancer | |
| S04 (02-10-25) | | |
| therapeutic target identification | rare diseases repurposing medicines | |
| S05 (09-10-25) | nocosomial inf/MRSA/phage antibacterials | |
| therapeutic target identification | Crispr/Cas9 gene editing huntington disease | |
| | AI in drug discovery / ML-powered medicine | |
| | AIDS - Lenacapavir : end of plague ? | |
| S06 (16-10-25) | | |
| structure based drug design | macrocycles and non druggable targets | |
| | chemoproteomics - NMEs | |
| | AIDS HIV from deadly virus to chronic disease | |
| S07 (30-10-25) | | |
| therapeutic modalities - NBEs | therapeutic peptides/incretins et al | |
| | biologicals on the rise MABs medicines | |
| | RNA therapeutics, antisense medicines | |
| | Wnt pathway - PROTACs vs molecular GLUEs | |
| S08 (06-11-25) | | |
| PHC personalized healthcare | BRCA1/2 preventive surgery/tumor board | |
| Human genomics | 4P medicine - GWAS - CTCs | |

Workshops

The Making Of An Innovative Medicine

(non exhaustive listing)



- Historical perspectives : the early days of modern pharmacy : ***Hopping on giant shoulders*** (well before the AI hypes !)



Sunday afternoon expt: a visit of the Pharmacy Museum of the University of Basel Switzerland

Happy Birthday ! Swiss Pharmacy Museum is celebrating 100 years



100 Jahre Pharmaziemuseum: «Körperlichkeit, Krankheit und Heilung betreffen uns alle»

«body awareness, disease and healing are us !

Mit einem Fest, einer Sonderausstellung und weiteren Events feiert das Pharmaziemuseum der Universität Basel sein 100-jähriges Bestehen. Sein Direktor, der Historiker Dr. Philippe Wanner, über Entstehung und Geschichte der Sammlung – und



460-370 BC

- The works of Hippocrates (460-370 BC) contain 300 medicinal plants classified by physiological action: Wormwood and common centaury (*Centaurium umbellatum Gilib*) were applied against fever; garlic against intestine parasites; opium, henbane, deadly nightshade, and mandrake were used as narcotics; fragrant hellebore and haselwort as emetics; sea onion, celery, parsley, asparagus, and garlic as diuretics; oak and pomegranate as adstringents



Ginseng root extracts (*Panax q.*) : evidence shows that taking **ginseng root** extracts daily for 12 weeks improves concentration and cognitive activities.
(cf pharmacognosy)



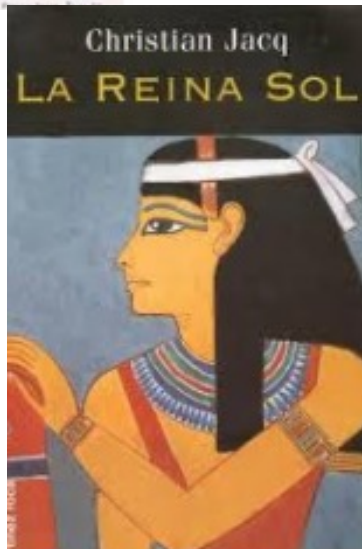
The Georg Ebers Papyrus.



Found in Egypt in the 1870s, the Ebers Papyrus contains prescriptions written in hieroglyphics for more than 700 remedies, including this one for an **acute asthma attack**.

From: University of Leipzig

- The Kahun (1825 B.C)
-gynecology
- The Ebers (1534 B.C?)
-internal medicine
- The Edwin Smith Surgical Papyrus (1600 B.C)
-surgical wounds and fractures



Historical perspective _ medicinal plant extracts



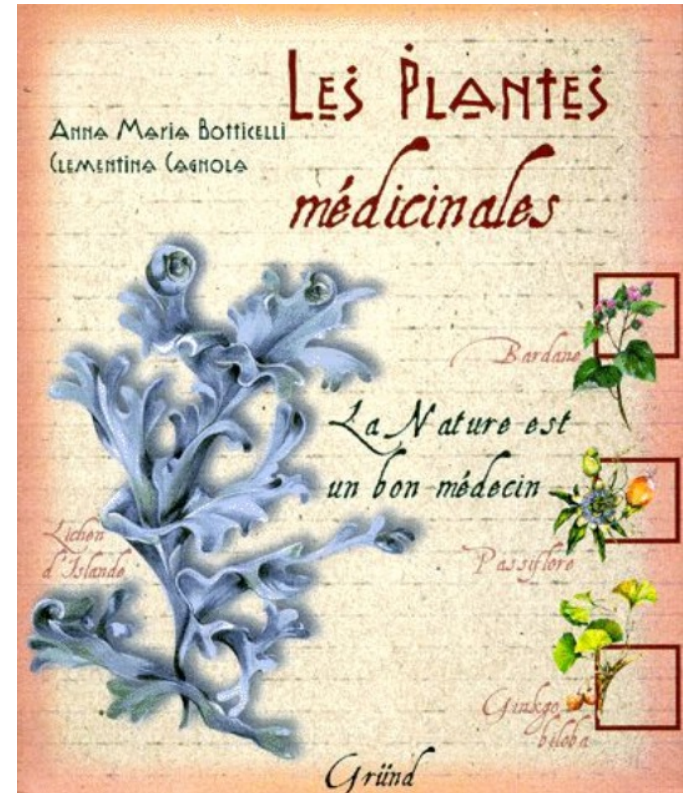
eg. *Papaver somniferum* (poppy seeds) known in the oldest civilisations as sleeping medicine



early past

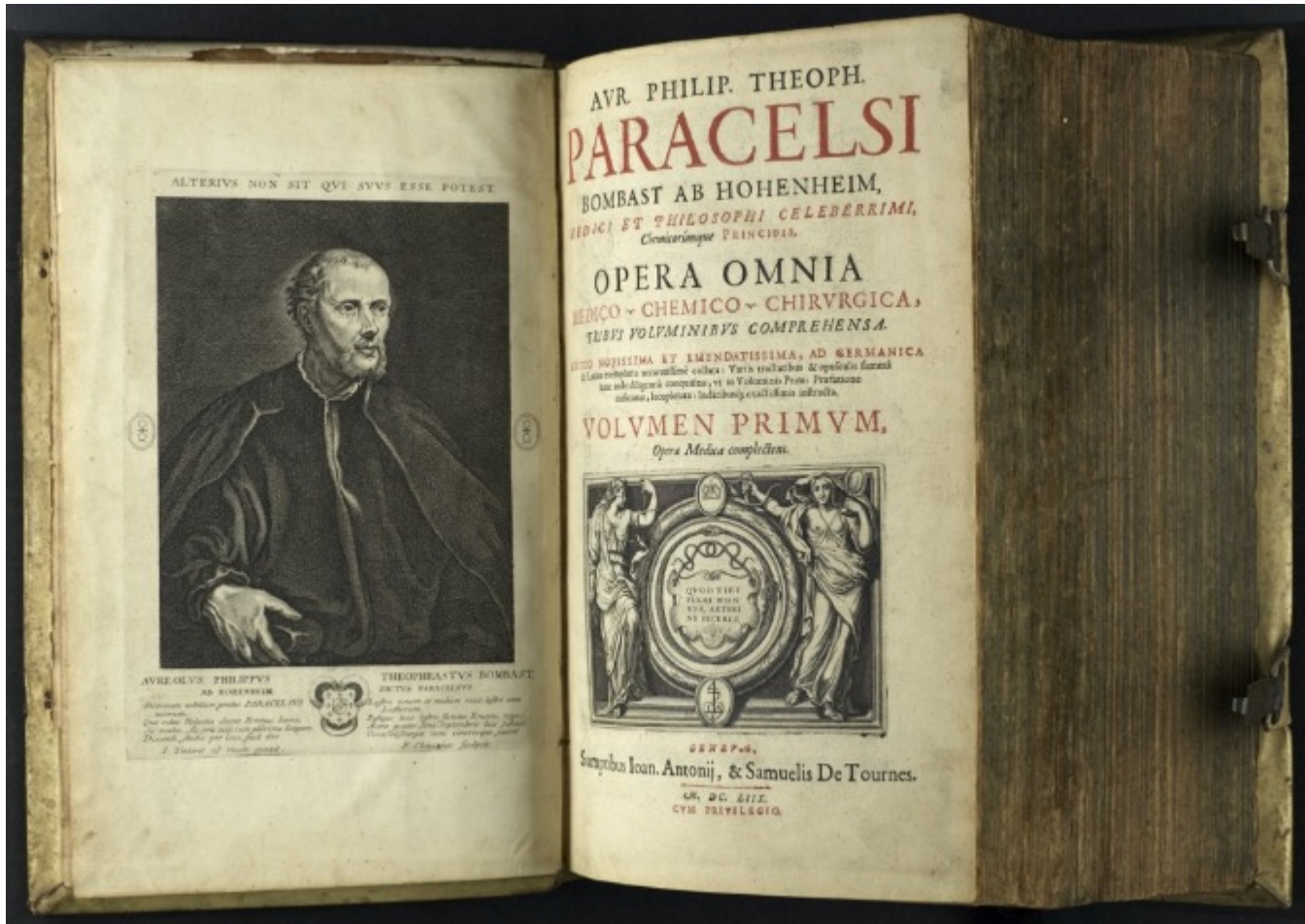


recent past



morphine binds opiate receptors (3 subtypes) which in turn mediate the opioid receptor signaling, and highlight advances in opioid molecular and behavioural pharmacology, widely used as analgesics in the clinic.

Historical perspective : Paracelsus : „sola dosis facit venenum”



Innovating medicine is difficult and often not comfortable : Paracelsus was rejected from various universities included Basel on his modern views on medicine



Auoleus Philipus Theostratus Bombastus von Hohenheim1493-1541

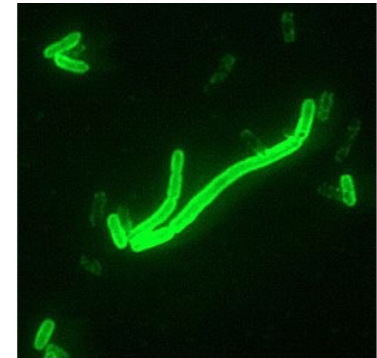
Paracelsus taught medicine (father of pharmacology) in Basel Switzerland

“solely the dose determines that a thing is not a poison”



**Marketplace of Napoli during plague near 1656
(Yersinia pestis)**

Infectious diseases before the antibacterial era



Yersinia pestis seen at 200x magnification with a fluorescent label.

Yersinia pestis



A scanning electron micrograph depicting a mass of *Yersinia pestis* bacteria in the foregut of an infected flea

Plague in ancient times
(now known as *Yersinia pestis*)

History of medicine by Jean Starobinski : a philosophical perspective

Je le soignai, Dieu le guérit.

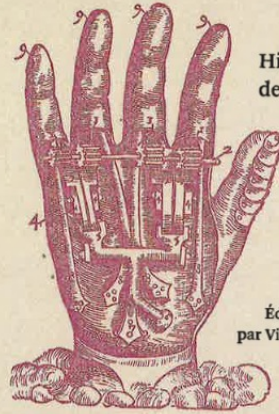


ambroise paré

www.citation-celebre.com



Jean
Starobinski



Histoire
de la médecine

Édition établie
par Vincent Barras

Héros-Limite



Vésale, étude de muscles, vue
frontale, XVI^e siècle.

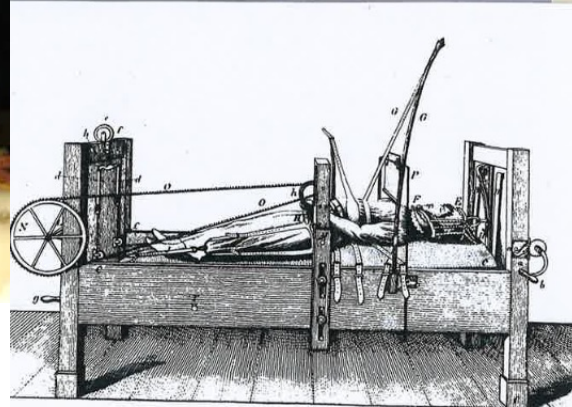


Planche anatomique
de la matrice, 1605.

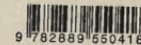


L'Histoire de la médecine de Jean Starobinski s'adresse non seulement au spécialiste, mais à chacun et chacune d'entre nous. Cet ouvrage demeure aujourd'hui encore l'occasion d'une réflexion portant sur les valeurs fondamentales de notre existence, et d'une prise de conscience critique de la médecine, car cette dernière ne nous rendra plus heureux que si nous savons exactement ce qu'il faut lui demander.

Illustrations : Fonds iconographique Nicolas Bouvier, Genève.



20 euros



S = !
VITALE

en quelques heures.
sauve des vies.

D'ALERTE

rés élevée ou
nature anormalement

s intenses, sueurs
tion rapide,
lement

ents cardiaques
ides

on, désorientation,
ence inhabituelle

vide, marbrée, bleutée

minute compte

on + ces signes
IMMÉDIATEMENT
NCES

Serendipity in medicine discovery

By C. Bohuon &
Monneret :
a sobering survey of
the pre placebo era

Sommaire

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| Préface | |
| Introduction | |
| L'acide valproïque | |
| L'amiodarone | |
| L'aspirine | |
| Les benzodiazépines | |
| La chlorpromazine | |
| Le cis-platine | |
| La clonidine | |
| Le cromoglycate de sodium | |
| La cyclosporine | |
| Le gardéнал | |
| Le Glivec | |
| L'héparine | |
| L'imipramine | |



Historical perspective : the future is the past only better ?
or how to measure the *disruptiveness* of a research discovery/paper ?



130 YEARS AGO : Montreal **1885**

Small Pox Victim: God's punishment ?



Edward Jenner invented patient
"vaccination" by scarification of cow pox
viruses and laid down the foundation of
immunology

TODAY's : Sierra Leone **2015**

EBOLA victims: all patients passed away

COVID **2019** world wide millions of deaths !



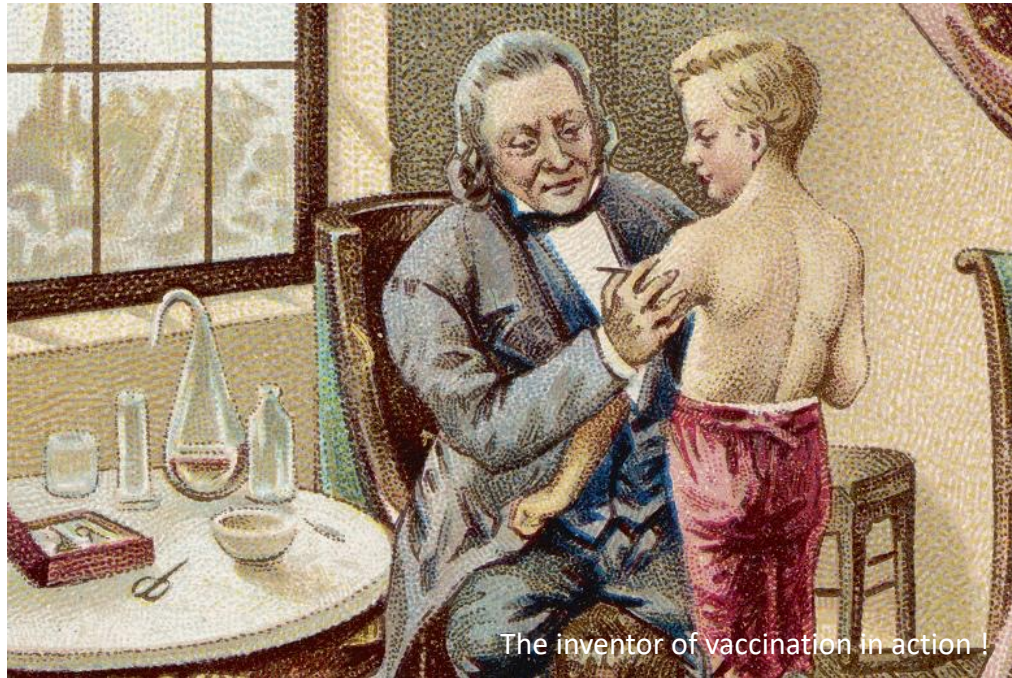
EBOLA'S LOST WARD

Two hundred years later we are still
striving at a number of viruses pandemia
and lots of unmet medical needs !

Historical true medical breakthroughs : the patient need



***The first steps in the development of a modern medicine ! Beginning of 19th century
Two centuries before the advent of therapeutic targets elucidation !
No knowledge what so ever of the underlying molecular mechanism (MOA) !***



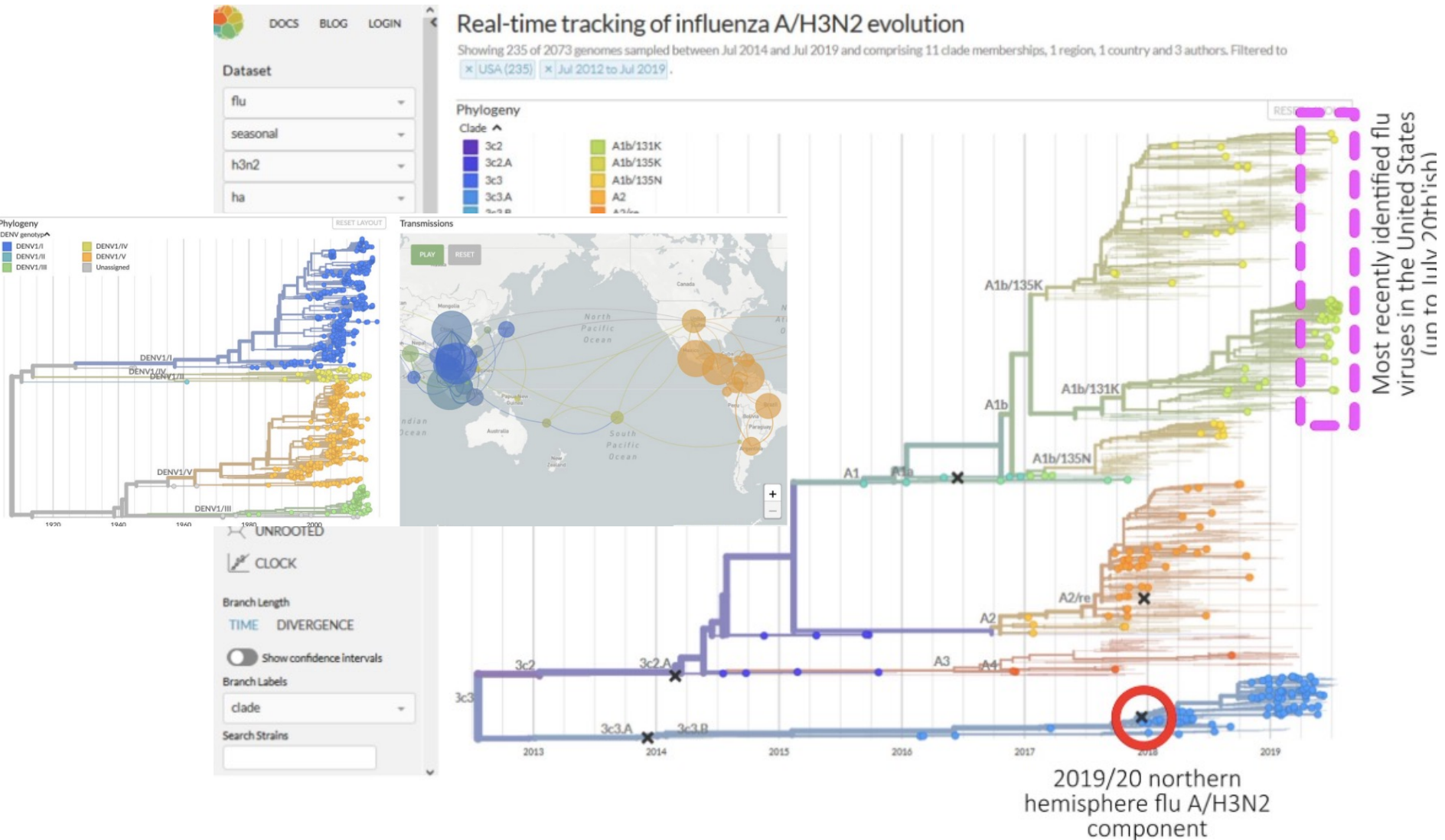
The inventor of vaccination in action !

WORKSHOP !

**Would Edward Jenner's smallpox experiment pass a research ethics committee today ?
How can we go about discovering innovative medicine in the highly regulatory context of today ? Is a single fatality in clinical setting entitled to stop 10 years of research ?
How do we innovate healthcare today ? How much is 3 months life extension worth ?**

Nextstrain : real time tracking of viral pandemic

Richard Neher biophysicist has been conducting research on epidemiological questions at the Biozentrum of the University of **Basel** since 2017.



Throughout history, pandemics have been a constant deadly threat challenging biomedical research and clinical setting



75



5M-10M*
DEATHS

The Cyprianic Plague
Mediterranean, 250-270

North Italian Plague
North Italy, 1629-1631
2M* DEATHS

Plague of London
London, 1665-1666
68K-100K DEATHS

Ebola Epidemic
West Africa, 2013-2015
11.5K* DEATHS

SARS
Global, 2003
774 DEATHS

Influenza Pandemic
Global, 1957-1959
1.1M* DEATHS

12.5M*
DEATHS

*Third Plague
Pandemic*
India, 1896-1920

5M-10M*
DEATHS

The Antonine Plague
Mediterranean, 165-190*

5M-20M*
DEATHS

The Justinianic Plague
Mediterranean, 541-544

The Black Death
Europe, 1346-1352
>40M DEATHS

Provençal Peste
Provence, France, 1720-1721
90K* DEATHS

Influenza Pandemic
Global, 1889-1891
1M-1.25M DEATHS

Great Pneumonic Plague Epidemic
Manchuria, 1909-1911
45K-60K DEATHS

Influenza Pandemic
Global, 1917-1919
25M-50M DEATHS

*approximate

LAST CENTURY OF PANDEMICS TIMELINE

There have been five main pandemics in the past one hundred years. These are summarised in the table below:

1918
1920

SPANISH FLU (H1N1)

A virus which originated in birds, mutated and then infected pigs, which went on to infect humans

CASES
500 MILLION
DEATHS
17 MILLION

3.4%

MORTALITY RATE

1920
PRESENT

HIV/AIDS

Originating from Chimpanzees, HIV kills humans by repressing immunity systems. Nobody dies of HIV, but they die of AIDS-related conditions.

CASES
75 MILLION
DEATHS
32 MILLION

42.7%

MORTALITY RATE

AIDS IDENTIFIED IN 1981

1956
1958

ASIAN FLU (H2N2)

(H2N2) from East Asia was nicknamed "Asian Flu". This virus comprised of 3 different genes and was the mildest of the 20th century pandemics.

