

# Conflict of Interest Disclosure

**Sanjiv Chopra, M.D., MACP**

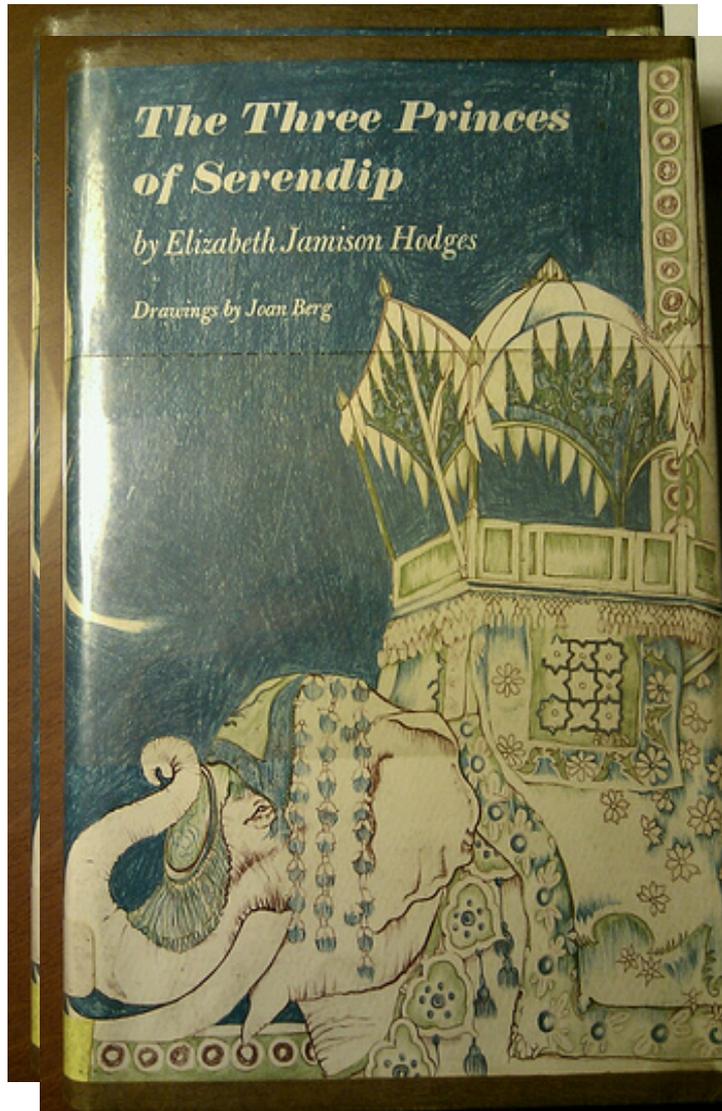
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# **The Top Stories In Medicine In the Last One Hundred Years**

**Sanjiv Chopra, M.D., MACP  
Professor of Medicine, Harvard Medical School**

**Marshall Wolf Master Clinician Educator  
Brigham and Women's Hospital**

# The Three Princes of Serendip



**Whose heroes were always making discoveries by accidents and sagacity, of things they were not in quest of.**

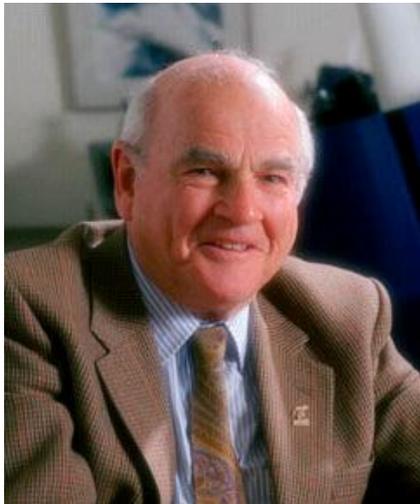
In the field of observation, chance favors only the prepared mind.



Louis Pasteur

# A Tale of Serendipity

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**Baruch Blumberg, M.D. and  
the Discovery of Australia  
Antigen**

# Polymorphism

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**Occurrence in the natural habitat of two or more discontinuous and presumably inherited forms of a species in such proportions that the rarest of them cannot be maintained merely by recurrent mutation.**

