

# ENVIRONMENTAL AND BEHAVIOUR CAUSES OF CARDIOVASCULAR DISEASE

*Gaetano Thiene*

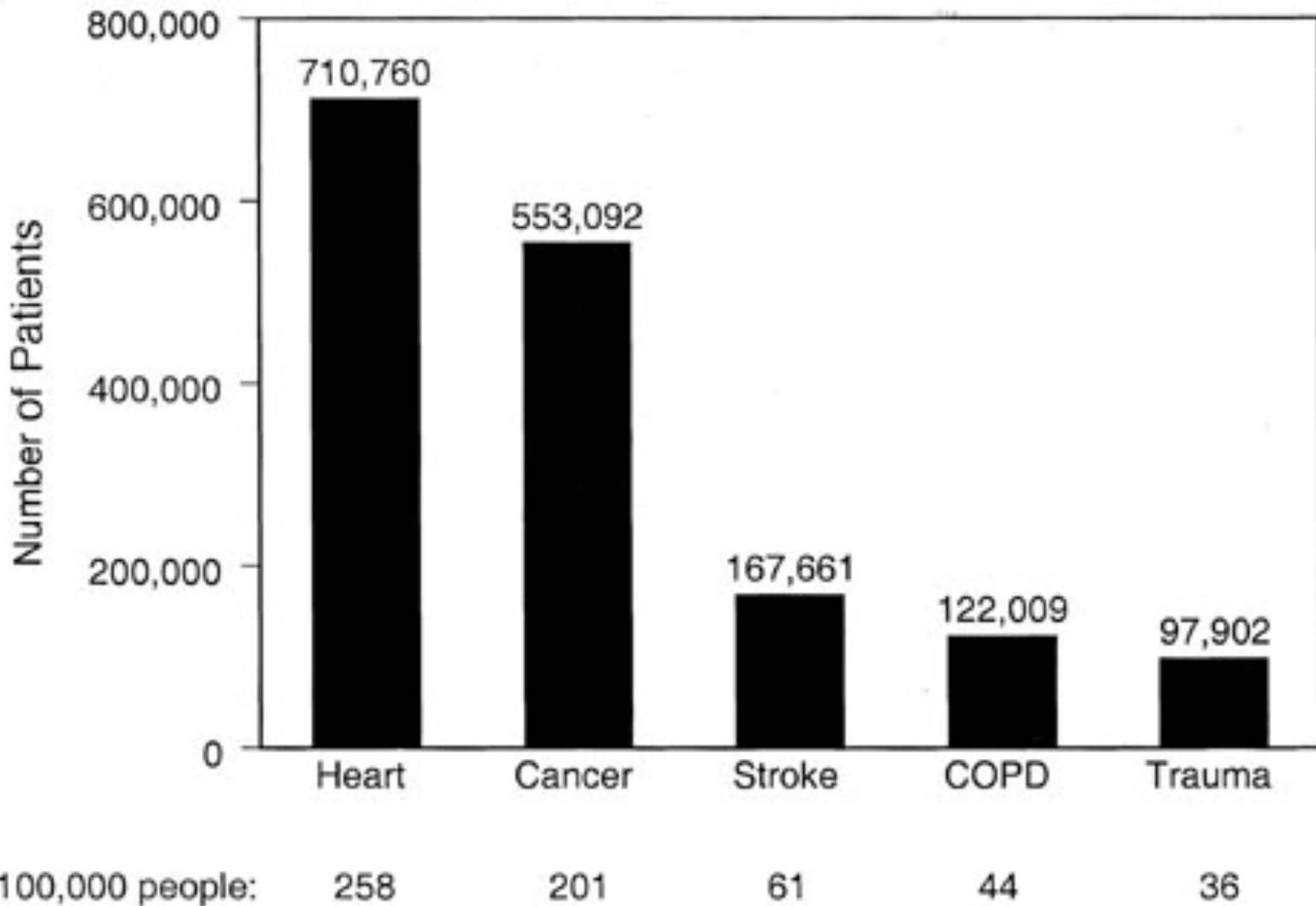
Università degli Studi di Padova



“Cardiac disease represents the  
worst calamity in terms of  
mortality”

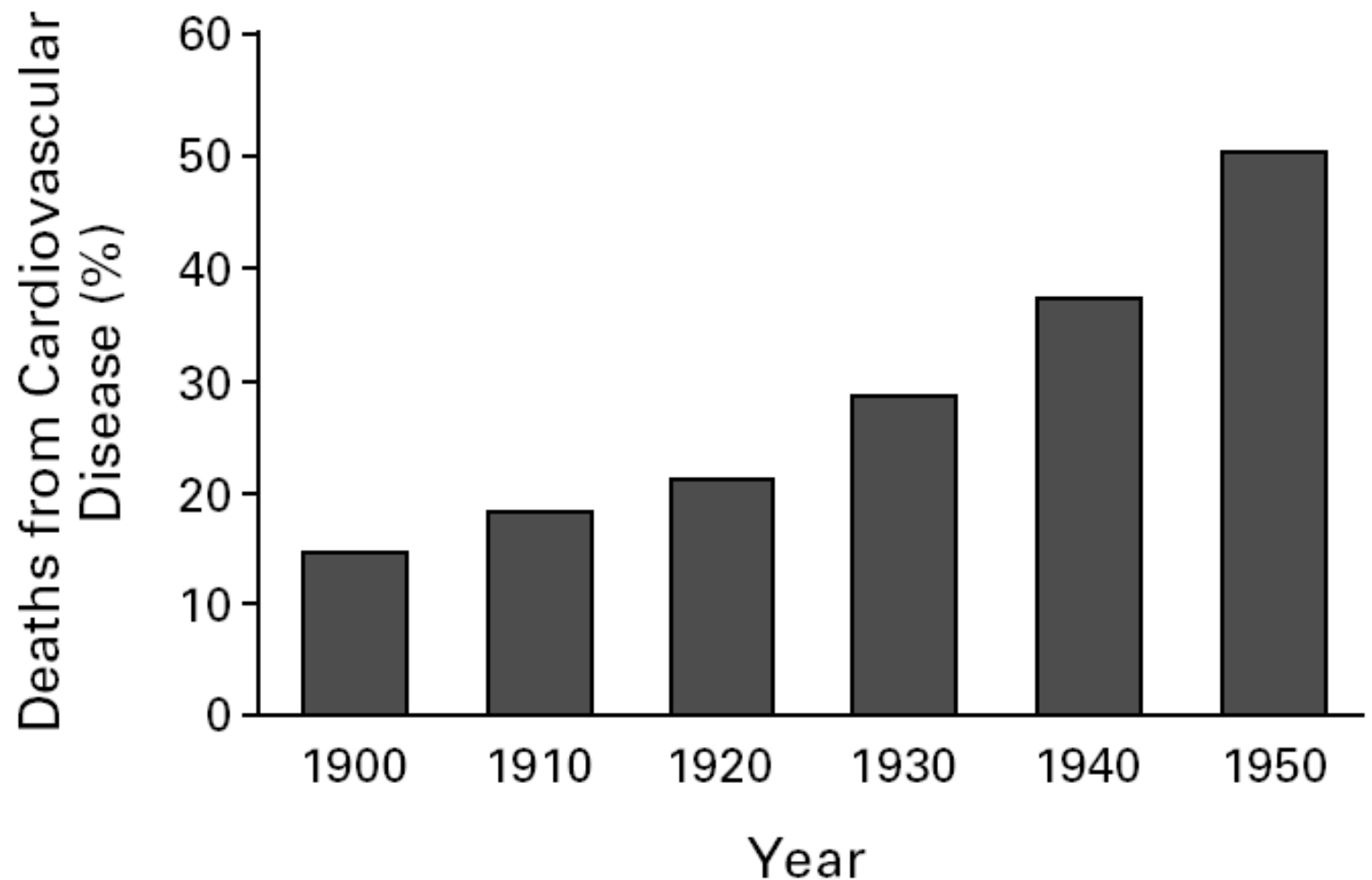
Washington Post,  
April 30, 1990





*from Topol EJ. Circulation  
Vol. 108, 2003 , Pages 108:III-6-III13*

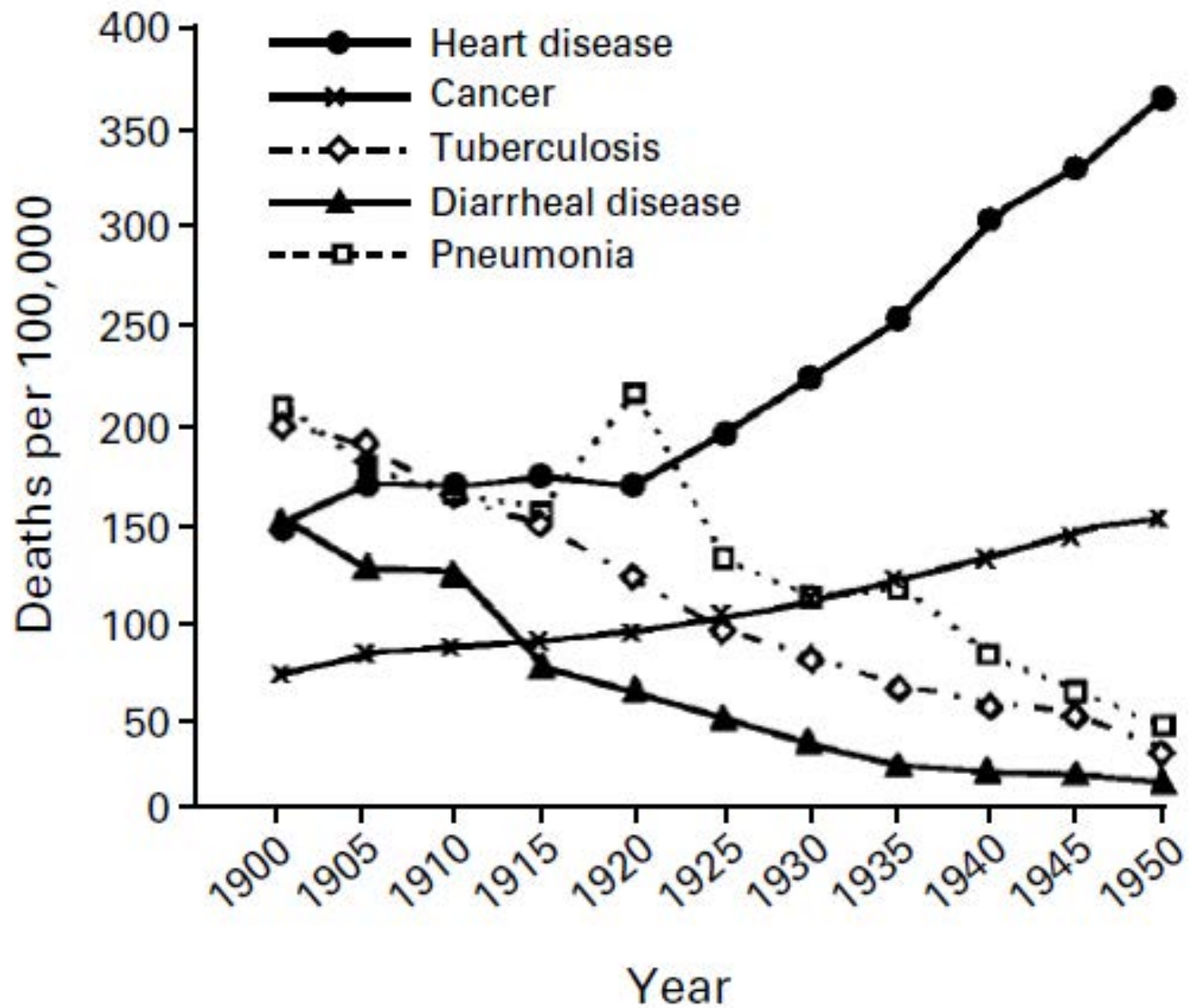




**Figure 2.** Percentage of Deaths from Cardiovascular Disease in the United States from 1900 to 1950.

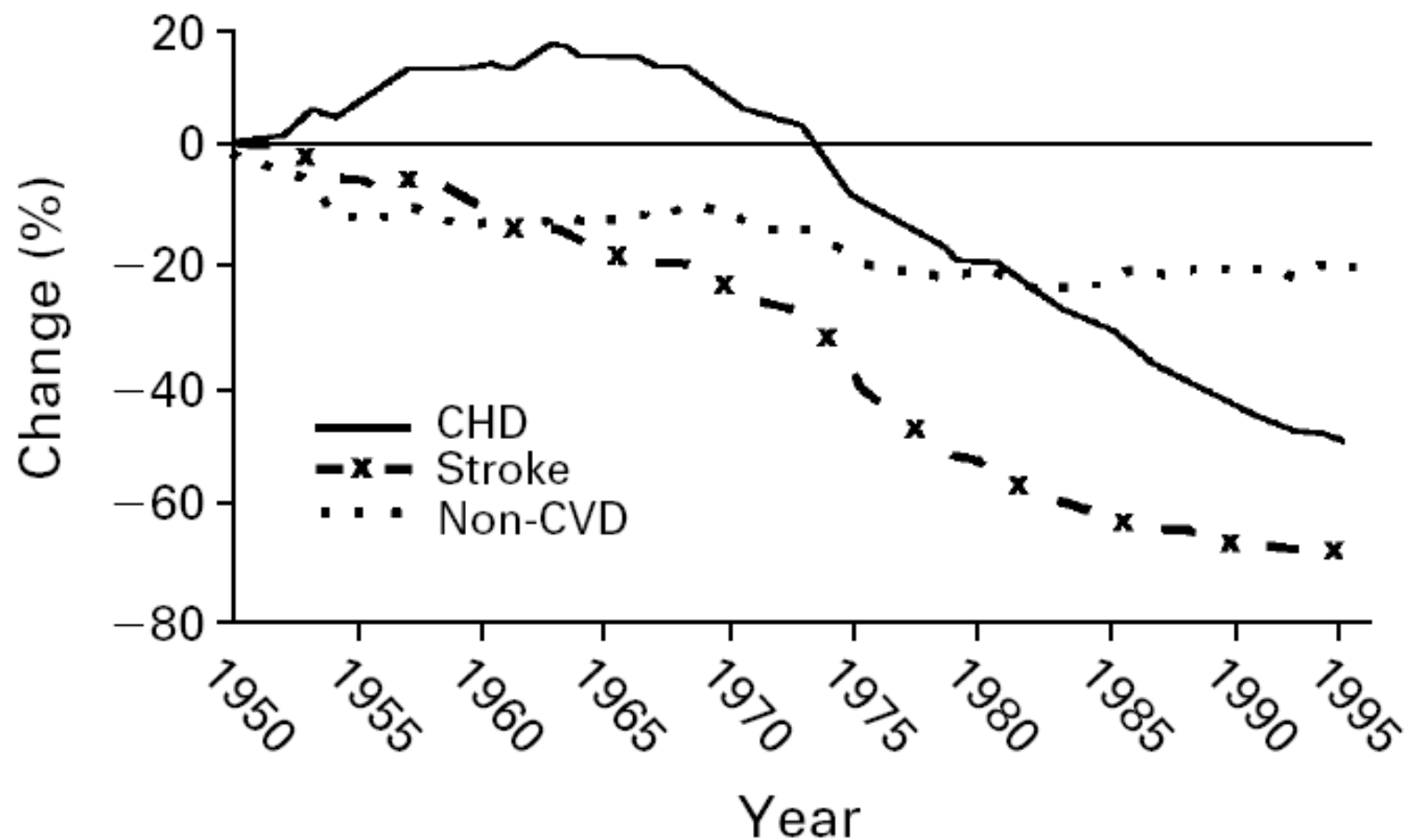
Data are from the Centers for Disease Control and Prevention.<sup>1</sup>





from Braunwald E, *The New England Journal of Medicine*  
Volume 50, No. 22, November 2007, Pages 2128-2130

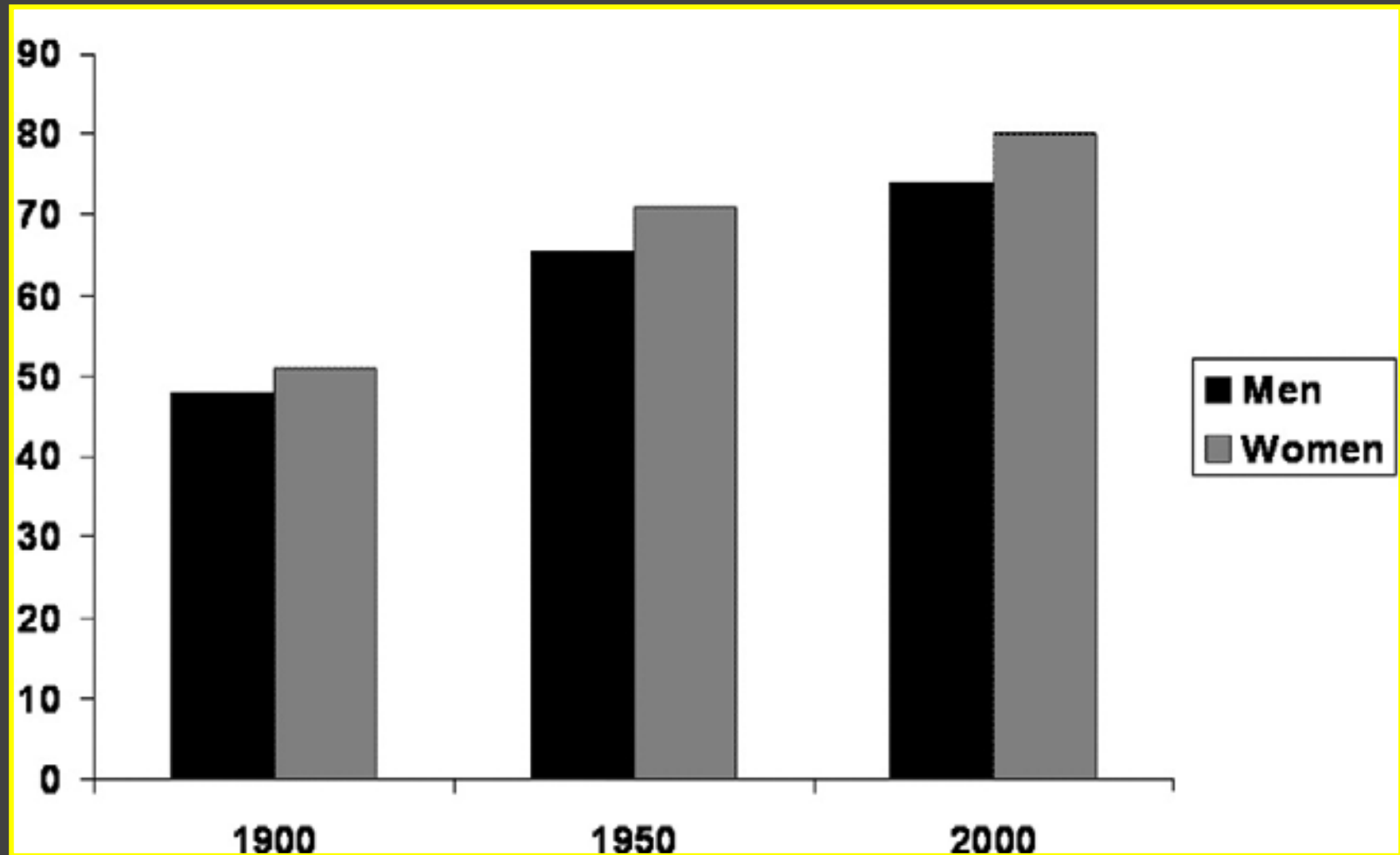




**Figure 5.** Changes in Age-Adjusted Death Rates from Coronary Heart Disease (CHD), Stroke, and Noncardiovascular Disease (Non-CVD) in the United States from 1950 to 1995.

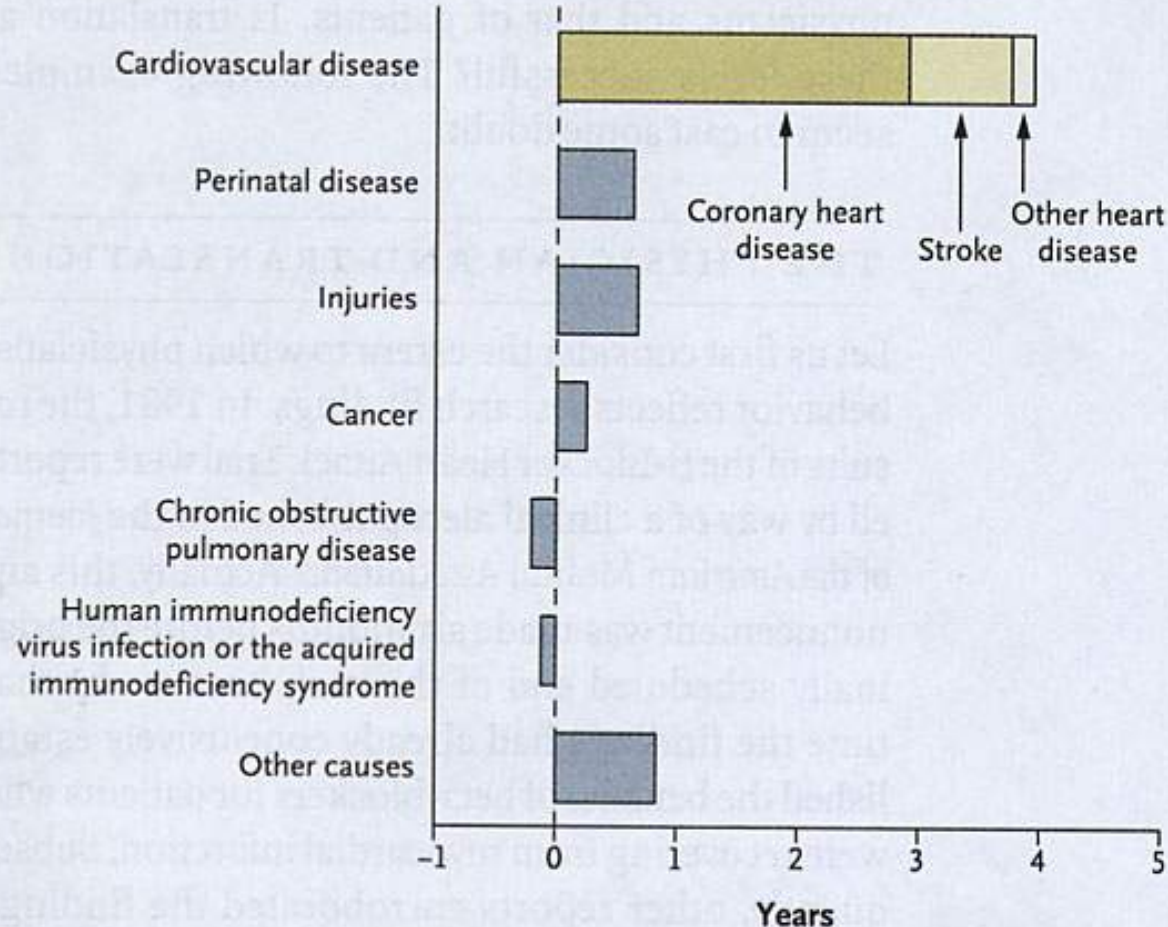
Data are from the National Heart, Lung, and Blood Institute.<sup>22</sup>

# Life Expectancy in the US



*from Jonas RA, The Journal of Thoracic and Cardiovascular Surgery  
Volume 134, Issue 1, July 2007, Pages 1-14*





**Figure 1.** Change in U.S. Life Expectancy between 1970 and 2000.

Between 1970 and 2000, life expectancy in the United States increased by 6.0 years overall, with 3.9 years of the increase due to reductions in mortality from cardiovascular causes. The data are from the Centers for Disease Control and Prevention.

*Lenfant C. The New England Journal of Medicine*  
*Volume 349, 2003, Pages 868-874*

# Achievements of Cardiovascular Medicine in the centuries:

- Discoveries in Anatomy, Physiology and Pathology: the dawn of Cardiovascular Medicine
- In vivo diagnosis becomes possible thanks to technologic innovation
- Heart diseases can be treated
- Prevention is nowadays feasible



# The dawn of Cardiovascular Medicine

- **ANATOMY:** Andrea Vesalio (1543)
- **PHYSIOLOGY:** Realdo Colombo (1559) and William Harvey (1628)
- **PATHOLOGY:** Giovanni Battista Morgagni (1761)





# Diego Rivera – Instituto Nacional de Cardiología, Mexico City



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# Robert Hooke (1635-1703) invents the microscope (1665)



## MICROGRAPHIA:

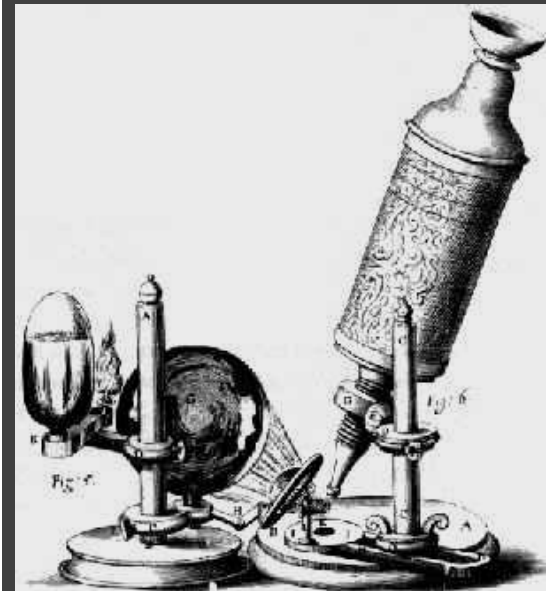
OR SOME  
*Physiological Descriptions*  
OF  
**MINUTE BODIES**  
MADE BY  
**MAGNIFYING GLASSES**  
WITH  
OBSERVATIONS and INQUIRIES thereupon.

By R. HOOKE, Fellow of the ROYAL SOCIETY.

*Non possum oculo quantum contendere Lincolni,  
Non tamen idcirco contemnas Lippum: innuigi. Horac. Ep. lib. 1.*



LONDON, Printed by Jo. Martyn, and Jo. Allestry, Printers to the  
ROYAL SOCIETY, and are to be sold at their Shop at the Bell in  
St. Paul's Church-yard. M DC LX V.