CASES
478 MILLION
DEATHS
1.1 MILLION

0.23%

MORTALITY RATE

1968
1969

HONG KONG FLU (H3N2)

(H3N2) originating from Hong Kong. The population was said to have some immunity from the N2 in the Asian flu pandemic.

CASES
200 MILLION
DEATHS
1 MILLION

0.5%

MORTALITY RATE

The future is the past : more pandemics, more zoonoses ... when, how massive ?



AIDS (HIV) pandemia (Kaposi sarcoma of bucal cavity)
1980's - today



Confronting asian flu H2N2 in 1957



Confronting SarsCoV2 in 2020

Throughout history a pandemic burst (of bacterial, viral or of zoonoses origin) is a constant threatful compaign of healthcare



MILLION COVID-19 DEATHS – A TIMELINE



JANUARY 2020

First death from COVID-19, reported in Wuhan, China.

JANUARY 2021

The U.S. continued to top COVID-19 death counts, but experts were hopeful the rollout of vaccines will help reduce mortality numbers.

JULY 2021

India accounted for almost a quarter of COVID-19 deaths during this period, driven by the delta variant. Later analyses said the total number was likely much higher, with one estimate putting the death toll at 3 million.

MARCH 2022

Several countries have started easing COVID-19 restrictions. But WHO officials continue to advise caution. While trends show COVID-19 cases are declining, they warn the pandemic is not yet over.

1

1M

2M

3M

4M

5M

6M

SEPTEMBER 2020

The U.S. topped total COVID-19 deaths during this period, reaching over 200,000.

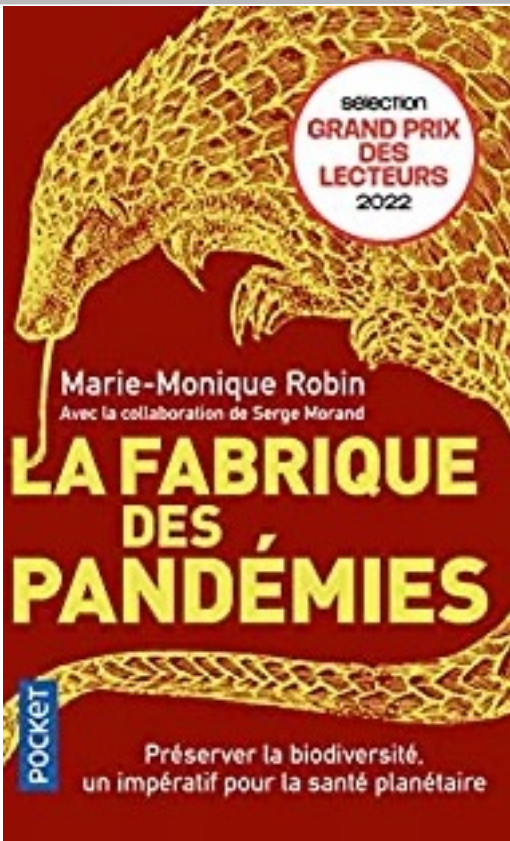
APRIL 2021

Uneven distribution of vaccines left several low- and middle-income countries with little to no access to doses.

NOVEMBER 2021

Official data showed the African region, excluding Egypt, had less than 150,000 deaths. But deaths in 13 countries had doubled since July, raising calls for more vaccine access as only 3% of the region's population was fully vaccinated.

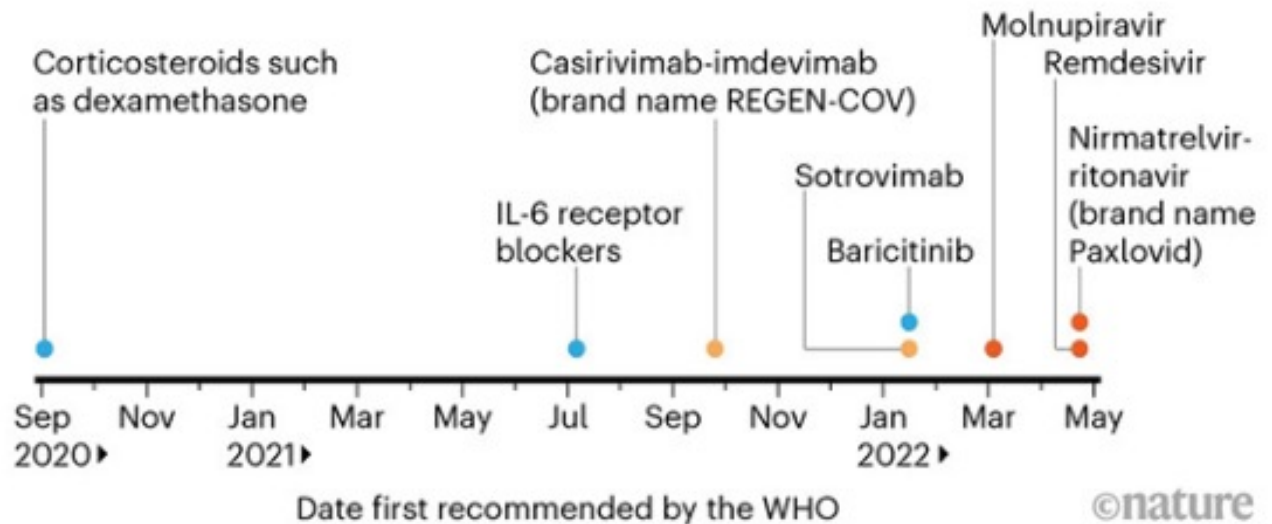
Throughout history Pandemias have been a constant companion today's SarsCoV2 pandemic from zoonoses origin



VIRUS-TAMING TOOLS

The virus that causes COVID-19 was identified only in early 2020, but the World Health Organization has already recommended more than half a dozen treatments for the disease. Still other therapies have been recommended by domestic agencies such as the US National Institutes of Health.

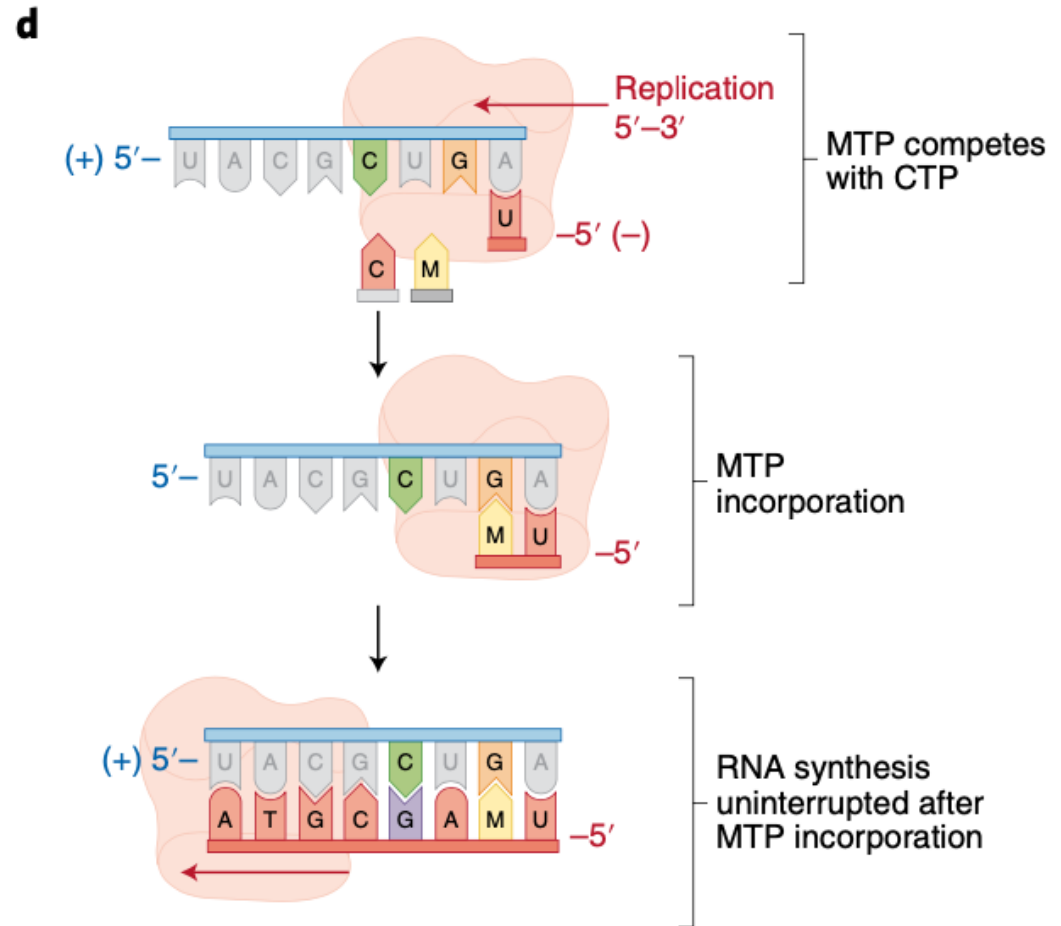
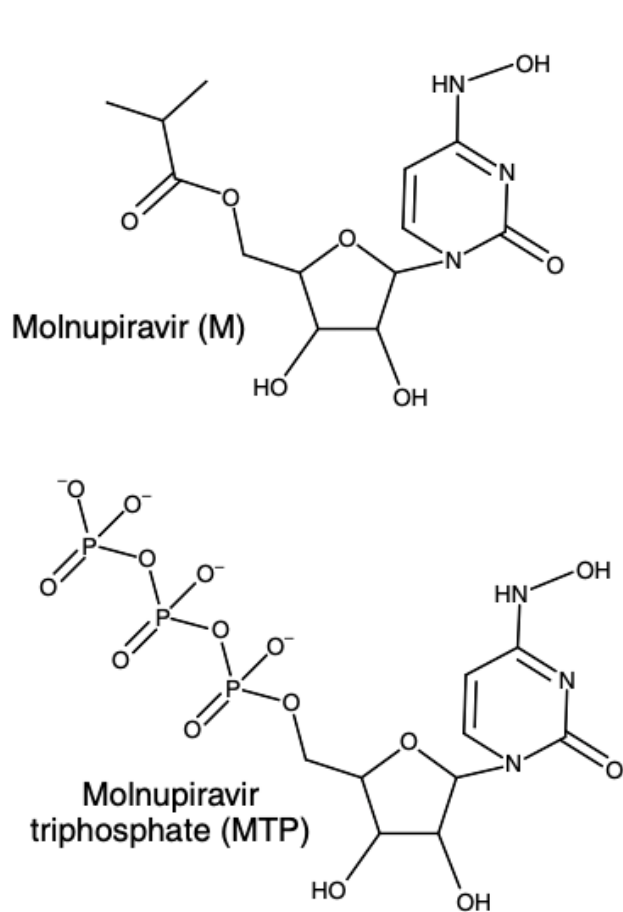
● Antiviral ● Monoclonal antibody ● Anti-inflammatory



©nature



Today's medicinal chemistry therapeutic armamentarium towards pandemics is on a steep learning curve



e

MTP directs the incorporation at either Gs or As with a high rate of mutagenesis leading to mutated SarsCoV2 RNA products

Paul Ehrlich coins the term
„chemotherapy“



AUG. 31, 1909: FIRST CHEMOTHERAPY DRUG TREATS SYPHILIS



**DOCTORS HAVE FAITH
IN EHRlich'S '606'**

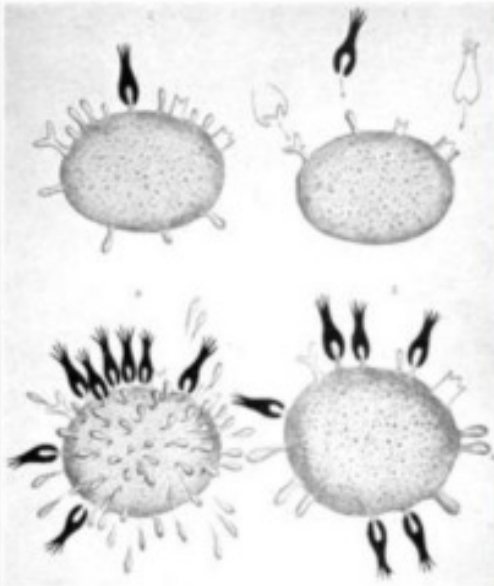
**Danger, All Admit, Attends
Faulty Technique in Using
the Blood Cure.**

IT MUST ENTER THE VEINS

**Fatalities Have Resulted Only Where
Salvarsan Has Been Introduced
Into Muscular Tissues.**

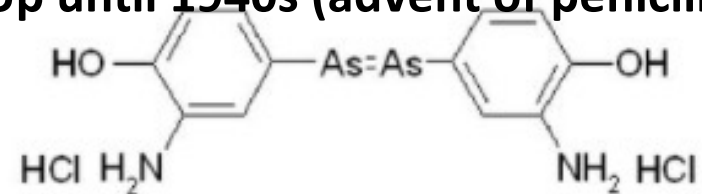
__1909: __After searching through hundreds of potential chemicals, a German immunologist discovers a compound that can selectively kill the parasitic spirochete that causes

Paul Ehrlich and the “Magic Bullet”



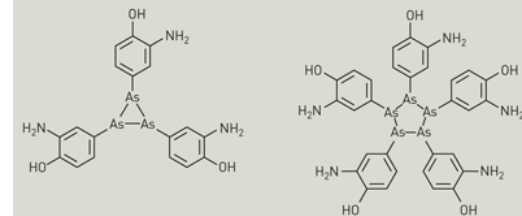
Up until 1940s (advent of penicilin)

Salvarsan-Compound 606
 Early antimicrobial chemical
 Introduced in 1910s
 Not 100% effective
 Long treatment: 1-2 years
Arsenical cpd Arsphenamine



MISTAKEN IDENTITY

Ehrlich's Salvarsan is actually a mixture of cyclic species



AUG. 31, 1909: FIRST CHEMOTHERAPY DRUG TREATS SYPHILIS

Paul Ehrlich coins the term „chemotherapy“

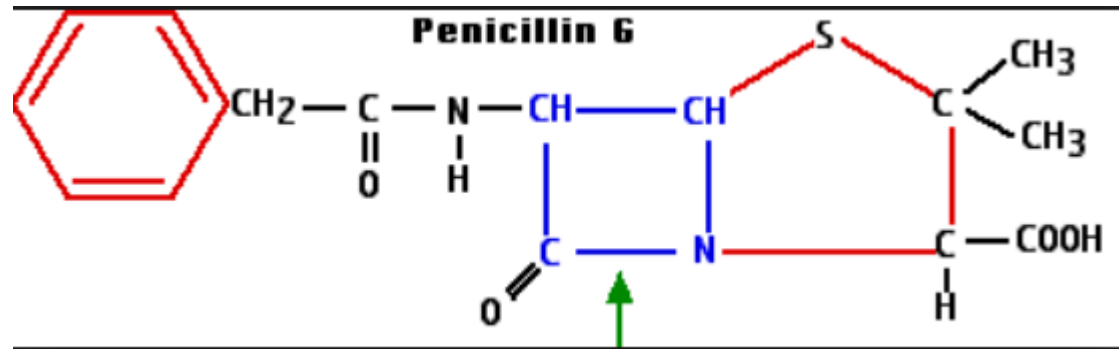


Ehrlich reasoned that by screening many cpds, he could discover anti microbials that do not kill the patient !
No placebo control trials ; no toxicology study except the patients themselves !



__1909: __After searching through hu
chemicals, a German immunologist discovers a compound
that can selectively kill the parasitic spirochete that causes

Historical medical breakthrough with impactful clinical value: debate : to whom penicilin's discovery?



“THE OLD WONDER” IS STILL FIRST LINE TREATMENT FOR SEXUALLY TRANSMITTED DISEASES SUCH AS SYPHILIS ! (45 x 10⁶ cases in 2015)



WORLDWIDE PAIN ASSISTANCE

SYPHILIS

Treponema pallidum

Exanthem

Syphilis

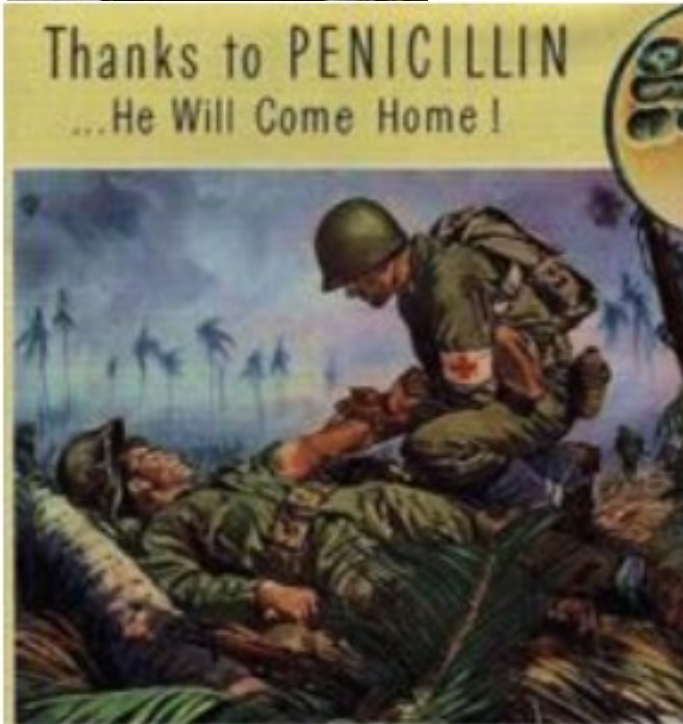
It is caused due to a bacterium called Treponema Pallidum which can be transmitted from an individual to other usually by sexual contact.

PainAssist.com

Historical medical breakthrough with impactful clinical value : 1940's and the New Wonder Drug From Mold

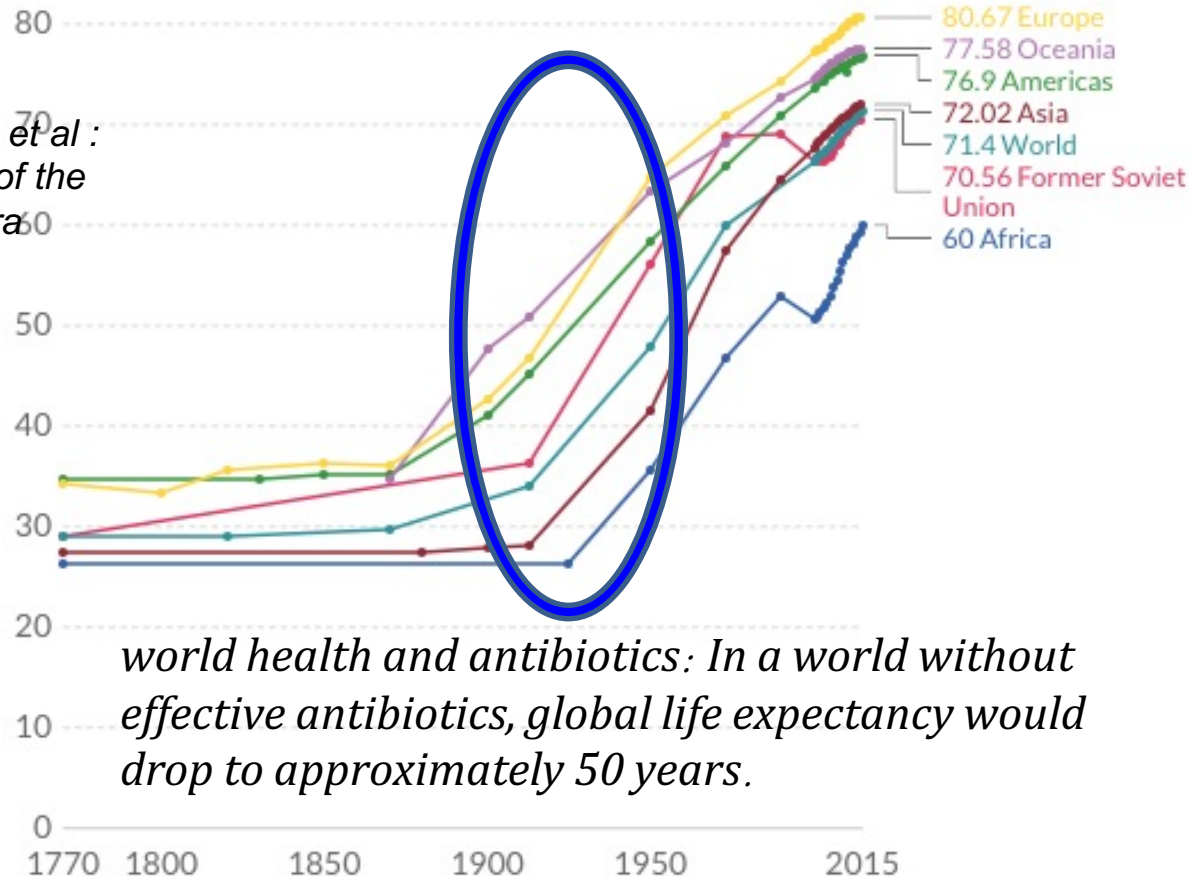


Sir A. Flemming et al :
the foundation of the
antibiotic era



Life expectancy globally and by world regions since 1770

Our World in Data



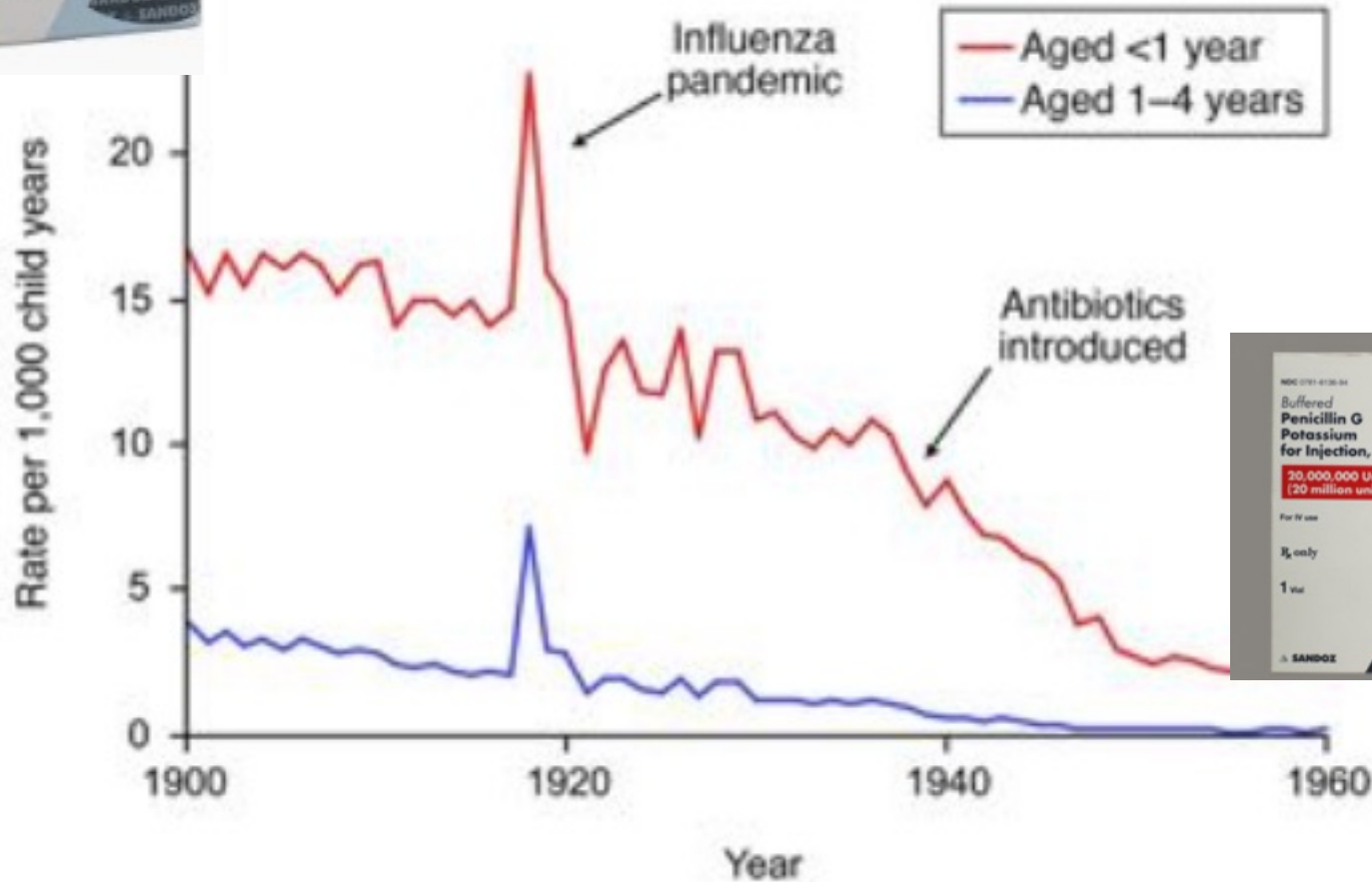
world health and antibiotics: In a world without effective antibiotics, global life expectancy would drop to approximately 50 years.