**E.B. Ford**

# A "New" Antigen in Leukemia Sera

Baruch S. Blumberg, MD and Harvey J. Alter, MD

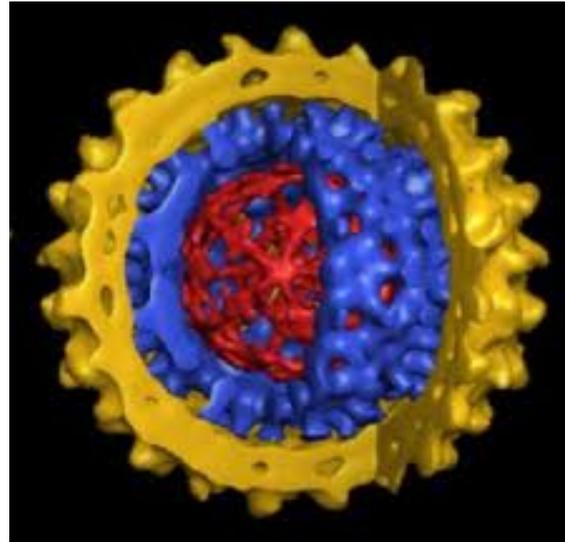
*JAMA. 1965;191(7):541-546.*



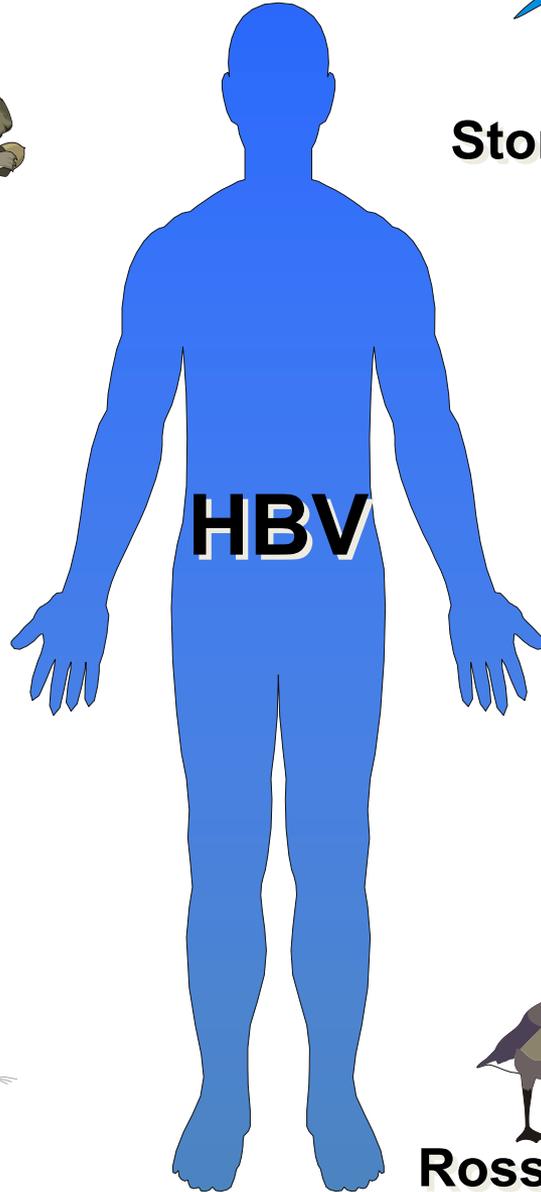
# Biology of Hepatitis B

- Nobel lecture December 13, 1976 by Blumberg
- Fascinating read in the July 1977 issue of Science

# The Hepatitis B Virion



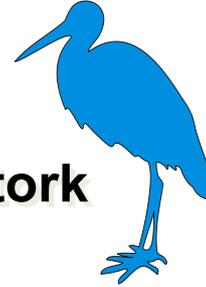
# Hepadnaviruses



**Tree squirrel**



**Stork**



**Woodly monkey**



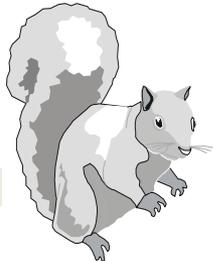
**Ground squirrel**



**Woodchuck**



**Arctic ground squirrel**



**Heron**



**Ross Goose**



**Duck**



# HBV Transmission



# Unusual Mode of HBV Transmission



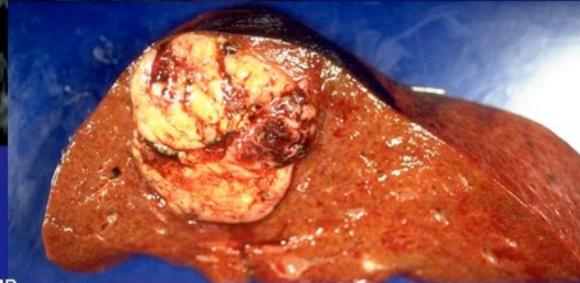
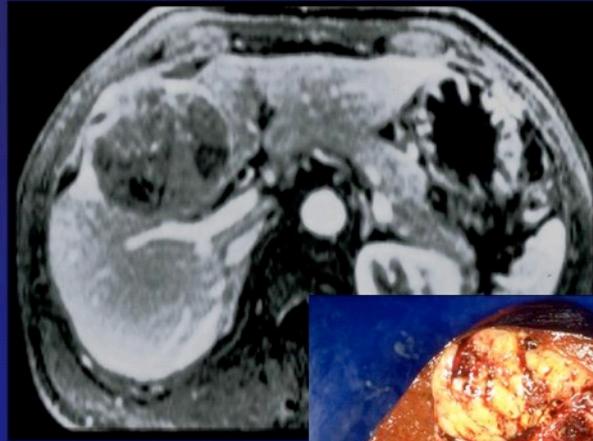
**Orienteering**

# World Wide Burden of HBV

**350 - 400 million people worldwide  
afflicted with chronic HBV.**

# PHCC in Chronic HBV

HCC



Courtesy of Nezam H. Afdhal, MD.