# Robert Koch (1843-1910) discovers the *Mycobacterium tuberculosis* (1882)

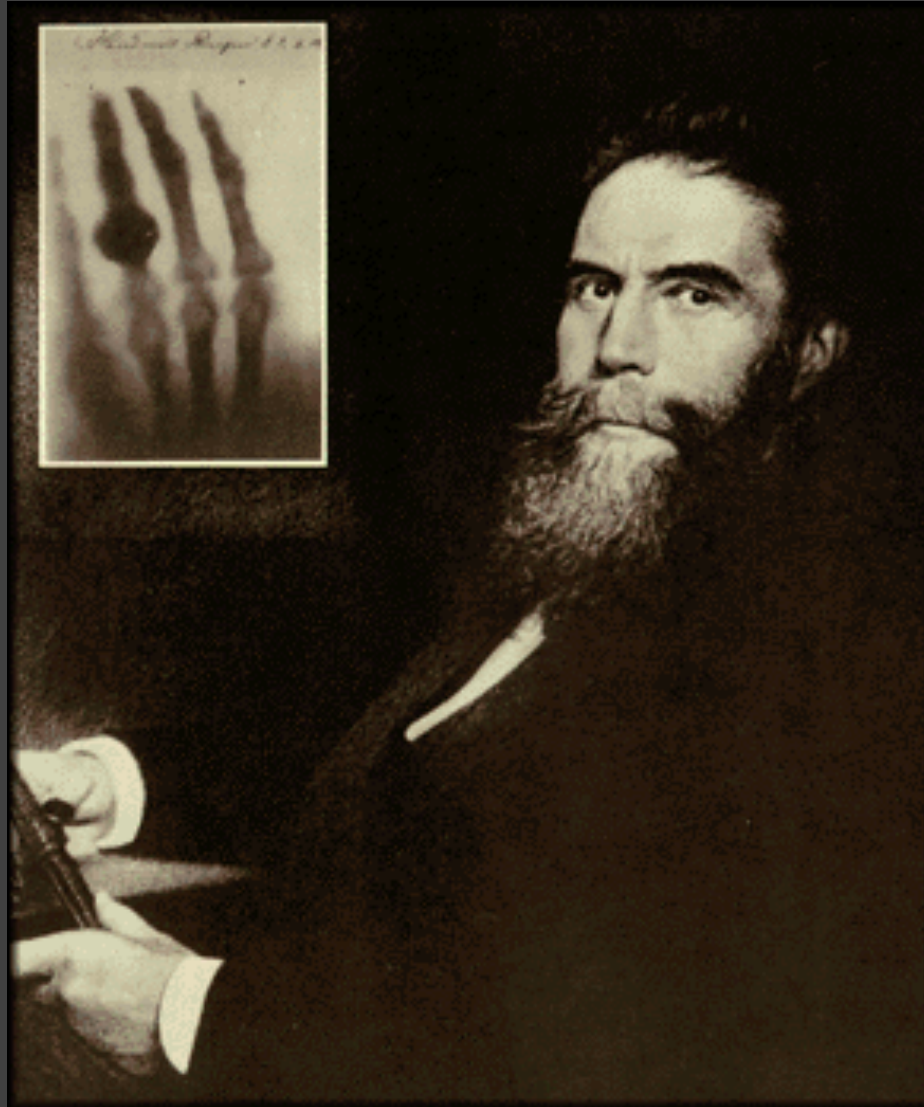




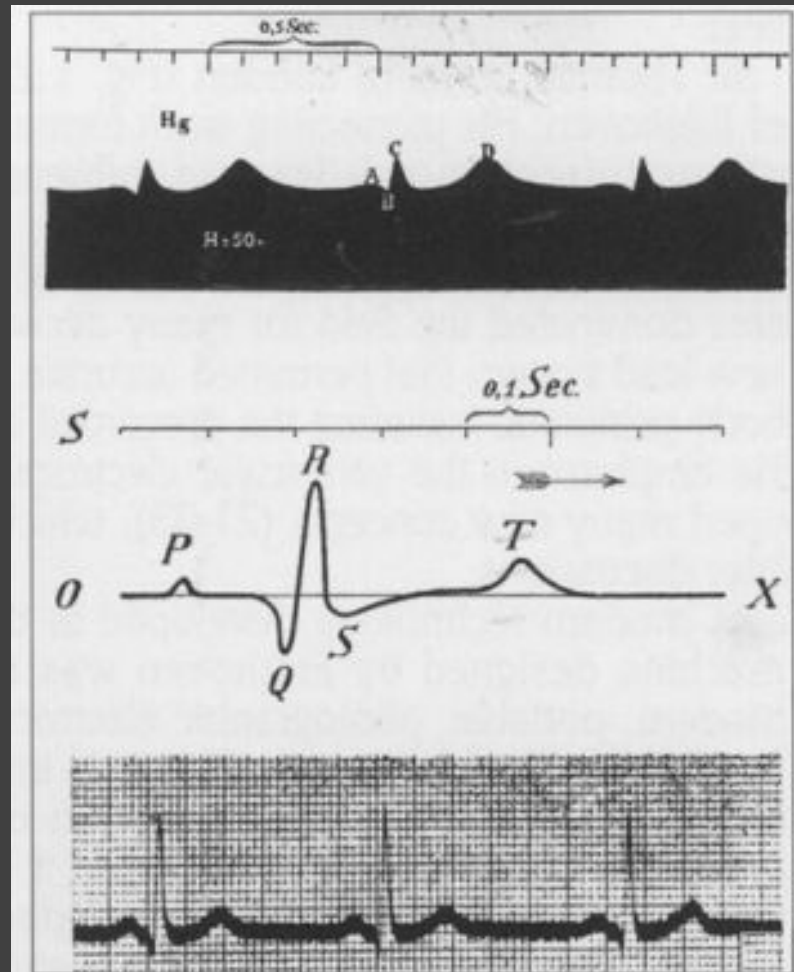
# René Laennec (1781-1826) invents the stethoscope (1816)



# Wilhelm Conrad Röntgen (1845-1923) invents radiography (1895)

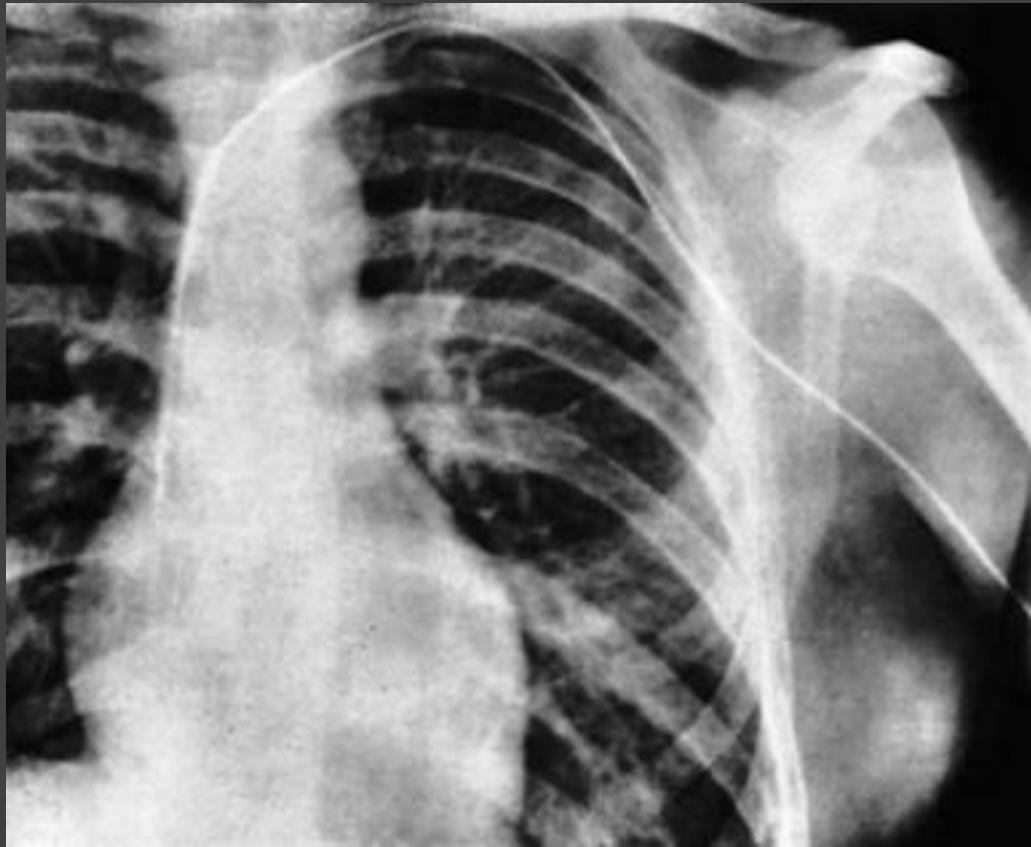


# Willem Einthoven (1860-1927) invents electrocardiography (1902)

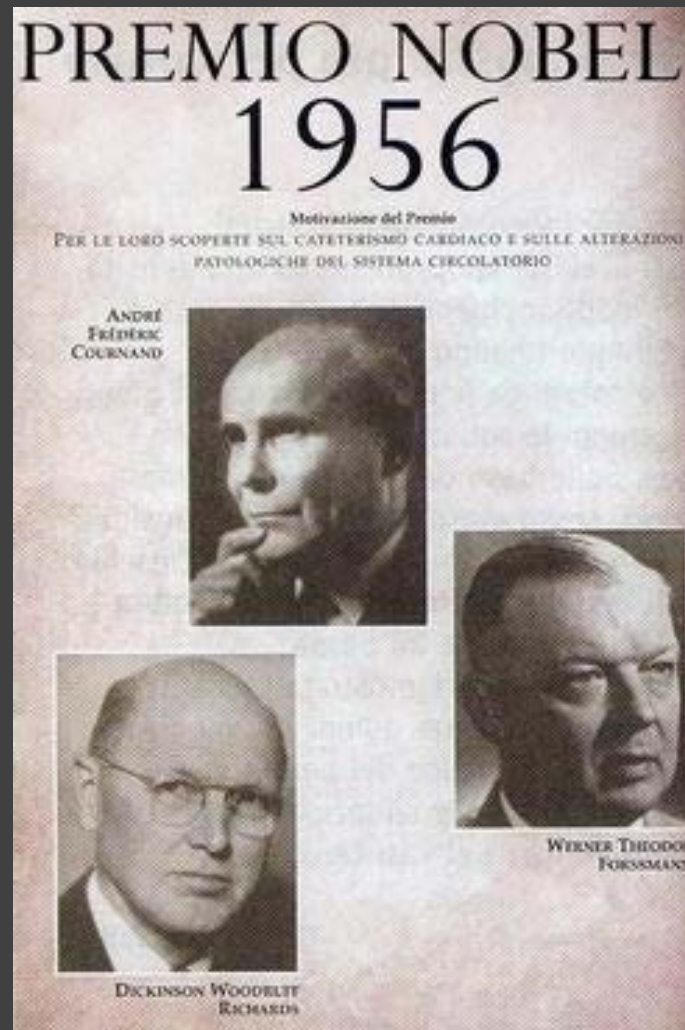




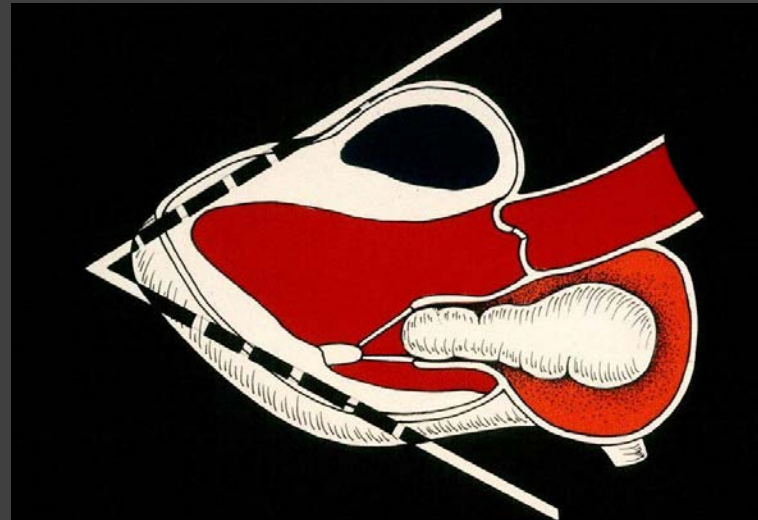
# Werner Forssmann (1904-1979) invents Cardiac Catheterization (1929)



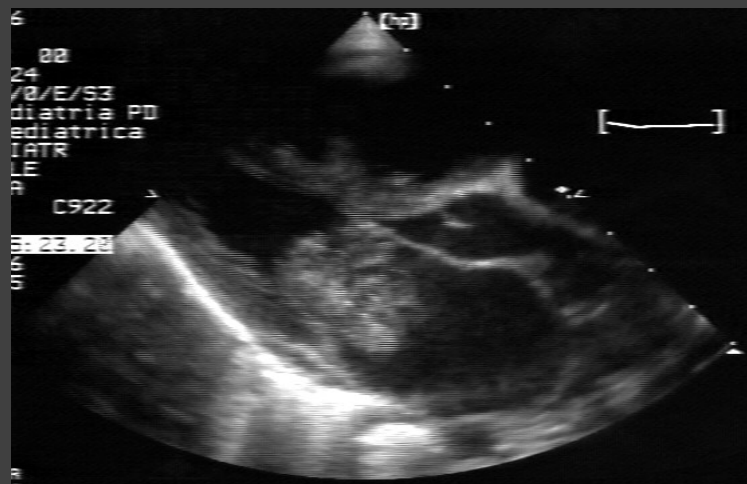
# Nobel Prize for Cardiac Catheterization



# Inge Edler (1911-2001) and Carl Hellmuth Hertz (1920-1990) apply echography to the heart (1952)

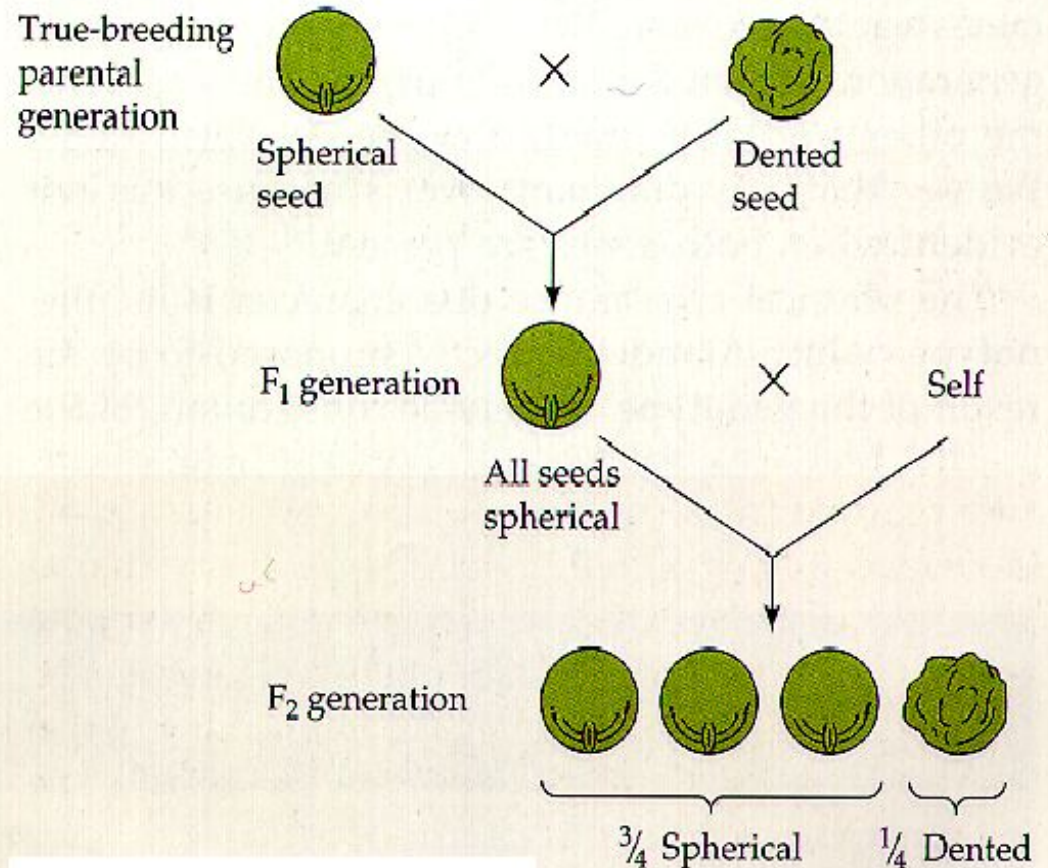
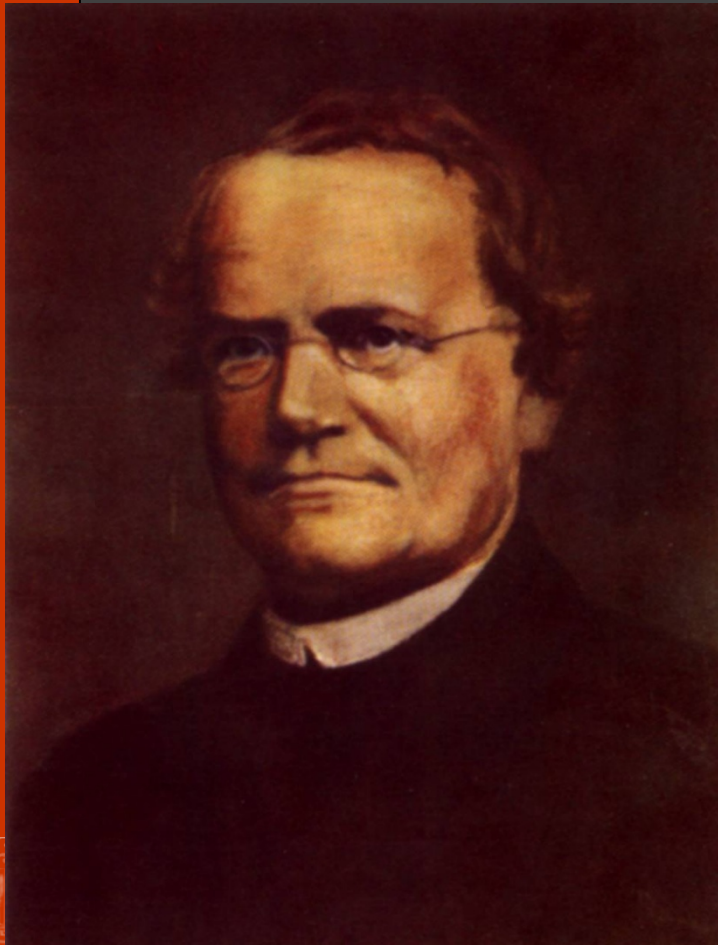


*Cardiovascular Pathology,  
University of Padua, Italy*

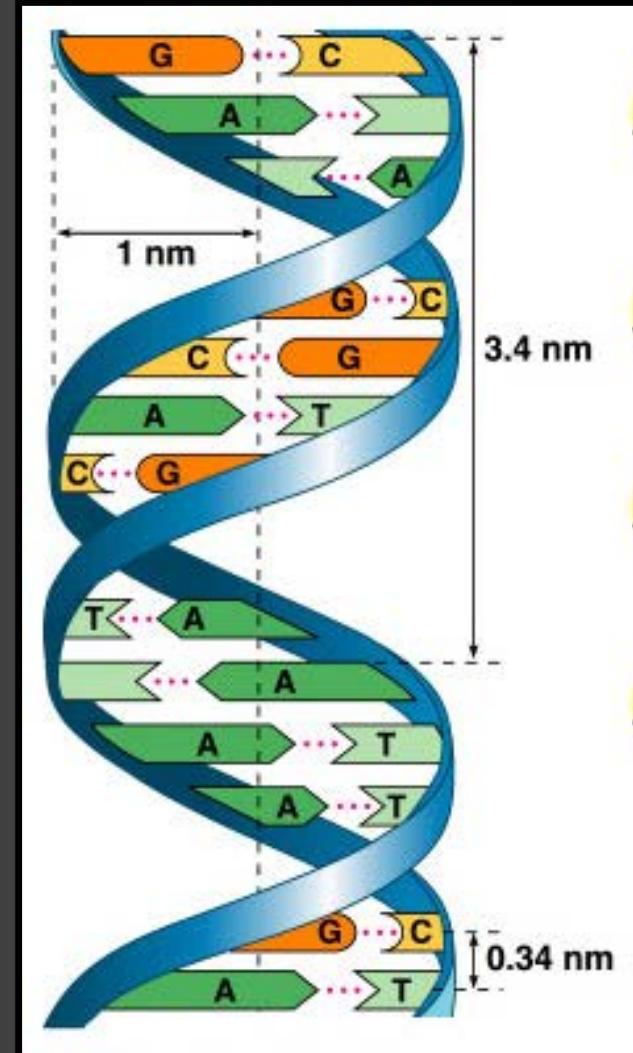
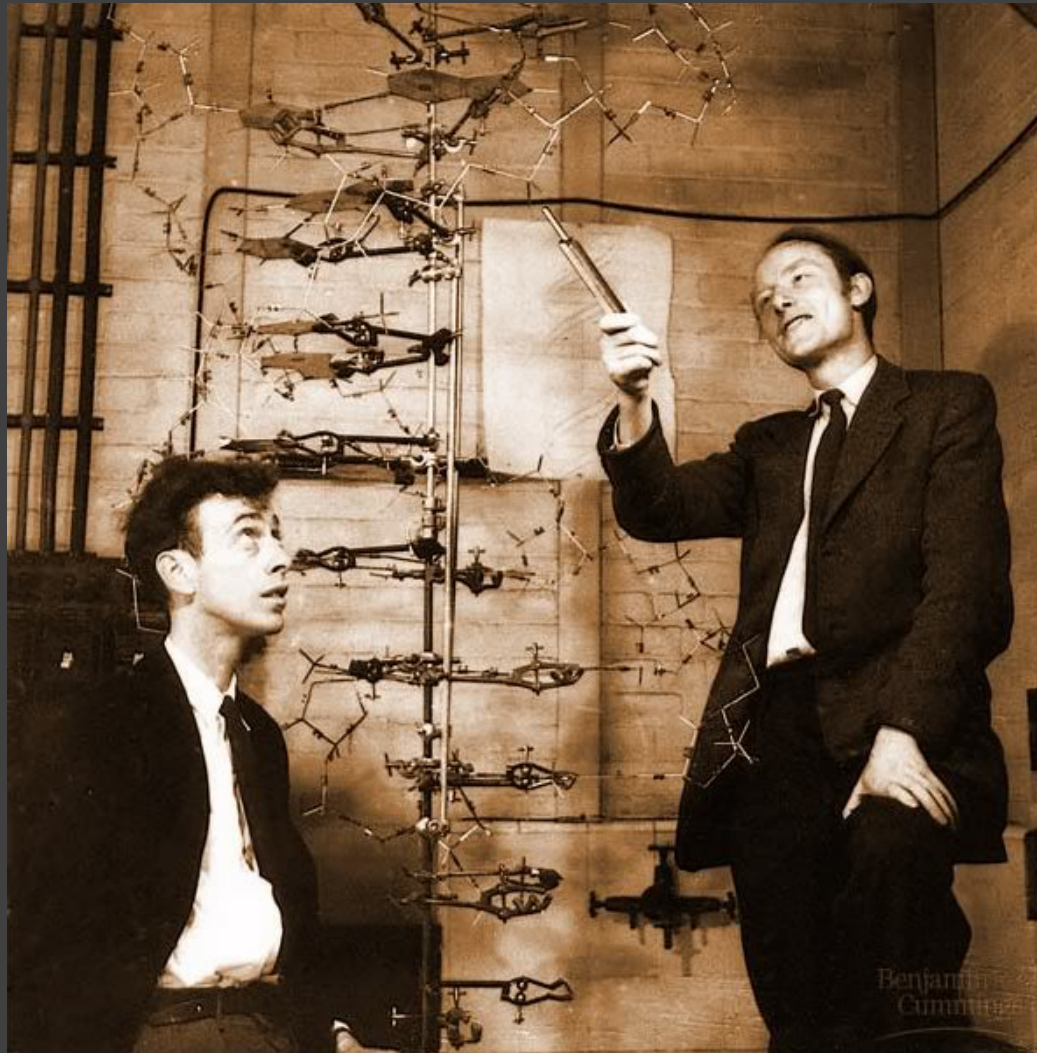




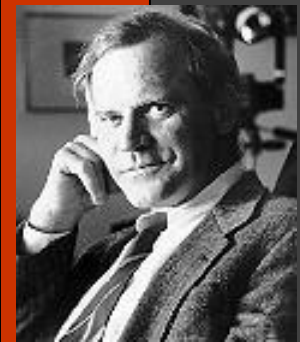
# Gregor Mendel (1822-1884) discovers the Principles of Genetic Heritage (Mendel's Laws)



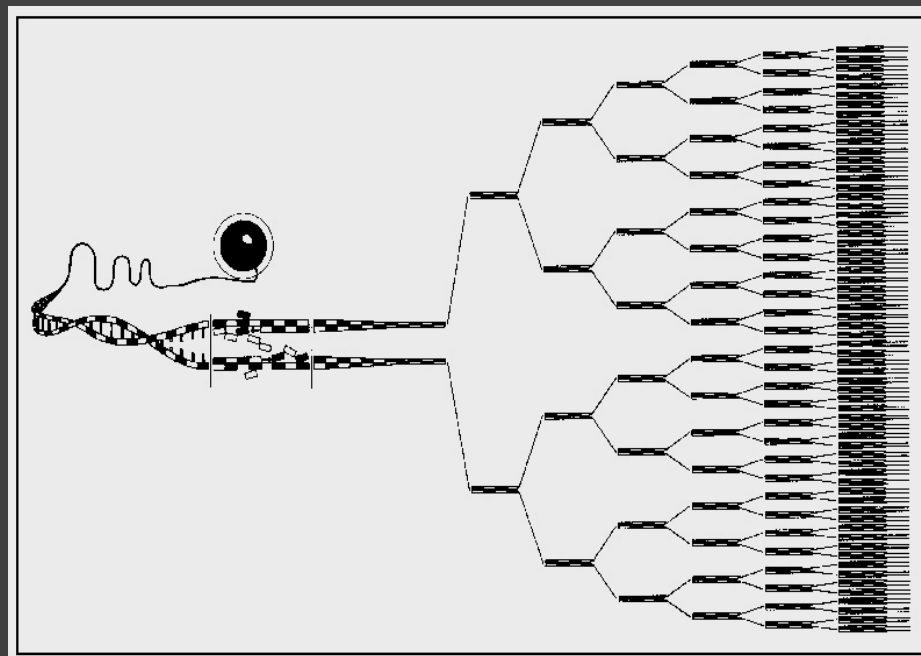
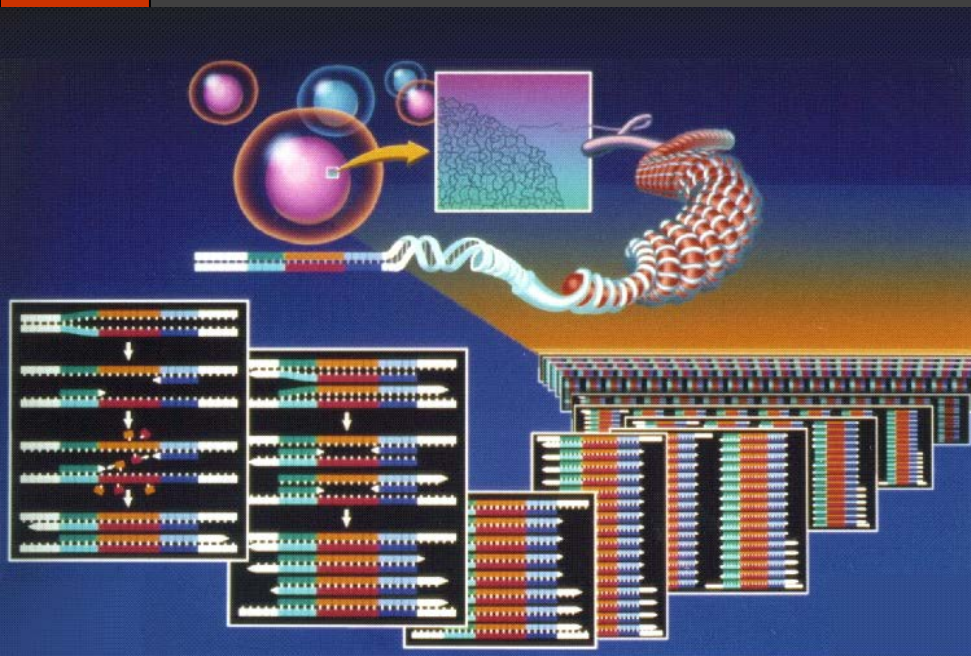
# James Watson (1928-) and Francis Crick (1916-2004) discovers the code of the life (1953)