Source: Life expectancy – James Riley for data 1990 and earlier; WHO and World Bank for later data (by Max Roser)
OurWorldinData.org/life-expectancy/ • CC BY

Historical true medical breakthroughs



THE ADVENT OF ANTIBIOTICS CHANGED OUR MEDICAL STATUS AND LIFE EXPECTANCY IN THE MID OF 20TH CENTURY : CHILDHOOD MORTALITY



1945 NL
Fleming,
Florey and
Chain



today 3000 types of resistant beta lactamase to antibiotics (ampicilin, methicillin, etc...)

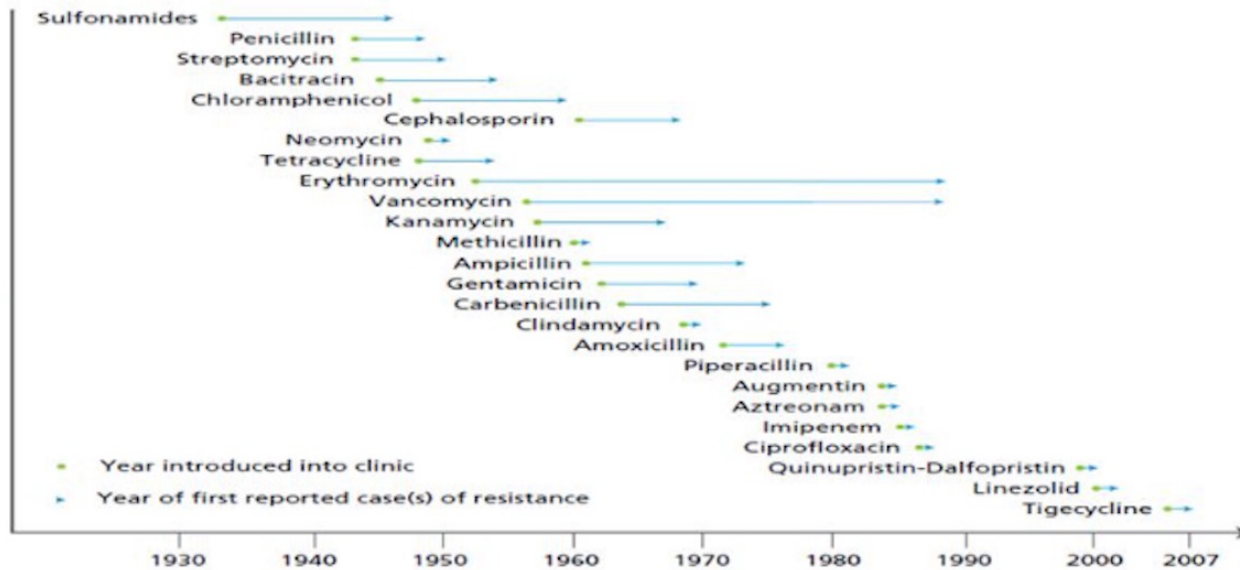


Threat and challenges of a postantibiotic era – stay tuned !

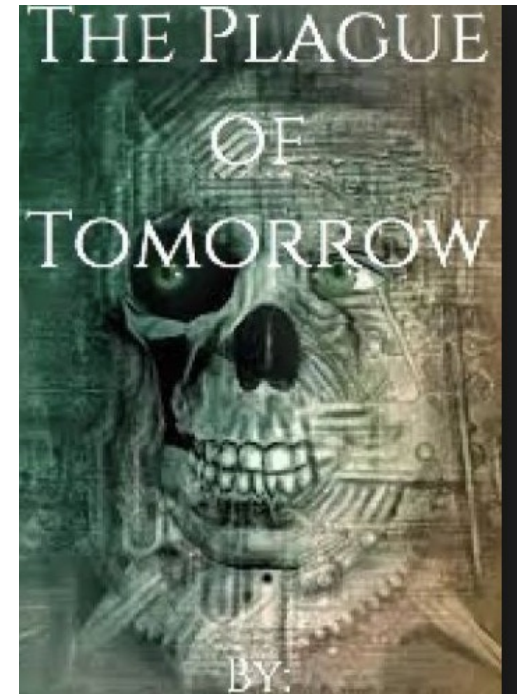


Emergence of antibiotic resistance

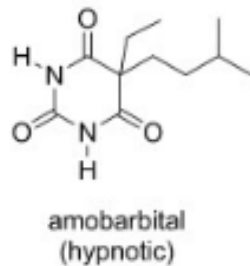
Antibiotic resistance threatens ability to control infection



Note: Some of the dates are estimates only.



Historical psychiatric care – electroshocks, lobotomy



Psychiatry 1940's: electroconvulsive therapies, electroshocks, lobotomy see eg. Angelina Jolie starring "Changeling"

Note: barbiturates act by hyperpolarization and opening of GABA receptor associated ion Cl channels leading to inhibition of neural activity, MOA unknown up until 1980's

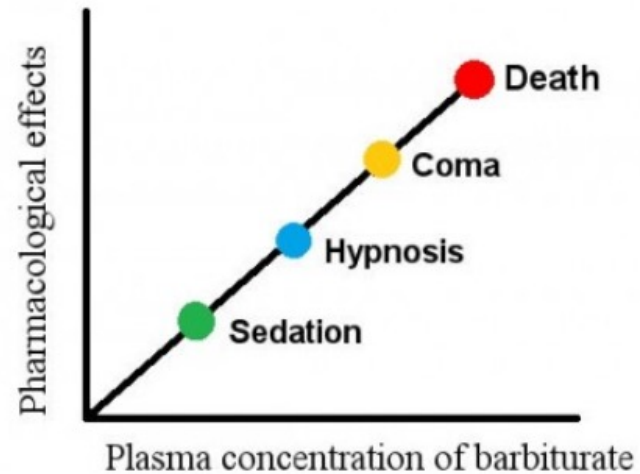
Historical medical breakthroughs and pitfalls



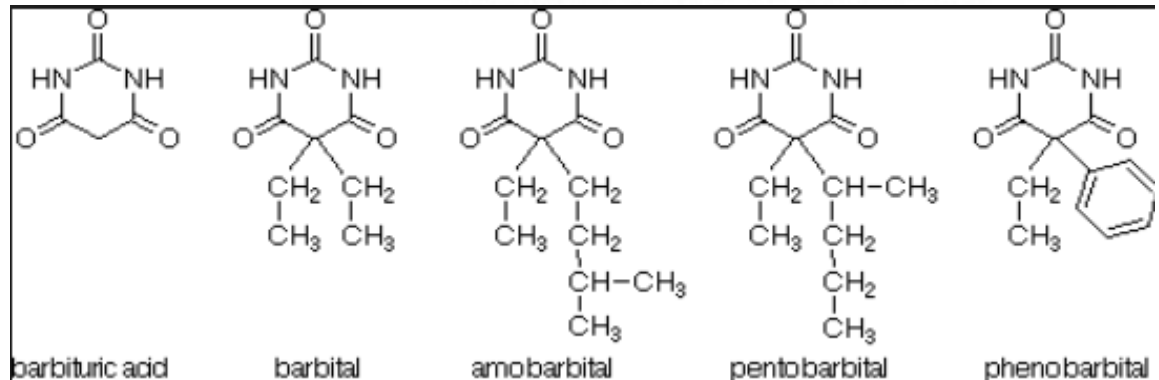
Before the Benzodiazepine Story: a number of fatalities on **barbiturates** overdose



Relationship between Plasma Concentration of Barbiturates and its Pharmacological Effects



Chemist A. von Baeyer : 1864 tested a derivative of urea and malonic acid on himself ! the first hypnotic sleep drug with fatal adverse effects (NL 1905)



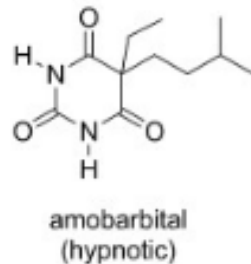
Historical psychiatric care-lobotomy



ANGELINA JOLIE JOHN MALKOV
A TRUE STORY
CHANGELING



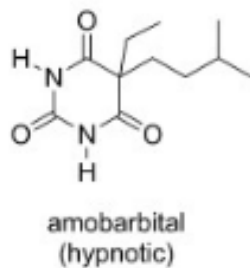
"Epic, Taut, Twisty and Compelling."



therapies, electroshocks, lobotomy
see eg. Angelina Jolie starring "Changeling"

Note: barbiturates act by hyperpolarization and opening of GABA_A receptor associated ion Cl⁻ channels leading to inhibition of neural activity, MOA unknown up until 1980's

Historical psychiatric care – electroconvulsive therapies

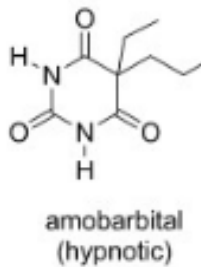


Psychiatry 1940's: electroconvulsive therapies, electroshocks, lobotomy see eg. Jack Nicholson starring "One flew over the cuckoo's nest"

Historical psychiatric care – reloaded by Jack Nicholson



"One Flew Over the Cuckoo's Nest" 1975



Historical psychiatric care – reloaded by «Le Temps d'Anna» a swiss movie



*Before the Benzodiazepine
discovery and others
serotonin uptake
inhibitors : **a true story of
fatal schizophrenia upon
lobotomy and***



Historical psychiatric care – reloaded by «Le Temps d'Anna» swiss movie



Before the Benzodiazepine discovery : a true story of fatal schizophrenia



More historical breakthrough medicines 1950s-1980's

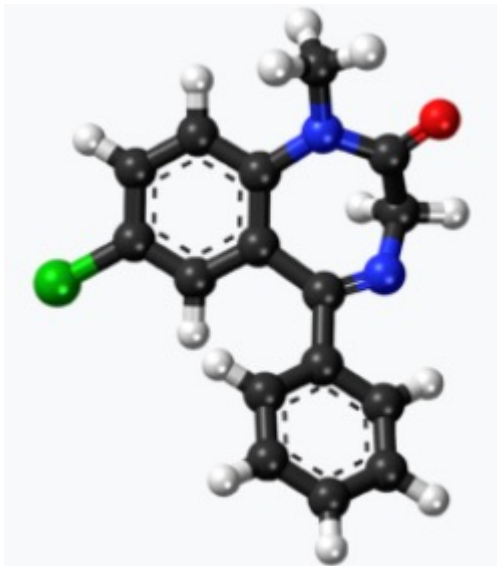


The advent of modern medicinal chemistry in drug development

BENZODIAZEPINES

1960 Valium® (diazepam)
Tranquilizer
(GABA receptor agonist)

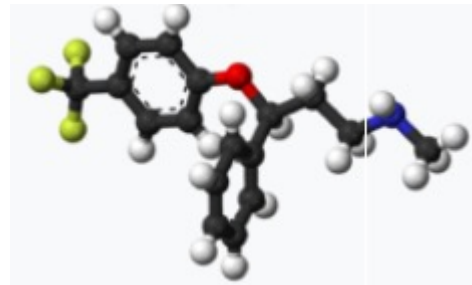
Leo Sternbach
Roche Ltd



SSRI selective serotonin reuptake inhibitors

1972 Prozac® (fluoxetine)
Antidepressant
(serotonin receptor)

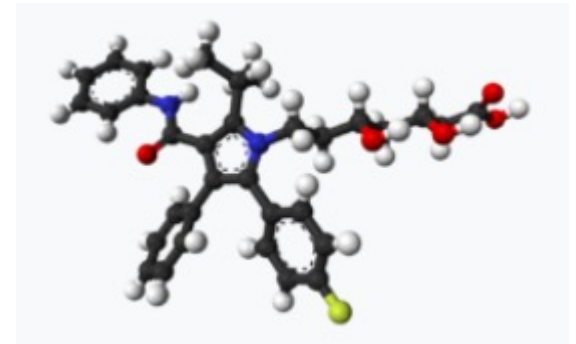
Eli Lilly Inc



STATINS

1985 Lipitor® (atorvastatin)
Lipid lowering, CVD
(HMGCoA reductase inhibitor)

Akira Endo (Lasker Award)
@ Sankyo/Warner-Lambert
Pfizer



Weekly Dose: Lipitor, the highest-selling drug of all time

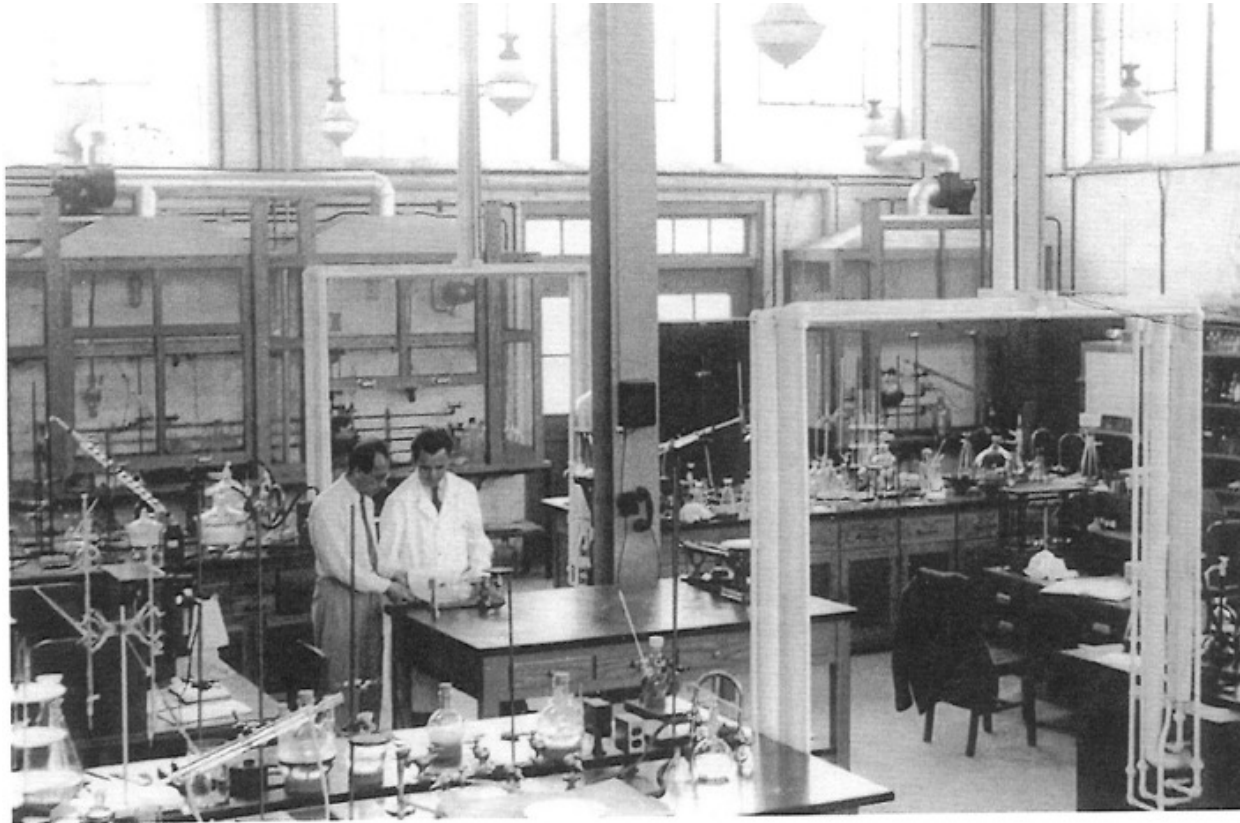


Historical medical breakthroughs 1940's @ Roche



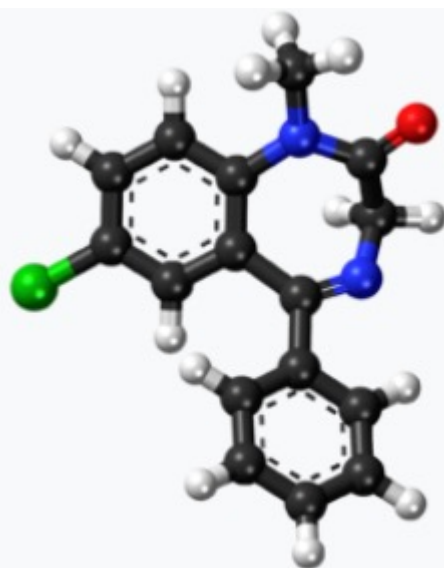
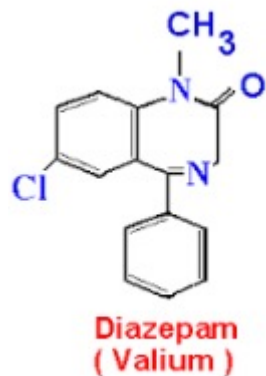
The Benzodiazepine Story: towards Leo Sternbach life time achievement

- 1940's
- WW II time
- ROCHE Inc hires Nazi refugee polnish chemist L. Sternbach
- primitive tranquilizers
anxiolytics: barbiturates with severe adverse effects and little therapeutic value
- **NO CELLULAR SIGNAL PATHWAY DECIPHERED !**
- **NO GENOME PROJECT**
- **TRIAL AN ERRORS NO HTS !**
- Secondary screens *in vivo*:
how to monitor a depressed anhedonic rodent in animal pharmacology ?