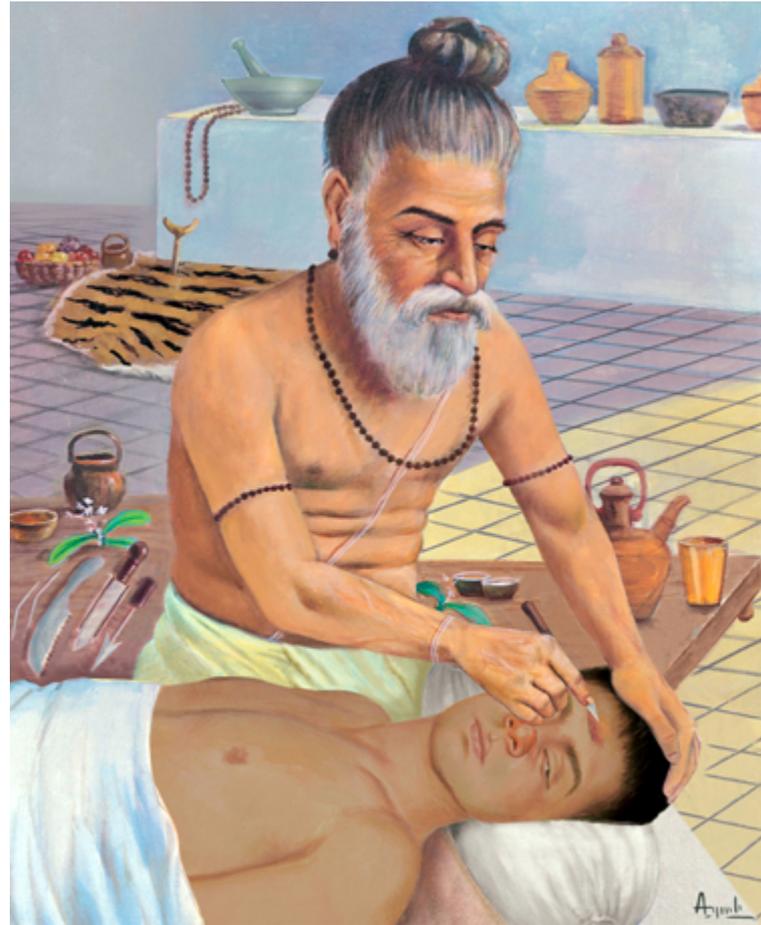
# The Hepatitis B Vaccine is Truly the First Anti-Cancer Vaccine !

Prevalence of HBsAg carrier rate in Taiwan decreased  
from 15% to 1.5% !

Childhood HCC mortality decreased by 75% !

Chen HL et al. JAMA 1996;276:906

Chang MH et al. N Engl J Med 1997;336:2855



**Sushruta:** 600-512 B.C. Indian Physician who advocated the Caesarian section, removal of kidney stones and cataracts, and catalogued 101 types of surgical instruments. He also wrote an excellent descriptions of a disease resembling **cholera** in the Sushruta Samshita in Sanskrit.

May God be with me! May Heaven bless this New Year. May it be a year of fruitfulness, of peace and prosperity; may it be a year of peace and unity for all mankind; **may the world be freed of cholera.**



Giacomo Meyerbeer 1791-1864

Cholera: A disease that begins, where other diseases end...with death.



## Two Seminal Observations in the Early 1960's

- Discovery of the sodium-glucose co-transport as the mechanism for intestinal glucose absorption (Robert K. Crane).
- Intestinal mucosa intact in cholera and capable of absorbing water.



**As a young physician working in Bangladesh, Dr. Richard Cash was instrumental in completing the first successful clinical trial of oral rehydration therapy on patients with severe diarrhea. He captured this image of a cholera patient who required nearly 150 liters of fluid resuscitation.**

# Haiti Earthquake, 2010

## Burden of Cholera

- More than 6% of Haitians afflicted
- 717,000 cases of **Cholera**
- 8,200 deaths



# Yemen Cholera Outbreak 2017

- A country ravished by war, economic collapse and near famine suffers from devastating cholera outbreak.
- 700,000 suspected cases in total with 7,000 new cases a day (October, 2017).

# Peter Bent Brigham Hospital, Boston 1954



# Bond of Brothers



Richard and Roland Herrick

# Richard, a difficult patient

“Since admission patient has been extremely uncooperative. Has knocked over infusions, has been restrained, has been moved to side room because of loud outbursts. Restless, cursing all members of the House Staff.”

“Rather a difficult p.m. . . . Is extremely uncooperative. Behavior erratic and unpredictable. Bit nurse on hand while bed linen being changed. . . .”

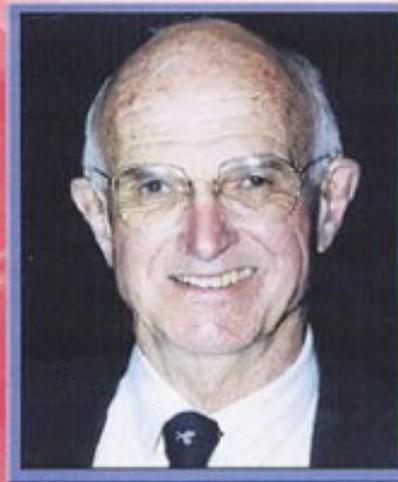
October 27<sup>th</sup>, 1954

# SCIENCE

UNLOCKING THE SECRETS OF

Profiling the Achievers in Science, Medicine & Technology

*Joseph E. Murray  
and the Story of the  
First Human Kidney  
Transplant*



*Joanne Mattern*

# Important Milestones

## First Successful ...

1954 **Kidney** Transplant

1967 **Liver** Transplant

1968 **Heart** Transplant

1968 **Pancreas** Transplant

1981 **Heart-Lung** Transplant

1989 **Living Related Liver** Transplant

2011 **Full Face** Transplant

2012 **Kidney** Transplant Chain



Artie was challenged by his  
cardiologist to run the  
Boston Marathon.