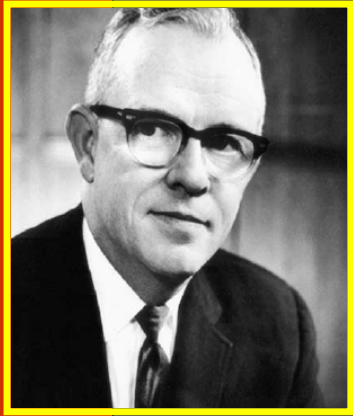




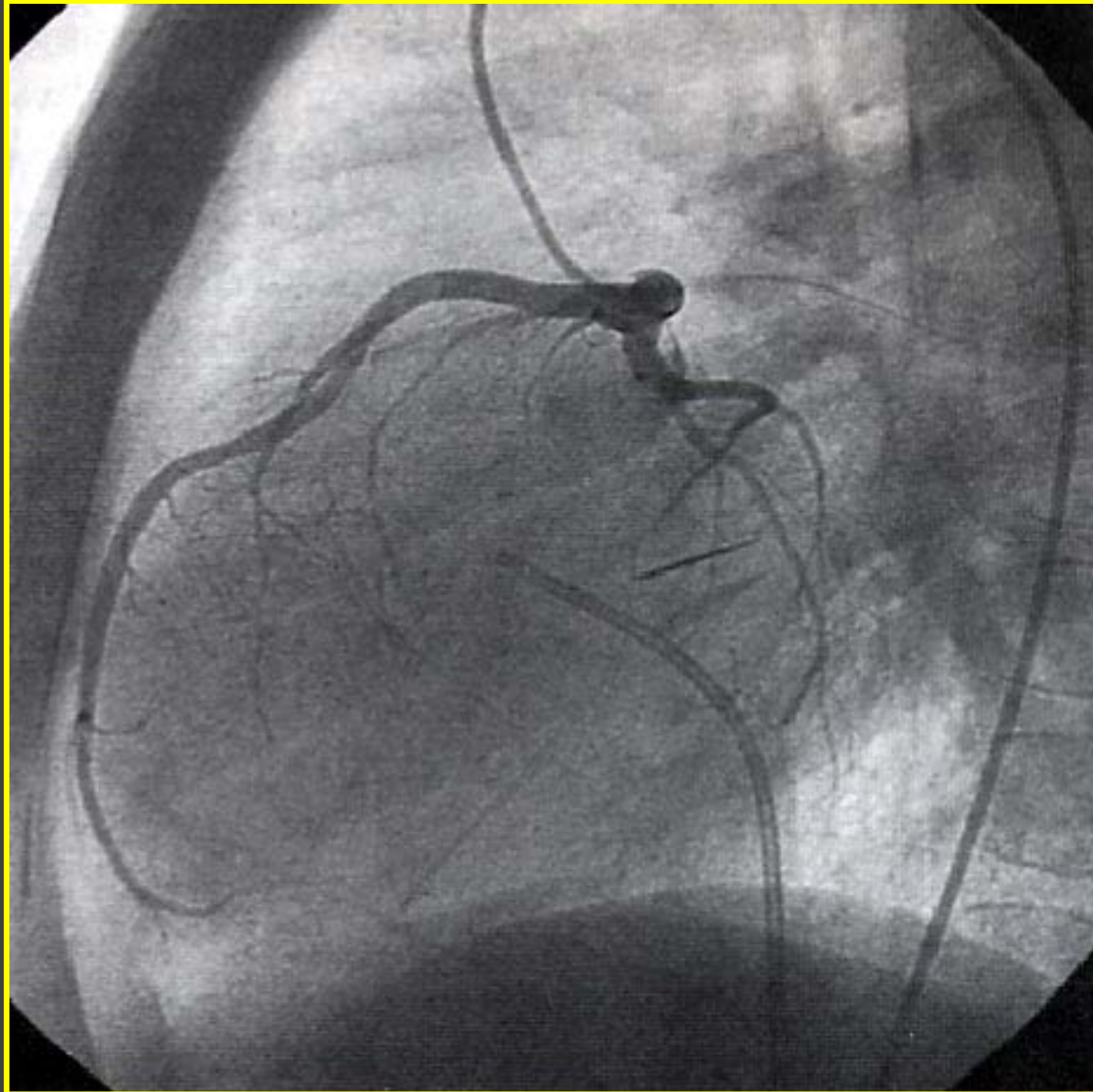


# Kary Banks Mullis (1944-) discovers the Polymerase Chain Reaction (PCR) (1985)

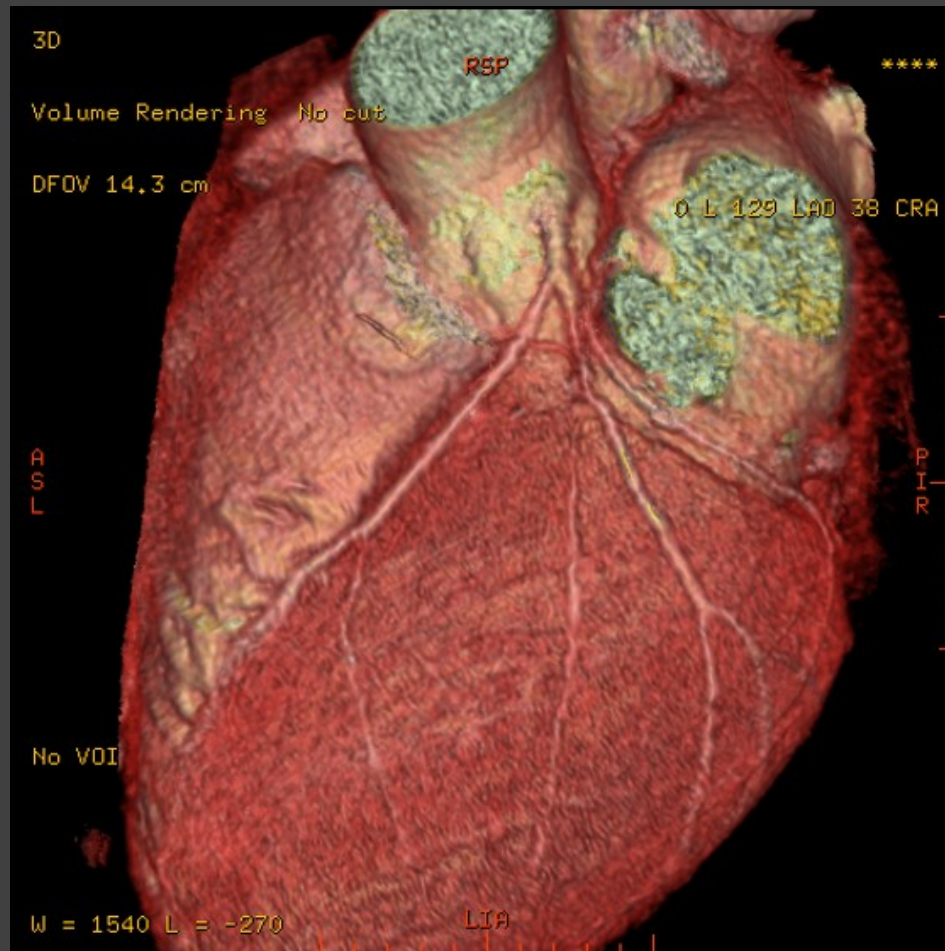




**Mason Sones (1918-1985)** invents  
in vivo Coronaroangiography (1958)

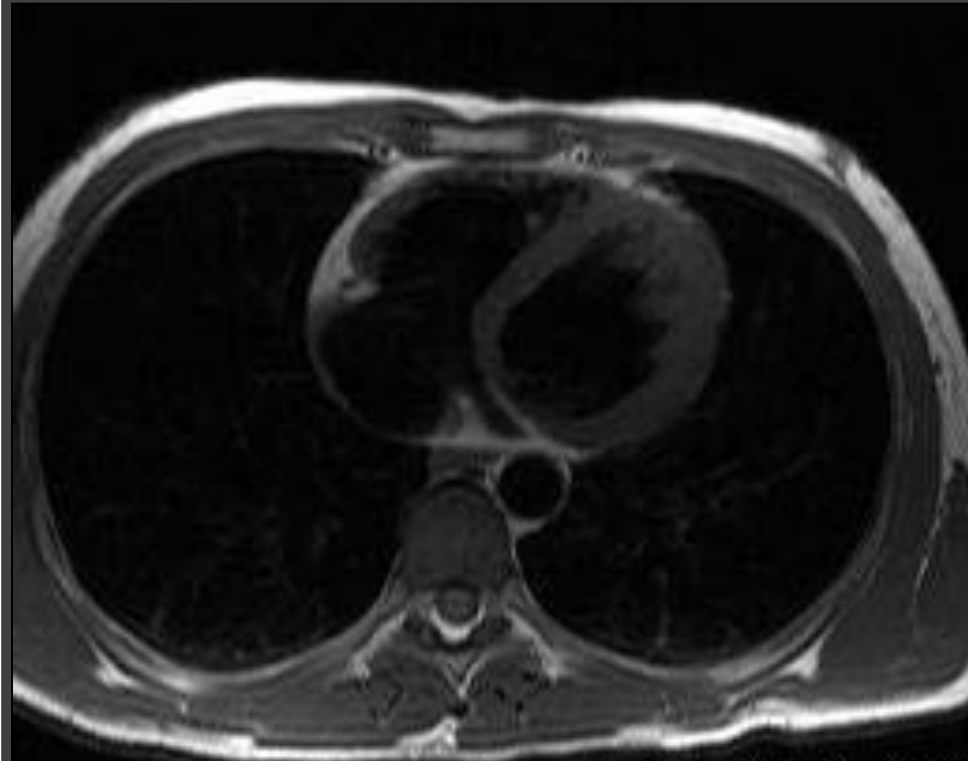
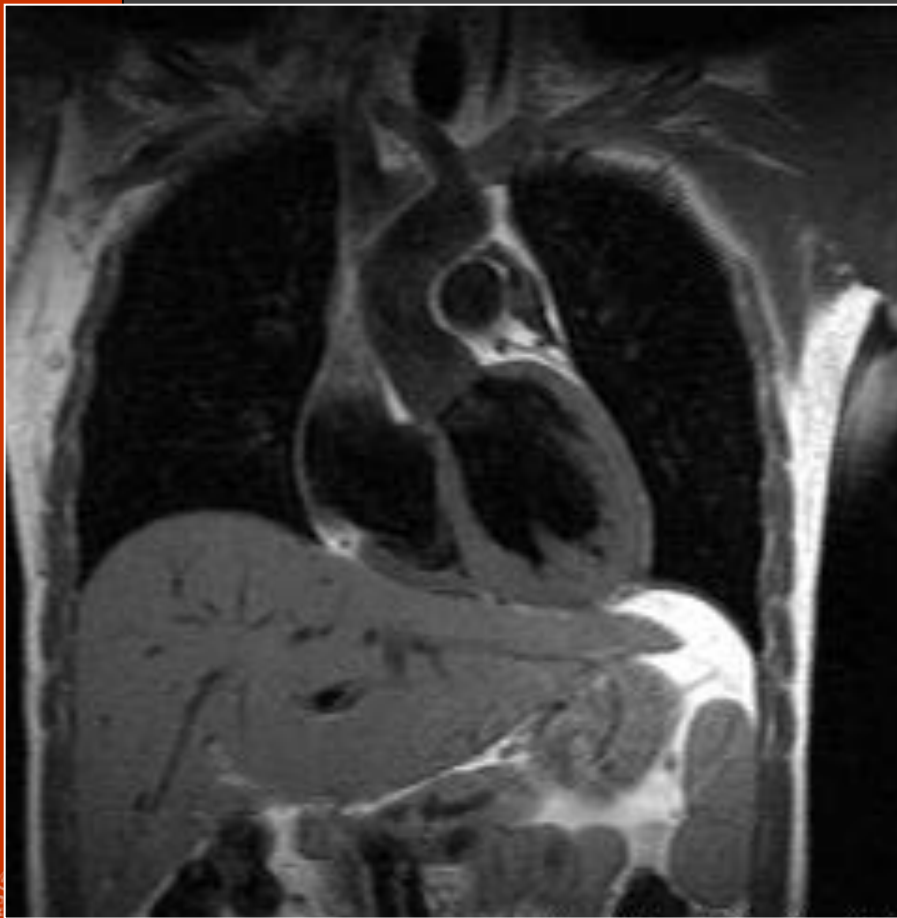


# Godfrey Hounsfield (1919-2004) and Allan Cormack (1924-1998) apply Computed Tomography to coronary arteries (1971)

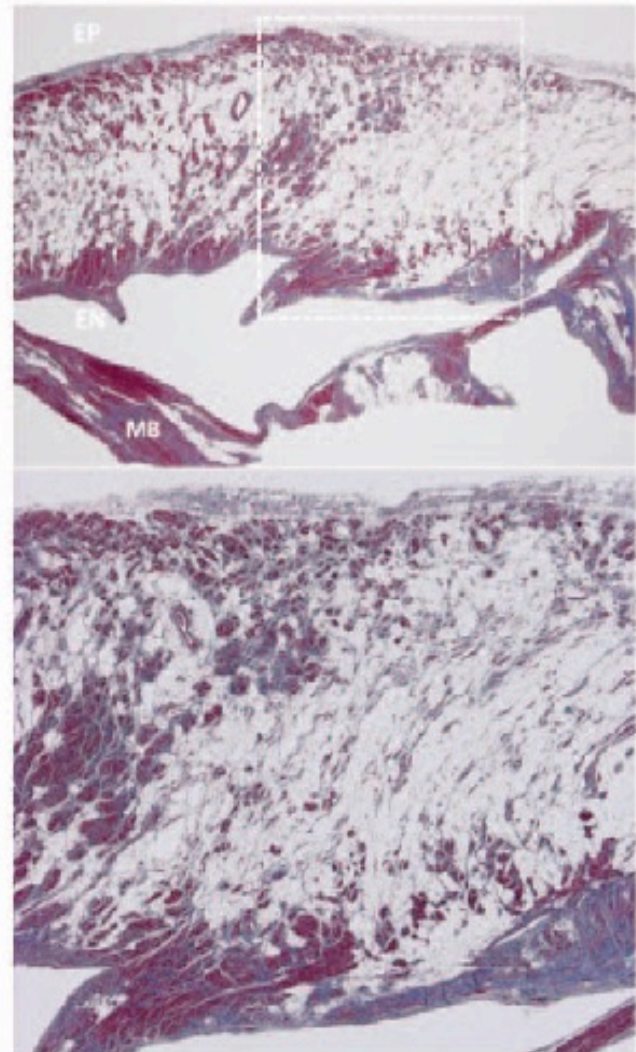
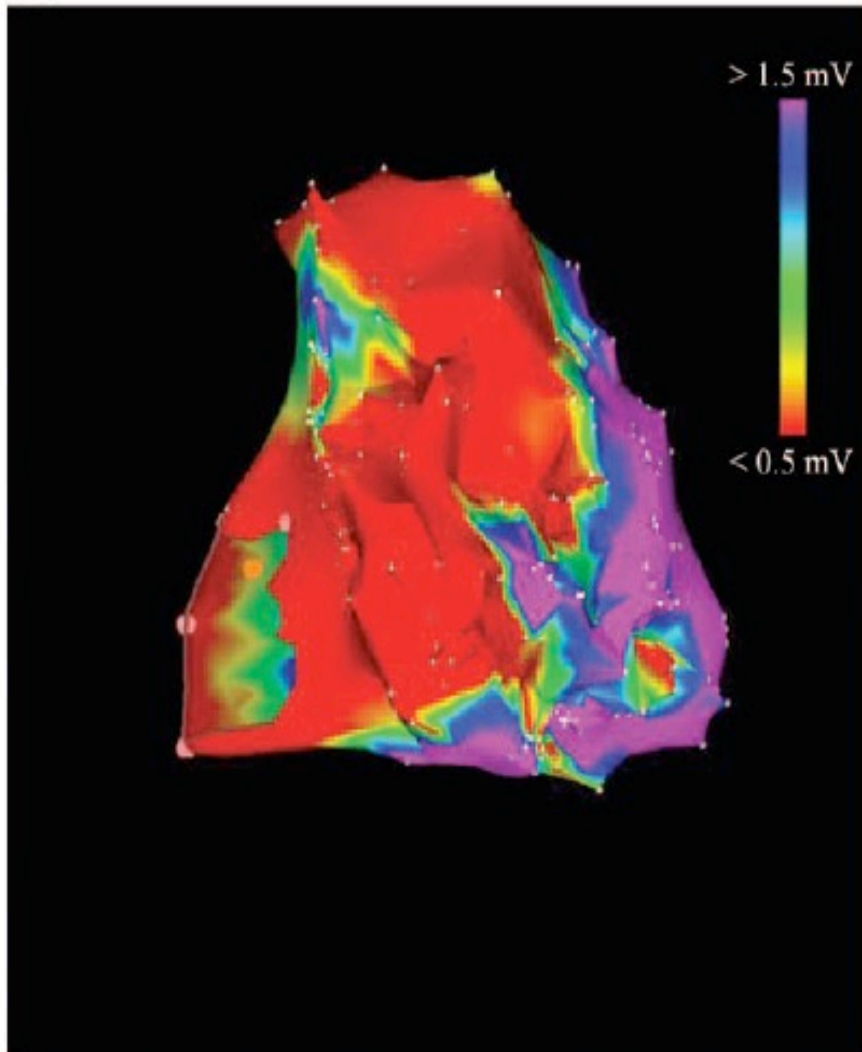




**Paul Lauterbur (1929-2007) and Peter Mansfield (1933-2017) apply Magnetic Resonance Imaging to the heart (1973-1976)**



# Lior Gepstein, Gal Hayam and Shlomo A. Ben-Haim invent Electroanatomic Voltage Mapping (1997)



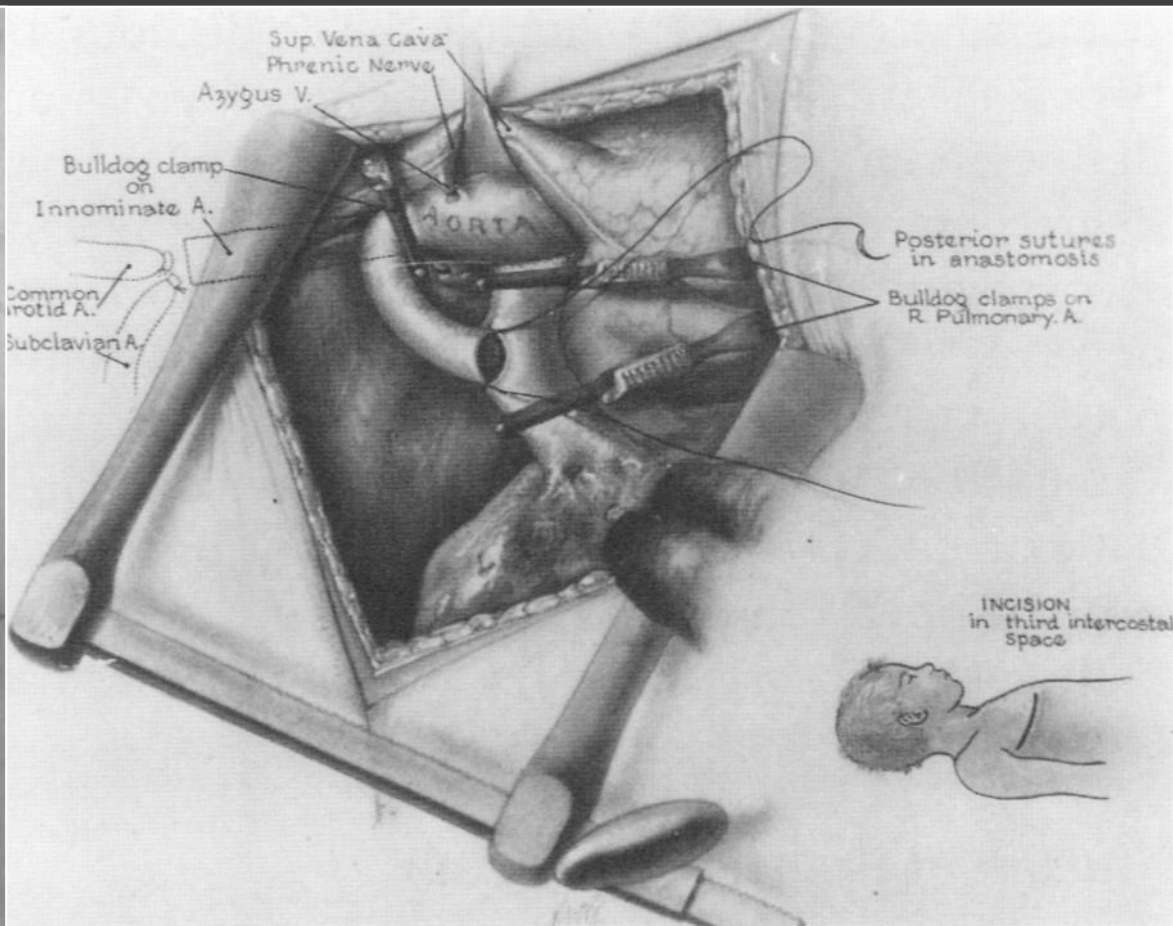
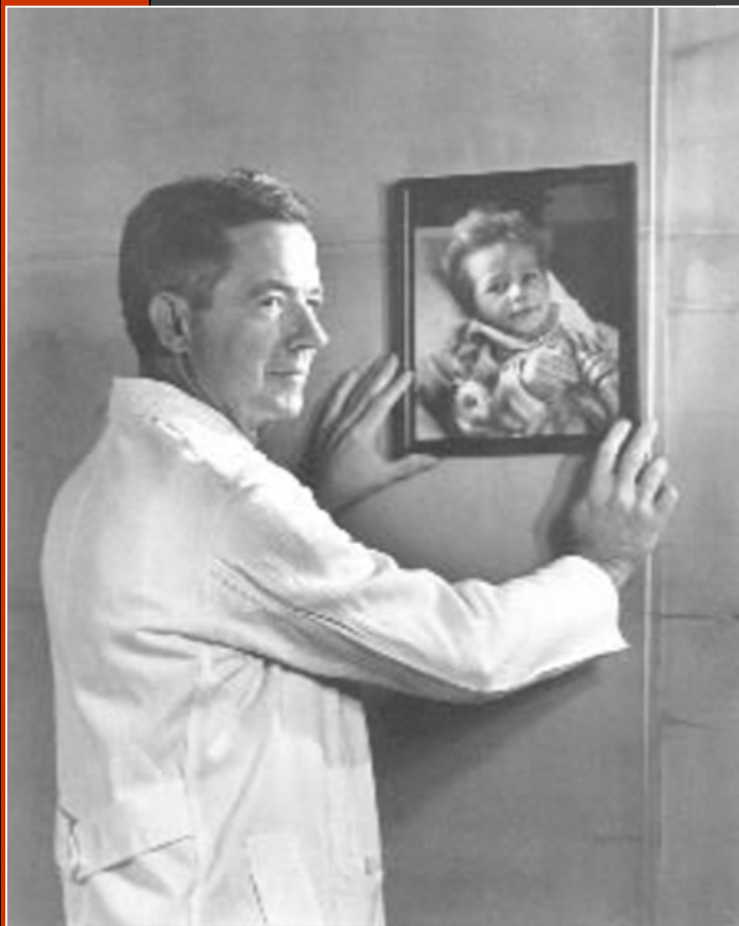
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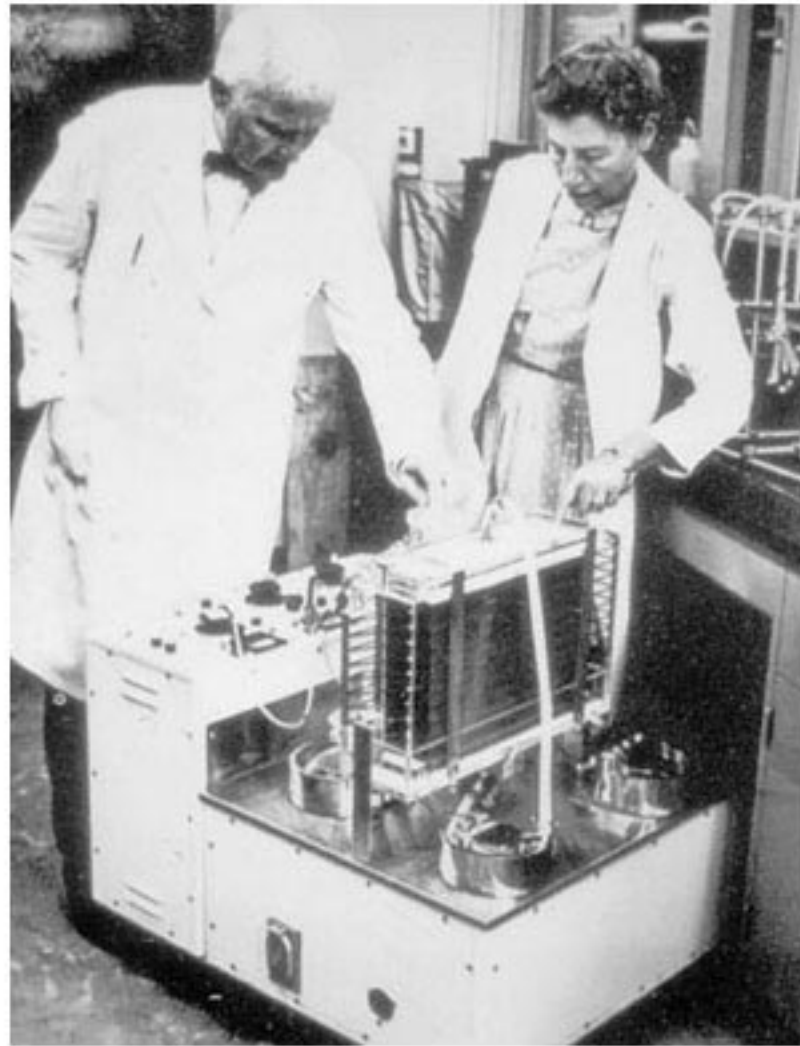




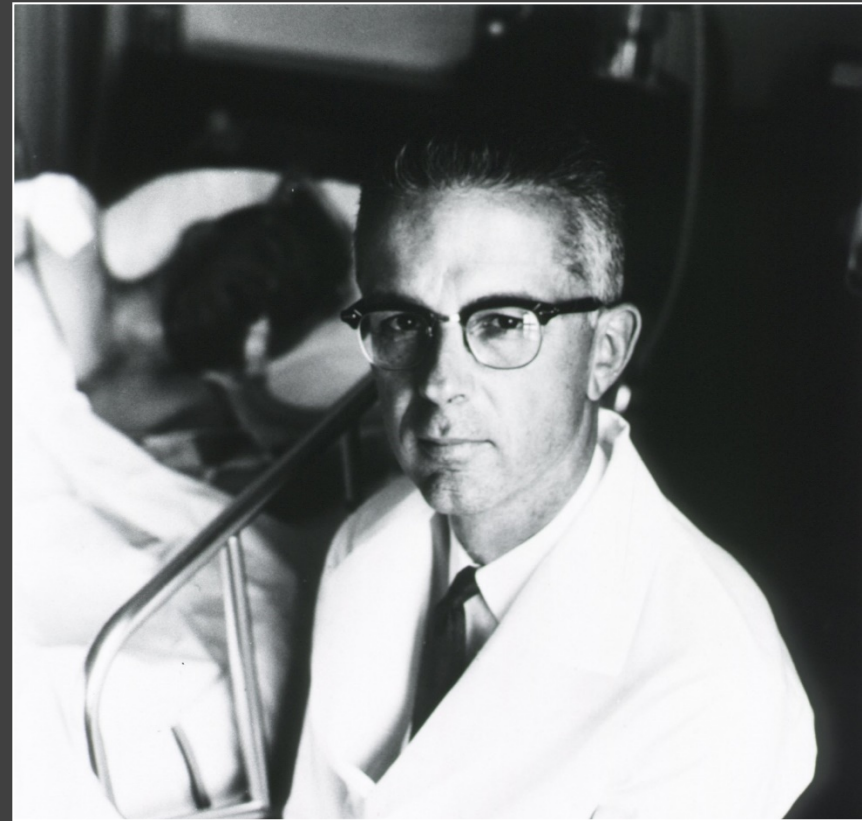
# Alfred Blalock (1899-1964) and Helen Taussig (1898-1986) cure blue babies with aortopulmonary shunt (1945)



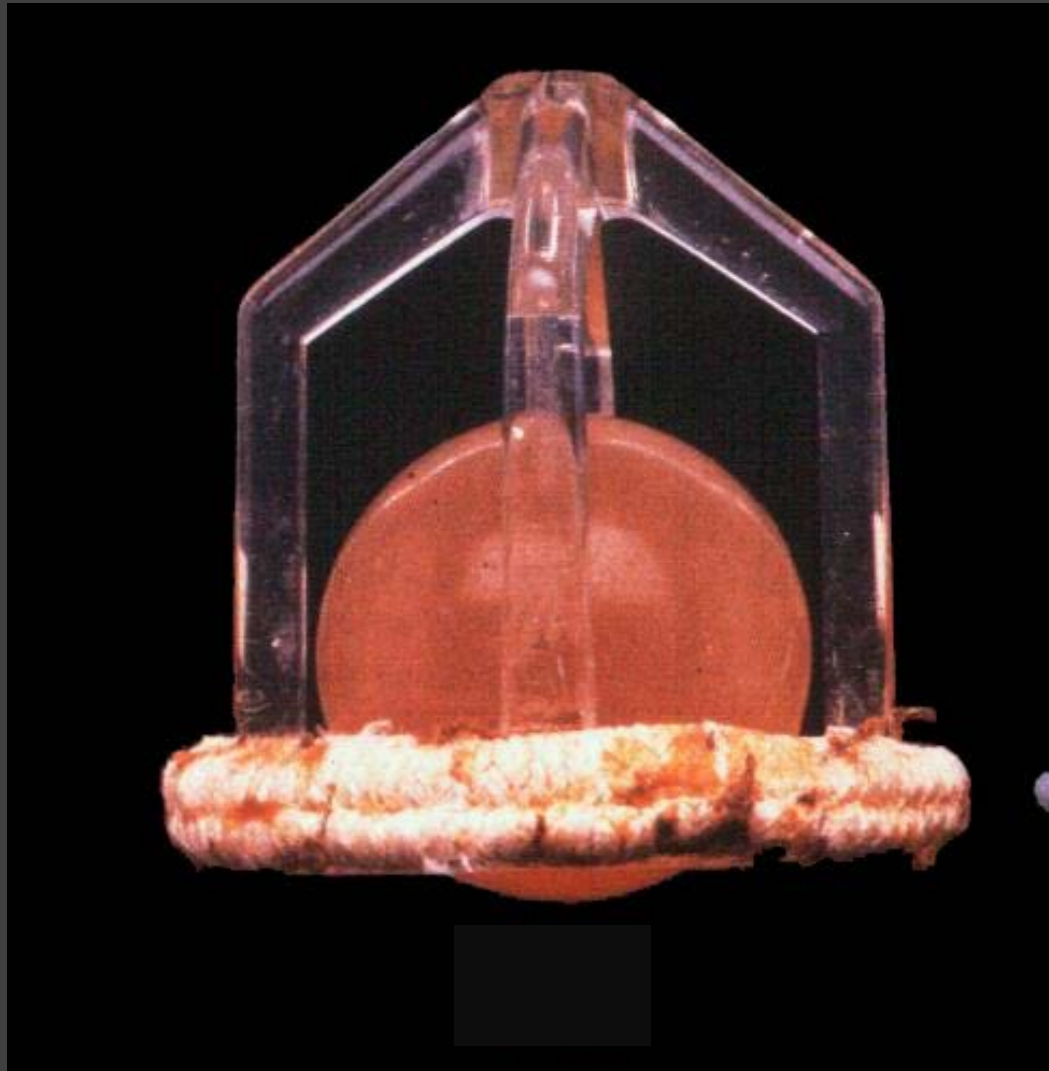
# John Heysham Gibbon (1903-1973) invents heart-lung machine (1953)