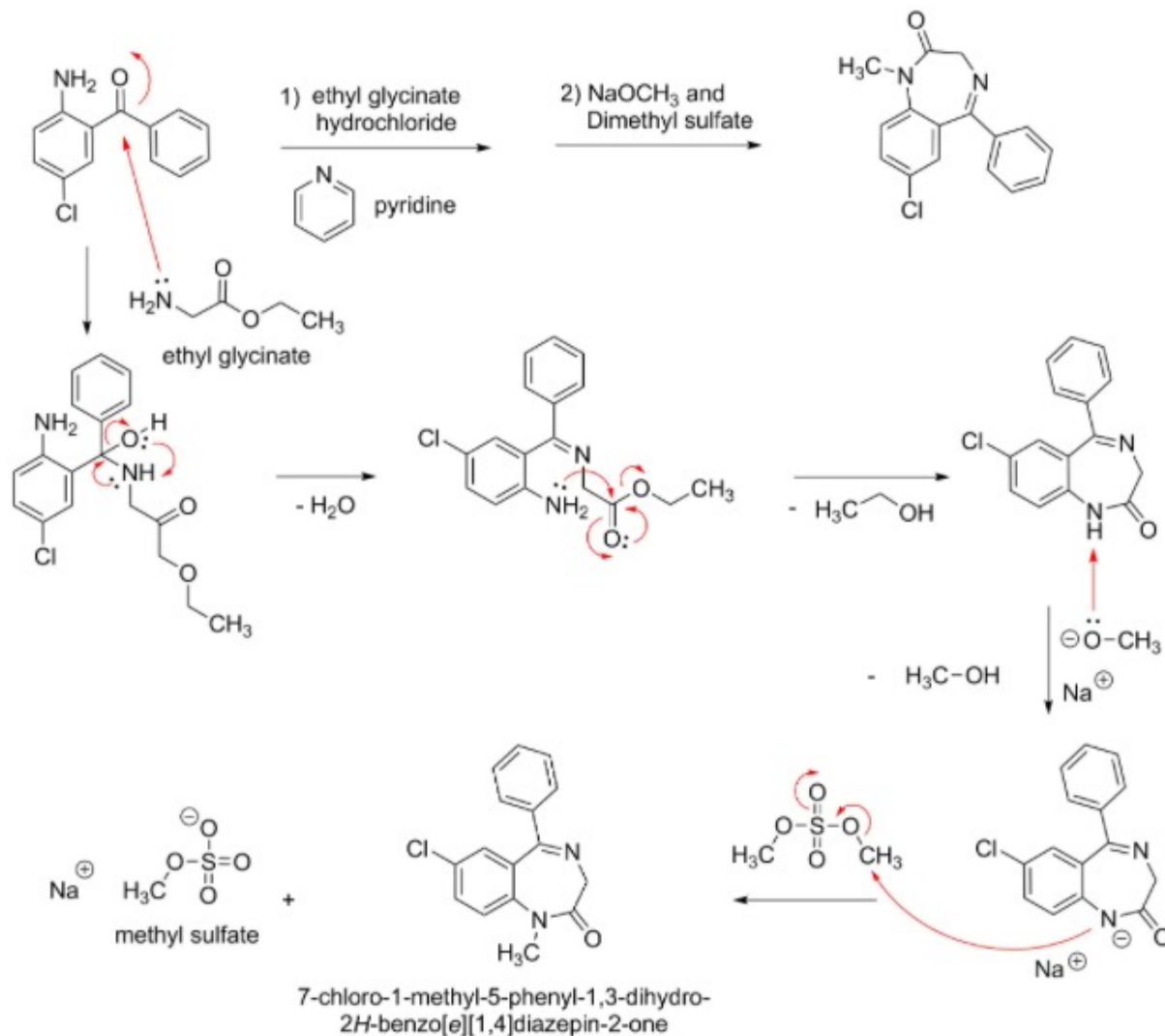


Leo Henryk Sternbach and Dr. Max Hoffer in the chemistry laboratory, building 25, Roche Nutley, 1941

The Benzodiazepine Story of Valium: Leo Sternbach life time achievement



Synthesis of Diazepam with (2-amino-5-chlorophenyl)(phenyl)methanone

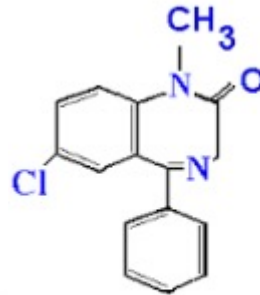


Historical medical breakthrough – the benzodiazepines

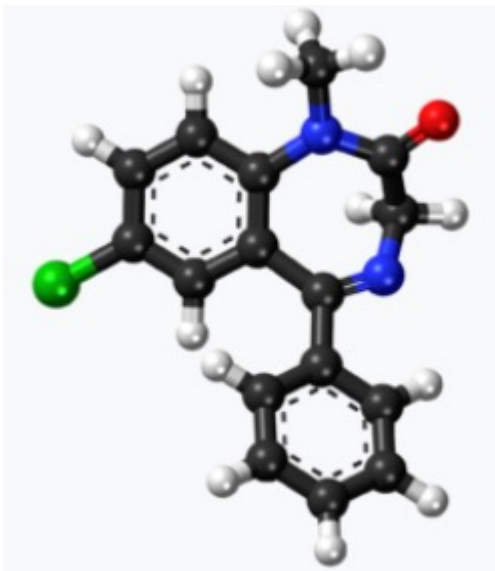


The Benzodiazepine Story of Valium®: Leo Sternbach life time achievement

1960's discovery of Valium®
(Diazepam) safe
tranquilizer, anxiolytic



**Diazepam
(Valium)**



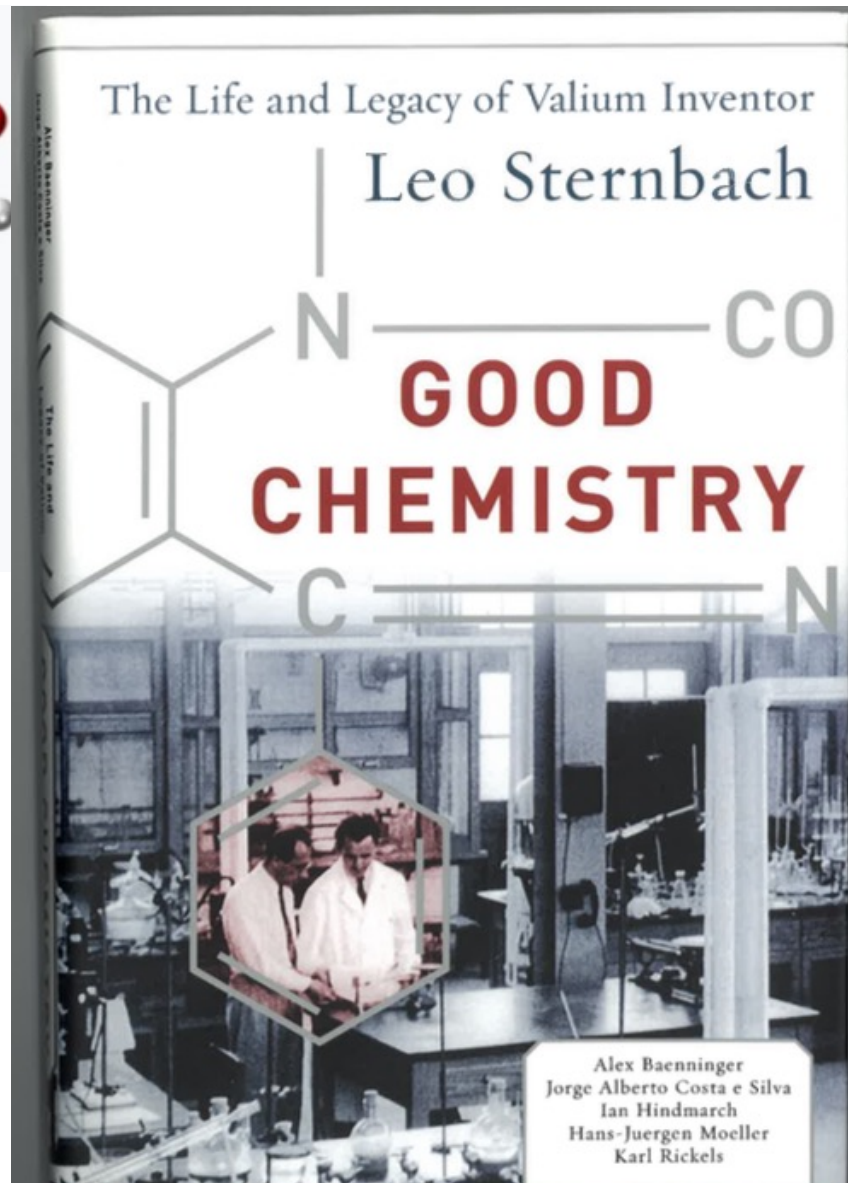
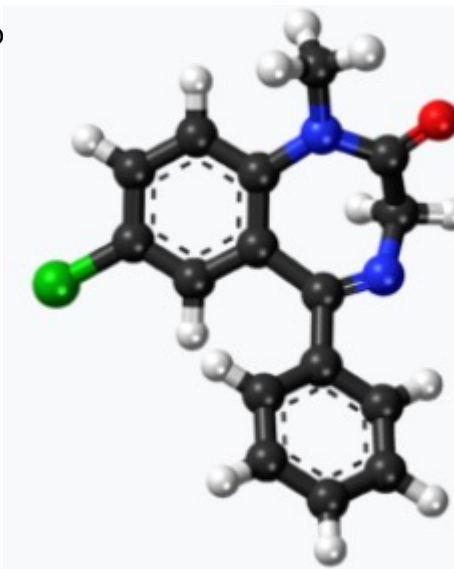
Leo Henryk Sternbach accepting award for Valium from Mr. Lindner on behalf of Roche, 1970

Historical medical breakthrough – the legacy of Leo Sternbach



1960's discovery of Valium®
(Diazepam) safe
tranquilizer, anxiolytic.

Today's "benzo" addiction
syndrome still a major
threat in psychiatric care



Historical medical breakthrough – Diazepam (Valium®)



20 YEARS AFTER THE DIAZEPAM DISCOVERY :

THERAPEUTIC TARGET IDENTIFIED !! A VERY SPECIFIC NEUROTRANSMITTER GABA RECEPTOR AGONIST

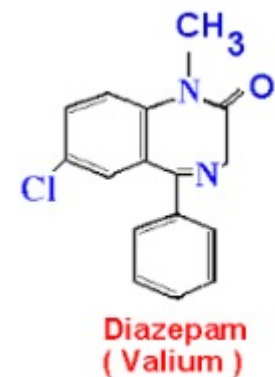
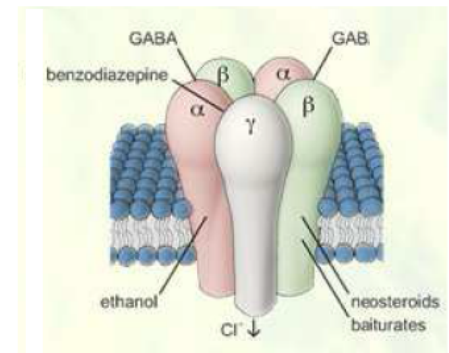
MARGINAL SIDE EFFECTS (ADDICTION), STILL IN CLINICAL USE TODAY AS VALIUM eg POST OP RELAXANT

Seeburg PH Barnard EA
Lab at Genentech. Nature
(1987) 328:221-227

The Benzodiazepine Story – Valium®: 20 years later !

GABA_A receptor (GABA_A R)

- pentameric **ligand-gated Cl⁻ channel** (endogenous: GABA)
- Clinically relevant **allosteric binding** sites for: BZD, Z drugs, barbiturates, **ethanol**
- Neuronal hyperpolarisation
- anxiety, fear, consciousness, seizures



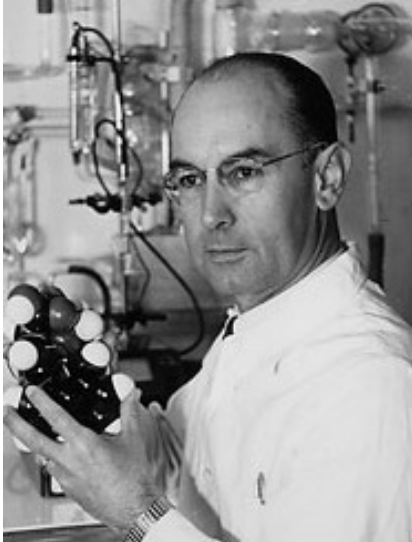
80th birthday LSD -1943-2023 - Lysergic acid diethylamide !

Psychiatry rediscovers in 2000's the LSD as a revolution in psychotherapy



1943-2018
Albert Hoffmann
@ Sandoz Ltd
Switzerland

*"the space medicinal
chemist"*

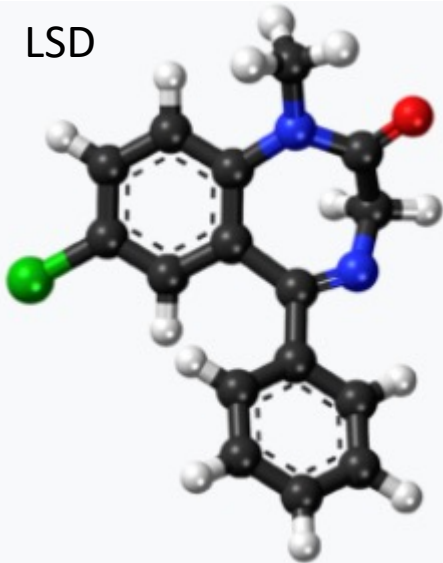


First « acid trip » in the lab on April 16, 1943 : for the first time an “acid trip” taken by its discoverer : while manipulating purified LSD, a drop fell on chemist Albert Hoffmann’s hand : upon absorption of the droplets, anguish, vertigo, supernatural visions, happiness and gratitude invaded his conscience.

Three days later, AH ventured to duplicate the “clinical experiment” : the unexpected **psychotropic surprise in the lab** - adverse and positive effects - resumed.

Albert Hoffmann could not anticipate at this point in time that his discovery would not only invade the hippies and pop song stages but also today’s psychiatric pharmacological armamentarium with resistant depressions. A. Hoffmann depicted his vivid memories on LSD as “Mein Sorgekind” (**my problem child**) !

LSD



***LSD – Basel in 1943* : historical breakthrough discovery of a psychotropic drug : the «acid trip» of A Hoffmann or how to reset your synaptome !**



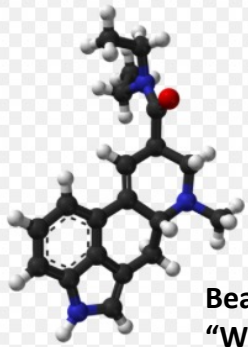
<https://www.youtube.com/watch?v=HBOPFWmZCdM>



LSD acid tab on the tongue : a day long trip, associated with psychedelic experiences in Wight Island Music Festival



1943 LSD
Albert Hoffmann
@ Sandoz Ltd
Switzerland



Beatles 1970's
"White is White" album : a "space" pop song
on Wight island UK

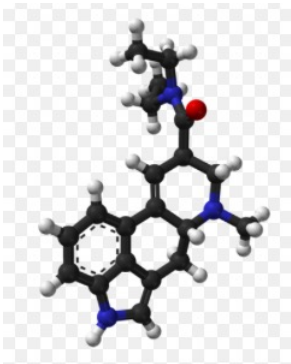


LYSERGIC ACID DIETHYLAMIDE : isolated as ergotamine, a chemical from the fungus ergot

A hippie's drug turns into an effective antidepression medicine as potent serotonin receptor agonist



As of today
LSD therapeutic target
identified ! X-ray
crystallography 5HT_{2c}

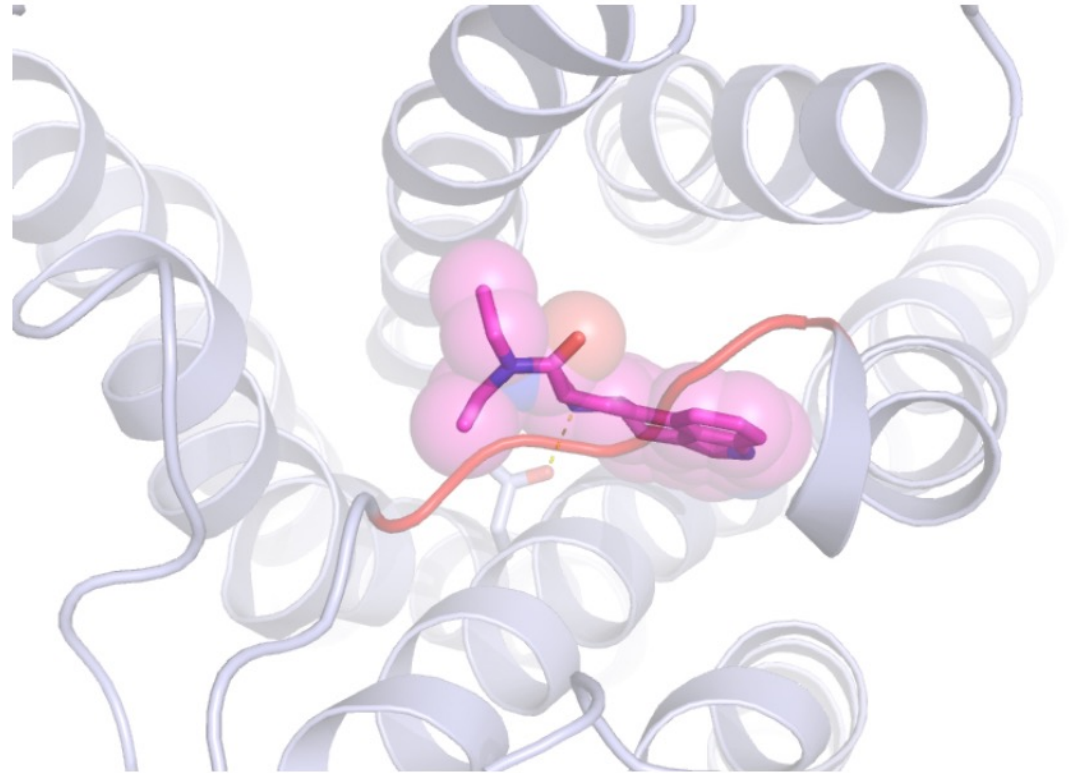


LSD wird meist auf Löschpapier aufgetragen und in den Mund gelegt. Es gibt die Droge aber auch als Pille.

**LSD in action : when attached to the serotonin receptor
psychiatry rediscovers in 2000's the LSD as a revolution in psychotherapy
with depression resistant inpatients (psychiatry ward)**



As of today
LSD therapeutic target
identified ! X-ray
crystallography 5HT_{2c}



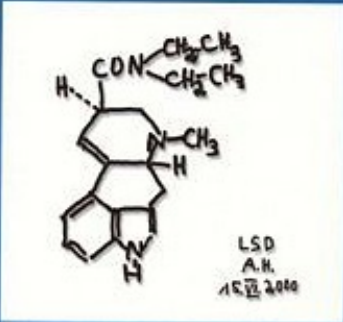

This is LSD attached to a brain cell
serotonin receptor

LSD and Albert Hoffmann : historical breakthrough psychotropic drug



Albert Hofmann

Die Mutterkorn-alkaloide



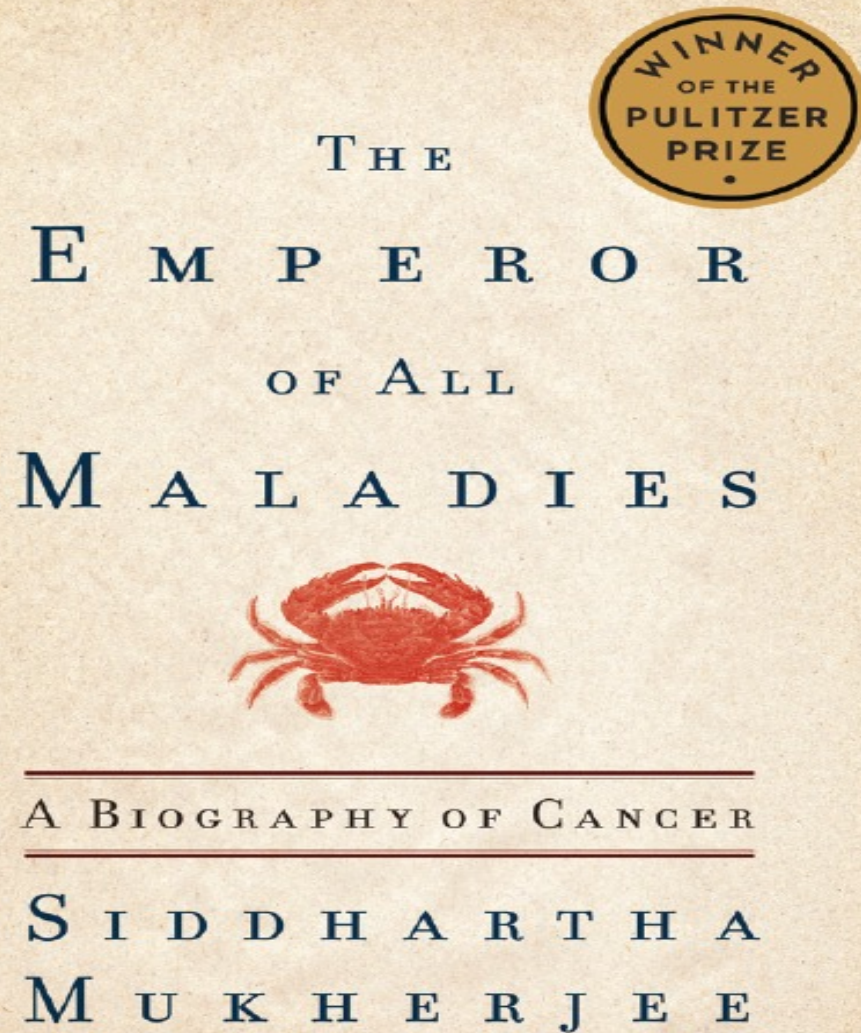
Vom Mutterkorn zum LSD – Die Chemie der Mutterkornalkaloide
Reprint der Originalausgabe

NACHTSCHATTEN VERLAG

Albert Hofmann

LSD
mein Sorgenkind

An oncologist view of patients facing their ordeal : historical perspective




"A compulsively readable, surprisingly uplifting, and vivid tale. Thrilling."
—O, THE OPRAH MAGAZINE




Tumor biology therapy : 1938 – what is missing as of today ?




**THE ONLY SAFE WEAPONS
AGAINST CANCER ARE**



SURGERY



X-RAYS



RADIUM

DO NOT TRUST YOUR LIFE TO OTHER METHODS

U.S. PUBLIC HEALTH SERVICE IN COOPERATION WITH THE AMERICAN SOCIETY FOR THE CONTROL OF CANCER

The poster features a vertical split background: light grey on the left and blue on the right. Three circular icons on the left represent surgery, X-rays, and radium. Red arrows point from the right side of the poster towards each icon. The text is in a bold, sans-serif font.

Tumor biology therapy : 1898 - discovery of Radium



UNE NOUVELLE DÉCOUVERTE. — LE RADIUM
M. ET M^{ME} CURIE DANS LEUR LABORATOIRE

THE PHYSIOLOGICAL ACTION OF RADIO-ACTIVE SUBS

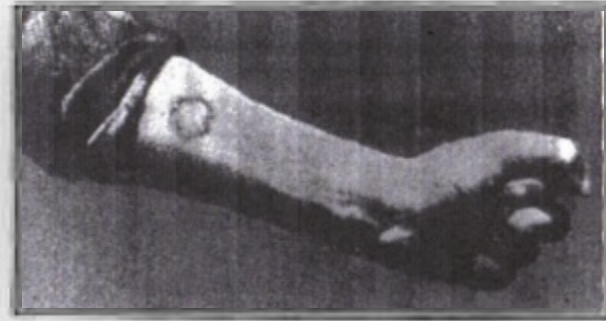


Fig. 51.

Professor Curie's arm, showing a scar resulting from a



MARIE CURIE and the Discovery of Radium



Radiotherapy : 1930's aftermath – the „radium girls“



blue bowl glowing: Marie Curie Sklodowska and Radium



Radiotherapy : 1917's aftermath – „les petites curies“

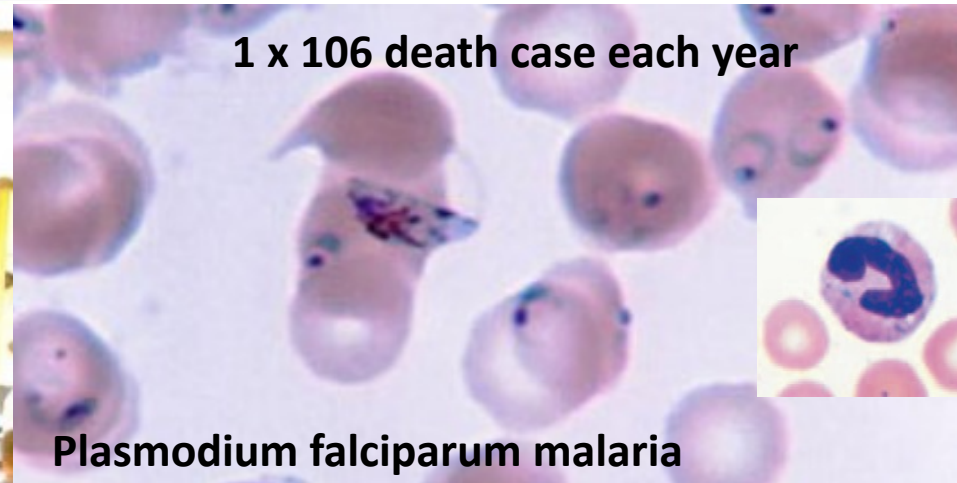


Xray radiology ambulances for war surgery

blue bowl glowing: Marie Curie Skolkova



Neglected tropical diseases – largely unmet medical needs !