# Artie Michaels' Inspiring Story

- Primary Sclerosing Cholangitis dx 1989.
- Liver transplant 1990. Surgery lasted 19 hrs.
- 1992 routine check-up, cardiologist challenges him to a race in the Boston Marathon.
- He ran it ... each mile was a major accomplishment. The strain was great but he completed the 26 mile run and finished the race ahead of the cardiologist who was 20 years his junior!

# **Kidney Transplant Chains**

**Historic record set involving 60 individuals, 30 donors and 30 recipients.**

**Carried out over 4 months, in 17 hospitals, in 7 states.**

The New York Times

# 60 Lives, 30 Kidneys, All Linked



**What is the Most Common  
Chronic Infection in Man ?**

# H. Pylori



# **Serendipity ...**

**After numerous attempts to culture the bacteria, Barry Marshall and Robin Warren finally visualized bacterial colonies in 1982.**

**They had unintentionally left their petri dishes incubating for 5 days over the Easter weekend.**



Marshall and Warren

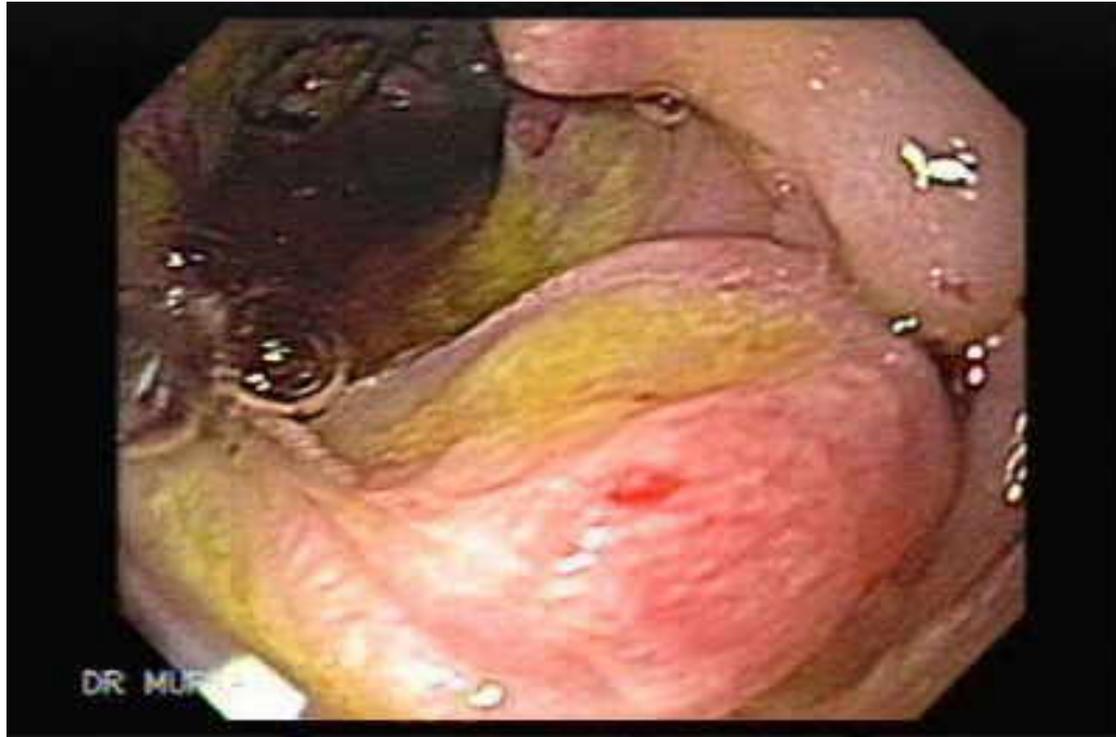
**Marshall BJ, Warren JR: Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration.**

**Lancet 1984;1:1311-5**

# More Than Half of the World

- ## Population Infected with H.Pylori !
- **100%** of infected patients have **gastritis**.
  - Less than **10%** develop **peptic ulcer disease**.
  - Less than **2%** develop **Gastric Cancer, Gastric Lymphoma** or **Gastric Maltoma**.