# Walton Lillehei (1918-1999) e John Kirklin (1917-2004) perform surgical repair of congenital heart disease (1953-54)



# Albert Starr (1926-) replaces heart valves with Mechanical Ball Valve Prosthesis (1960)





**Viking Bjork (1918-2009)** invents the tilting disk mechanical valve prosthesis (1968)

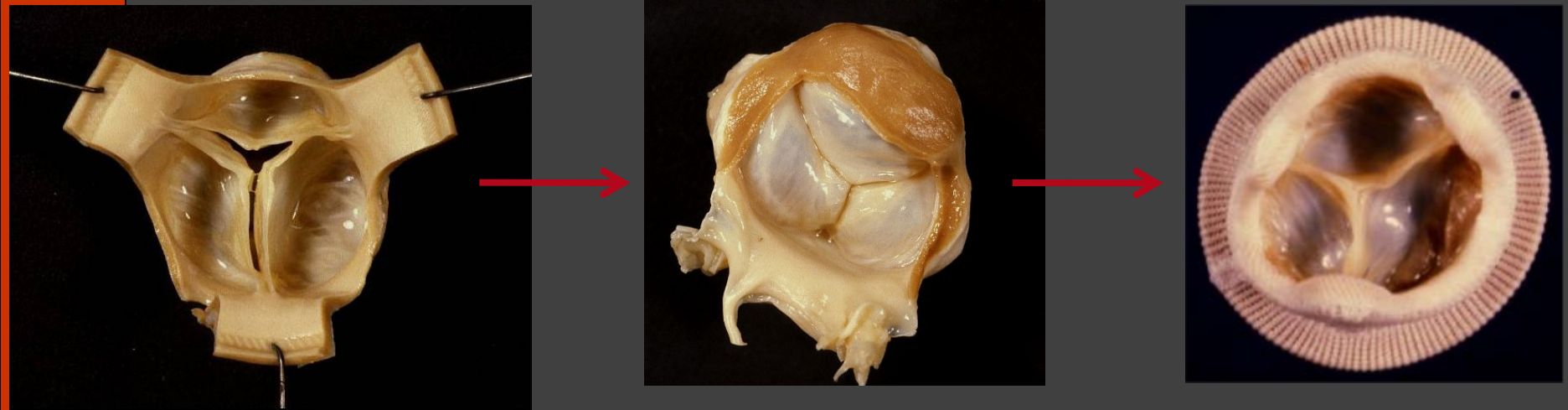


# Franco Vallana (1943-) invents bileaflet Mechanical Valve Prosthesis (1990)

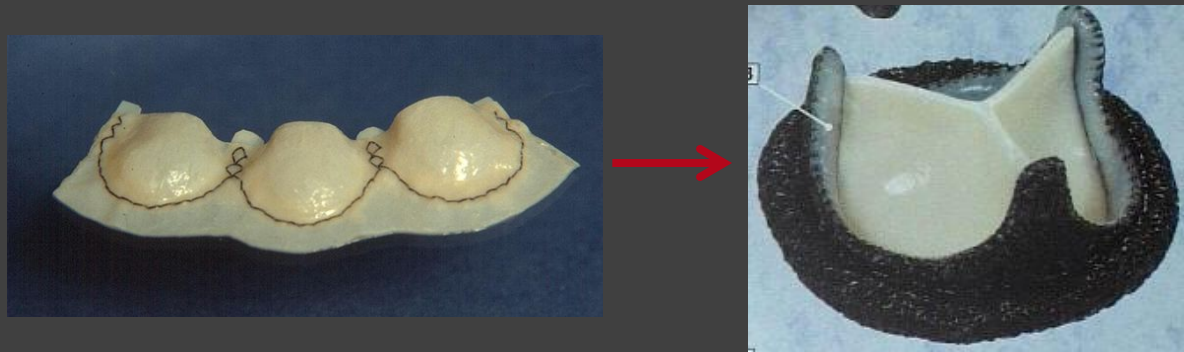


# Glutaraldehyde-fixed Valve Bioprostheses are employed in the clinical setting

Alain Carpentier (1933-) invents Porcine Aortic Valve (1967)

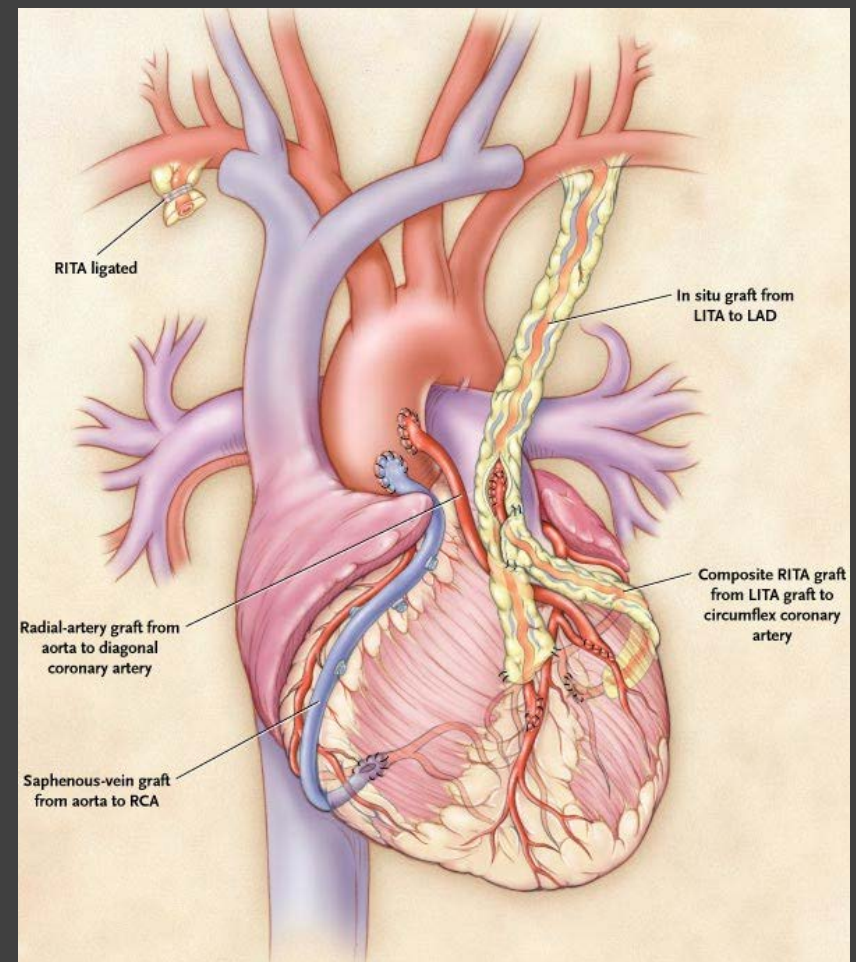


Marian Ionescu (1929-) invents Bovine Pericardial Valve (1971)





# René Favaloro (1923-2000) performs aorto-coronary by-pass (1967) with autologous saphenous vein





# Christian Barnard (1922-2001) performs the first human cardiac transplantation (1967)

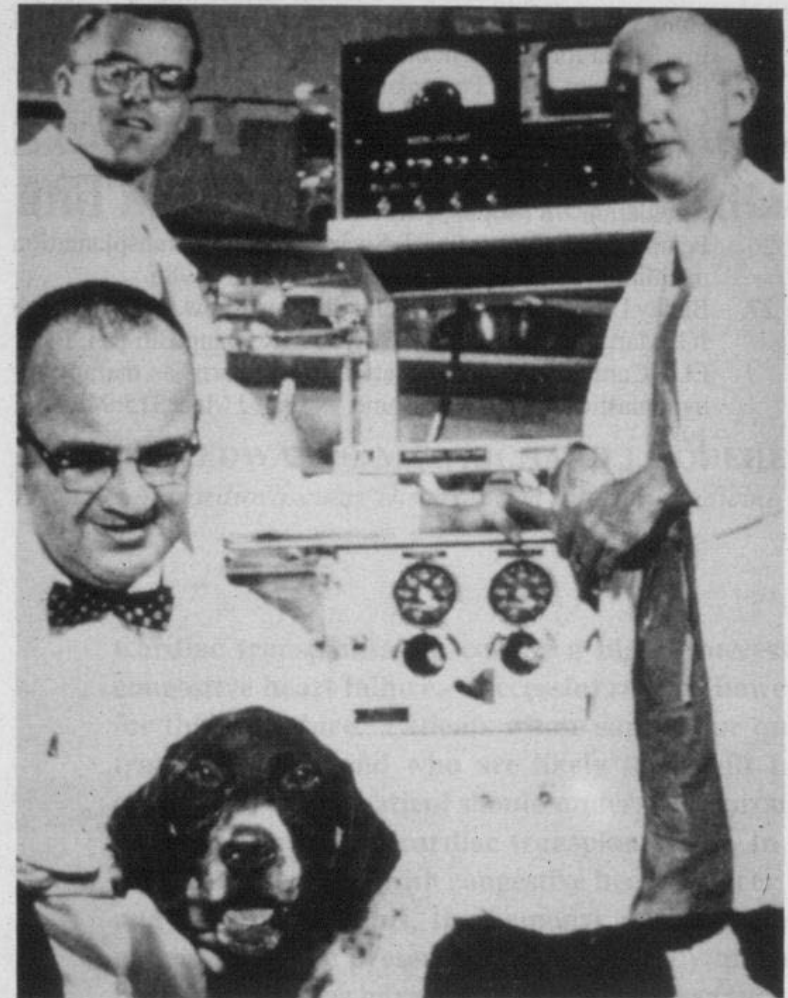


Fig. 4. Norman E. Shumway, M.D., Ph.D. (right), Richard R. Lower, M.D. (left), and Raymond C. Stofer, D.V.M. (kneeling), Stanford University, 1960.

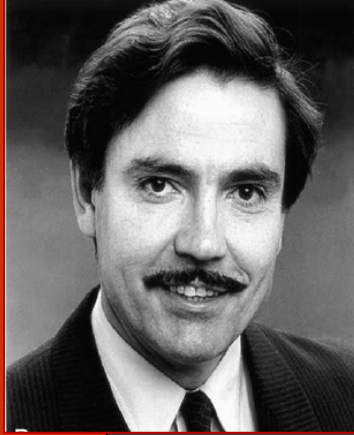
# Domingo Liotta (1924-) and Denton Cooley (1920-2016) implant total artificial heart in a man (1969)



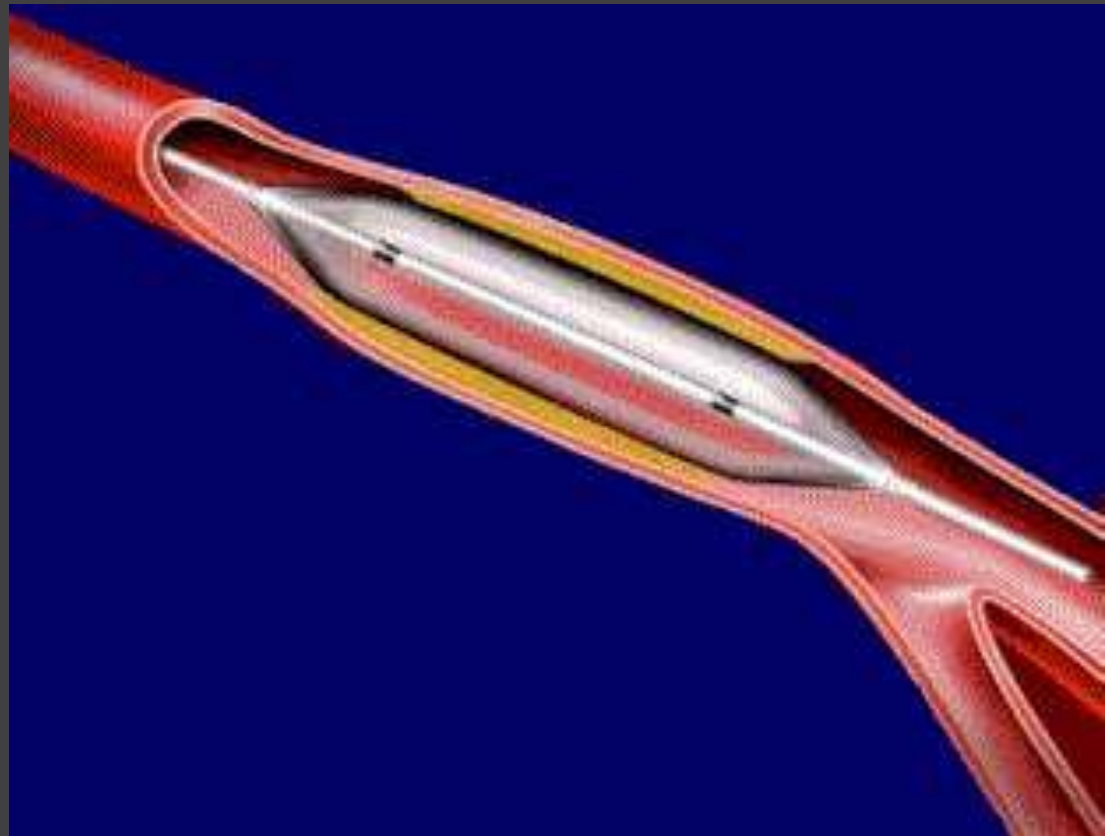
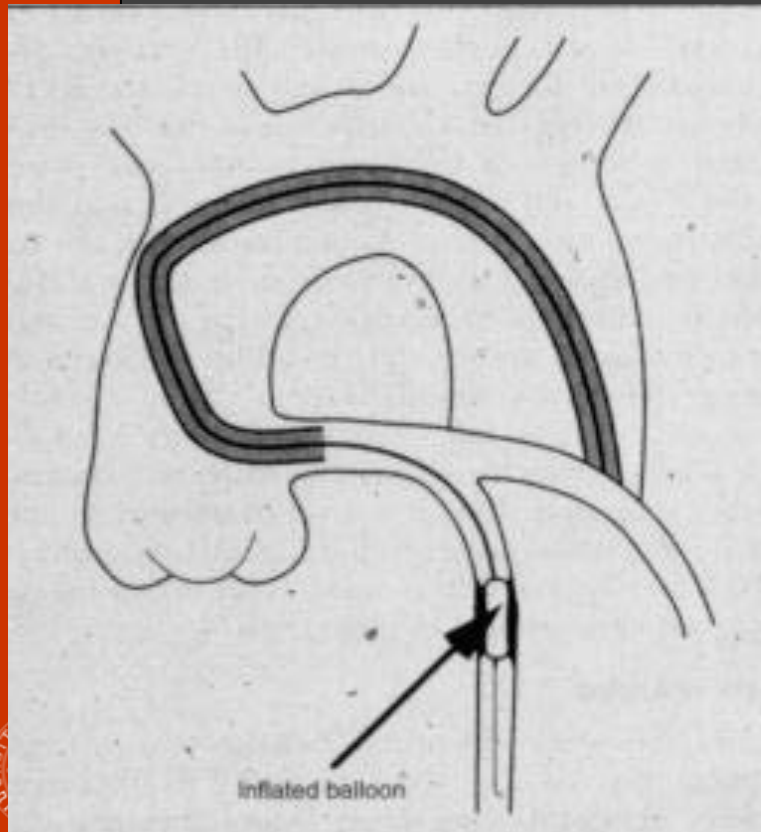
**Heart diseases can be treated  
by interventional cardiology**



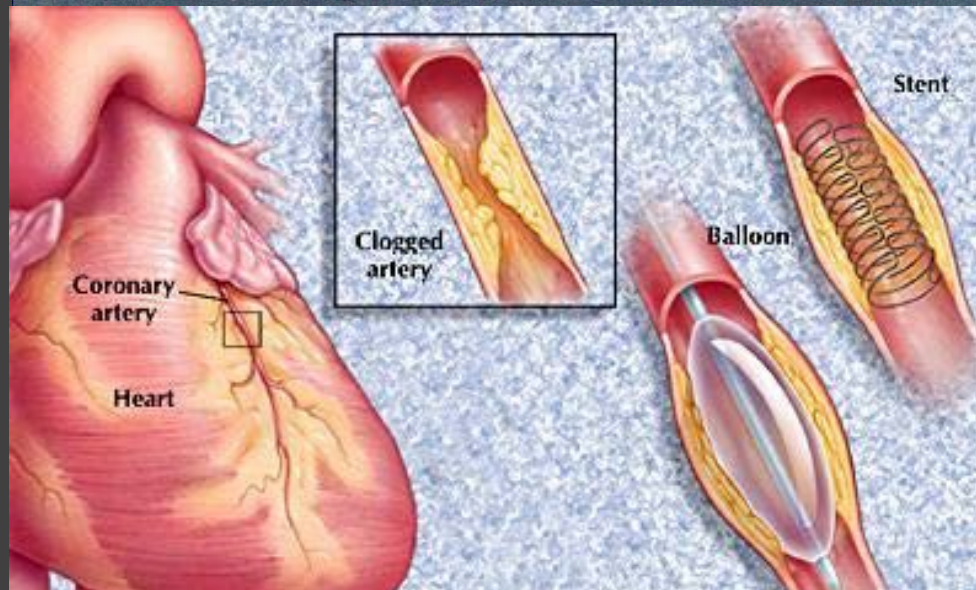
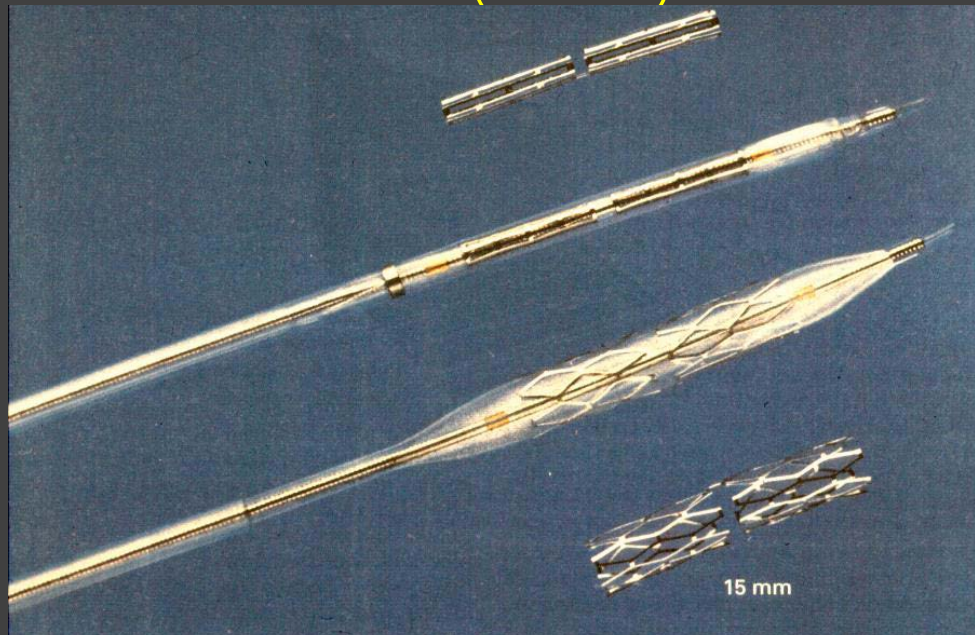




**Andreas Gruentzig (1939-1985)**  
performs the first percutaneous coronary  
balloon angioplasty (1977)



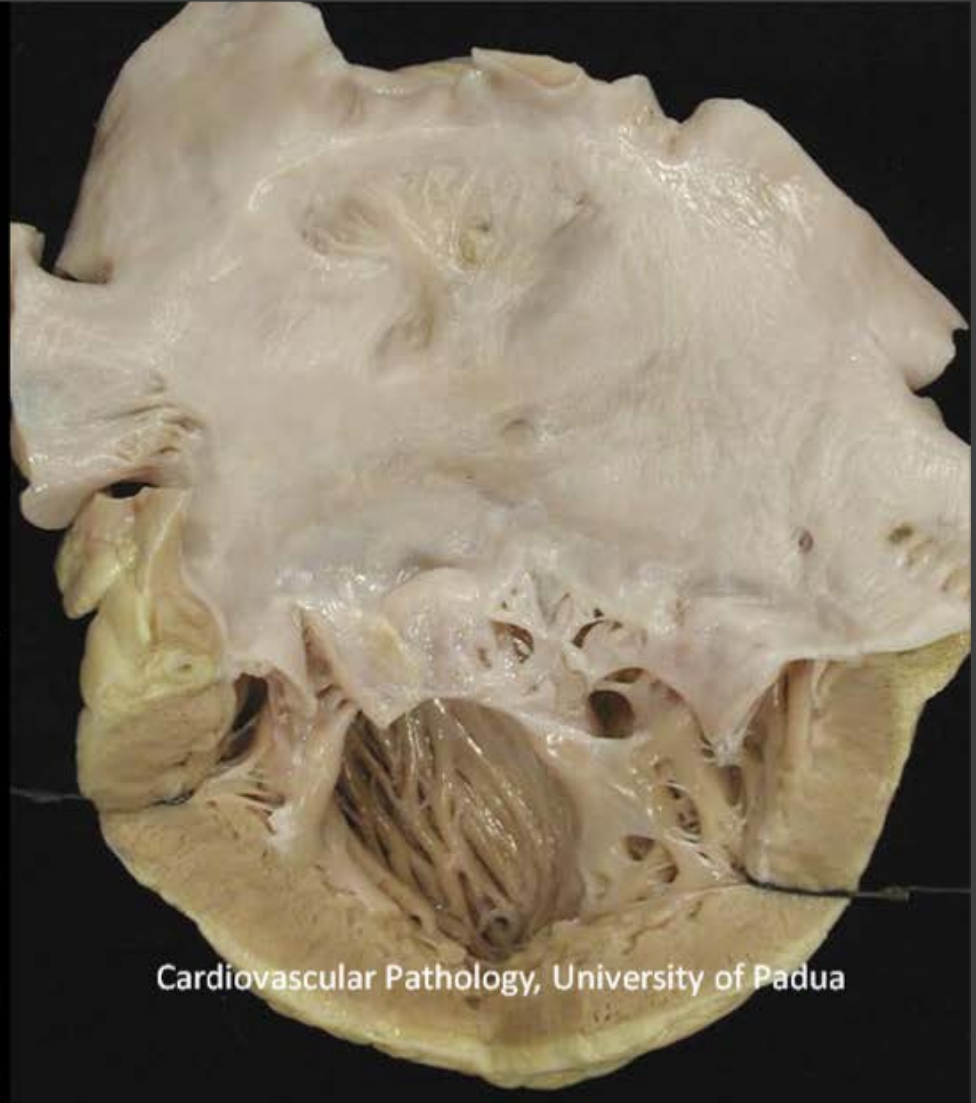
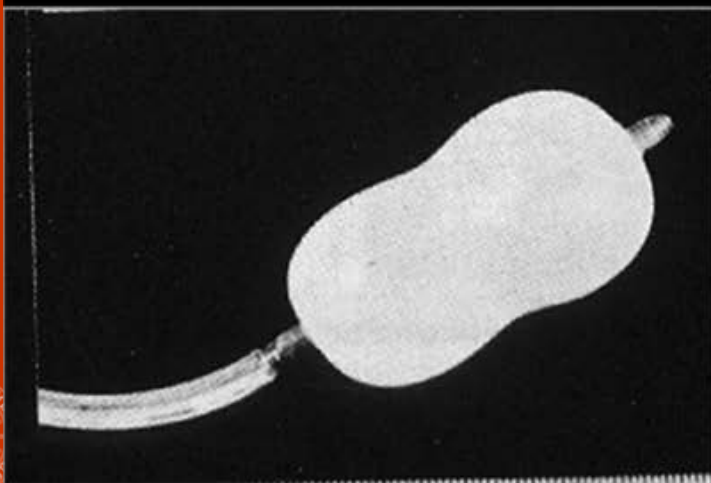
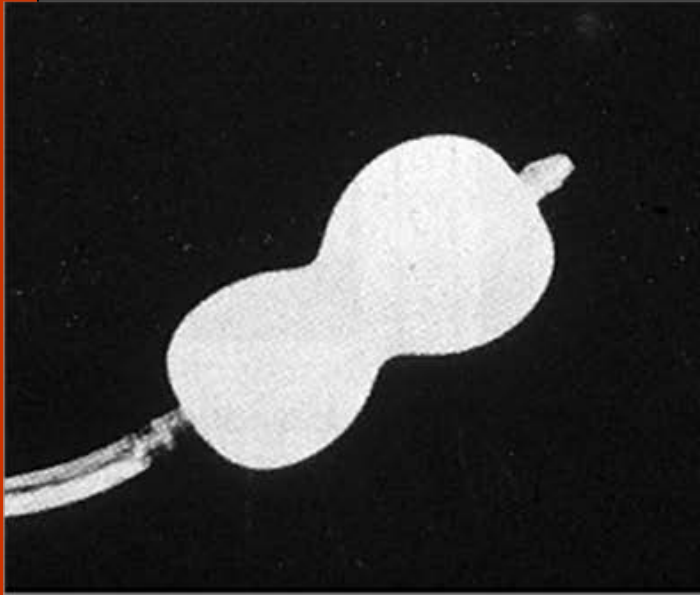
# Ulrich Sigwart (1941-) implants coronary stent (1986)



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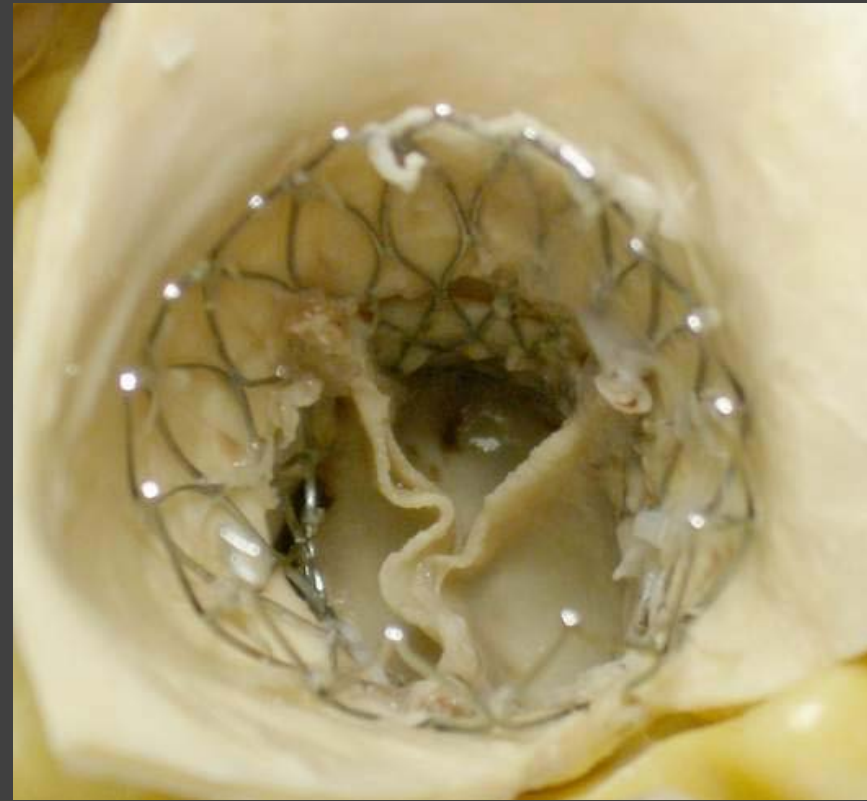