1 x 10⁶ death case each year

Plasmodium falciparum malaria

MALARIA, LESHMANIASIS, FILARIASIS etc.

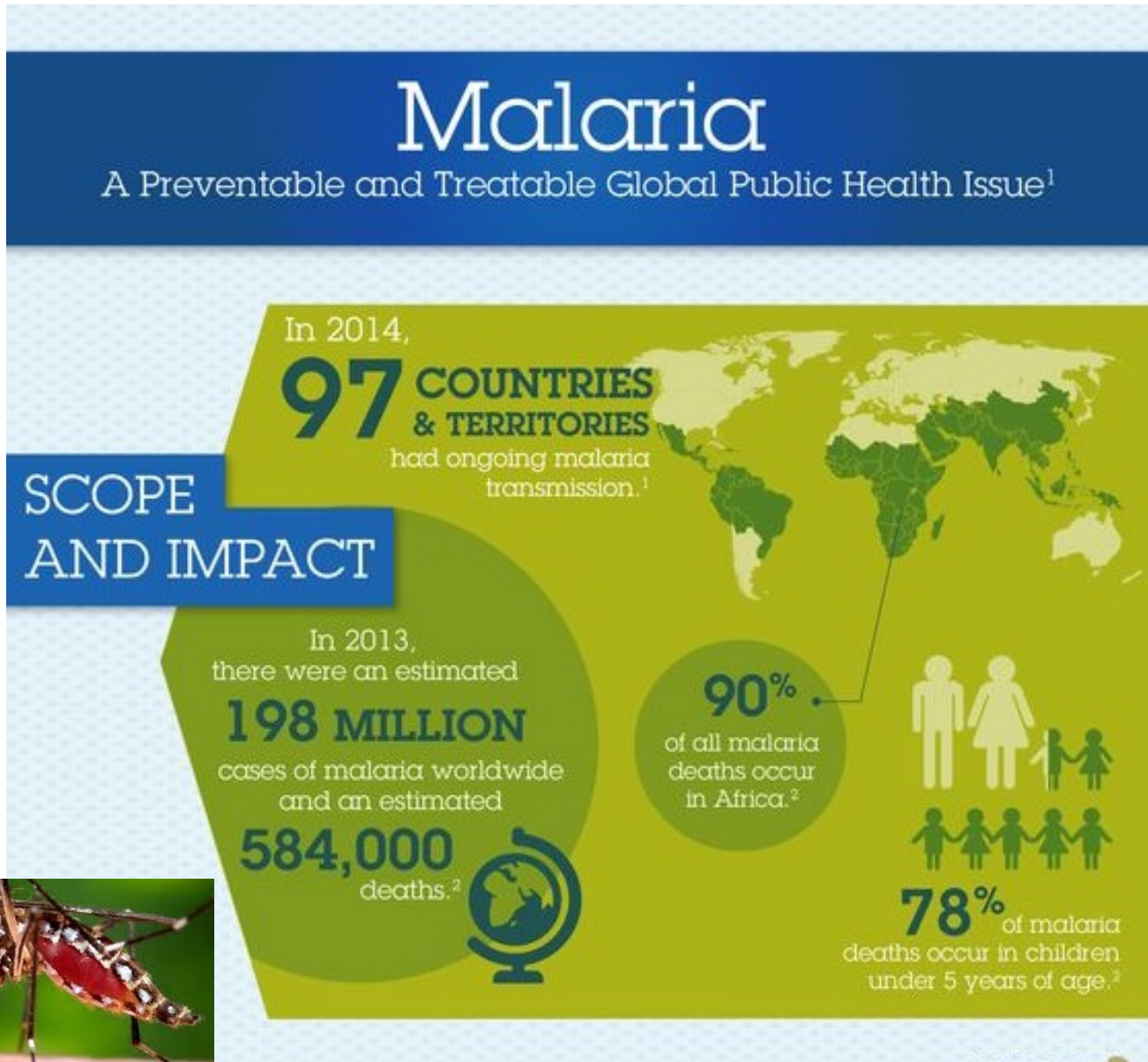
OLD NEGLECTED MEDICAL NEED

PUBLIC HEALTH ISSUE !

WORKSHOP !

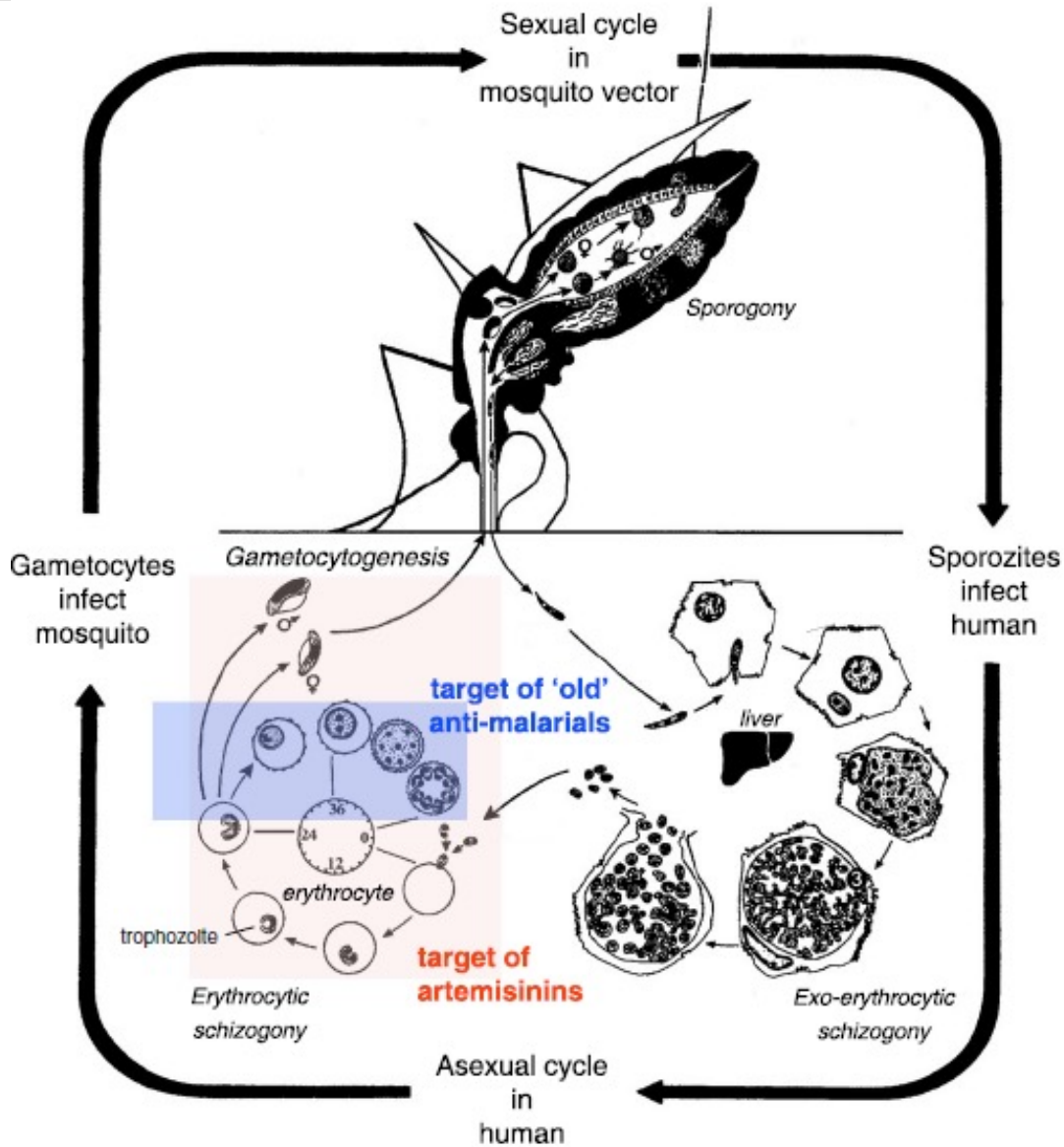
**SHORTAGE OF EFFICACIOUS MEDICINES
(eg ARTEMISIN) !**

The Making Of An Innovative Medicine: historical perspective Artemisinin



The Making Of An Innovative Medicine: historical perspective

Artemisinin



The Making Of An Innovative Medicine: historical perspective artemisinin



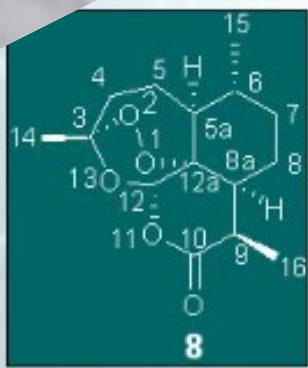
Artemisinin: A major breakthrough in malaria chemotherapy

- In 1967, the Chinese government started a search for new antimalarial drugs from indigenous plants.
- The first written record of *Artemisia annua* for Emergency Use was in 1955.
- In 1972, the Chinese government named Qinghao as a source of new antimalarial drugs.

Plants in the News
October 9 2015



Nobel Prize in Physiology or
Medicine awarded to Tu Youyou
for the development of artemisinin



The Making Of An Innovative Medicine: historical perspective

A visit to the TPI in Basel website !



Swiss TPH 

Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut

<https://www.swisstph.ch/de/>



Historical breakthrough medicines



1920 : life expectancy of diabetes children is about 10-15 years !

Frederick Banting became as a GP interested in diabetes mellitus: he became aware of the scientific reports on stenosis of pancreas leaving the Langerhans islets intact and killing the trypsin producing cells. He left aside all his clinical duties to prove his hypothesis and received help from C Best to isolate upon 10 days ligature beagle dog pancreas islets: kids receiving those extracts however experienced no real benefit from this extract injection (5g/L to 4g/L and severe side effects ! Geat disappointment ; F. Banting went on and reasoned that the extracts contained impurities such as bacteria. He decided to further purify.



WORKSHOP !

Session 2: Historical breakthrough medicines



Frederick Banting then turned to a medical doctor biochemist James Collip who worked on an almost pure pyrogene free pancreatic insulin injectable. The efficacy was closed to the miracle! glycemia dropped from 5g/L to 1g/L !! The kids came out of coma and were starting a new life !

Frederick Banting eventually received a well deserved Nobel Prize in 1923.

Sofar millions of diabetic patient's life has been safed thanks to Frederick Banting resilience and perseverance and benefited from this breakthrough ! F Banting coined the name «insulin» from «insula» in latin (for islet/island of Langerhans) and became one of the most successful drug hunter ever in biomedical history.

Very few life threatening diseases have been cured sofar to such a extend of efficacy in modern medicine.

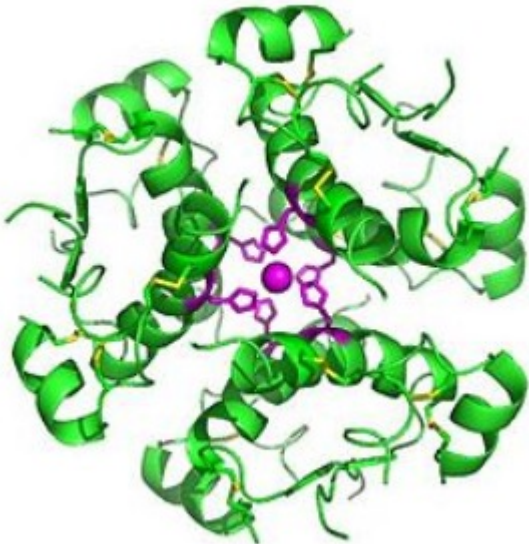
1920 : life expectancy of diabetes children is about 10-15 years !

Today diabetic patients live almost like healthy subjects !

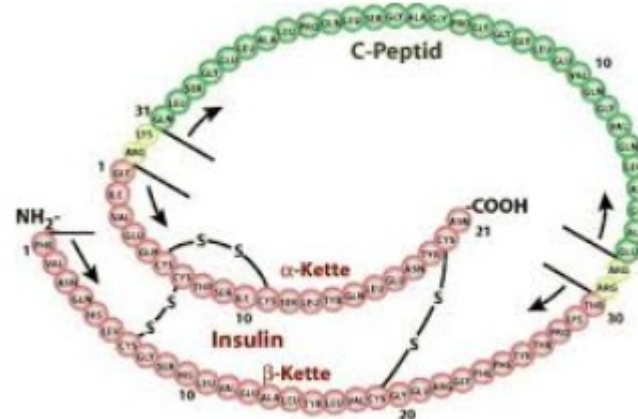
Historical breakthrough medicines



INS



Frederick Banting became as a GP interested «by accident» to help many kids in life threatening conditions purified extracts from dog ligatured pancreas : kids experienced no real benefit up until the dog pancreas extracts got purified. Later insulin has been extracted from porcine pancreas and provided by Eli Lilly USA



1960s : shortage of porcine insulin: bacterial recombinant insulin came to the rescue (first «biological» ever) Axel Ullrich et al. 1970s !

FROM AN HISTORICAL PERSPECTIVE THESE MEDICINE WERE TRUE INNOVATIONS ! TODAY'S REGULATORY AUTHORITIES WOULD PROBABLY NOT LET THEM PASS THROUGH THE REGISTRATION

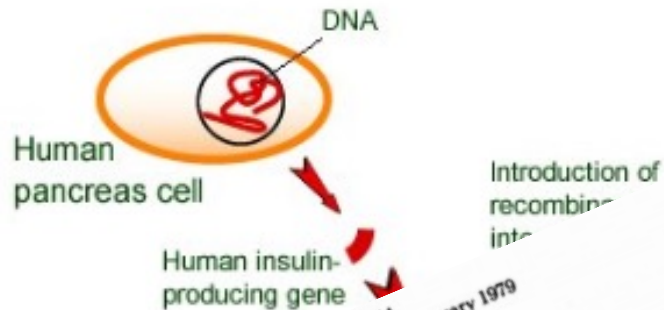
Rat insulin genes: construction of plasmids containing the coding sequences.

Ullrich A, Shine J, Chirgwin J, Pictet R, Tischer E, Rutter WJ, Goodman HM.



Abstract

Recombinant bacterial plasmids have been constructed that contain complementary DNA prepared from rat islets of Langerhans



Proc. Natl. Acad. Sci. USA
Vol. 76, No. 1, pp. 106-110, January 1979
Biochemistry

Expression in *Escherichia coli* of chemically synthesized genes

(plasmid construction/lac operon/fused proteins/radioimmunoassay/peptide purification)

DAVID V. GOEDEL*†, DENNIS G. KLEID*, FRANCISCO BOLIVAR*, HERBERT L. HEYNEKER*, DANIEL G. YANSURA*, ROBERTO CREA*‡, TADAOKI HIROSE‡, ADAM KRASZEWSKI‡, KEIICHI ITAKURA‡, AND ARTHUR D. RIGGS†‡

*Division of Molecular Biology, Genentech, Inc., 460 Point San Bruno Boulevard, South San Francisco, California 94080, and †Division of Biology, City of Hope National Medical Center, Duarte, California 91010

Communicated by Ernest Beutler, October 3, 1978

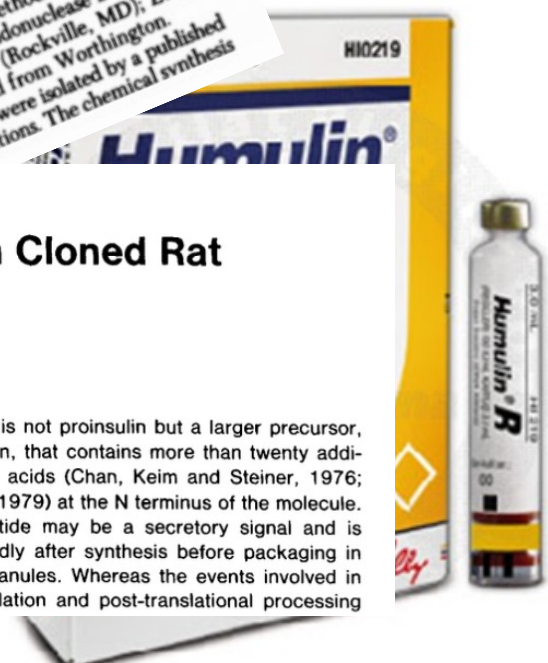
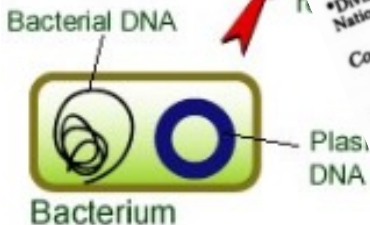
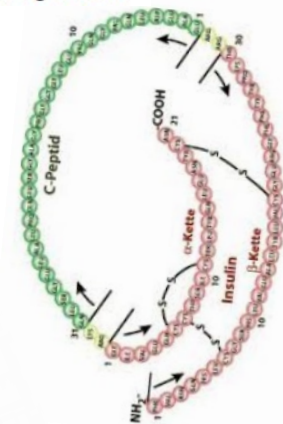
Enzymes and DNA Preparations. T4 DNA ligase and T4 polynucleotide kinase were purified as described (6). Restriction endonuclease *EcoRI* was purified by the procedure of Greene et al. (7); *HindIII* was purified by a method developed by D. Goeddel (unpublished). Restriction endonuclease *BamHI* was purchased from Bethesda Research (Rockville, MD); *E. coli* β -galactosidase was purchased from Worthington. The chemical synthesis of insulin A and B chains was carried out by the method of Goeddel (unpublished). The chemical synthesis of insulin A and B chains was carried out by the method of Goeddel (unpublished). The chemical synthesis of insulin A and B chains was carried out by the method of Goeddel (unpublished).

Cell, Vol. 18, 533-543, October 1979, Copyright © 1979 by MIT

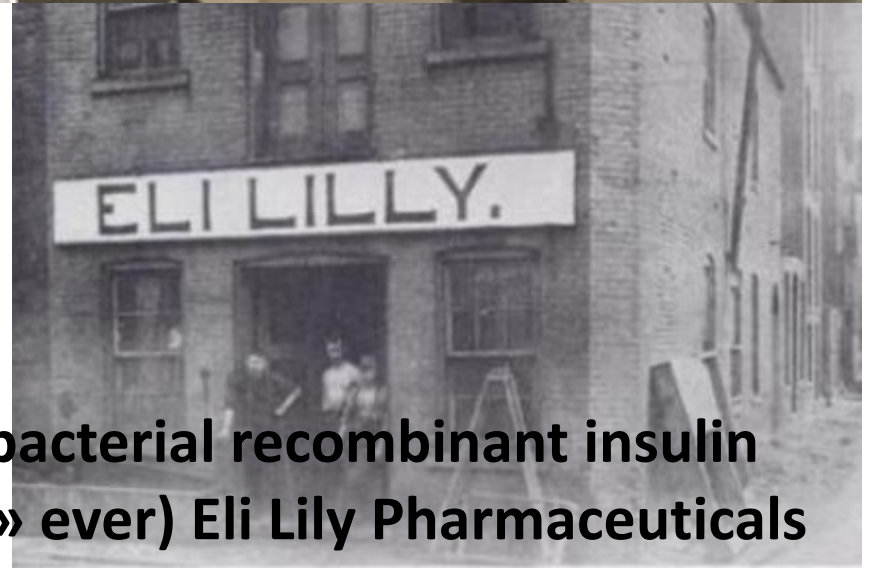
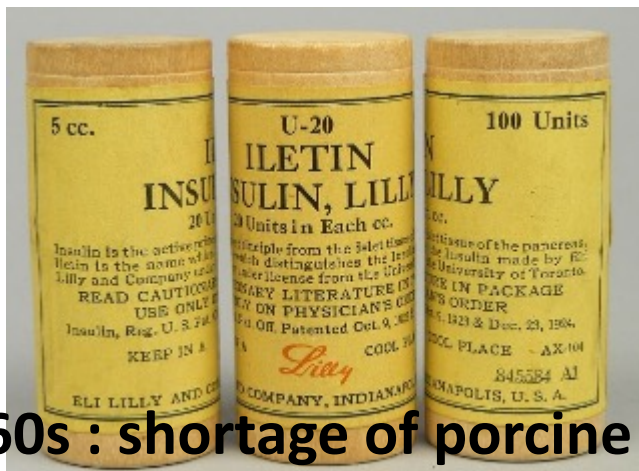
Isolation and Characterization of a Cloned Rat Insulin Gene

Barbara Cordell, Graeme Bell, Edmund Tischer, Frances M. DeNoto, Axel Ullrich,* Raymond Pictet, William J. Rutter and Howard M. Goodman
Howard Hughes Medical Institute Laboratory
Department of Biochemistry and Biophysics
University of California, San Francisco
San Francisco, California 94143

Insulin mRNA is not proinsulin but a larger precursor, pre-proinsulin, that contains more than twenty additional amino acids (Chan, Keim and Steiner, 1976; Chan et al., 1979) at the N terminus of the molecule. This prepeptide may be a secretory signal and is cleaved rapidly after synthesis before packaging in secretory granules. Whereas the events involved in insulin translation and post-translational processing



Historical breakthrough medicine : Eli Lilly insulin



1960s : shortage of porcine insulin: bacterial recombinant insulin came to the rescue (first «biological» ever) Eli Lilly Pharmaceuticals

Historical breakthrough medicines

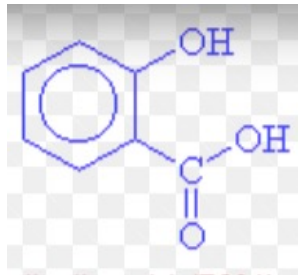
The advent of placebo controlled clinical trials



The advent of modern medicinal chemistry in drug development

Salicylic acid

Pain, antiinflammatory, cardio portective



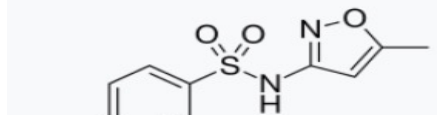
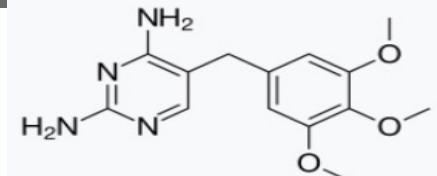
Isotretinoin 1969

Severe acne, ichthyosis, birth defects



Bactrim

Antimicrobial sulfamethoxazol and trymethoprim



Trimethoprim (top) and sulfamethoxazole (bottom)

FROM AN HISTORICAL PERSPECTIVE THESE MEDICINE WERE TRUE INNOVATIONS ! TODAY'S REGULATORY AUTHORITIES WOULD PROBABLY NOT LET THEM PASS THROUGH THE REGISTRATION



Historical breakthrough medicines and the german medicinal chemistry



The advent of modern medicinal chemistry in drug development



The kolbe schmitt reaction has been invented in the 1930's for the preparation of aromatic hydroxy acids. Usually the substitution occurs ortho to the phenolic hydroxy group