# Gastric Maltoma



# **Karl Schwarz's Dictum 1910**

**No Acid, No Ulcer**

# **2012 Dictum**

**No H.Pylori, No Ulcer**

**So Is It**

**pH or Hp ?**

Enough said about the topic  
(NSAID)

# Essentially 3 Causes of Duodenal Ulcer

Acid Hypersecretion

H.Pylori

NSAIDS

# **Medical Imaging**

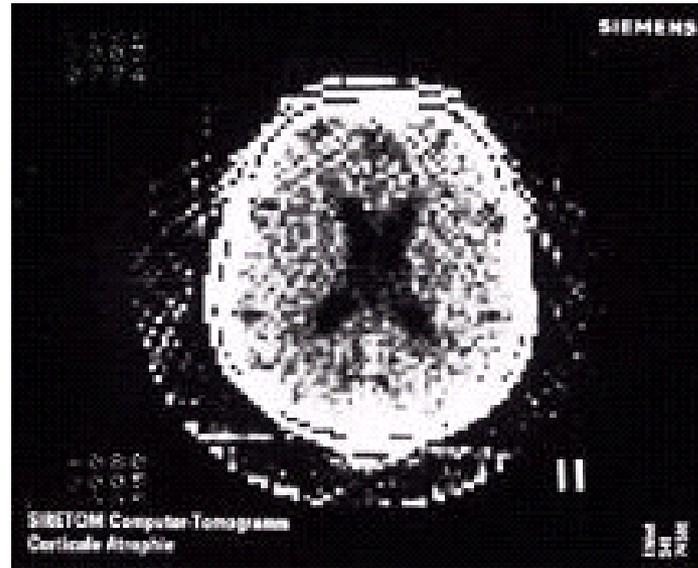
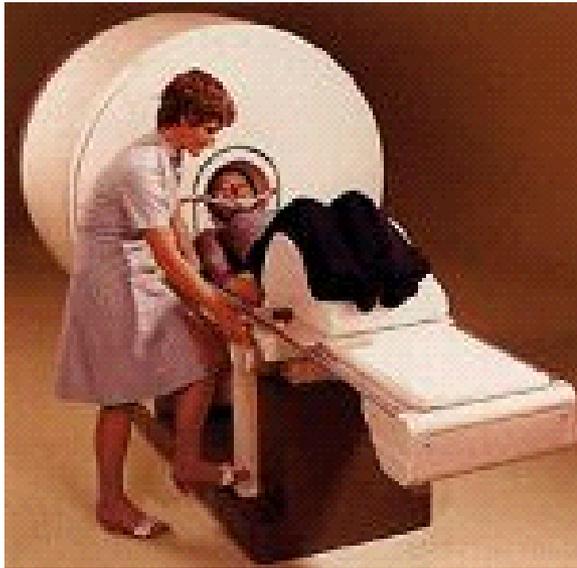
**From the very first x-ray to molecular imaging**



Wilhelm Röntgen



# First CT scan image



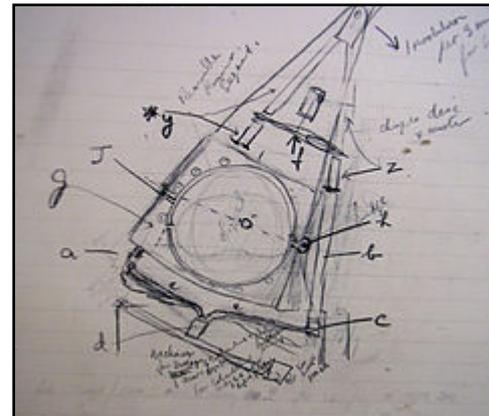
CT was invented in 1972 by British engineer Godfrey Hounsfield of EMI Laboratories, England and by South Africa-born physicist Allan Cormack of Tufts University, Massachusetts. Hounsfield and Cormack were later awarded the Nobel Peace Prize for their contributions to medicine and science. The first CT scanner developed by Hounsfield in his lab at EMI took several hours to acquire the raw data for a single scan or "slice" and took days to reconstruct a single image from this raw data.