# Kanji Inoue invents Balloon Mitral Commissurotomy (1982)



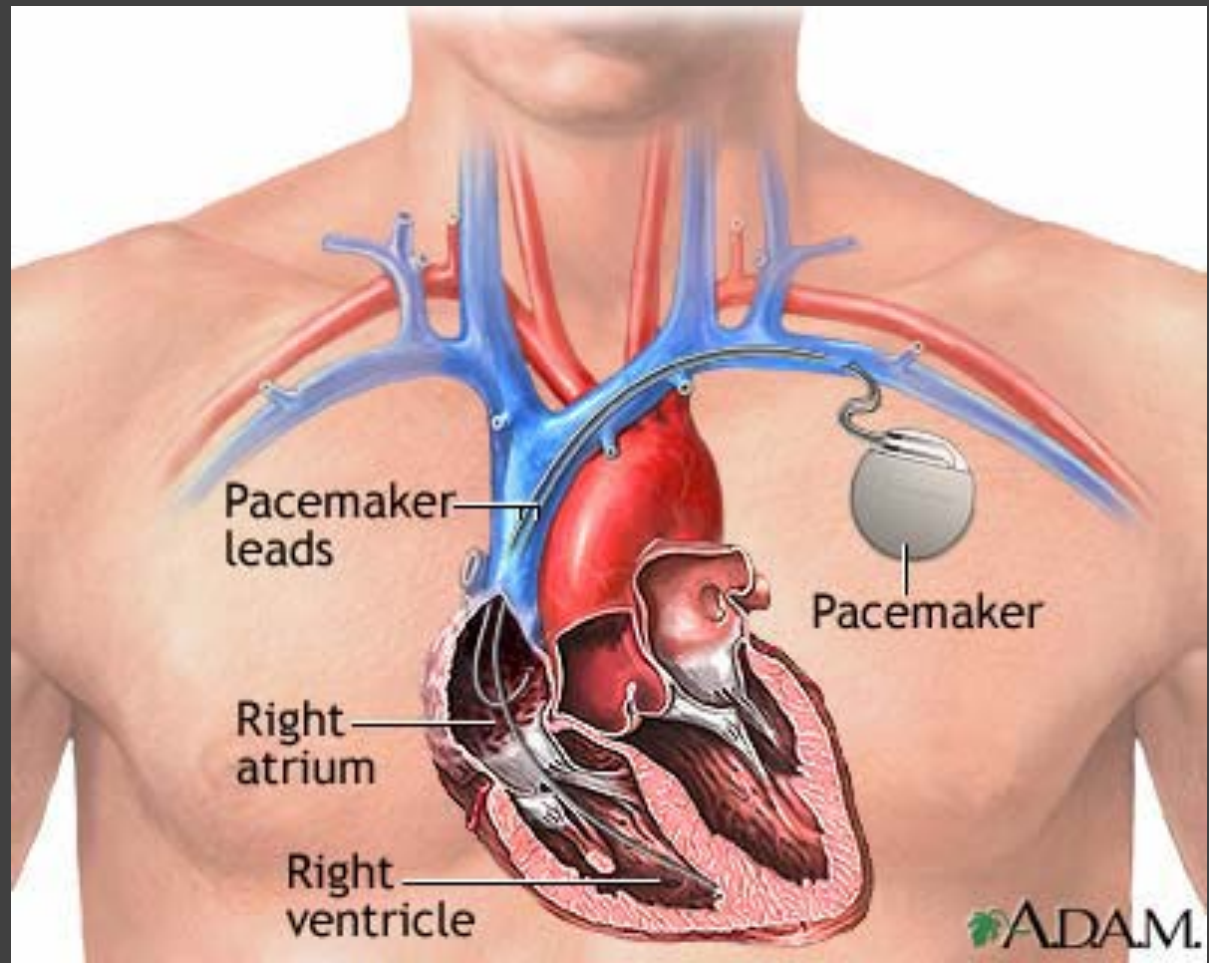
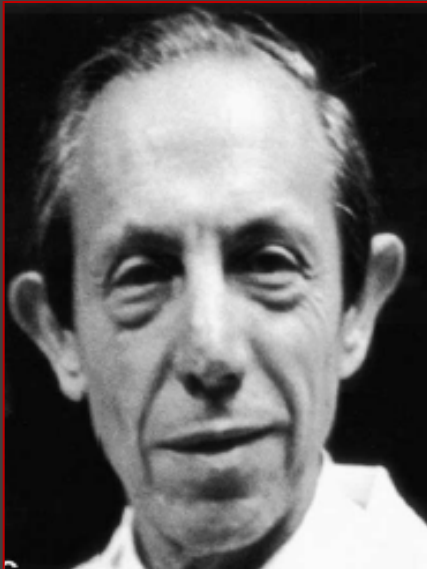
Cardiovascular Pathology, University of Padua

# Alain Cribier (1945-) first implants Transcatheter Aortic Valve Bioprosthesis (1986)





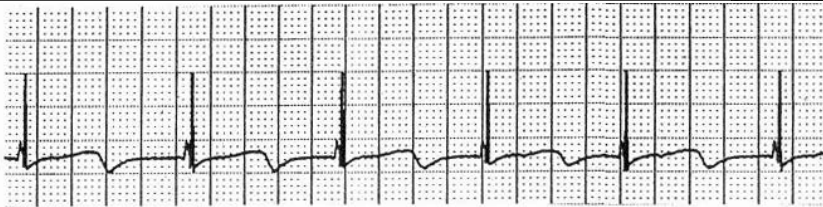
# Paul Zoll (1911-1999) invents Pacemaker (1956)



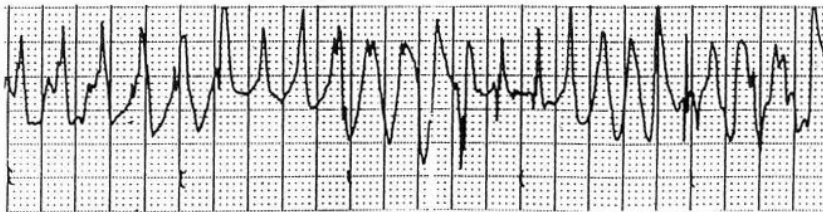
# Michel Mirowski (1924-1990) invents Implantable Cardioverter Defibrillator (1980)



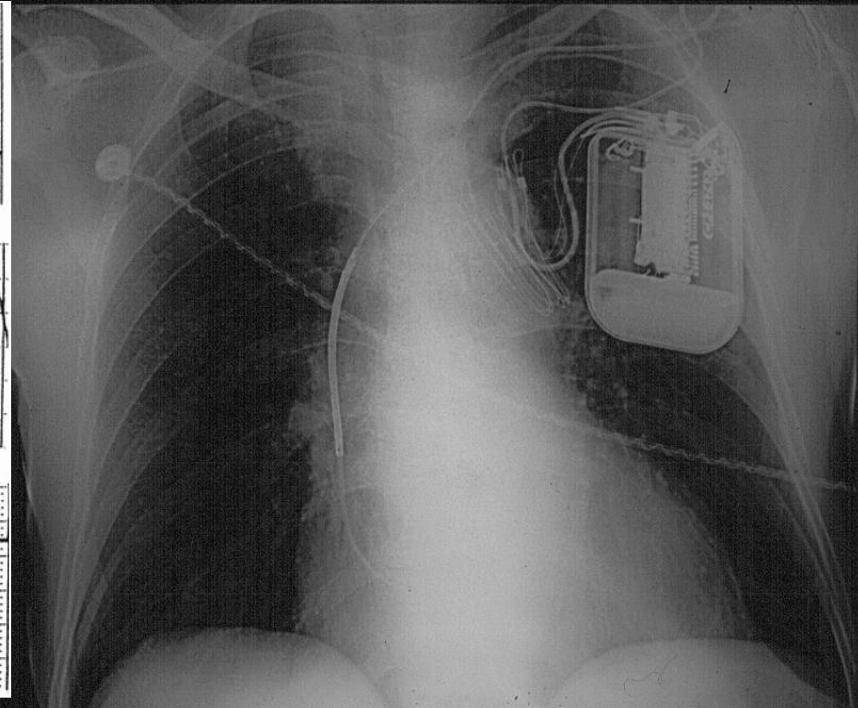
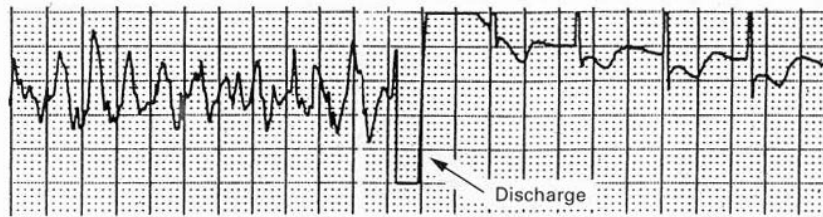
Sinus rhythm



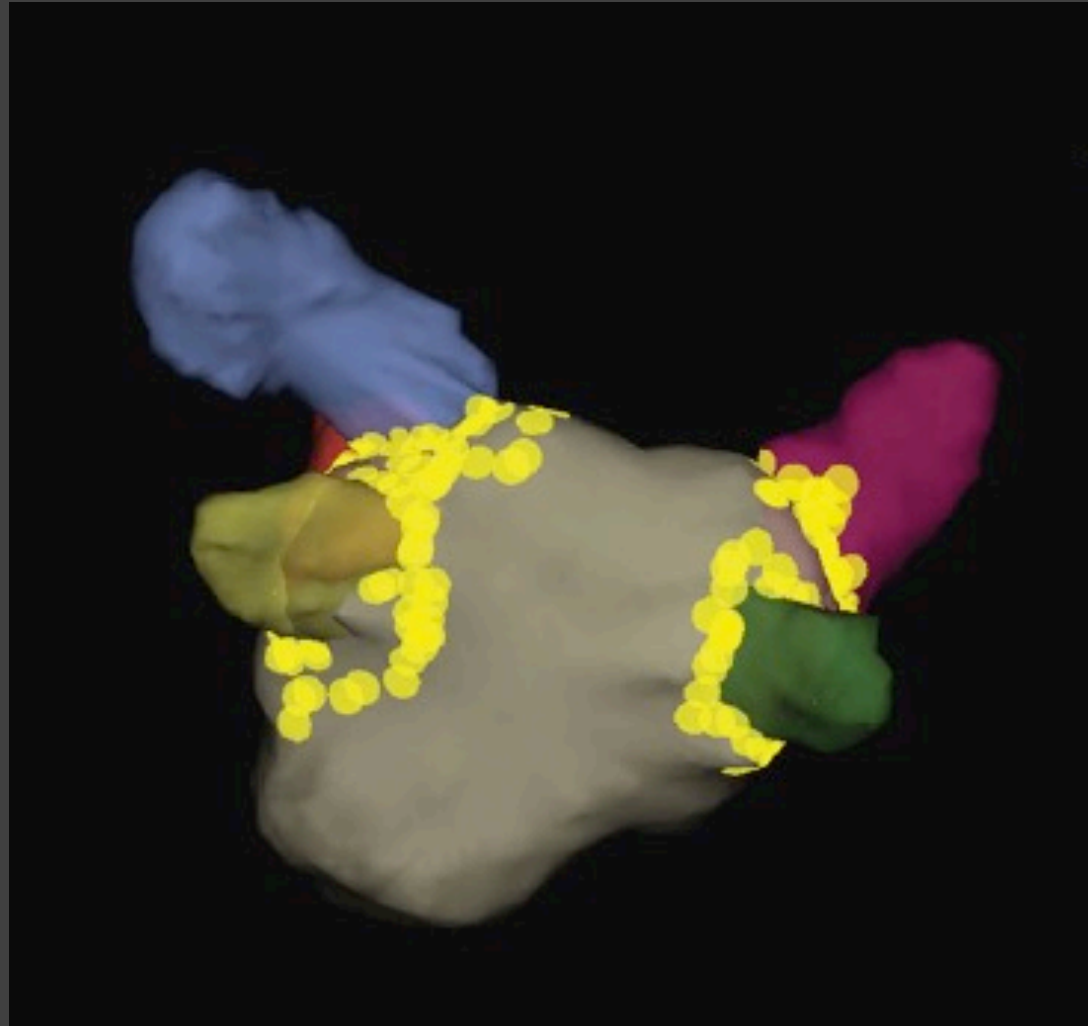
Torsade de pointes



Ventricular fibrillation  
and sinus rhythm



**Michael Haissaguerre (1955-)** ablates the triggering of atrial fibrillation around the origin of the pulmonary veins (1998)



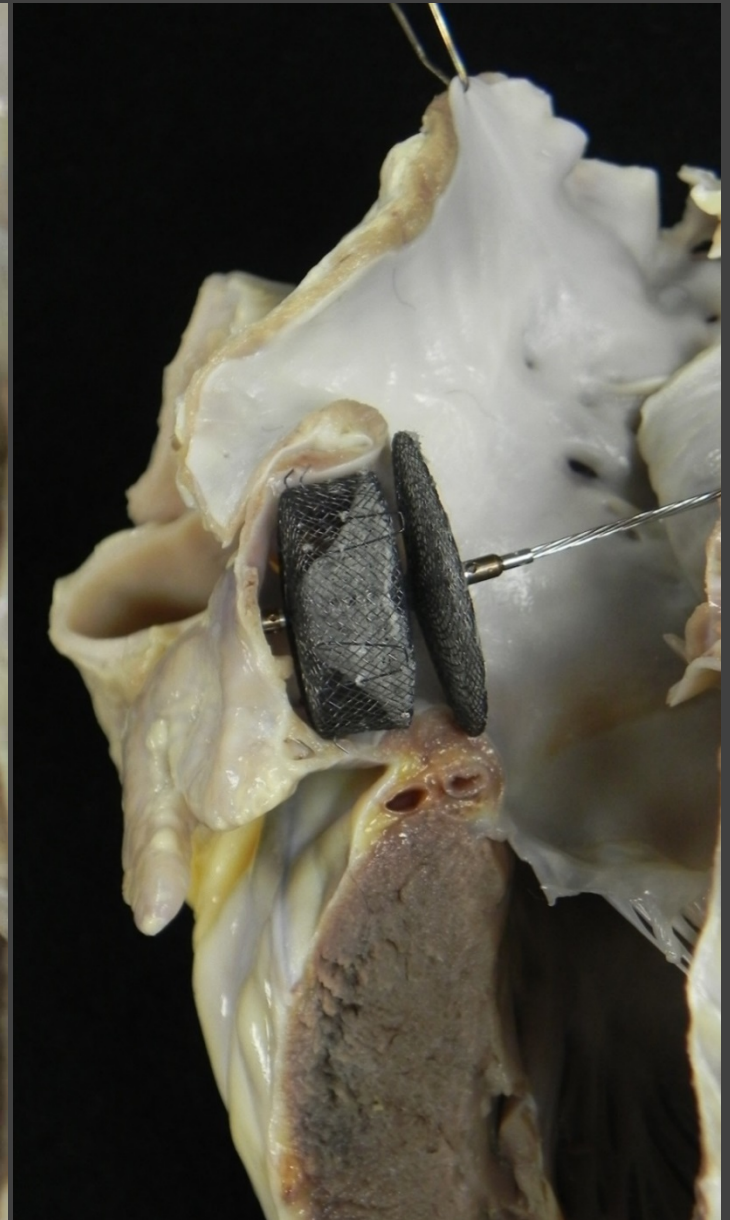
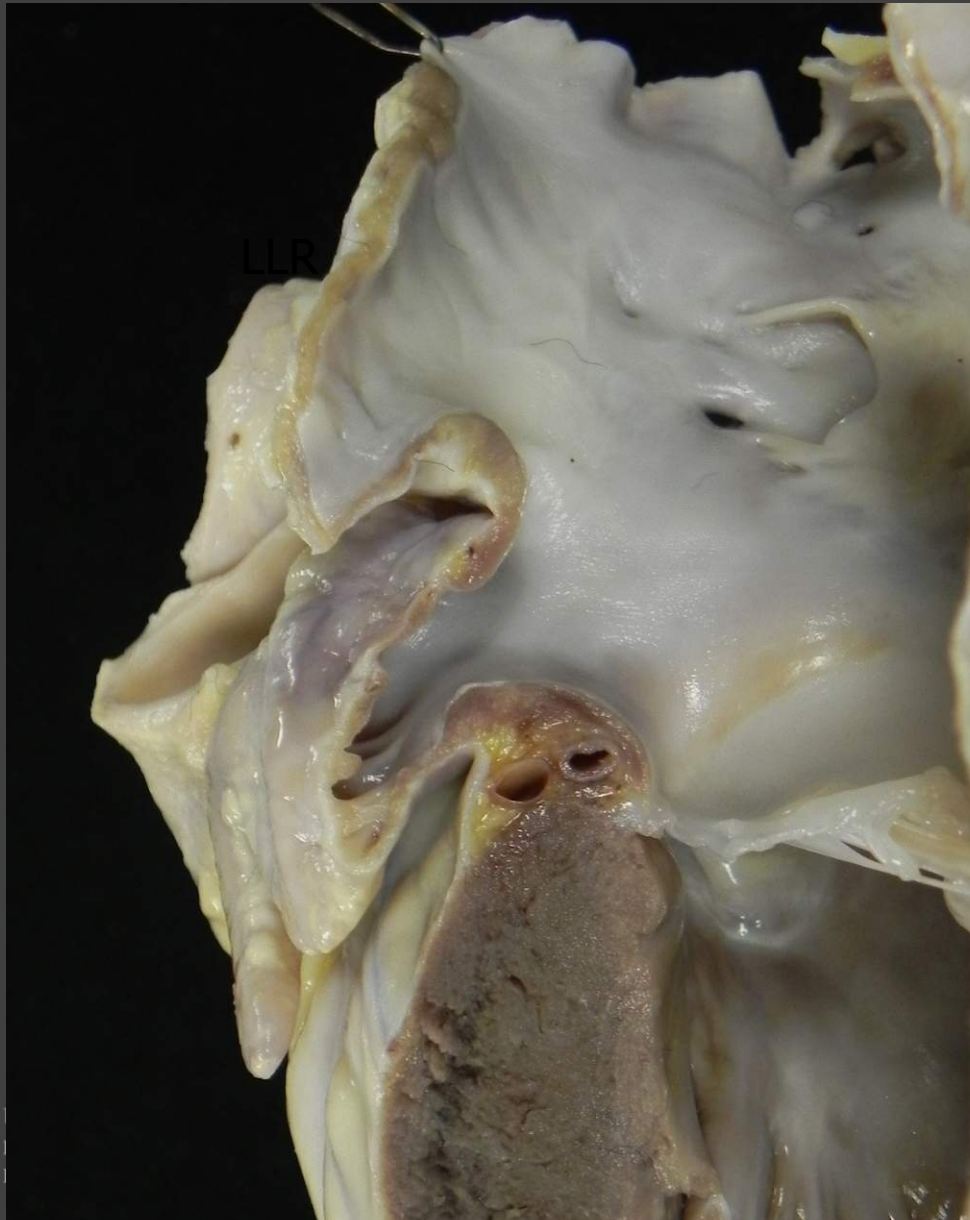


Left atrial appendage is a 'Santa Barbara'  
for the risk of stroke





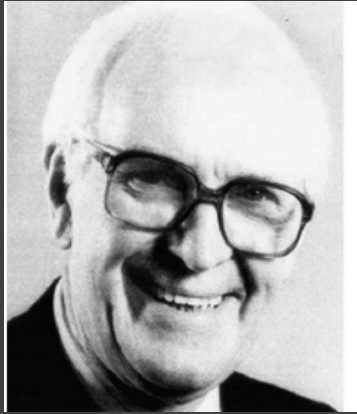
# Closure of left atrial appendage orifice by Amplatzer occluder device



# Heart diseases can be treated by drugs



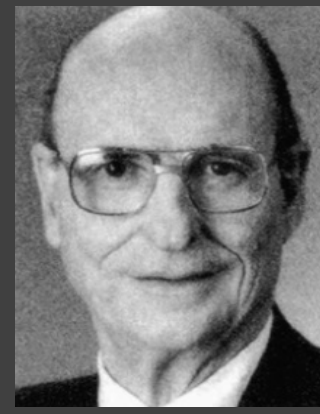
# Cardiovascular Pharmacology



JW Black



DW Cushman

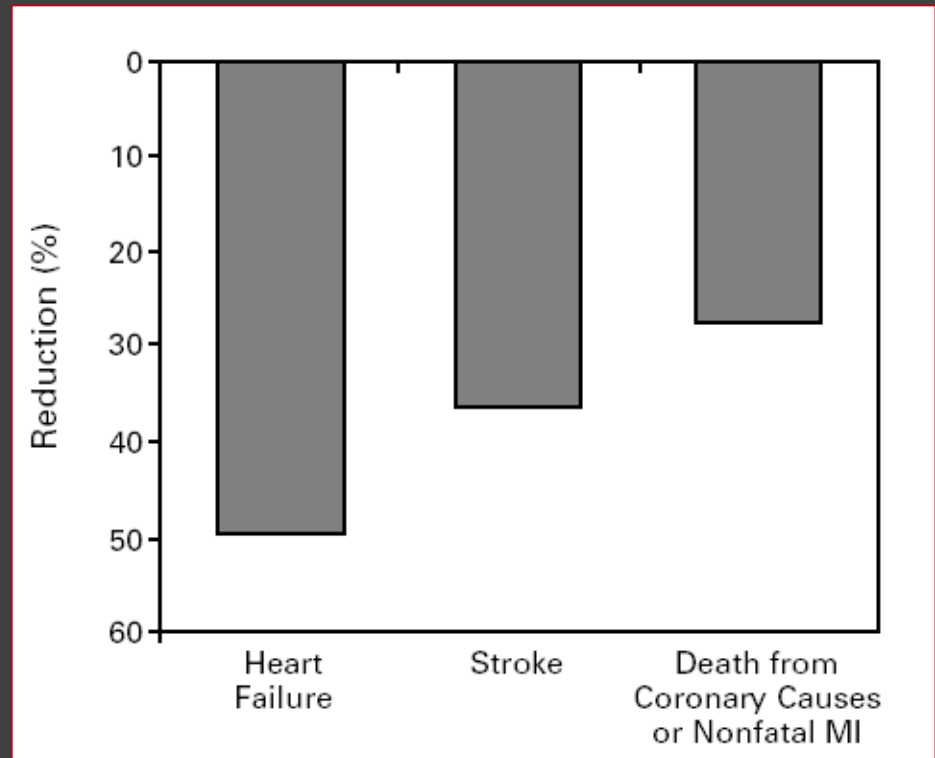


MA Ondetti



A. Endo

- Beta-blockers
- ACE-inhibitors
- Statins
- Anticoagulants
- Antiplatelets
- Thrombolytic drugs

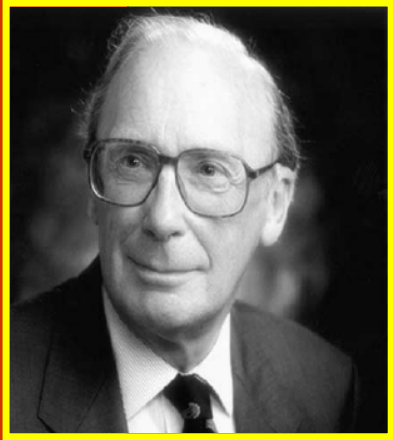


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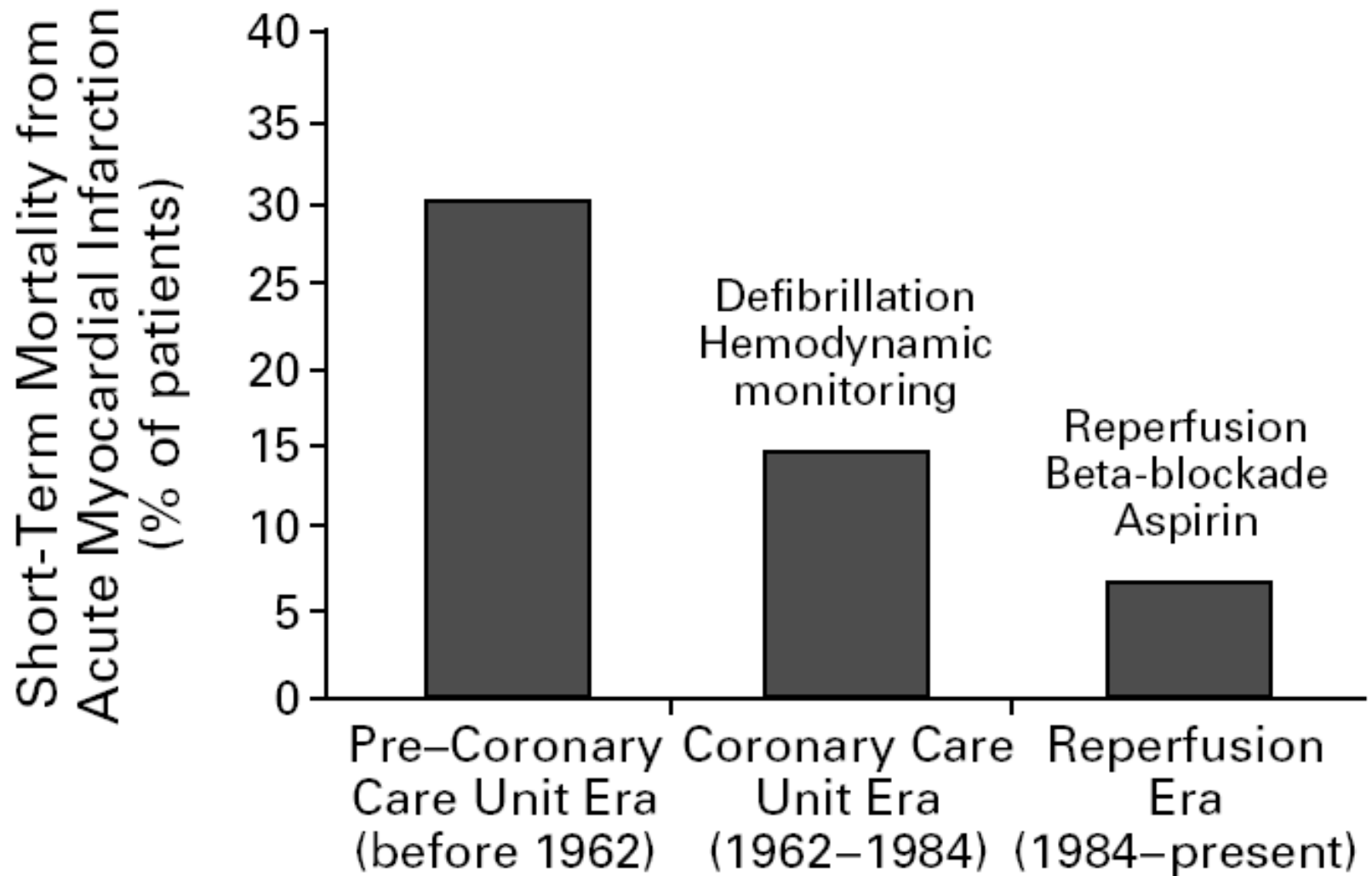


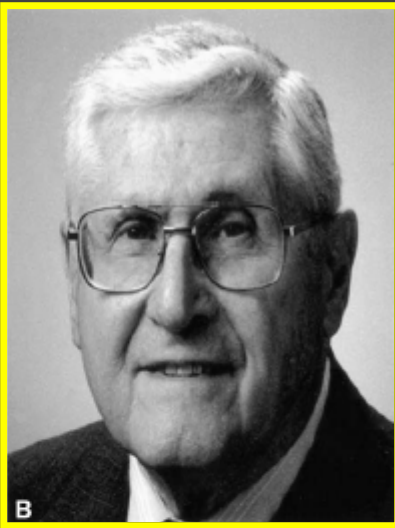
# Desmond Julian introduces Coronary Care Unit (1961)



- Care in a single, separate site
- ECG monitoring with alarm system and prompt treatment of ventricular fibrillation (VF)
- Specially trained medical staff