FROM AN HISTORICAL PERSPECTIVE THESE MEDICINE WERE TRUE INNOVATIONS ! TODAY'S REGULATORY AUTHORITIES WOULD PROBABLY NOT LET THEM PASS THROUGH THE REGISTRATION

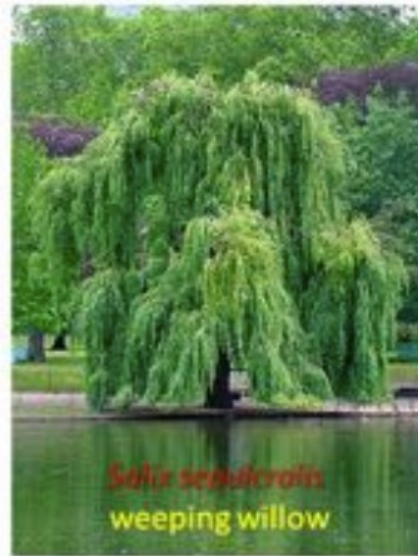


Aspirin : from tree bark to modern medicine



Aspirin - from tree bark to modern medicine

Aspirin



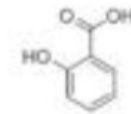
百年名藥-阿斯匹靈

- Analgesic-止痛
relieve minor aches and pains
- Antipyretic-解熱
reduce fever
- Anti-inflammatory-消炎



Hippocrates

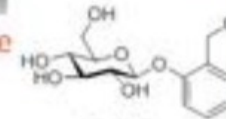
460 B.C and 377 B.C



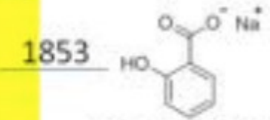
Salicylic acid



Hermann Kolbe

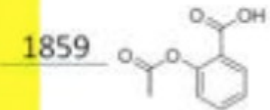


Salicin



1853

sodium salicylate



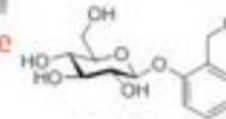
1859

Acetylsalicylic acid

1897

1897

1899



Salicin



Felix Hoffmann
in Bayer AG

1974

prevention of strokes
and heart attacks





Historical breakthrough medicines



The advent of modern medicinal chemistry in drug development

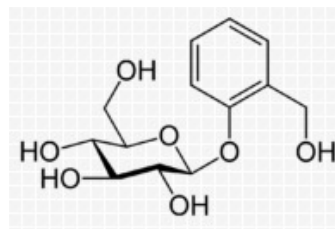
The salicin in willow bark converts to salicylic acid



Known in chinese medicine
Extracts from white willow bark in
1821
Isolation of salicylic acid from
SALICILIN in white willow bark in
1838

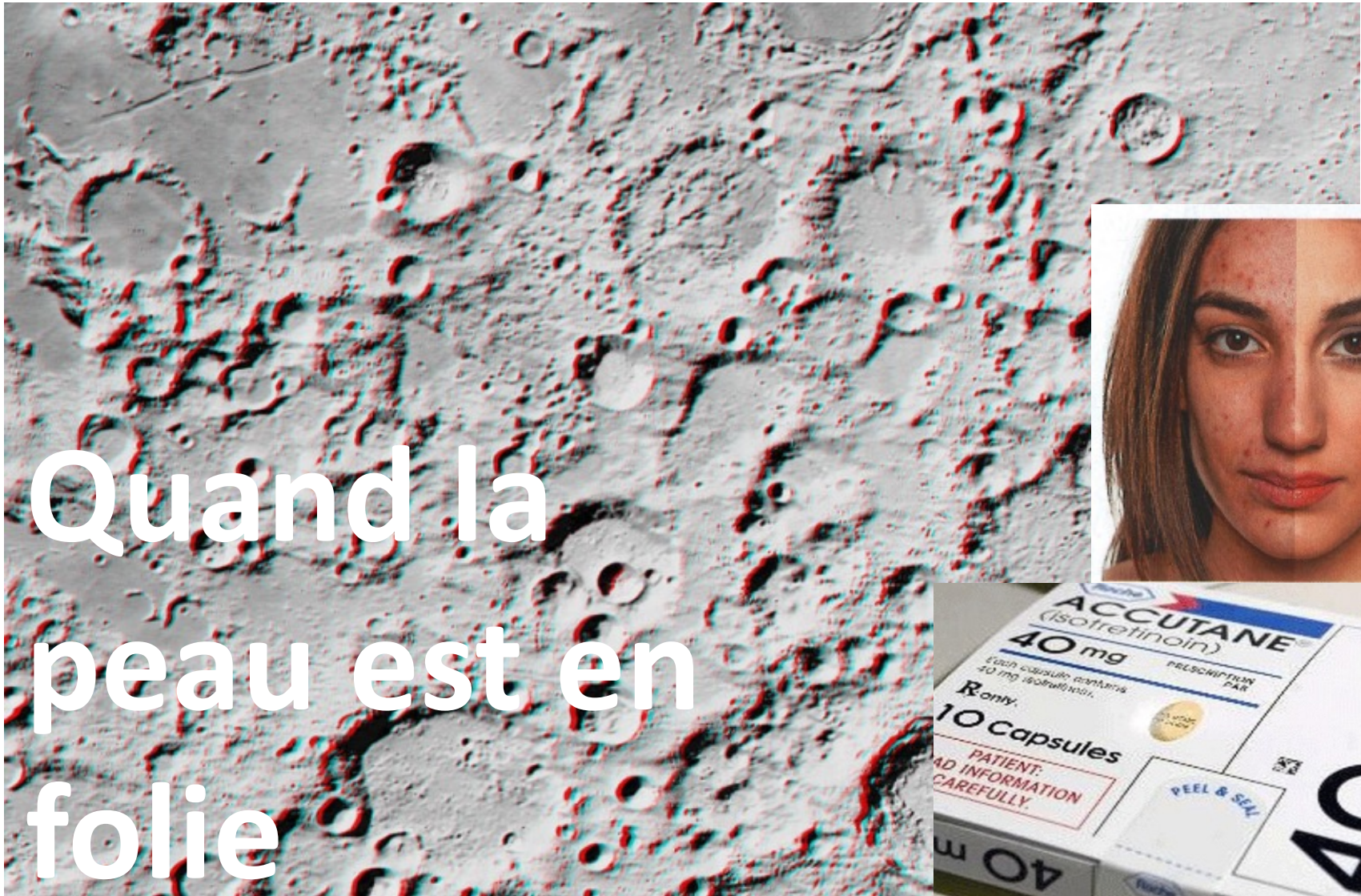
Salicylic acid

Pain, antiinflammatory, cardio protective

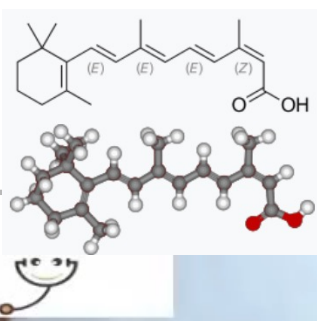


FROM AN HISTORICAL PERSPECTIVE THESE MEDICINE WERE TRUE INNOVATIONS ! TODAY'S REGULATORY AUTHORITIES WOULD PROBABLY NOT LET THEM PASS THROUGH THE REGISTRATION

case study : 80 % of young adults suffer from acne
Accutane® (isotretinoin) 1969



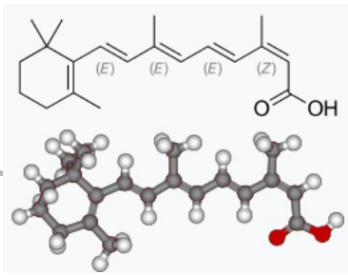
Quand la
peau est en
folie



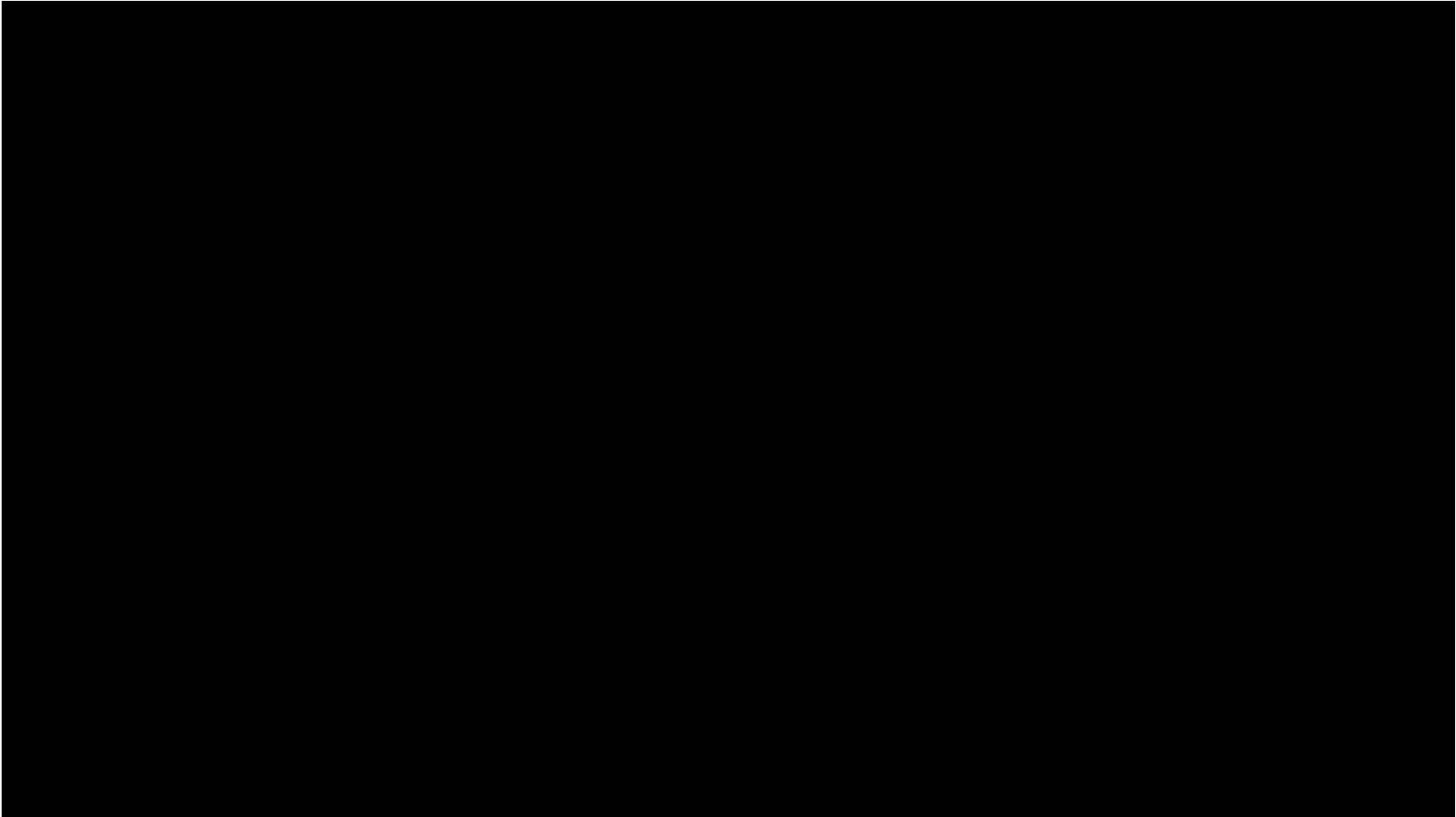
Let's do what patient needs next !



Can you think of any pharmacological intervention to alleviate pain of this patient ?



severe acne : accutane (13cis RA) transformation



case study : 80 % of young adults suffer from acne



Karate kial is my savior....

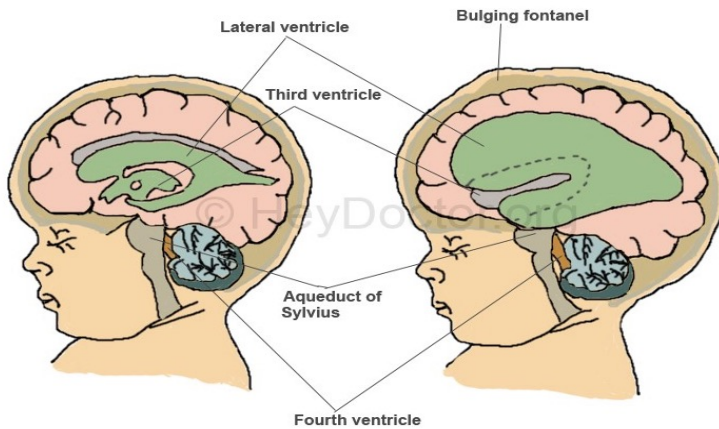


Isotretinoin (13-cis RA) like excess of Vitamin A

**THERAPEUTICALLY
HIGHLY VALUABLE !
ACUTE TREATMENT !
HYPERTRIGLYCERIDEMIA
RED FLAG: NO CHILD
BEARING WOMEN !**

- Animal teratology studies
 - Vitamin A, many retinoids
 - produce congenital anomalies in different species
 - **Central nervous system, head, limbs, cardiovascular system defect**
 - All-trans-retinoic acid (tretinoin)
 - Isomer of isotretinoin that is readily formed when isotretinoin is ingested
 - **craniofacial abnormalities** in rats, rabbits, and monkeys
 - Isotretinoin
 - produces congenital anomalies in a number of species, including humans
 - **Hydrocephalus, microcephaly, ear, face, limb abnormalities**

workshop: excess and/or retinoid deficiencies

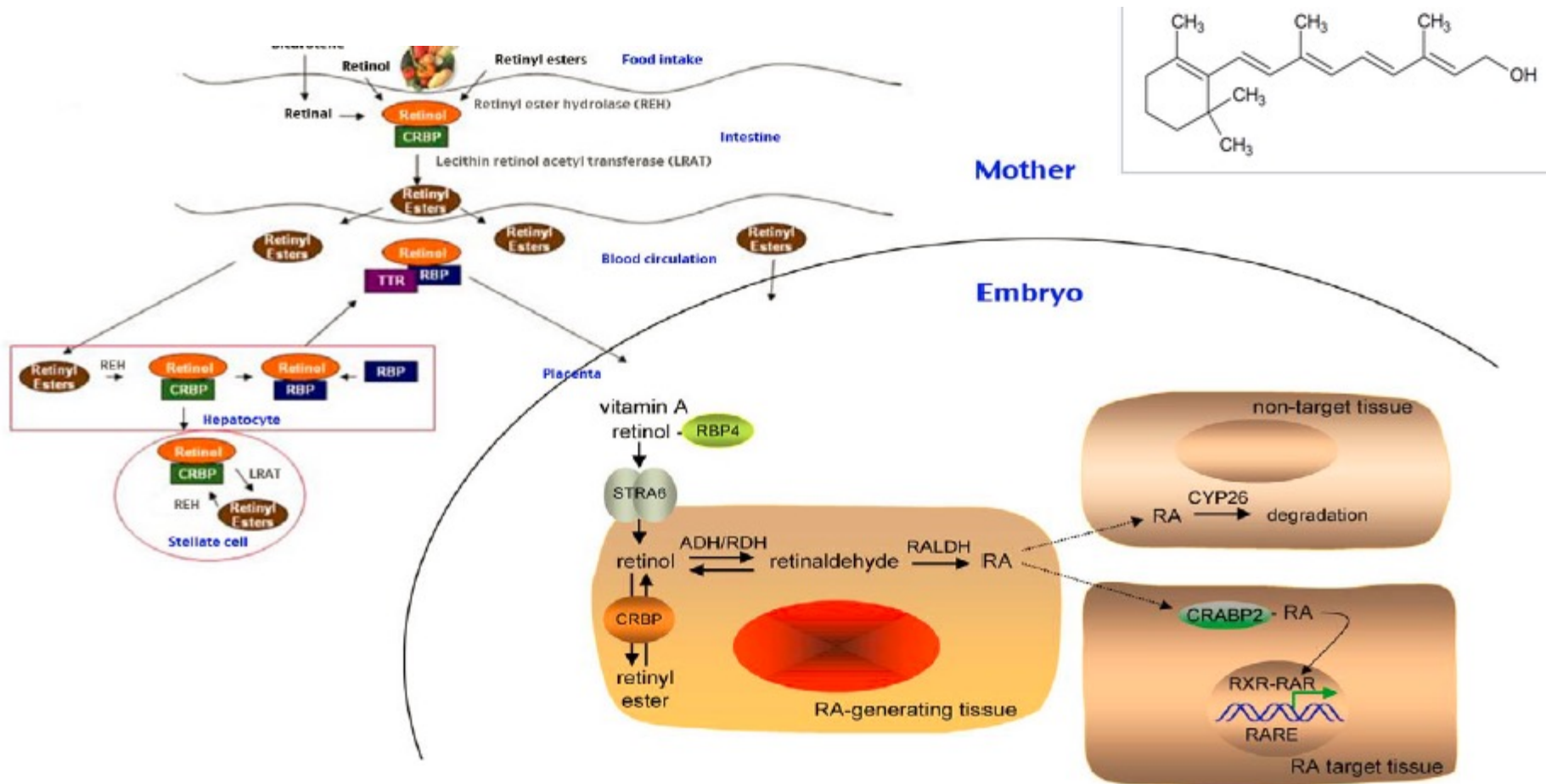


**THERAPEUTICALLY
HIGHLY VALUABLE !
ACUTE TREATMENT !
HYPERTRIGLYCERIDEMIA
RED FLAG: NO CHILD
BEARING WOMEN
(hydrocephalus,
polydactily etc)**





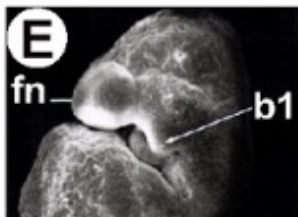
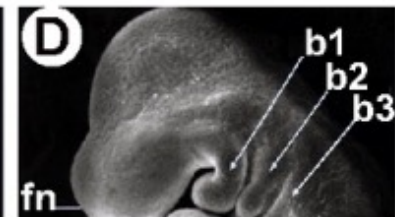
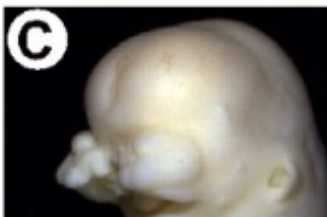
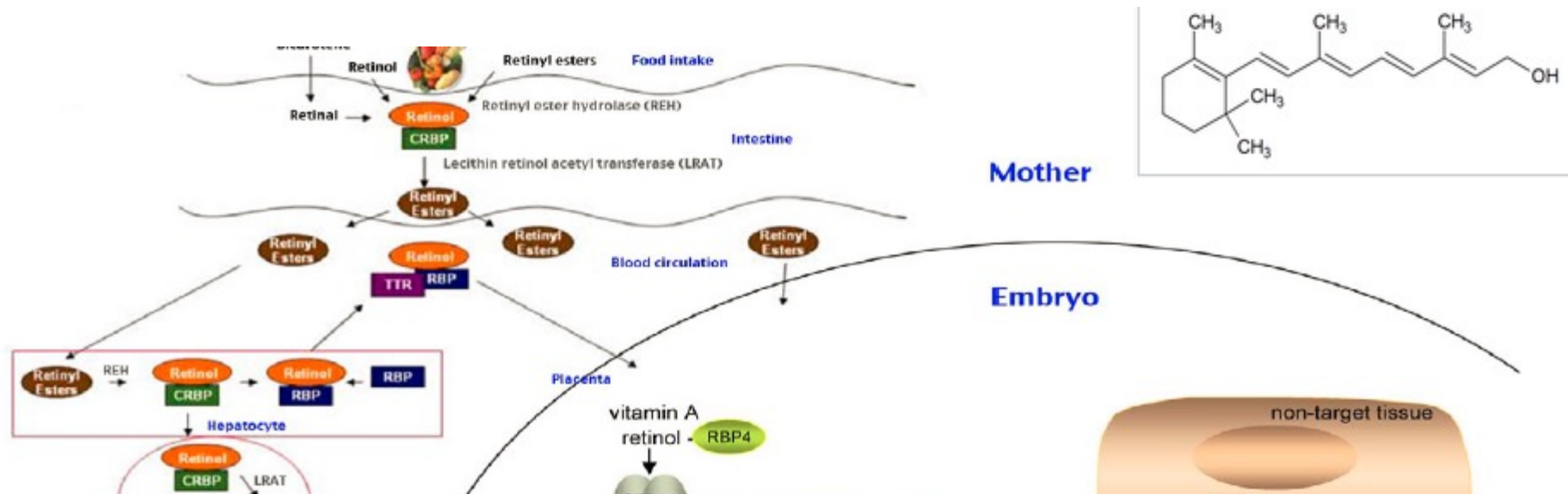
RAR/RXR (isotretinoin) dependent nuclear signaling



Retinoic acid availability is a result of a balance between storage (retinyl ester) and production. Its activity is the result of the balance between CYP26-mediated degradation and binding to its receptor(s). Its function during embryonic development is tightly regulated by those two processes.