# Nobel Prize 1979

## Godfrey N. Hounsfield



## Allan M. Cormack



**EMI - Electric and Musical Industries Ltd**

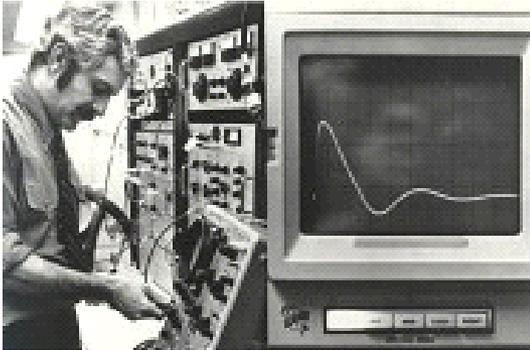
**Investor in:**

**Airborne RADAR, CT Scanners, and...**

# EMI - Electric and Musical Industries Ltd

Investor in Airborne RADAR, CT Scanner, and **the BEATLES**





Dr Raymond Damadian developed first MR scanning machine



Post doc fellows



First human MR image – chest of his fellow, Dr Minkoff

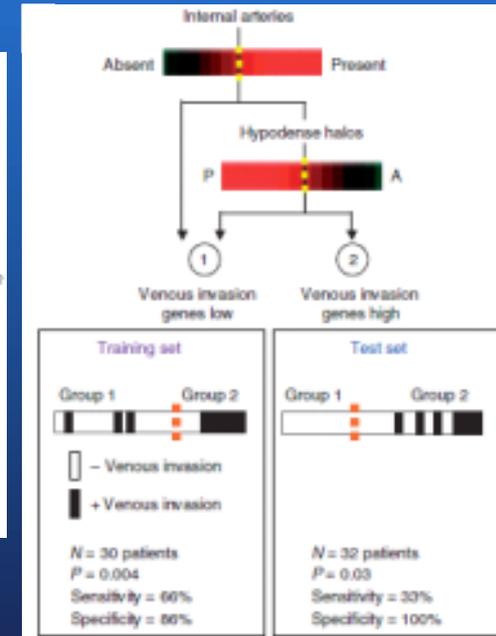
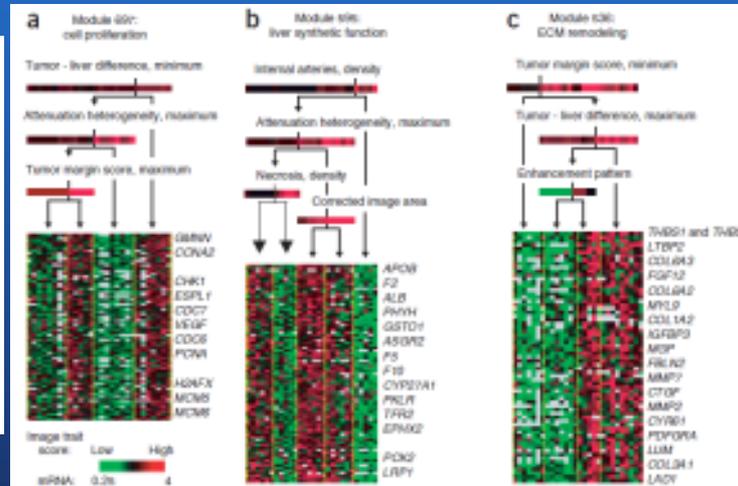
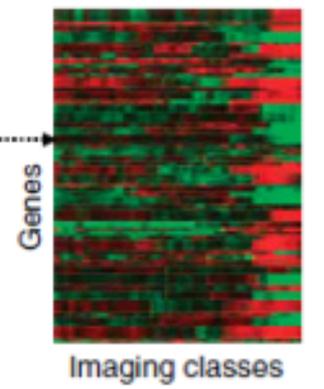
# Linking gene expression and imaging traits

## Imaging traits in HCC

Constructing an association map

Molecular portraits of HCC derived from imaging traits

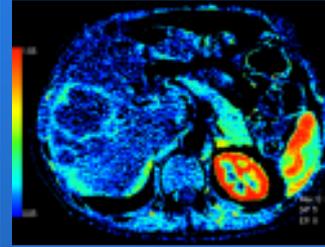
Imaging traits that predict venous invasion