# Decline of mortality from Myocardial Infarction

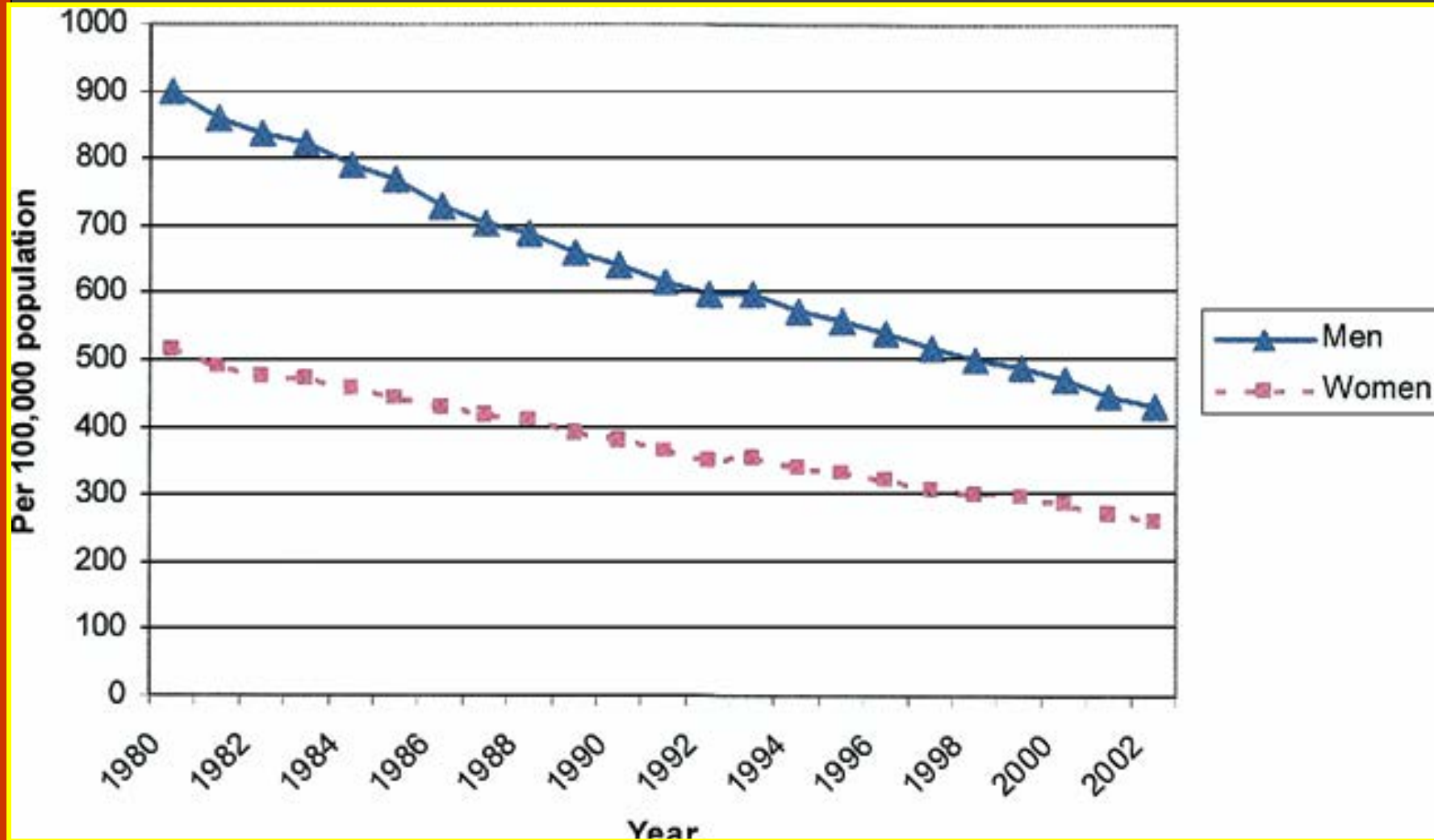




## William Kannel identifies coronary risk factors in the *Framingham Study* (1961)

- Smoke
- Hypertension
- Hypercholesterol
- Diabetes
- Obesity

# Trends in Age-Adjusted Mortality Rates from Coronary Artery Disease in Adults Aged >35 yrs in US



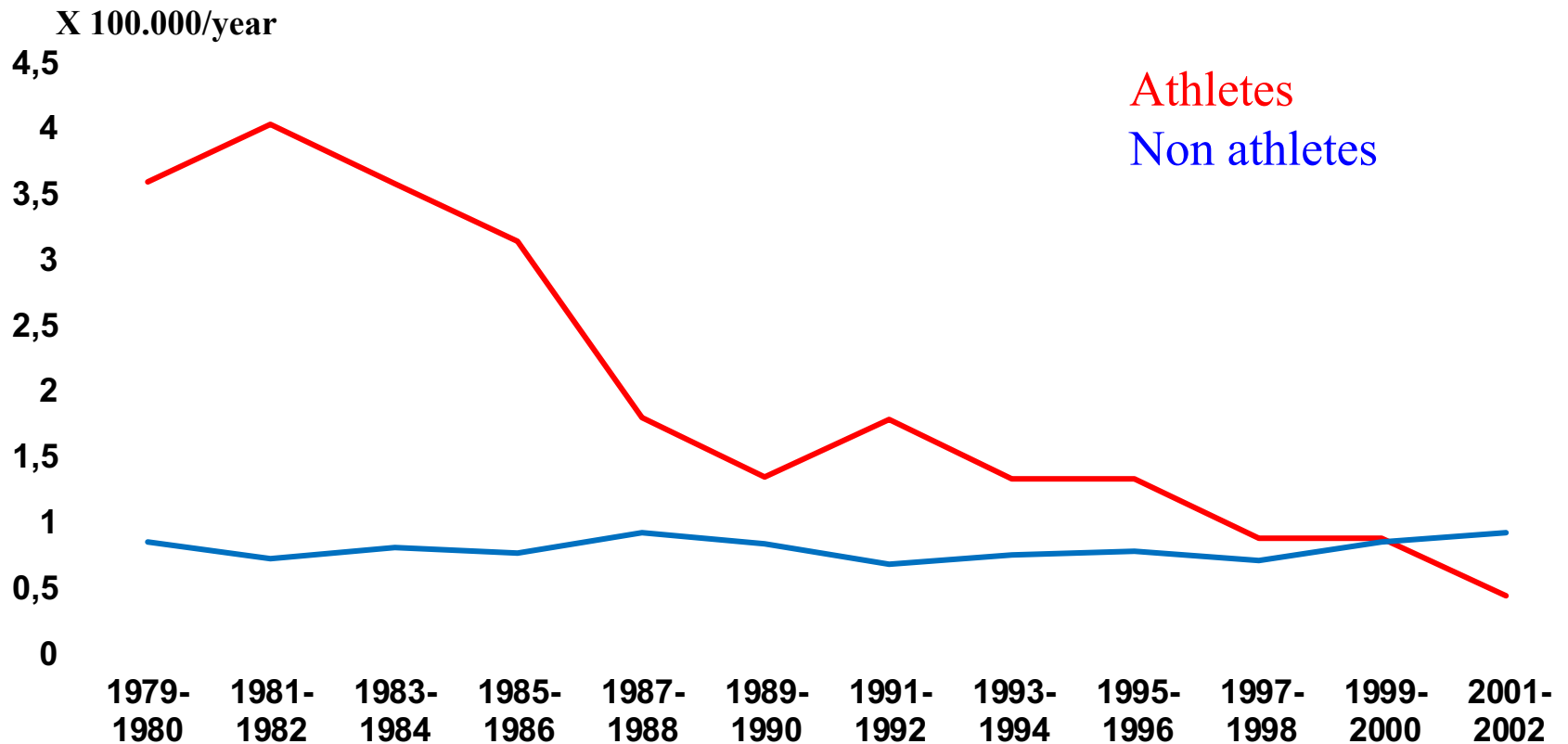
from Ford ES & Capewell S. *The Journal of the American College of Cardiology*  
Volume 50, No. 22, November 2007, Pages 2128-2130





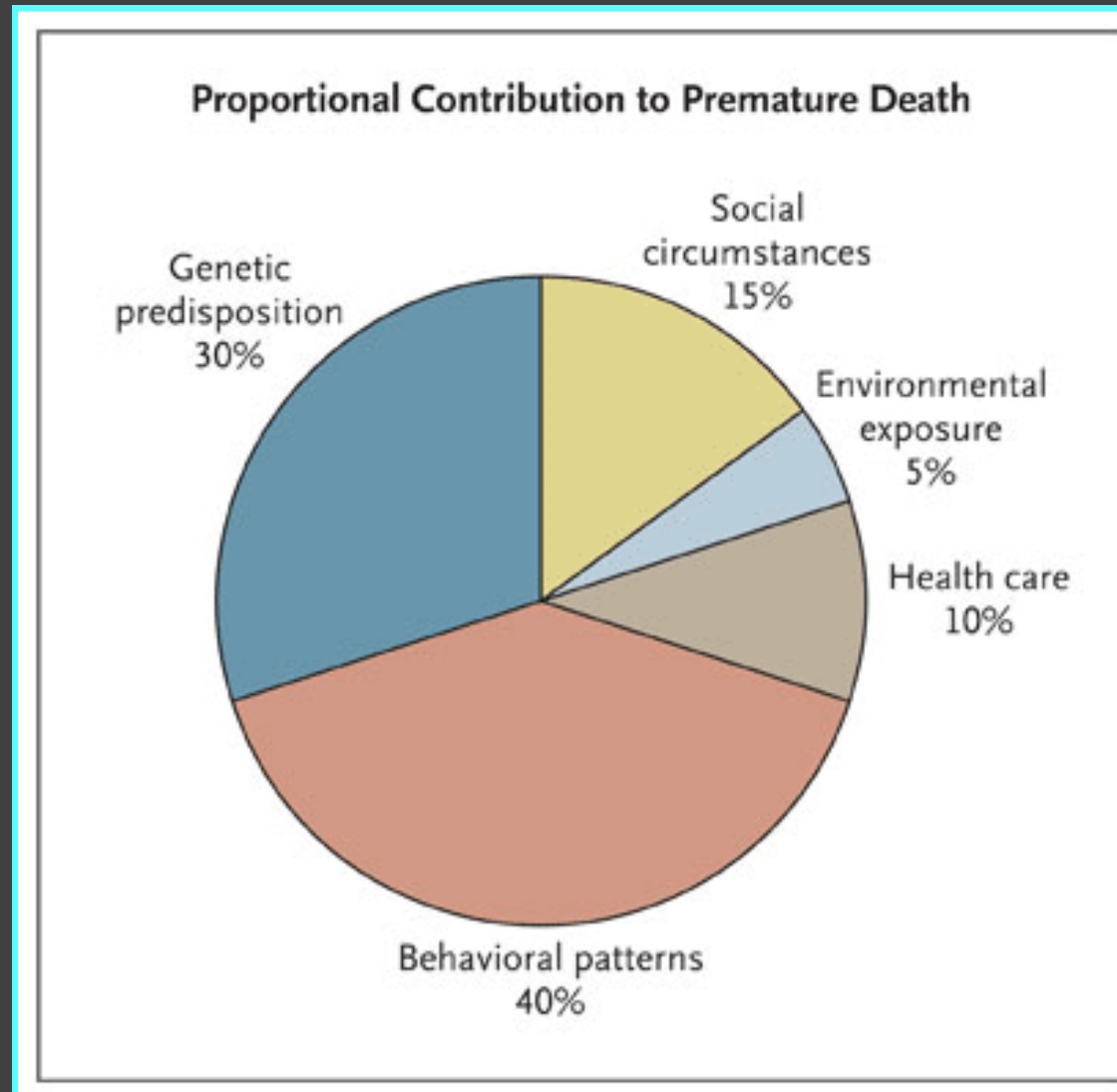
# TIME-TREND OF SUDDEN CARDIAC DEATH INCIDENCE IN ATHLETES VS NON-ATHLETES

Veneto Region of Italy 1979-2002



• D.Corrado, G. Thiene JAMA , 2007

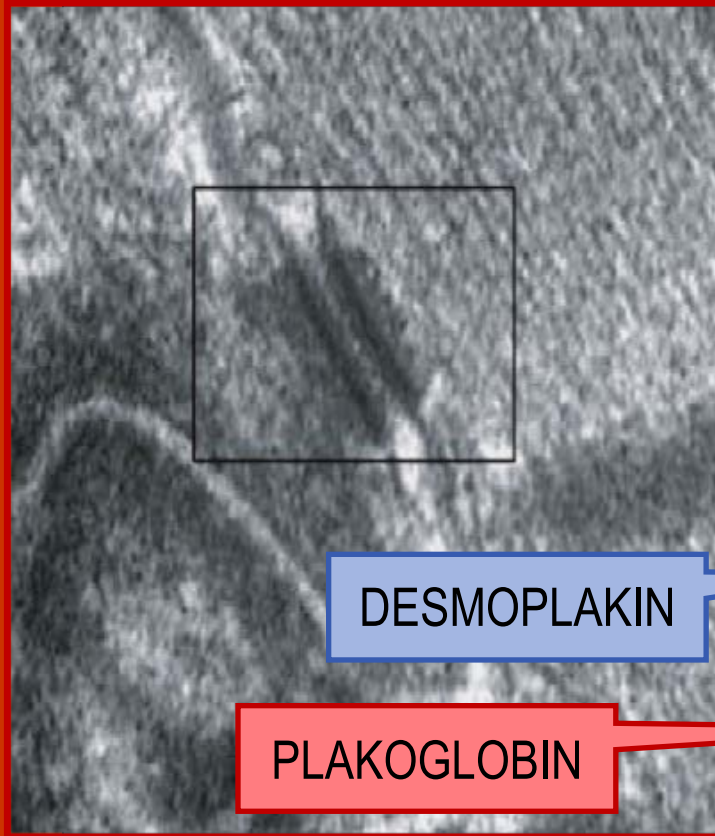
# Determinants of Health and their Contribution to Premature Death



*from Schroeder SS. The New England Journal of Medicine  
Volume 357, No. 12, September 20, 2007, Pages 1221-1228*

# Arrhythmogenic RV Cardiomyopathy: A DESMOSOMAL DISEASE

Basso C et al. *Lancet* 2009;373:1289-300



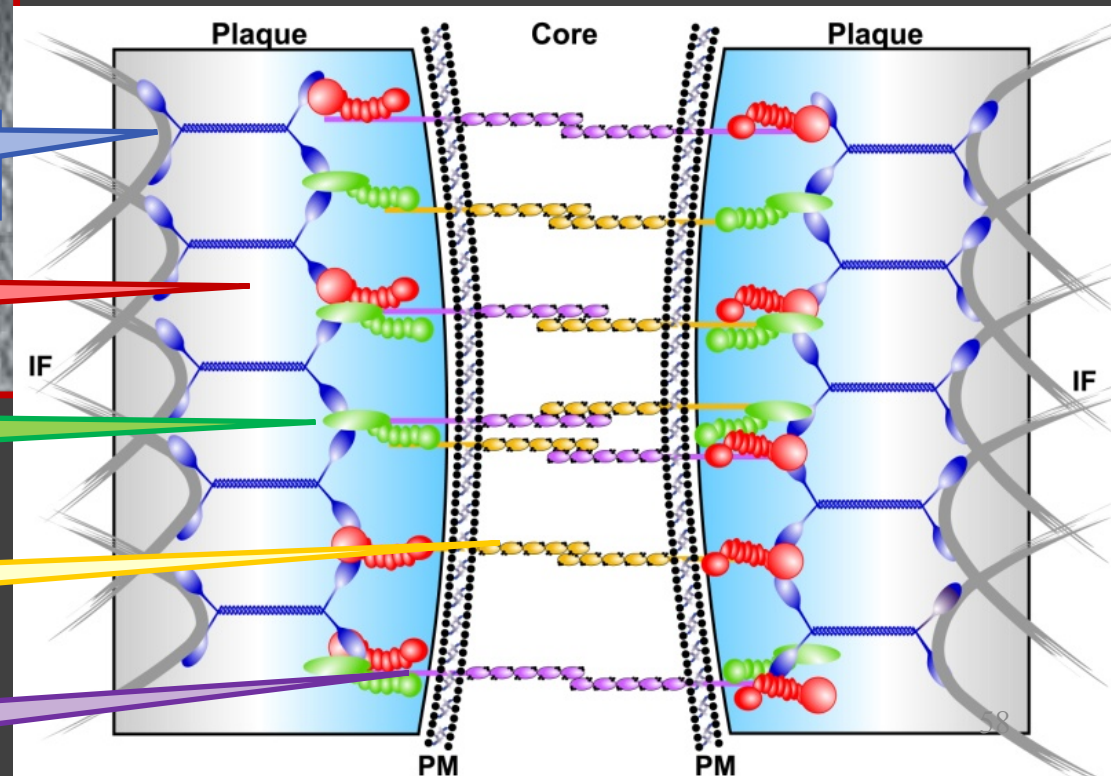
DESMOPLAKIN

PLAKOGLOBIN

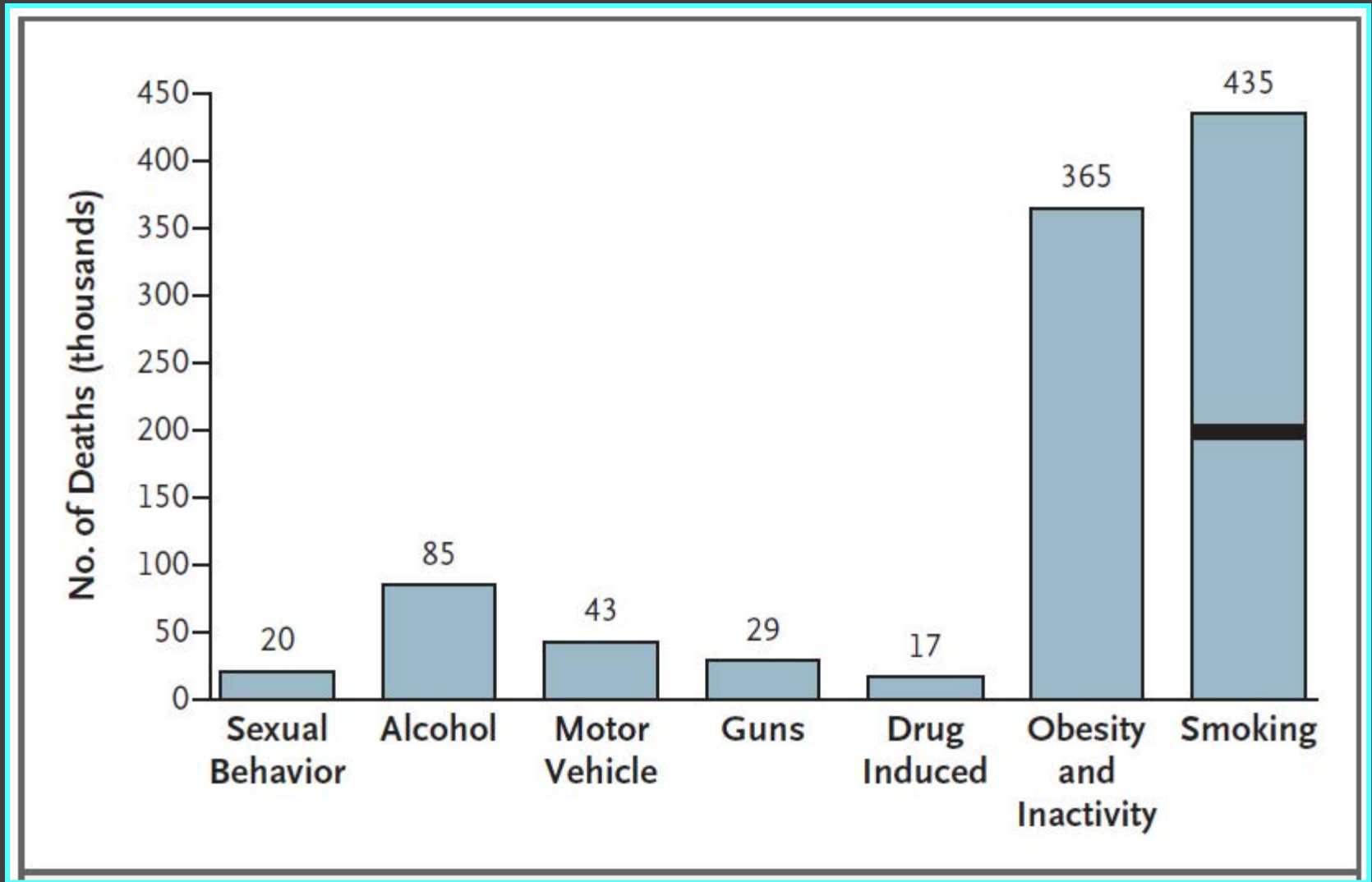
PLAKOPHILIN 2

DESMOCOLLIN-2

DESMOGLEIN-2



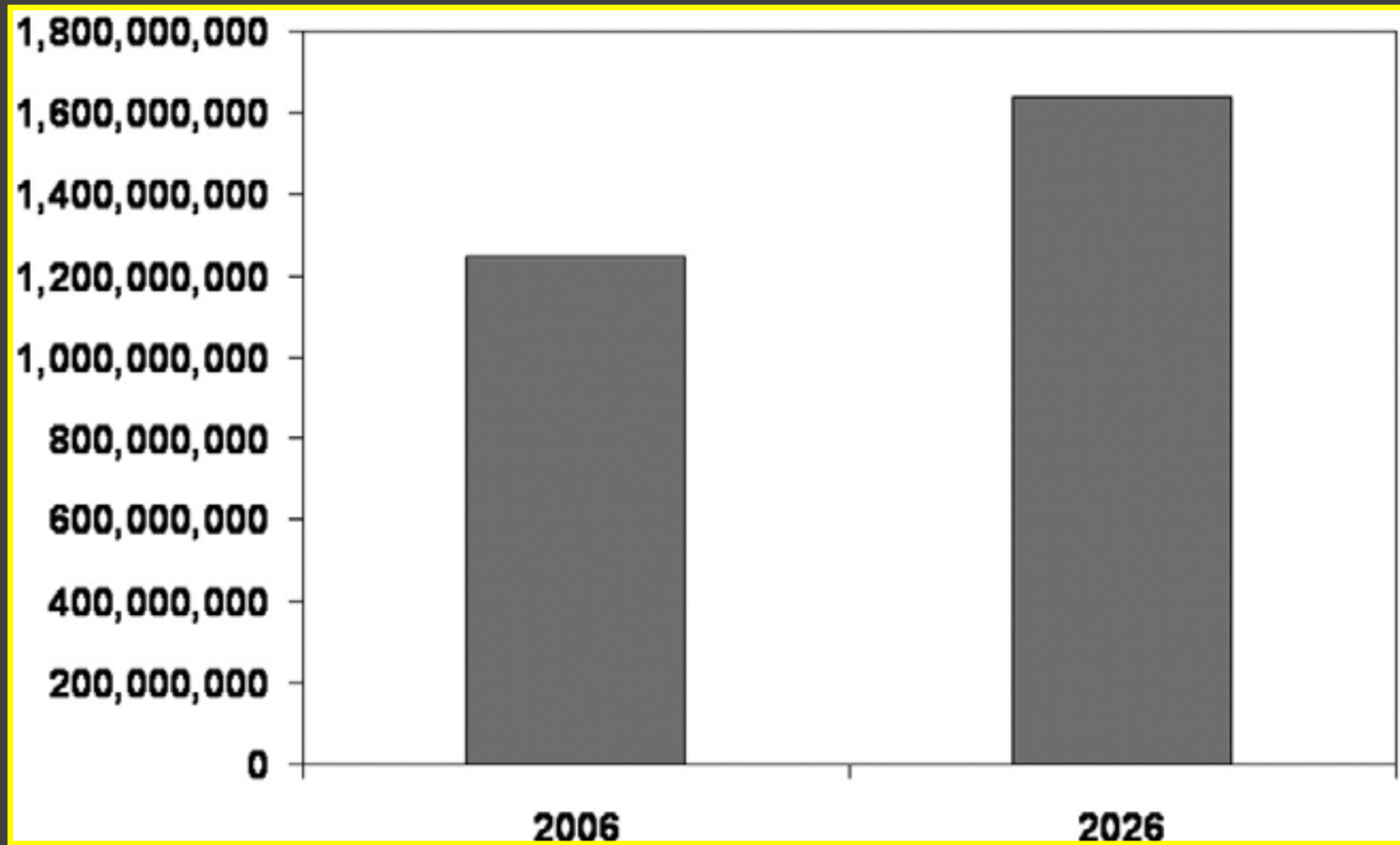
# Number of US Deaths from Behavioral Causes, 2000



from Schoroeder SS. *The New England Journal of Medicine*  
Volume 357, No. 12, September 20, 2007, Pages 1221-1228







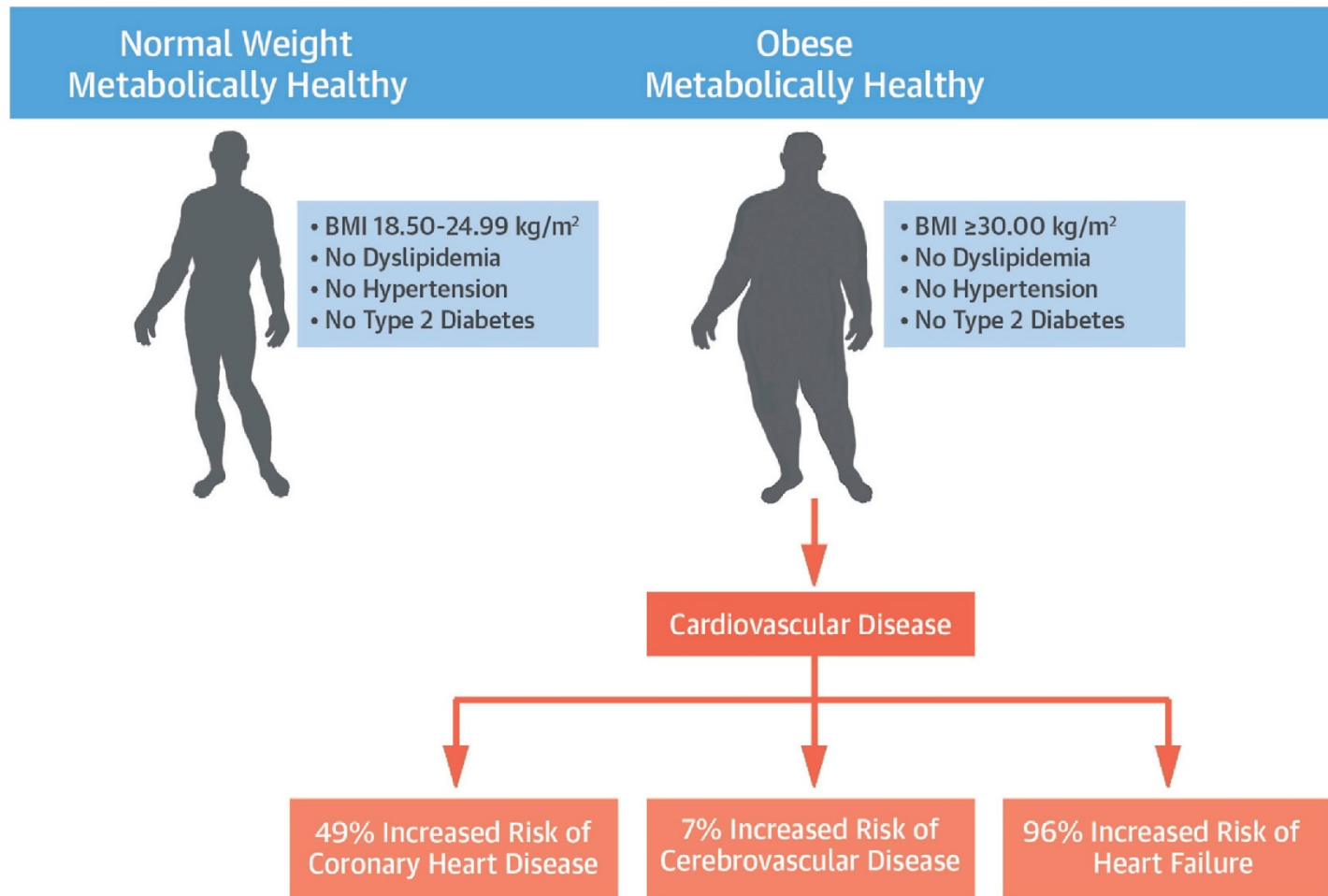
Total number of smokers is projected to increase by more than 30% globally in the next 20 years. Data were obtained from “Tobacco is impoverishing people and nations, WHO warns” available at:

<http://www.wpro.who.int/NR/rdonlyres/7321AD83-6AB5-4071-B374-535C243684DA/0/TobaccoImpoverishing.pdf>

*from Jonas RA. The Journal of Thoracic and Cardiovascular Surgery  
Volume 134, No. 1, 2007, Pages 1-14*



## CENTRAL ILLUSTRATION: Metabolically Healthy Obese and Incident Cardiovascular Disease



Caleyachetty, R. et al. J Am Coll Cardiol. 2017;70(12):1429-37.