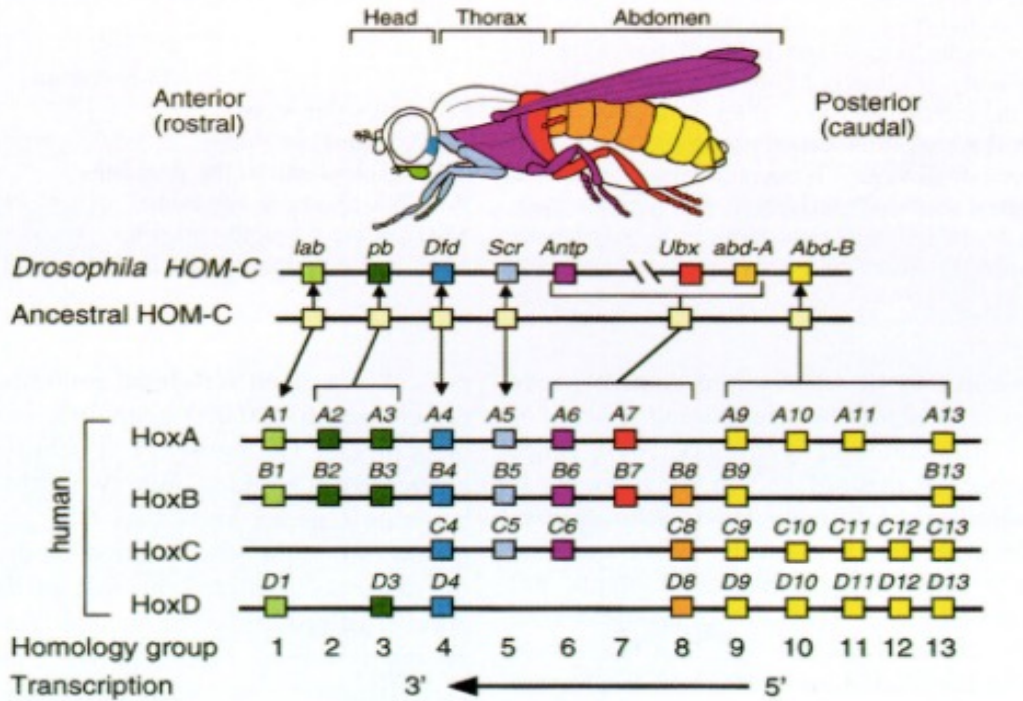


RAR/RXR (isotretinoin) dependent nuclear signaling

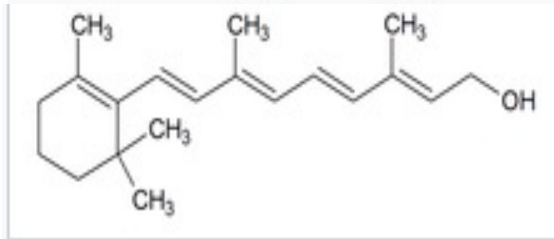
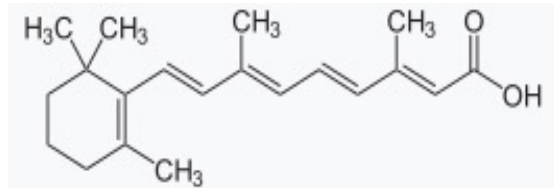


Retinoic acid biosynthesis. (A) The oxidation of retinol into retinaldehyde and retinoic acid (RA). Enzymes responsible for each of the catalytic steps are shown, with enzymes that are

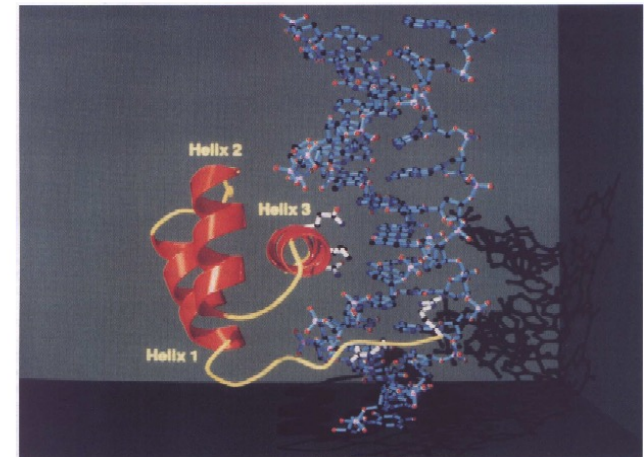
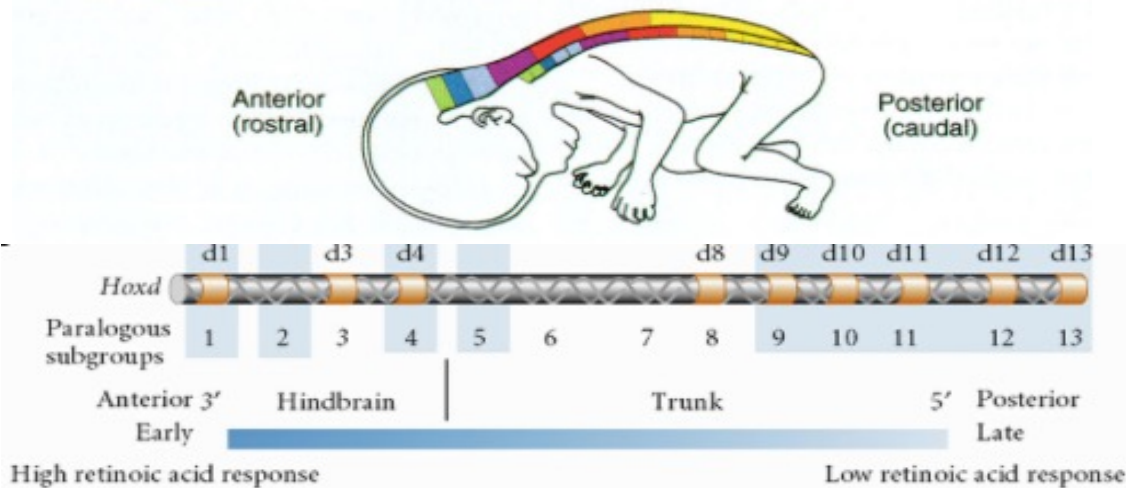
RAR/RXR - dependent nuclear signaling



retinoic acid vitamin A



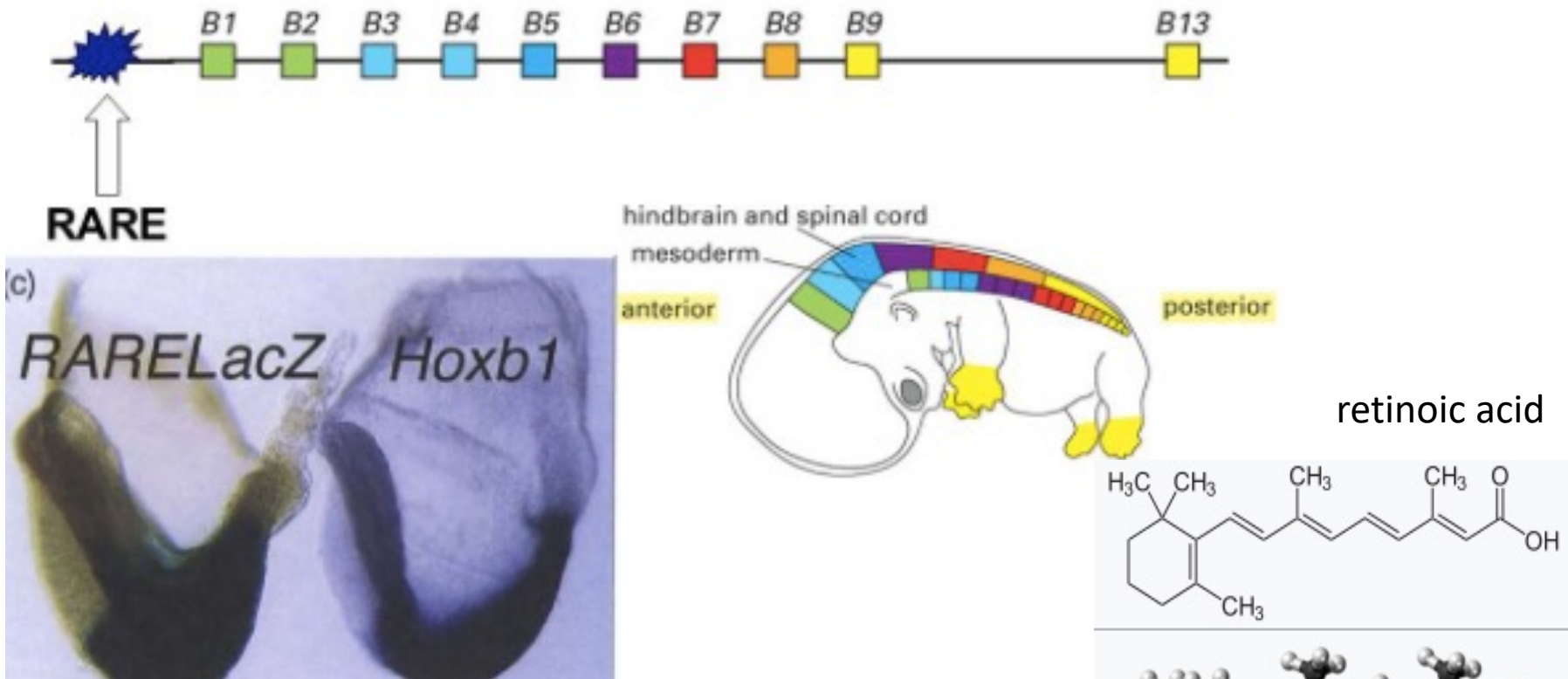
J.-Y. VOLLMER AND R. G. CLERC



RAR/RXR - dependent nuclear signaling



Hox complexes have a retinoic acid receptor response element (RARE) in the DNA before paralogue 1. This DNA enhancer element controls expression of many genes in the complex. In retinoic acid teratogenesis, Hox gene expression borders move into more anterior regions.



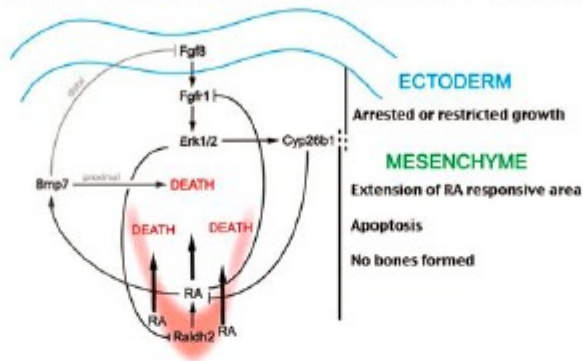
retinoic acid (and 13-cis RA) belong to the retinoid cpd class, whose potent morphogenic activity cannot be dissociated from its unique efficacious property in clinical dermatology



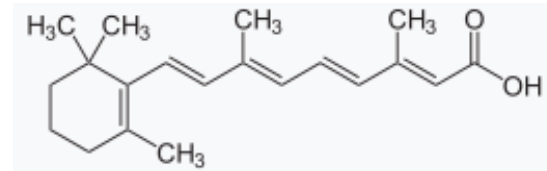
RAR/RXR- dependent nuclear signaling

In presence of an excess of retinoids antiproliferative and pro-apoptotic signaling overcome the distal mitogenic and survival signaling.

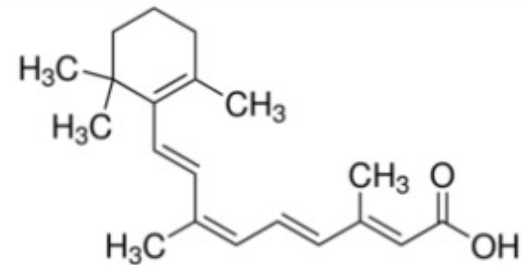
Limb growth is impaired due to massive cell death.



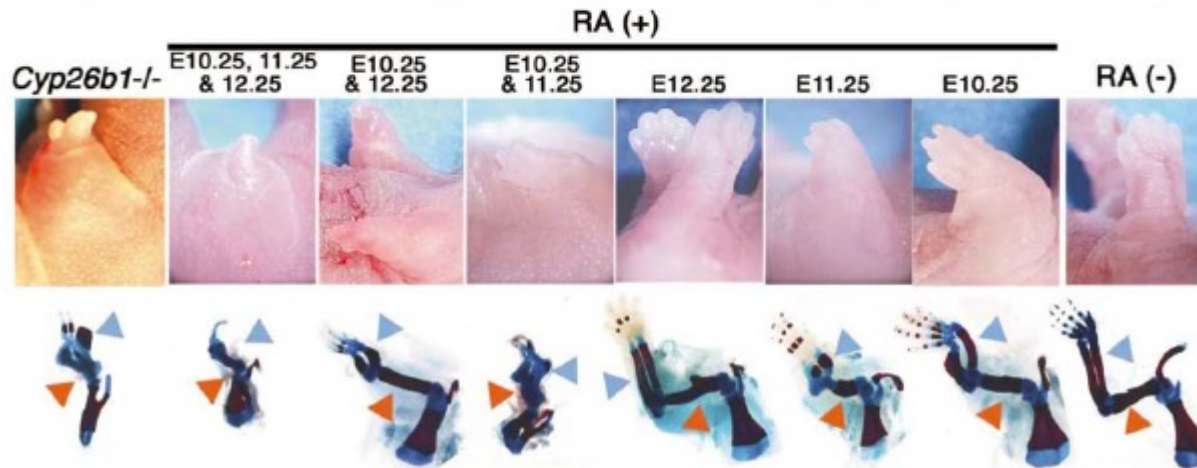
RA(all-trans)



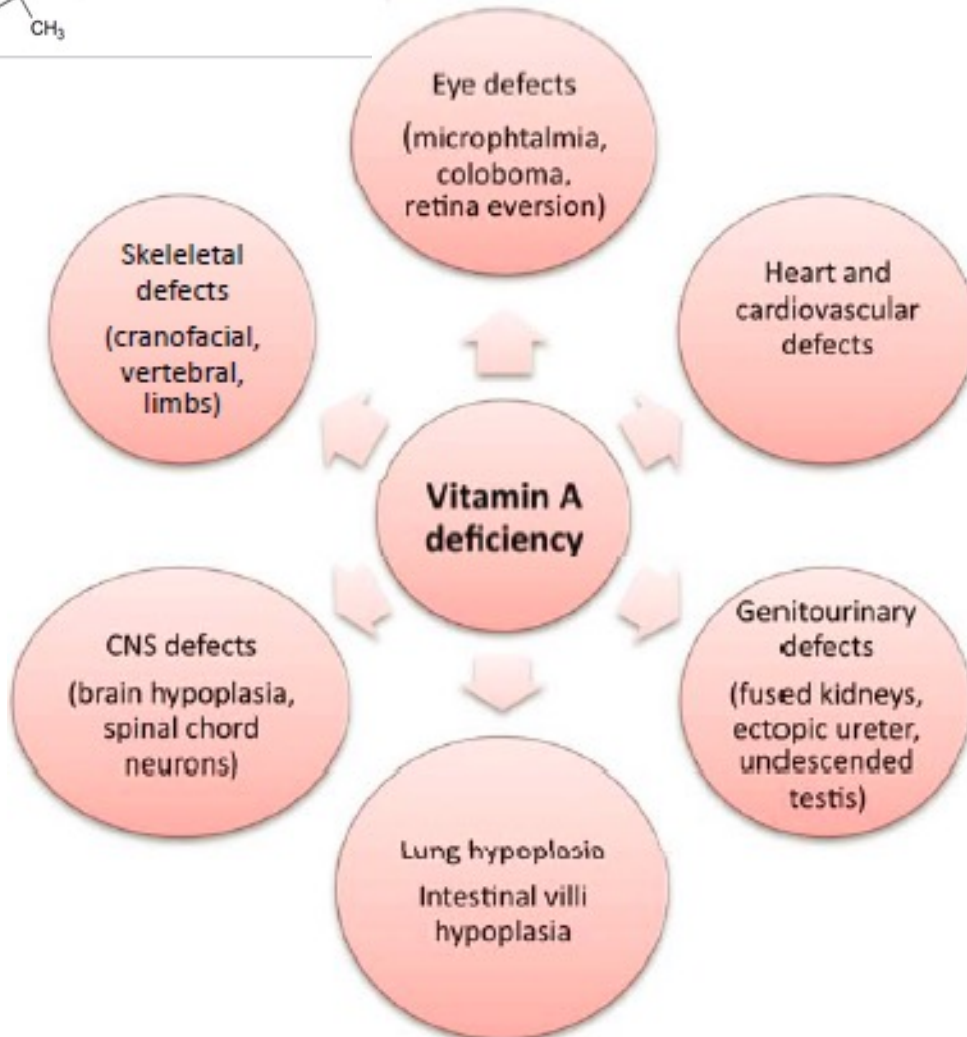
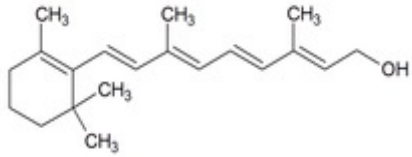
9-cis



Type and severity of limb defect depends on period of exposure and duration. Mouse experiment where RA was given at 1, 2 or 3 successive developmental time points

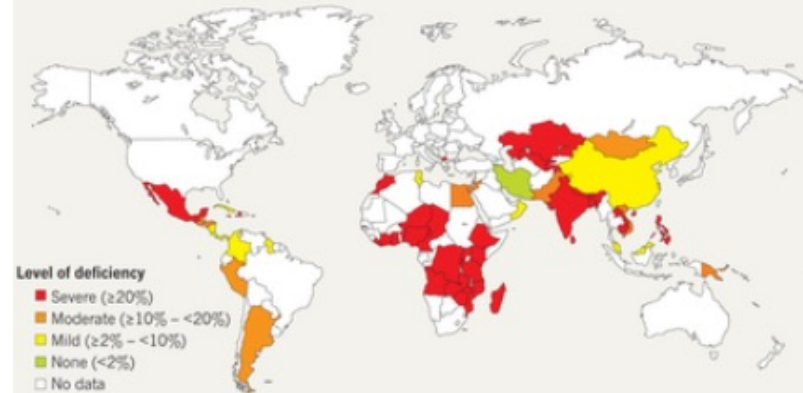


workshop: excess and/or deficiencies of retinoids



PREVALENCE OF VITAMIN A DEFICIENCY

Map showing level of serum retinol (an indicator of vitamin A deficiency) in pre-school age children. Data were collected by the World Health Organization between 1995 and 2005 from populations at risk.



Estimates of vitamin A deficiency are based on low serum retinol concentration $< 0.70 \mu\text{mol l}^{-1}$

**VITAMIN A SUPPLEMENT CAMPAIGNS
GOLDEN RICE DISCOVERY IN CH !**



Nobody likes scars : 80 % of young adults suffer from acne



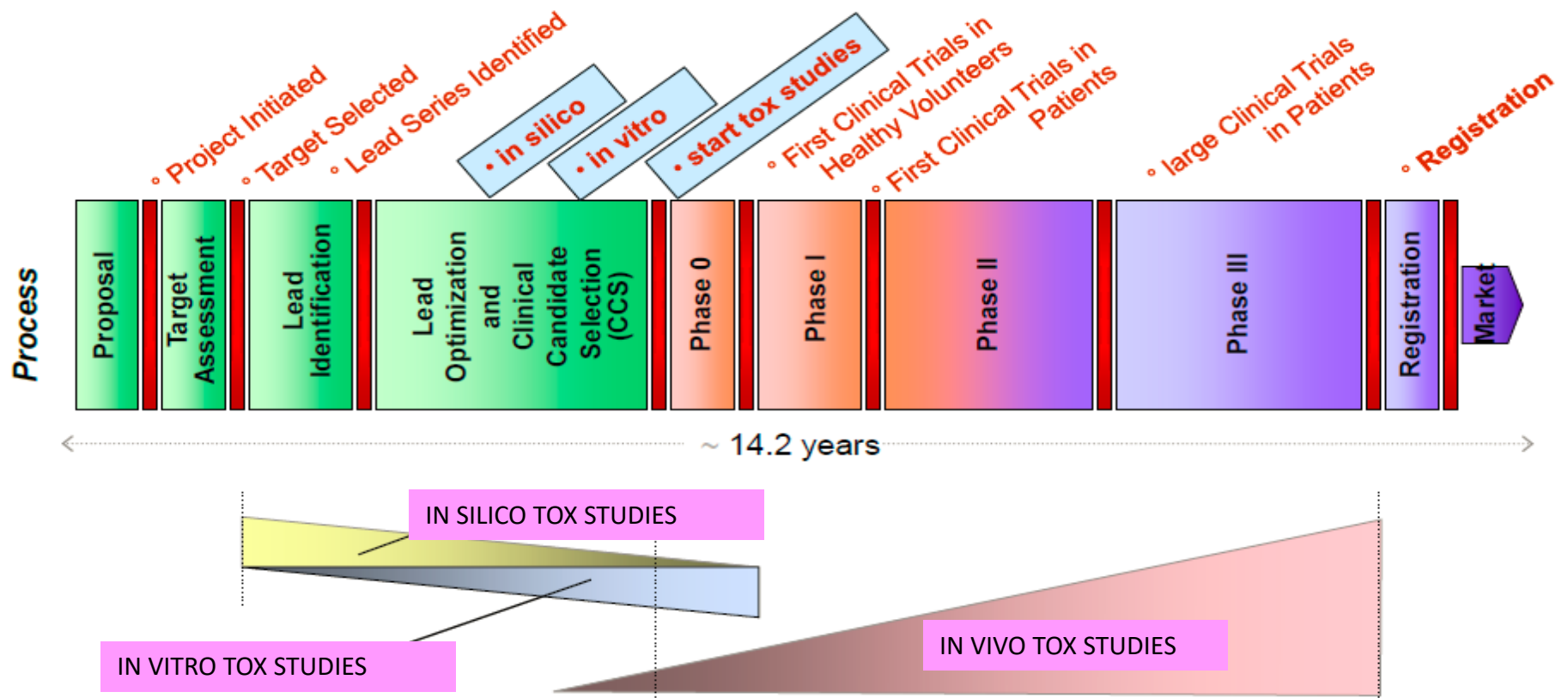
case study : severe acne ; still today the only „last resort“ medicine ! 



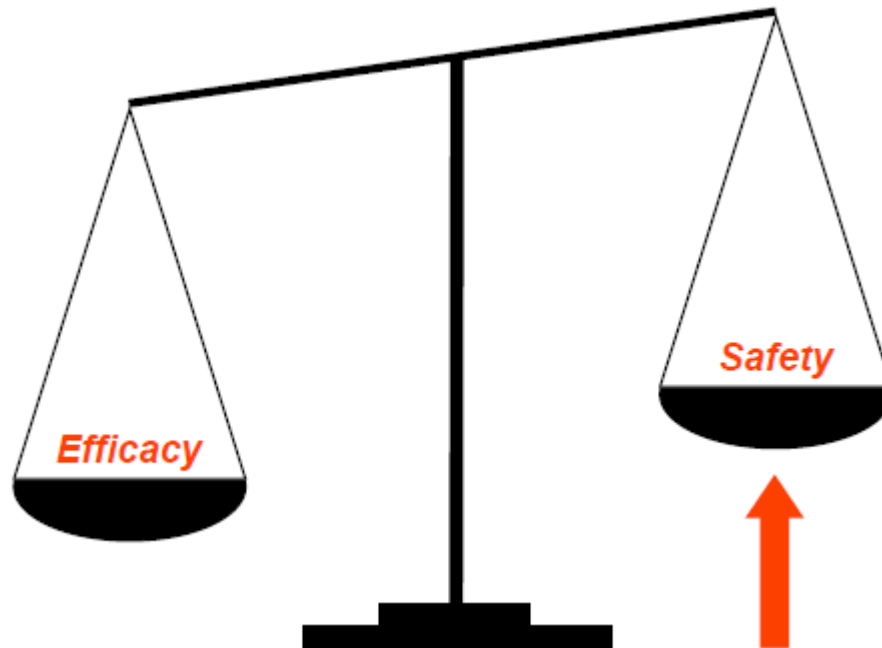
Historical breakthrough medicines – from today’s perspective



IN THOSE DAYS REGULATORY (FDA; EMEA) WAS EASY: **NO “STANDART OF CARE” TO BEAT -NO PLACEBO CONTROLLED DOUBLE BLIND CLINICAL TRIALS:** THESE MEDICINES WERE THE FIRST “FIRST IN CLASS” ! INVESTIGATIVE TOXICOLOGY AND PRECLINICAL **SAFETY BEARLY INEXISTANT-** NO CELLULAR SIGNAL PATHWAY IDENTIFIED ! **“ORPHAN DRUGS”** NO HUMAN GENOME SEQUENCE - NO MOLECULAR BIOLOGY - NO TRANSLATIONAL BIOMEDICINE ! TRIAL AND ERROR APPROACH ! TODAY NO FDA REGISTRATION DELIVERY FOR THOSE WONDER DRUGS !!