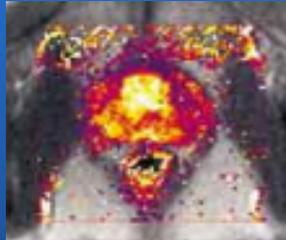
Contrast  
Ultrasound



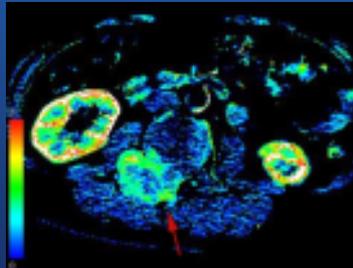
CT Perfusion  
mapping



Functional MRI



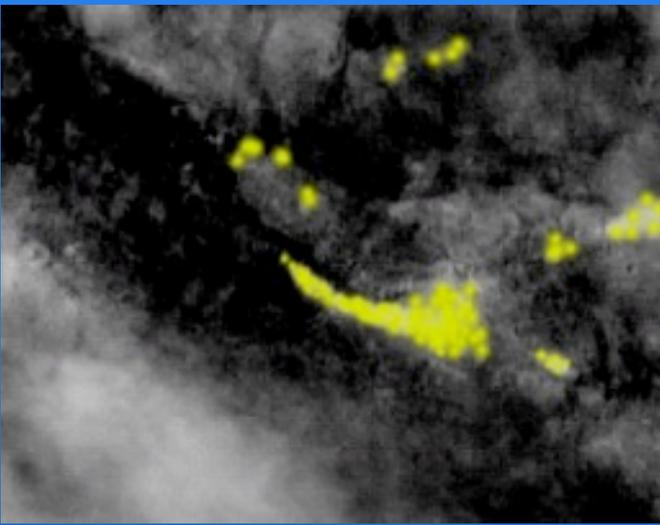
PET



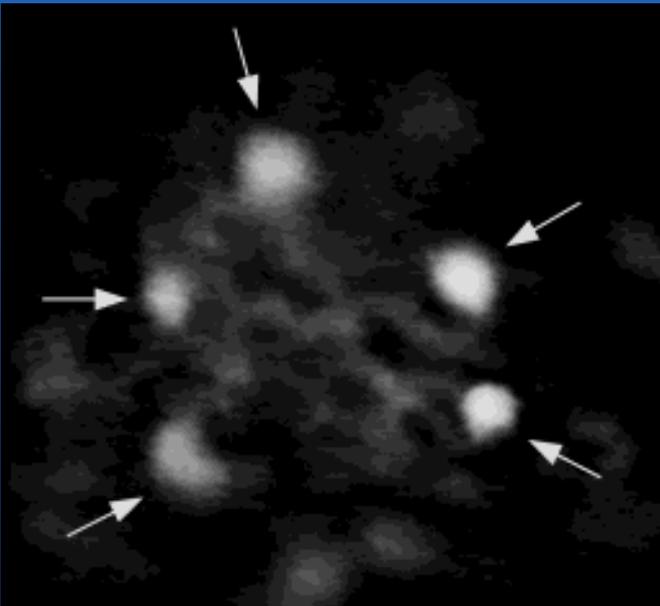
Optical  
Imaging



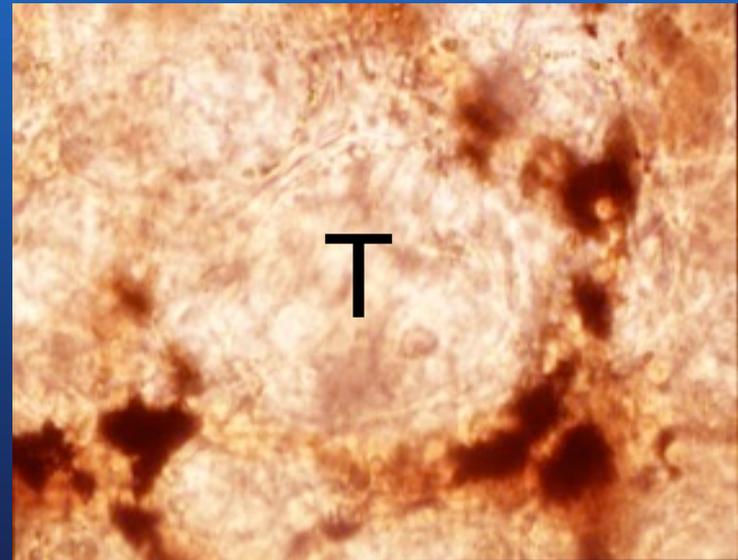
# Molecular imaging of Liver Tumor growth