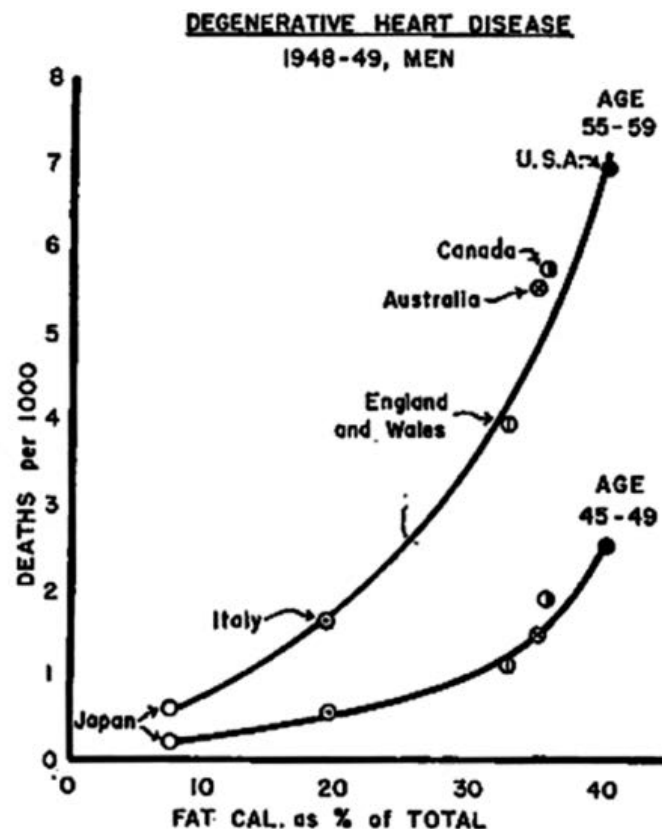
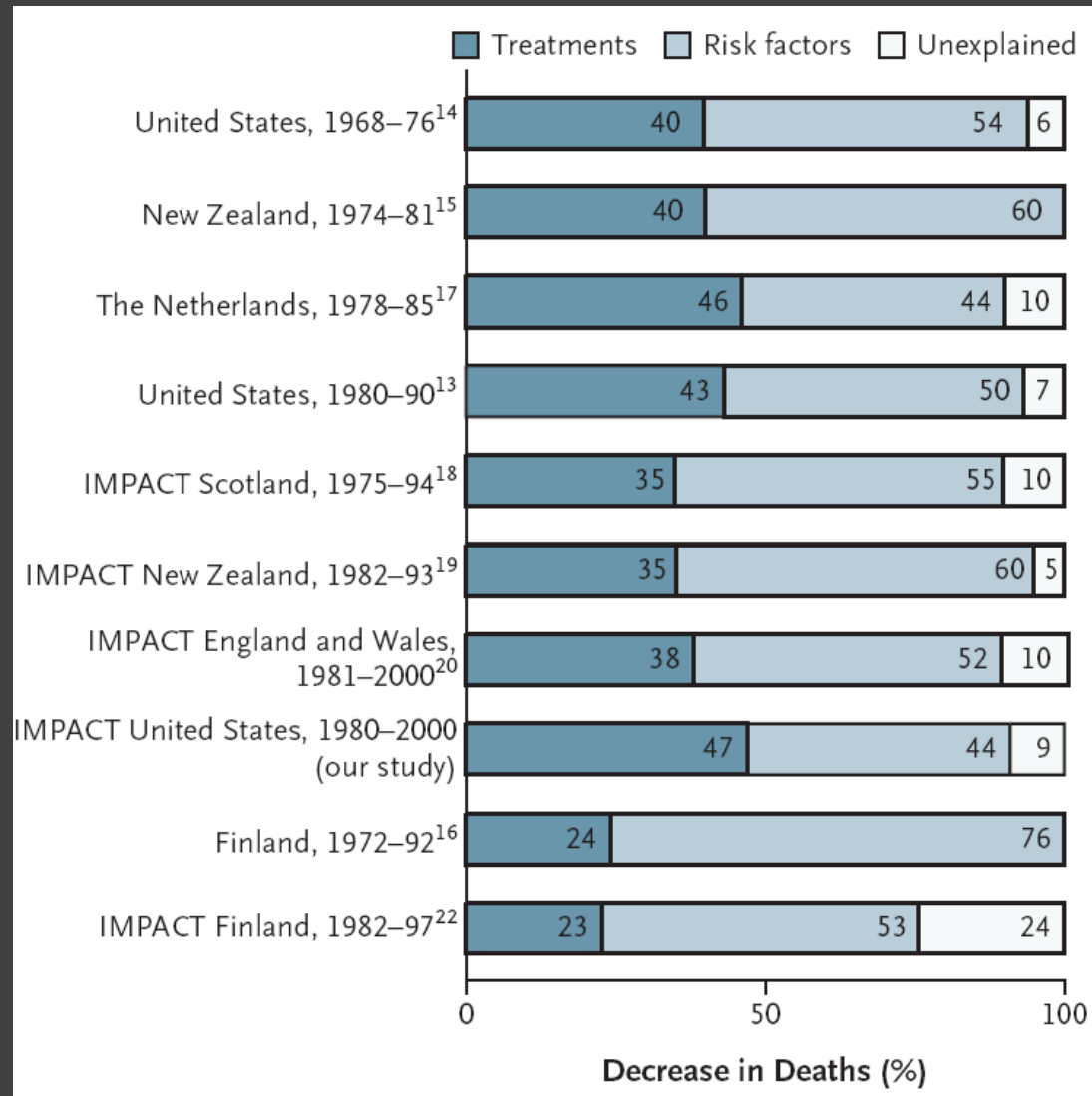


FIG. 2. Mortality from degenerative heart disease (categories 93 and 94 in the Revision of 1938, categories 420 and 422 in the Revision of 1948, International List. National vital statistics from official sources. Fat calories as percentage of total calories calculated from national food balance data for 1949 supplied by the Nutrition Division, Food and Agriculture Organization of the United Nations.

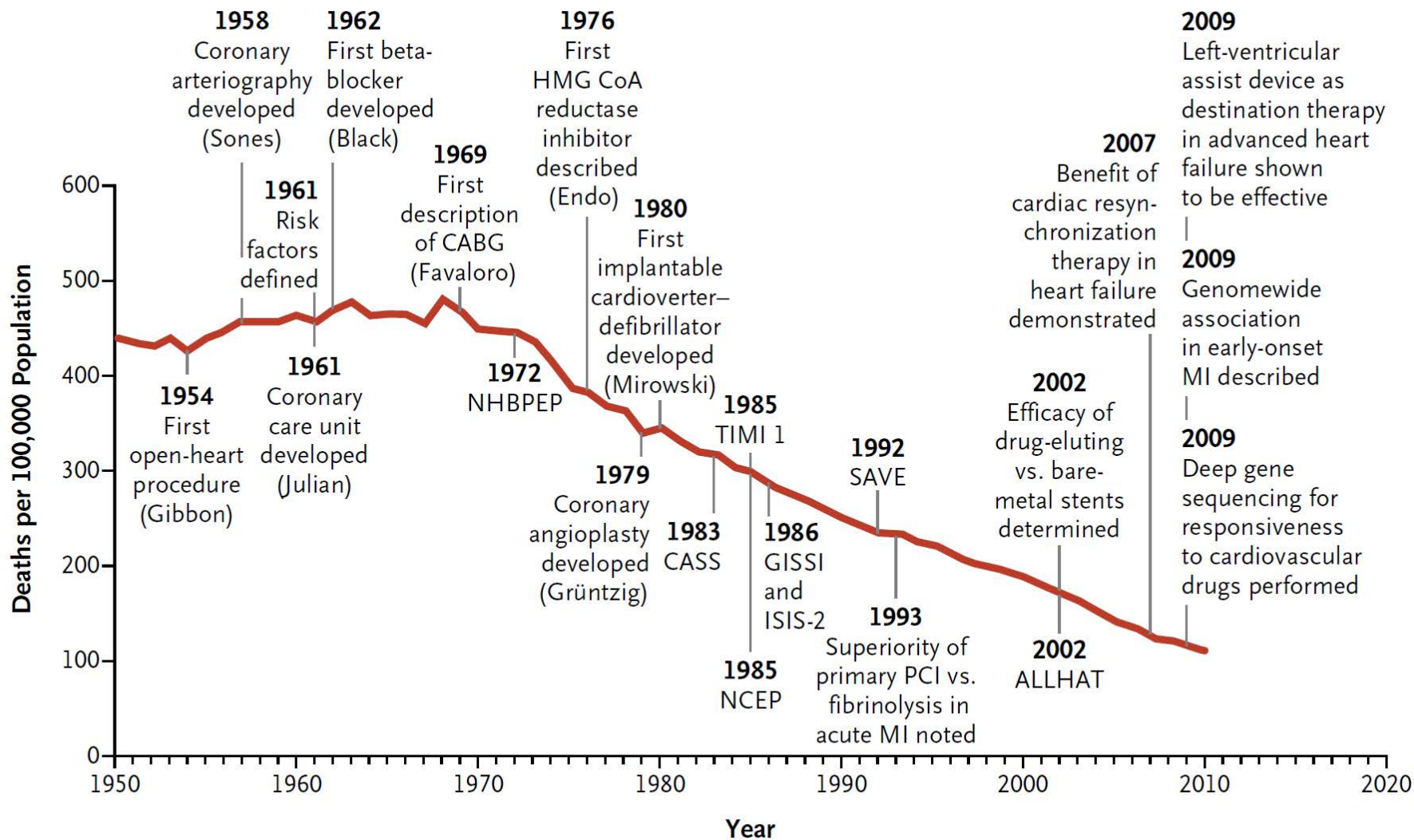


# Decrease in Deaths from Coronary Artery Deaths According to Treatments and Risk-Factor Changes



from Ford ES. *The New England Journal of Medicine*  
Volume 356, No. 23, June 7, 2007, Pages 2388-2398





**Figure 1.** Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances.

2003 → 2020

2020 →



A  
DISCOURSE  
UPON THE INSTITUTION OF  
MEDICAL SCHOOLS  
IN AMERICA

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BY JOHN MORGAN M.D.

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Reproduction through a Gift from the  
Philip H. and A.S.W. Rosenbach Foundation  
upon the occasion of the  
TWO HUNDREDTH ANNIVERSARY  
OF THE  
SCHOOL OF MEDICINE of  
the UNIVERSITY OF PENNSYLVANIA  
THE *First American Medical School*  
1765 – 1965

“According to the learned  
Gaubius, ‘*Medicine is the  
guardian of life and health,  
against death and disease*’”



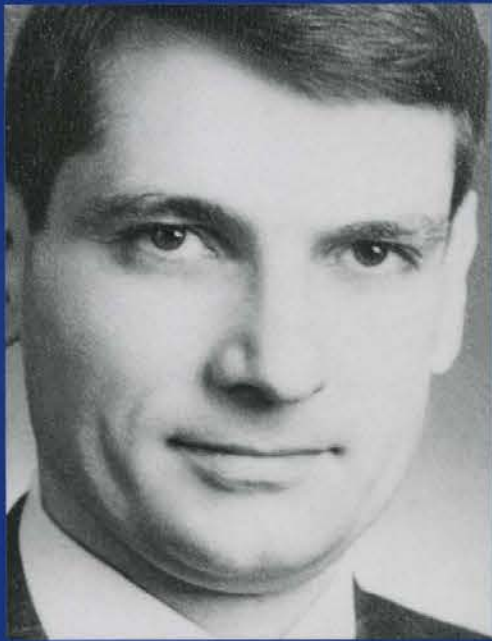
Hyeronimus David Gaubius  
(1705-1780)





# Picasso, Science and charity, 1897





# GIANCARLO RASTELLI

*Un cardiocirurgo  
con la passione dell'uomo*

*I have always believed that  
the first mercy the patient  
should receive from the  
doctor is the trust on  
science*

Giancarlo Rastelli, 1961



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DI PADOVA

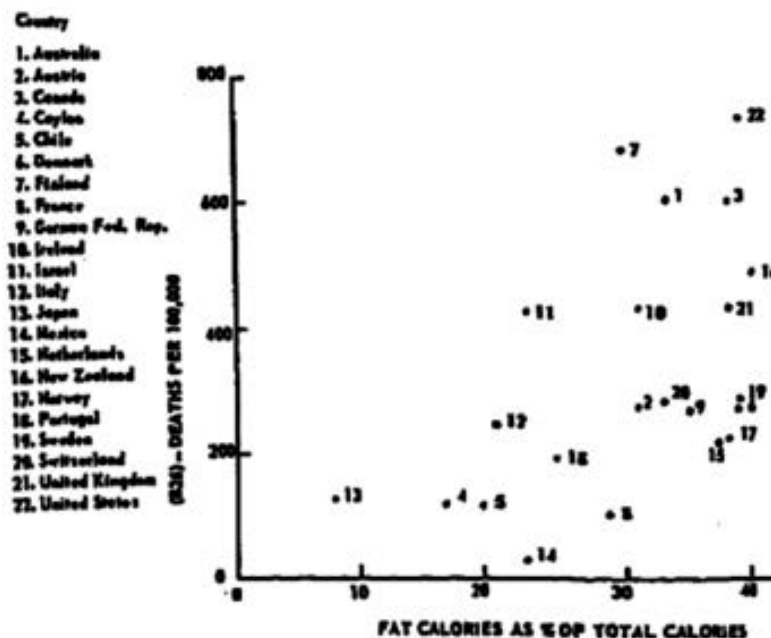


From: Ferrara I: Introduction Why and how do cardiologists need to take an interest and lead prevention programmes?

Eur Heart J. 2017;38(44):3255-3257. doi:10.1093/eurheartj/ehx622

Eur Heart J | Published by Oxford University Press on behalf of the European Society of Cardiology 2017.



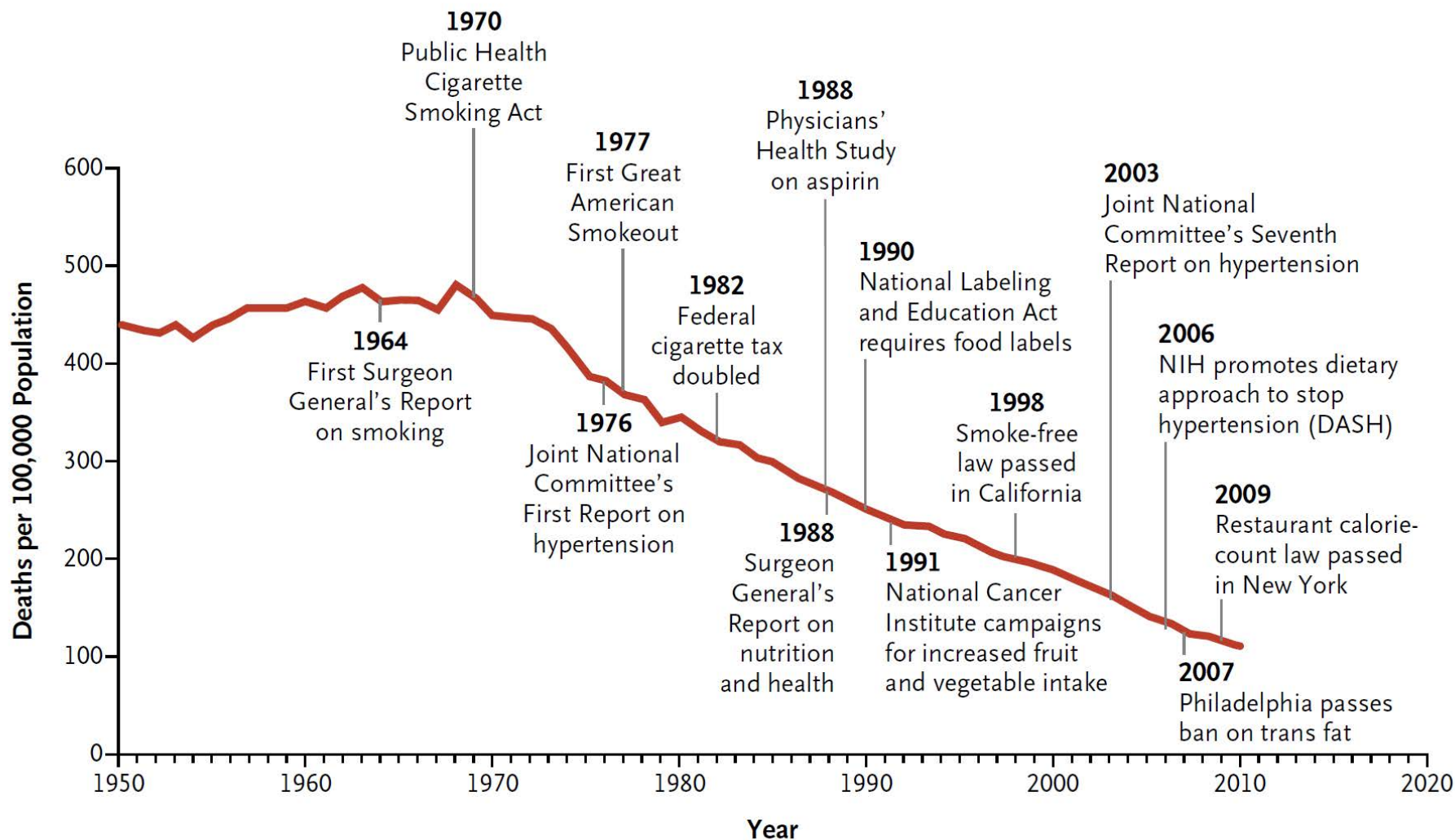


**FIG. 3.** Mortality from arteriosclerotic and degenerative heart disease (B-20) and fat calories as per cent of total calories in males fifty-five to fifty-nine years. Calculated from national food balance data by F.A.O. (see text for definition).

From: The Seven Countries Study

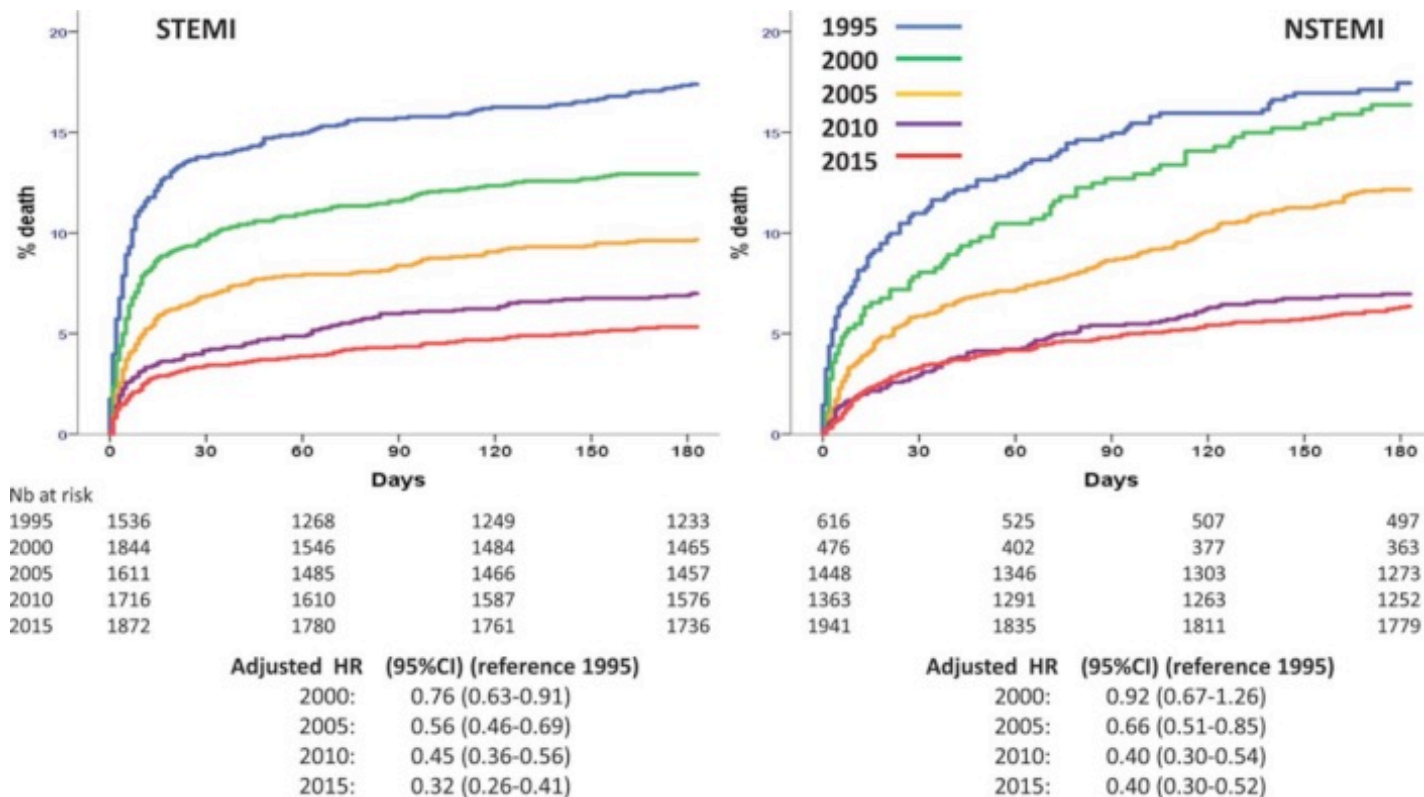
Eur Heart J. 2017;38(42):3119-3121. doi:10.1093/eurheartj/ehx603

Eur Heart J | Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2017. For permissions, please email: journals.permissions@oup.com.



**Figure 1.** Decline in Deaths from Cardiovascular Disease in Relation to Important Public Health and Primary Care Interventions.

## Cumulative 6-month mortality in patients with STEMI and NSTEMI by year of survey.



Etienne Puymirat et al. Circulation. 2017;136:1908-1919



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*The* NEW ENGLAND JOURNAL *of* MEDICINE

20<sup>th</sup> NEJM ANNIVERSARY ARTICLE

# A Tale of Coronary Artery Disease and Myocardial Infarction

Elizabeth G. Nabel, M.D., and Eugene Braunwald, M.D.

N Engl J Med 2012;366:54-63



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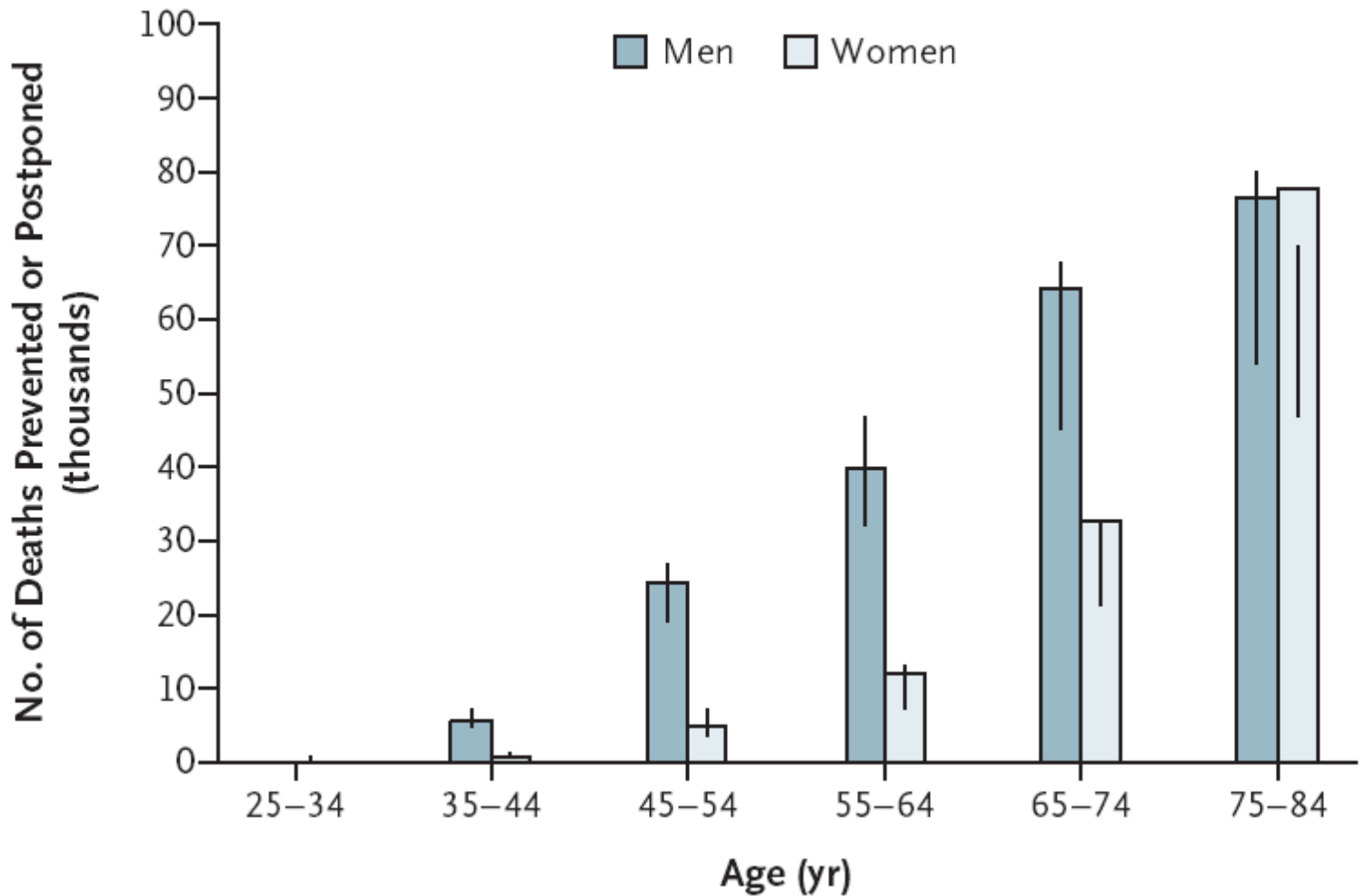
## Determination of the Cause of Death: its Relationship to Cardiac Disease and Autopsy Findings *Jesse E. Edwards (I)*

At this point in the history of medicine, the leaders in the field of diagnostic aids have come from a class of people familiar with the autopsy, and development of these tests and many others have been supported by anatomic observations made by pathologists and clinicians working together at the autopsy. Now, persons in the diagnostic fields are being educated and trained in a period not only of declining incidence of autopsy, but, worse than that, absence of the clinician from the few autopsies that are being performed...