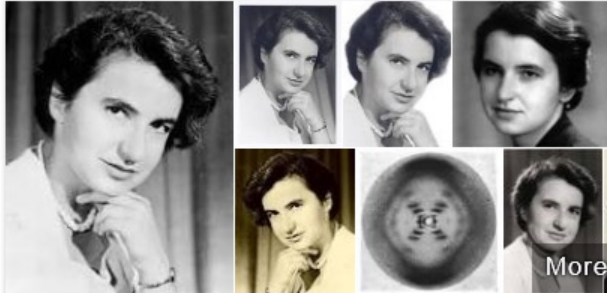
Safety (acceptable adverse effects) is what patients care first over efficacy !



VALIUM : a game changer in psychiatric therapeutic options (introducing however addictive behaviours)

- A BALANCING ACT : NO THERAPIES WITHOUT ADVERSE EFFECTS !
- ANY THERAPEUTIC PHARMACOLOGICAL INTERVENTION SHOULD HOWEVER BE SAFE, DEVOID OF UNDESIRABLE ADVERSE EFFECTS
- INVESTIGATIVE TOXICOLOGY IS KEY !

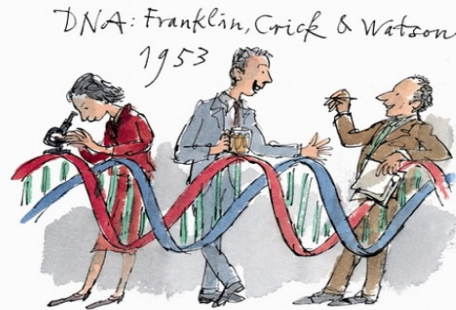
Hopping on giant shoulders



Rosalind Franklin

Chemist

“She was best in science, best at maths, best in everything. She expected that if she undertook to do something, she would be in charge of it.” By the age of 15, over objections from her father, who thought she should go into social work; Franklin decided to become a scientist.



No. 4356 April 25, 1953

NATURE

737

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

¹ Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1929).

² Langmuir, H., *M. S., Mem. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).

³ Von Arx, W. S., *Woods Hole Papers in Phys. Oceanogr. Meteor.*, **11** (3) (1950).

⁴ Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey¹. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons:

(1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates repel each other. (2) Some distances appear to be too small.

Another three-chain structure suggested by Fraser (in the phosphates are on the outside, linked together by a structure as described is rather unsatisfactory for this reason.

We would like to suggest a structure which is radically different from the above. It is a double helix of the sugar-phosphate chains, with the bases on the inside. The two chains are intertwined, and the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.

is a residue on each chain every 3.4 Å. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions



Francis Harry Compton Crick (1916-2004)



James Dewey Watson (1928 -)



Maurice Hugh Frederick Wilkins (1916-2004)

devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

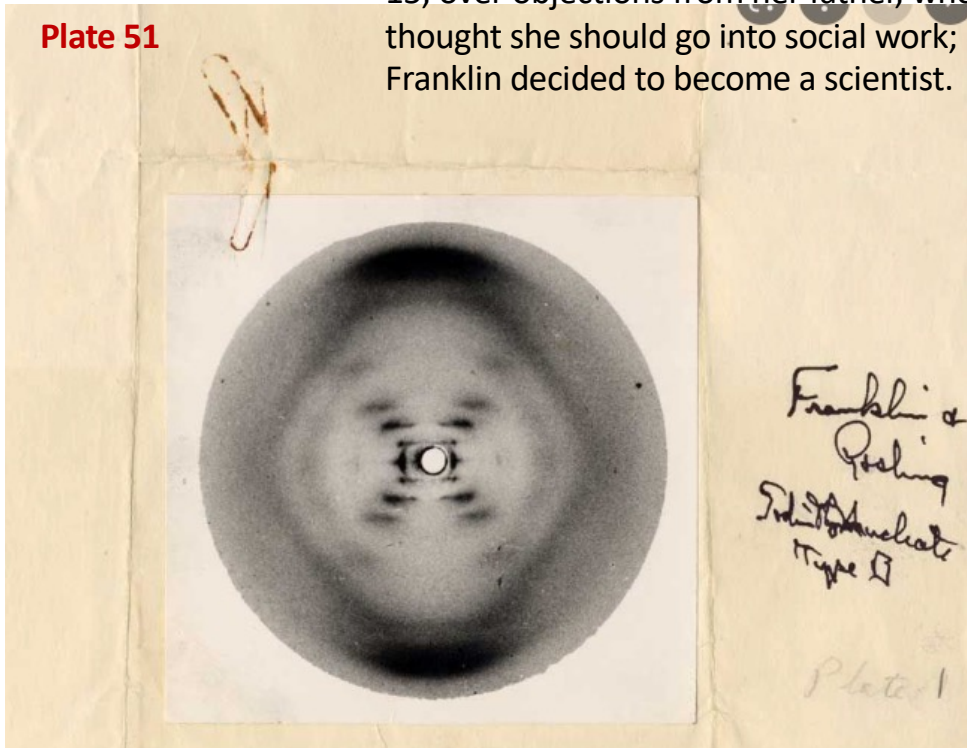


Plate 51

Franklin & Gosling
Ribonucleate
Type B

Plate 1

Thank you
Rosalind!

D.N.A

The advent of biologicals and biomarkers

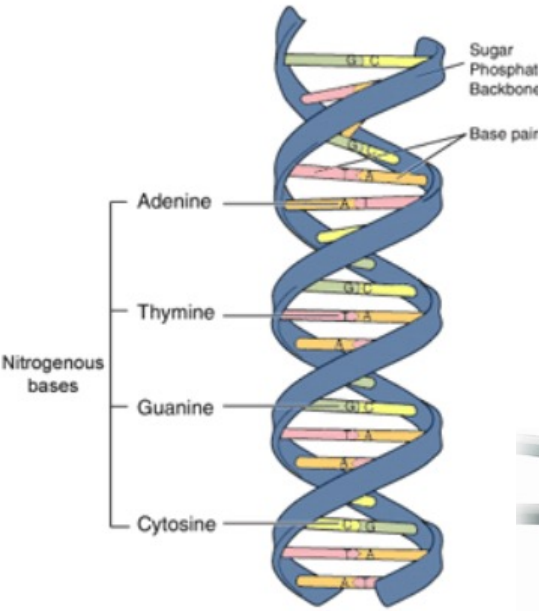
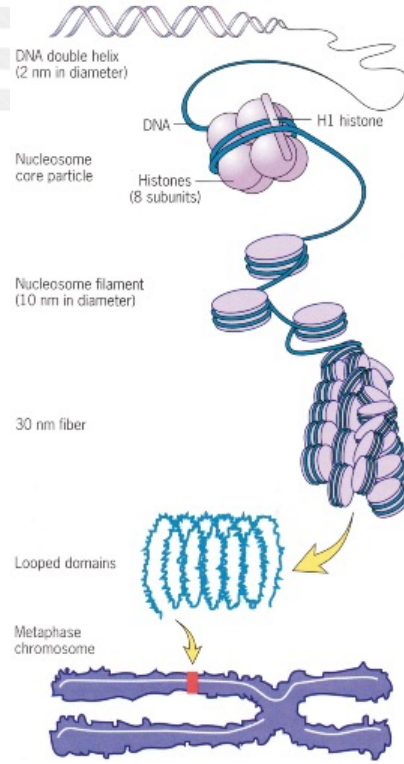
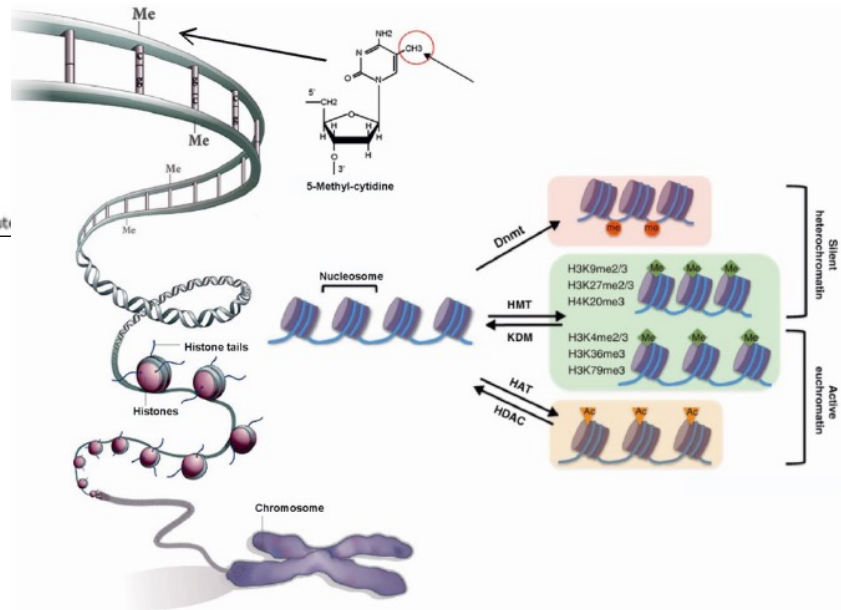
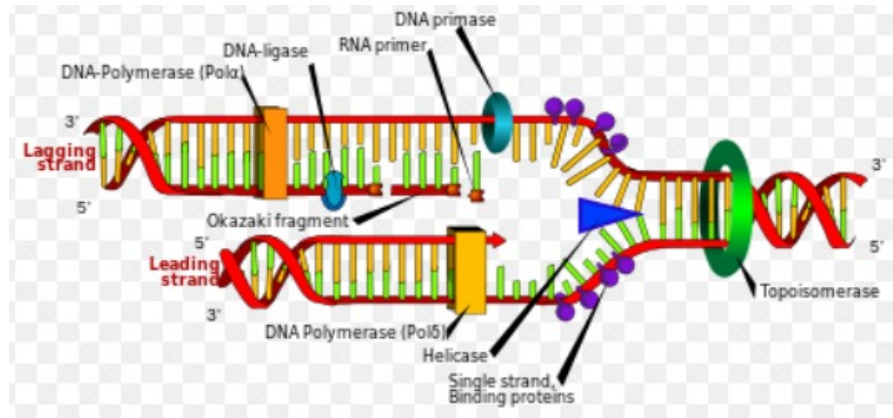


Image adapted from: National Human Genome Research Institut



The advent of biologicals and biomarkers

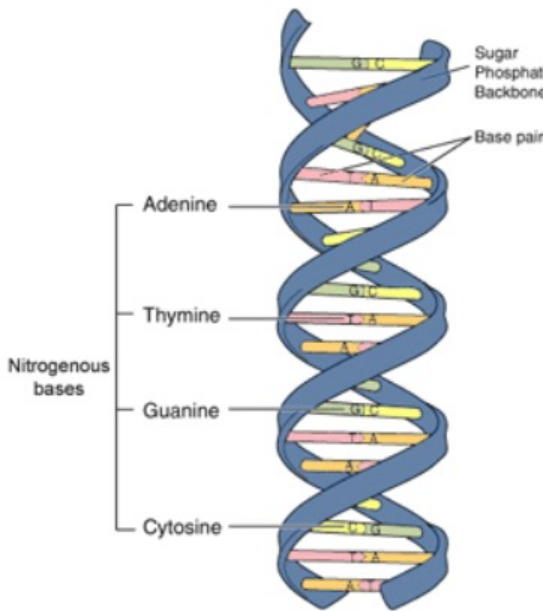
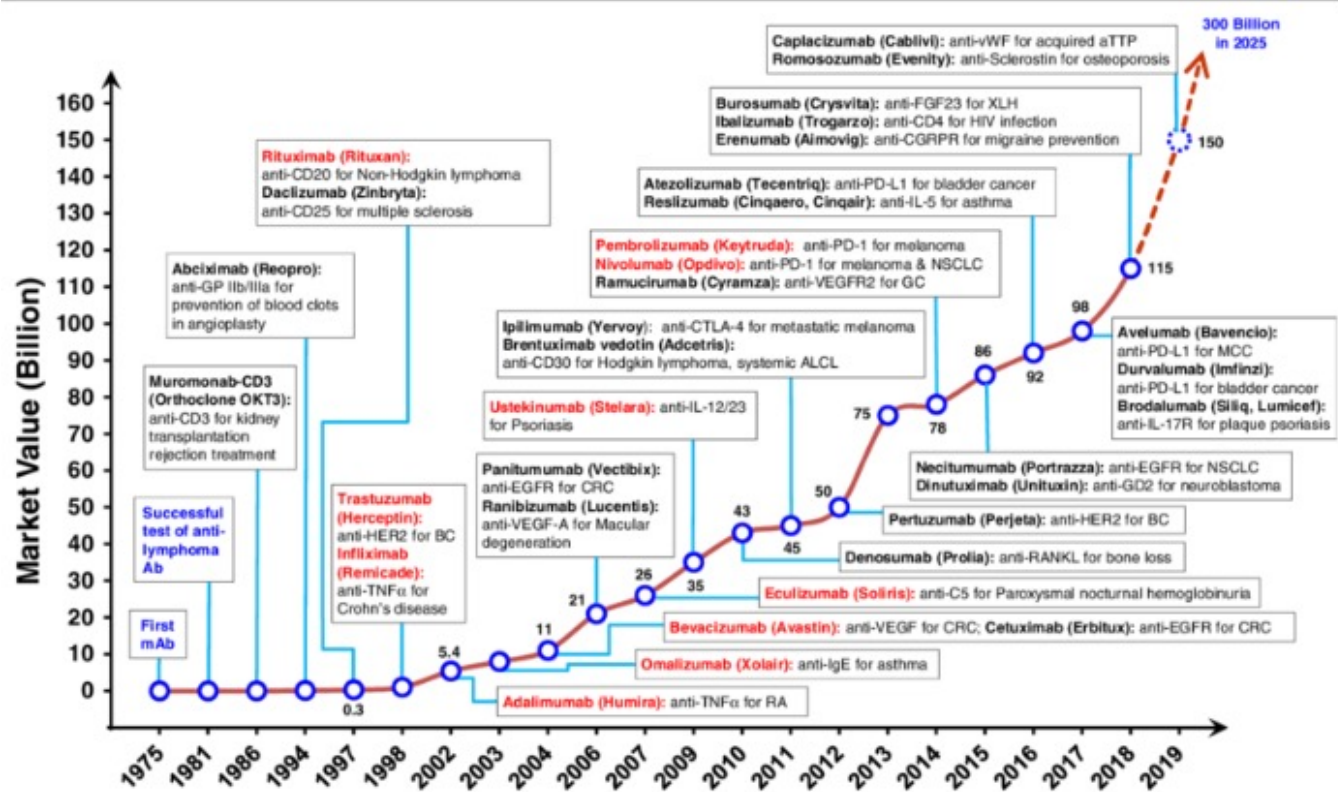


Image adapted from: National Human Genome Research Institute.



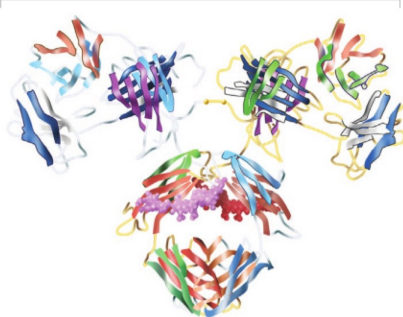
Acetylsalicylic acid
Small molecule

21 atoms

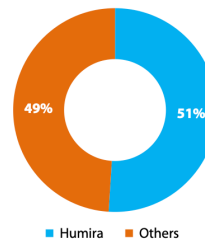


IgG1 antibody
Biologic medicine

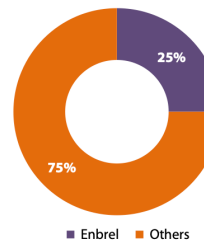
> 20,000 atoms



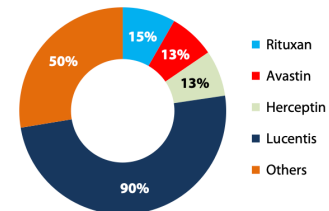
AbbVie: Humira Sales vs. Total Revenues (2012)



Amgen: Enbrel Sales vs. Total Revenues (2012)



Genentech (Roche): Rituxan, Herceptin, Avastin, and Lucentis vs. total revenues (2012)



The looming crisis in drug development : is the future the past only better ? 



**ARRESTED
DEVELOPMENT ?
FINANCIAL CRISIS AND
REGULATORY
PRESSURES THREATEN
THE DISCOVERY OF NEW
MEDICINE ! AND ITS
LOCAL PRODUCTION**

ARRESTED DEVELOPMENT – TOWARDS A NOVEL PARADIGM ?

Drug development : QUO VA DIS ?



Kinch M. et al 2016: "A prescription for a change" UNC Press

- The days where morphine, penicillin, valium, etc. shaped growth of Eli Lilly, Merck, Roche, Sandoz, Pfizer and Ciba-Geigy (to cite only the dominant innovators of the 20th century) are over.
- Large companies became dependent on pharmaceutical "blockbusters" (over >1 \$ billion annual sales) that they cannot replace to maintain market expectations.
- Mergers, acquisitions and down sizing R+D profoundly affected the ability to support productive internal R+D programs. Also as a consequence of this turn around, the number of biotech start-ups is declining.
- **WHAT DO WE DO ? AN UNPRECEDENTED EFFORT OF COMMUNICATION BETWEEN ACADEMIA, COMMERCIAL, FEDERAL AND FINANCIAL INSTITUTIONS AND THE PUBLIC-PRIVATE PARTNERSHIPS WILL BE REQUIRED TO ALLOW TRANSLATIONAL RESEARCH CONDUCTED AND NEW MEDICINES TO BE DISCOVERED IN THE FUTURE**
- **RARE DISEASES APPROACHES ! LINE EXTENSION IN OTHER DISEASE AREAS !**

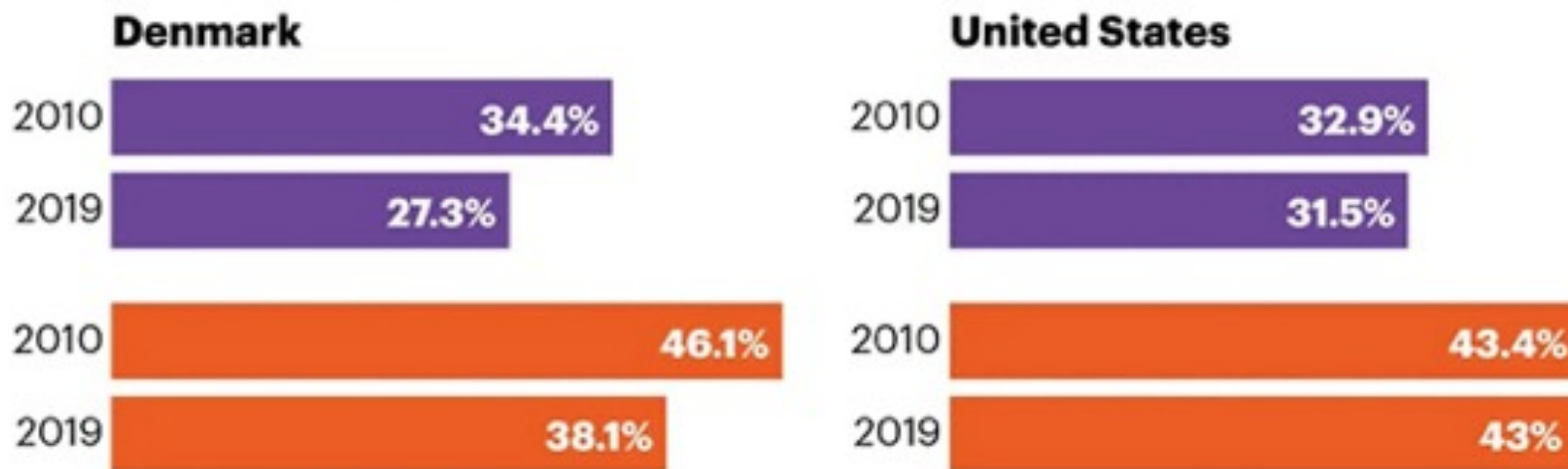


MOST AND LEAST IMPROVED

Among 25 high-income countries, the chance of dying from a non-communicable disease between 2010 and 2019 declined the most in Denmark, whereas the United States recorded the smallest decline.

Chance of dying from a non-communicable disease

■ Women ■ Men





A Prescription for Change

*THE LOOMING
CRISIS IN DRUG
DEVELOPMENT*



MICHAEL KINCH

- **LOOKING INTO INNOVATIVE SOLUTIONS TO THE CURRENT LOOMING CRISIS**
- **HOW TO BRIDGE THE “VALLEY OF DEATH” ?**



WORKSHOP !

- Hopping on giant shoulders : the advent of modern medicines : the fabulous chances

- “CHANCES FAVORS PREPARED MINDS”

(Louis Pasteur dixit)

Jean Starobinski



Histoire
de la médecine

Édition établie
par Vincent Barras

Héros-Limite

Claude Bohuon et Claude Monneret

FABULEUX HASARDS

HISTOIRE
de la DÉCOUVERTE
de MÉDICAMENTS

EDP
SCIENCES

Le hasard ne favorise
que des esprits préparés

The Life and Legacy of Valium Inventor

Leo Sternbach




Alex Barenninger
Jorge Alberto Costa e Silva
Ian Hindmarch
Hans-Juergen Moeller
Karl Rickels

HOME REVIEWING



- **Review historical drug structures and drug examples**
- **Look up an historical drug not shown in this course session S02 and learn about it**
- **Review lecture notes from each session**
- **Formulate Quescussions, be vocal !**

A man in a blue tank top and khaki pants is walking a tightrope on a steep, grey rock cliff. He is leaning forward, balancing himself. A blue rope is attached to his harness and hangs down. The background shows a valley with green trees and distant mountains under a clear sky.

**It is not
because things
are difficult
that we do not
dare;
it is because
we do not dare
that they are
difficult.**

Seneca

Enjoy an inspiring next week end !



Alv Laiets/GR
O. Kubitz, Aug. '16

ZUNÄCHST BERGWETTER





THANK YOU.....

DO YOU HAVE ANY QUESTIONS ?