Macrophage recruitment from sinusoids



into developing tumors



to support tumor growth

# From Salvarsan to **Penicillin**



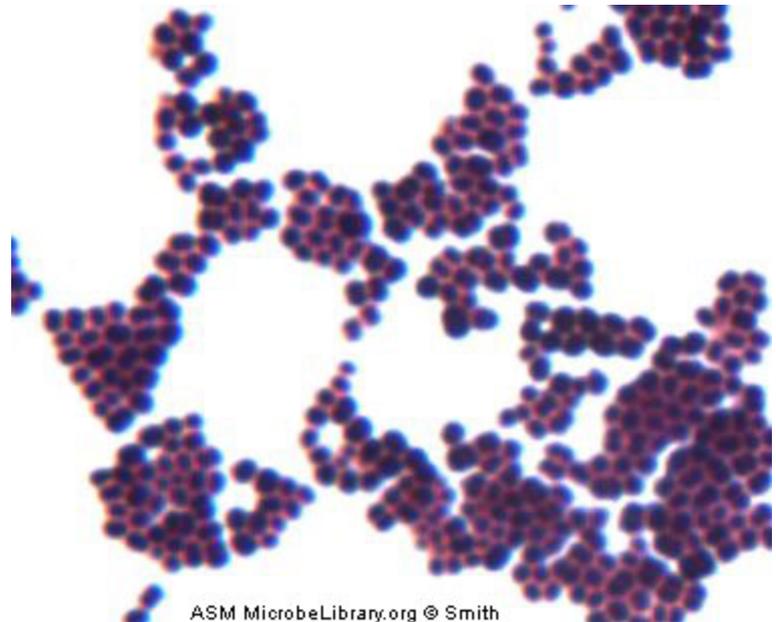
# The Mold in Dr. Florey's Coat

The Story  
of the  
Penicillin  
Miracle

ERIC LAX

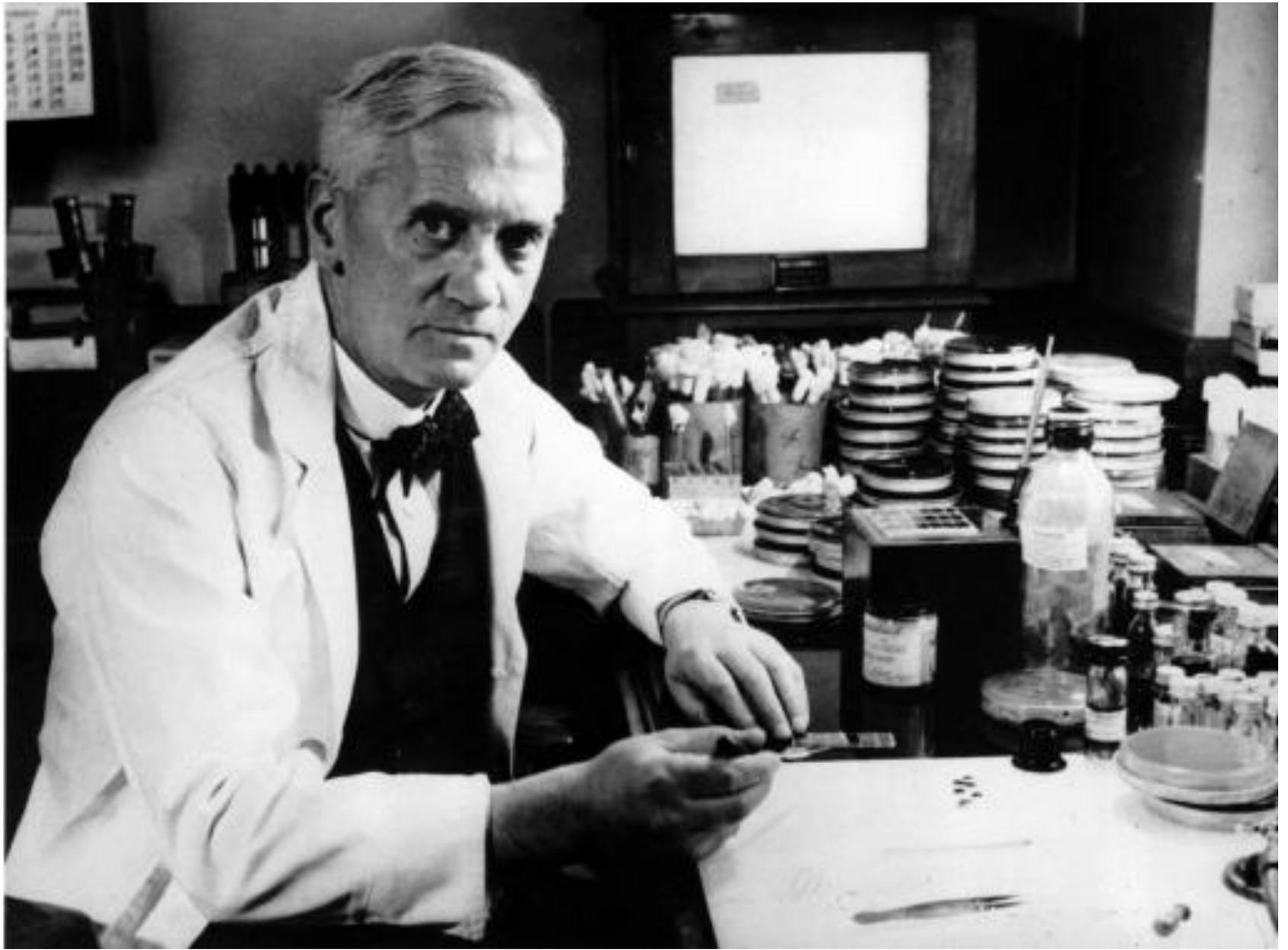


"Admirable, superbly  
researched . . . perhaps  
the most exciting tale  
of science since the apple  
dropped on Newton's head."  
—Simon Winchester,  
*The New York Times*



ASM MicrobeLibrary.org © Smith

FI



It was a Warm Summer Night in 1928

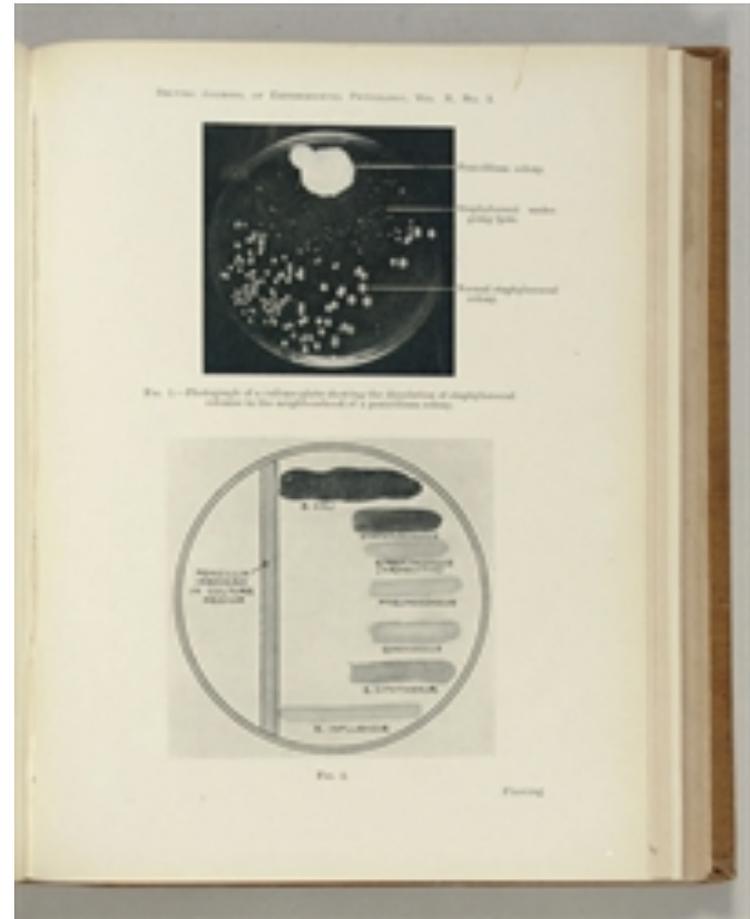


When he returned from vacation he  
observed...

An agar plate of  
staphylococci and the effect  
of the mold *Penicillium  
notatum*



**FLEMING, Alexander** *On the Antibacterial Action of Cultures of a Penicillium, with special reference to their use in the isolation of B. Influenzae.* In: *The British Journal of Experimental Pathology*, volume 10, pp.226-236. **1929.**



# Attempts to develop a drug

- Lysozyme research;
- In 1935 he largely abandoned this work