*Mayo Clin Proc 1999;74:739*

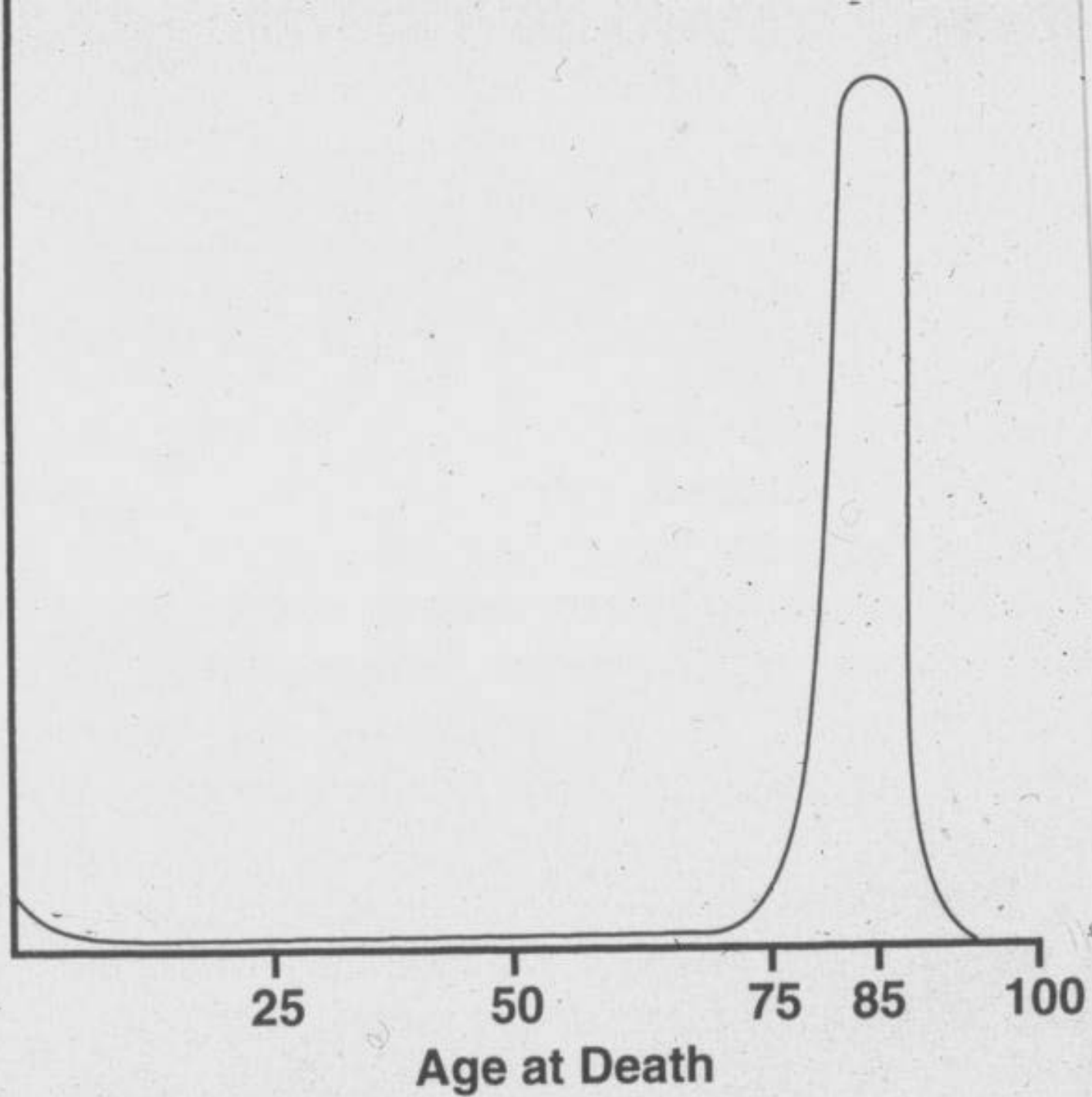


# Estimated and Observed Reductions in Death from Coronary Heart Disease in the US between 1980 and 2000 Stratified to Age and Sex



from Ford ES. *The New England Journal of Medicine*  
Volume 356, No. 23, June 7, 2007, Pages 2388-2398

**Number of Persons**



# In vivo diagnosis became possible thanks to technologic revolution

- Microscope, Robert Hook (1665)
- Stethoscope, René Laennec (1818)
- Genetic Heritage, Gregor Mendel (1865)
- Radiography, Wilhelm Roentgen (1895)
- Electrocardiography, Willelm Einthoven (1902)
- Cardiac Catheterization, Werner Forsmann (1929)
- Electron Microscope, Max Knoll and Ernst Ruska (1931)
- Echocardiography, Inge Edler and Carl Hellmuth Hertz (1952)
- Life Code, James Watson and Francis Crick (1953)
- Coronarography, Mason Sones (1958)
- Computed Tomography, Godfray Hounsfield and Allan Comak (1971)
- Magnetic Resonance, Christian Lauterbur and Peter Mansfield (1973)
- Polymerase chain reaction, Robert Mullis (1985)
- Electroanatomic Mapping, Lior Gepstein, Gal Hayam and Shlomo A. Ben-Haim (1997)



# Magnetic Resonance: Navigation in the Living Human Body



*Courtesy of Dr Martina Perazzolo Marra*



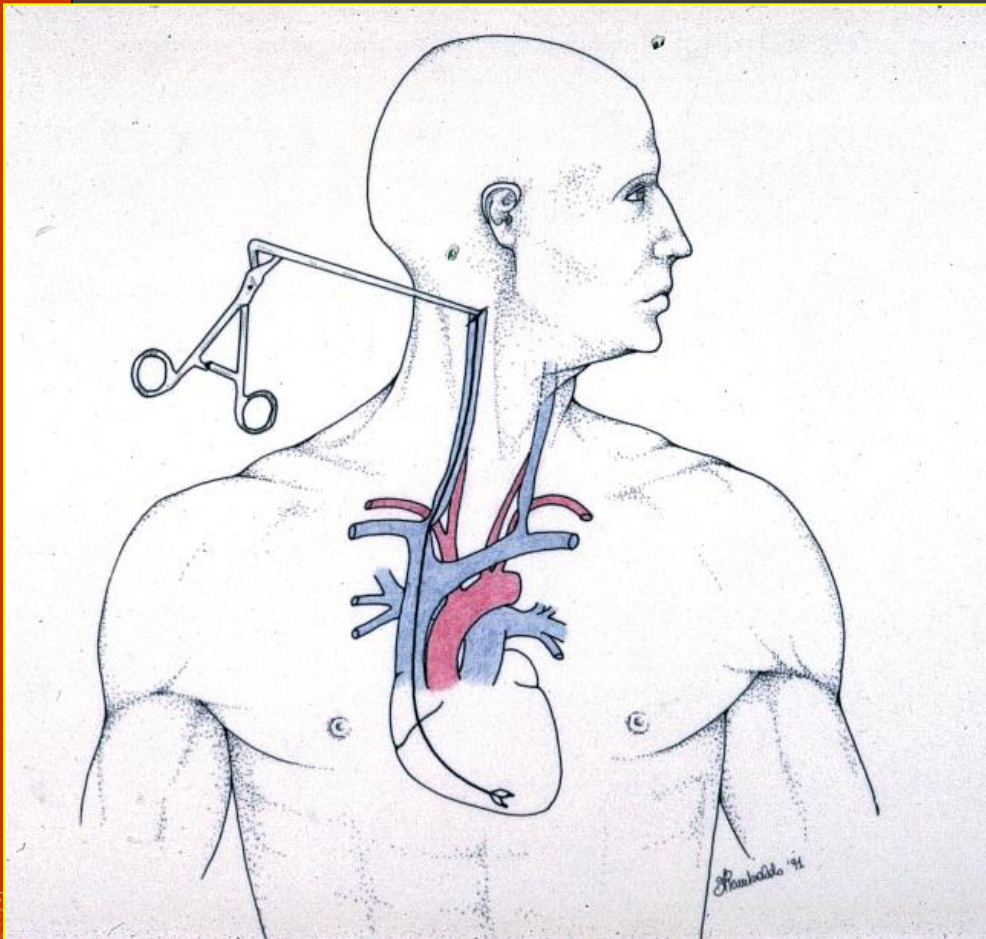
# Heart diseases can be surgically treated

- Extracardiac correction of congenital heart diseases
- Open heart surgery with extracorporeal circulation
- Prosthetic valve replacement
- Aorto-coronary bypass
- Cardiac transplantation with homologous or total artificial heart
- Endomyocardial biopsy



# Cardiac rejection monitoring through endomyocardial biopsy

Margaret Billingham, 1980



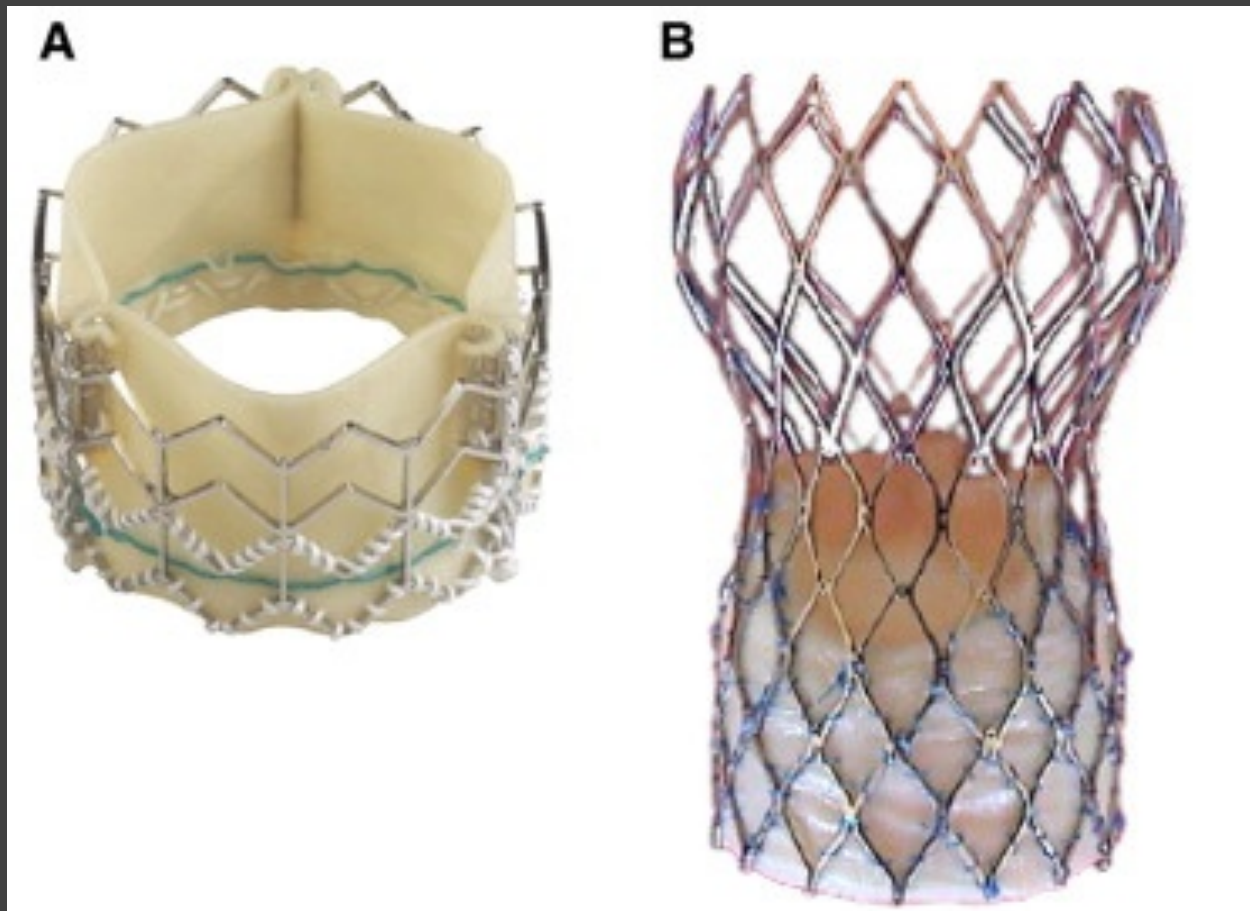




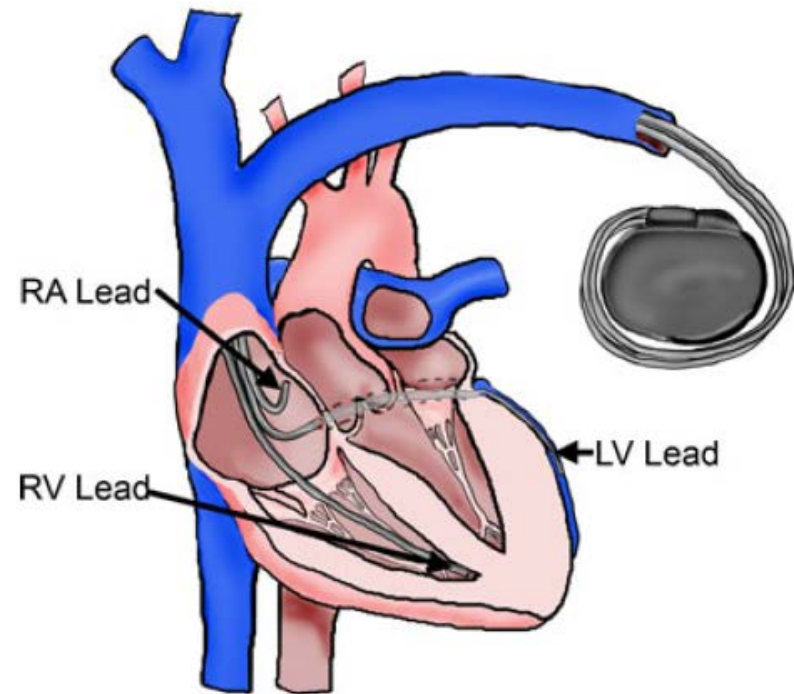
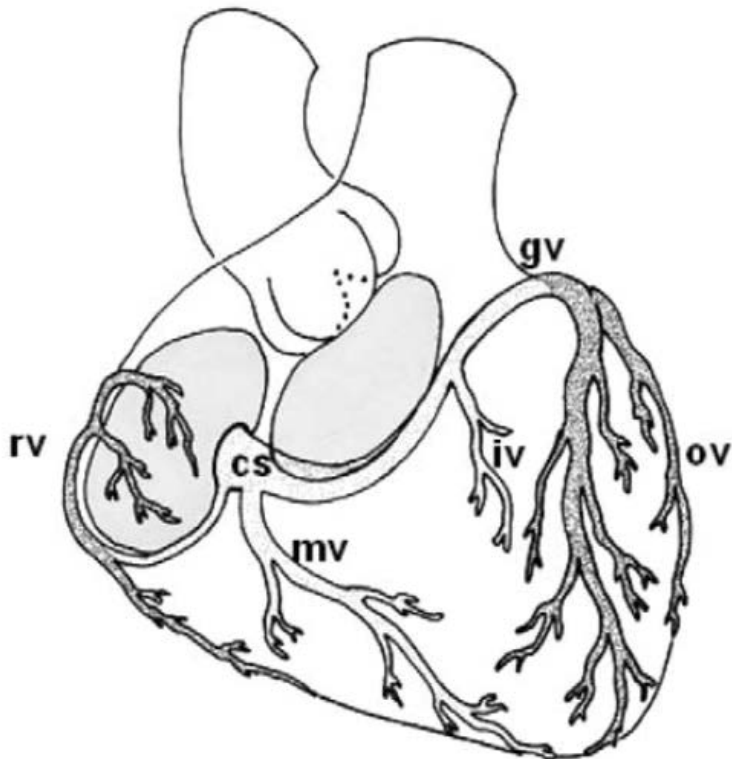


# Transcatheter Aortic Valve Implantation

## Alain Cribier, 1986



# Ventricular resynchronization, the cardiac veins as a pathway for therapy



# Heart diseases can be prevented

- **Prevention**

- Identification of risk factors (1961)
- Coronary Unit (1961)
- Physical activity and pre-participation screening (1982)
- Molecular screening for identification of genetically determined diseases

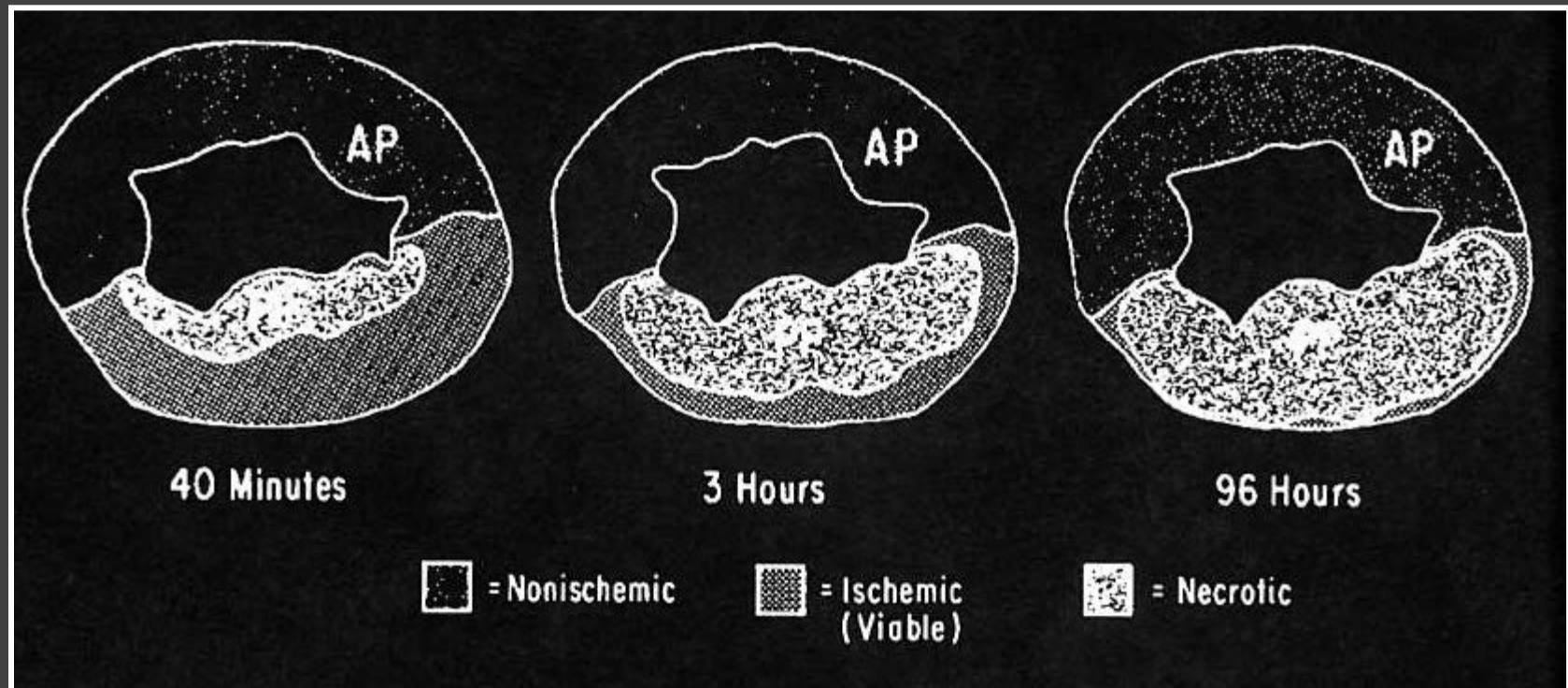


# The "Wavefront Phenomenon" of Myocardial Ischemic Cell Death

## II. Transmural Progression of Necrosis within the Framework of Ischemic Bed Size (Myocardium at Risk) and Collateral Flow

KEITH A. REIMER, M.D., PH.D., AND ROBERT B. JENNINGS, M.D.

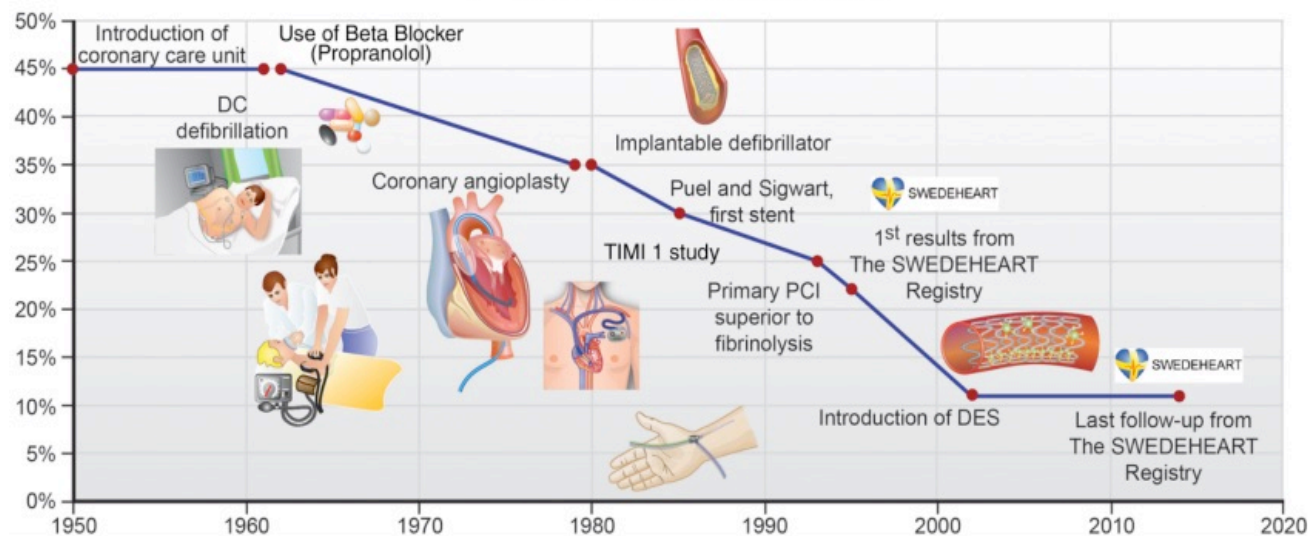
*Department of Pathology, Duke University Medical Center, Durham, North Carolina 27710*

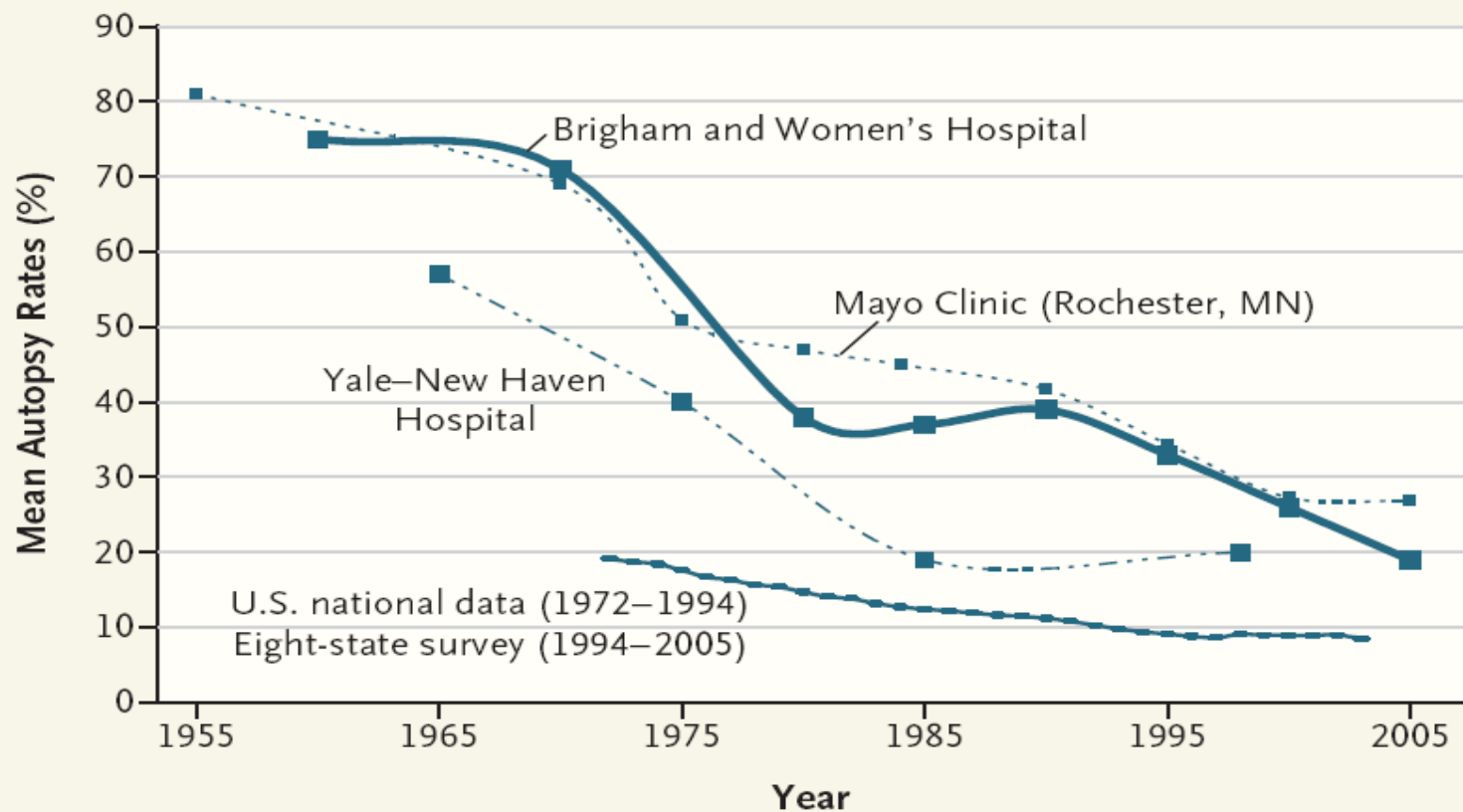






### Cardiovascular Mortality Over Years





### Trends in U.S. Autopsy Rates.

Rates are from various published sources contained in a systematic review,<sup>1</sup> publicly available national data, a survey of centers performing autopsies in eight states (Illinois, Indiana, Louisiana, Minnesota, Nebraska, North Dakota, South Dakota, and Wisconsin),<sup>2</sup> and personal communication with pathologists at individual institutions. Autopsy rates at many institutions are inflated by the inclusion of forensic cases and stillbirths.

## The Vanishing Nonforensic Autopsy

Kaveh G. Shojania, M.D., and Elizabeth C. Burton, M.D.

N Engl J Med 2008;358:873-875 90



## Determination of the Cause of Death: its Relationship to Cardiac Disease and Autopsy Findings *Jesse E. Edwards (II)*

... Unless that trend reverses itself, it is my prediction that the day will come when current and future teachers will miss the fundamental instruction on which the practice of medicine has been built. To overcome the deficiency, there will need to be a return to the autopsy with a promise for future developments in the field of diagnostic testing.

*Mayo Clin Proc 1999;74:739*



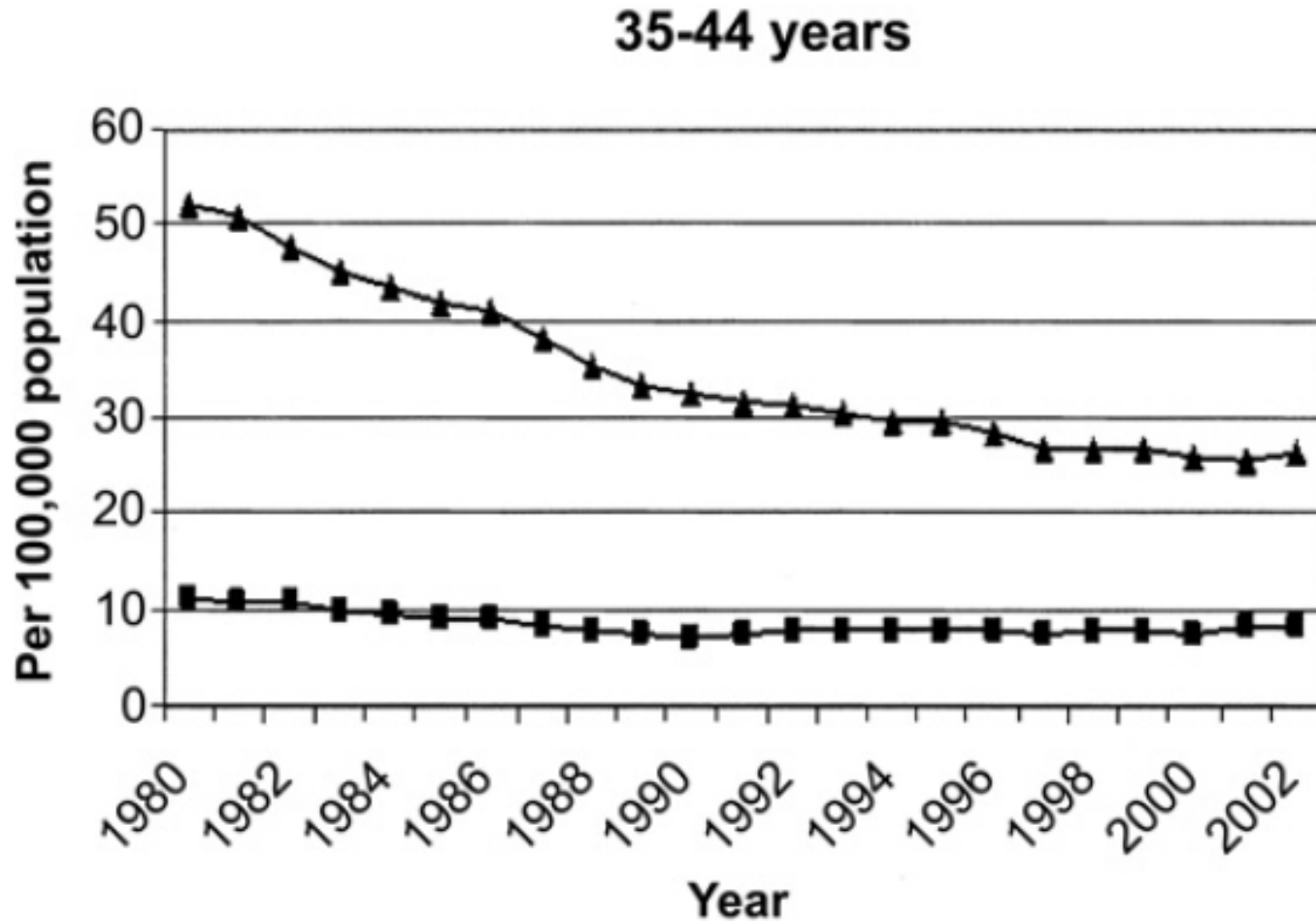


William Withering (1741-  
1799)



*Digitalis purpurea*

# Trends in Age-Specific Mortality Rates from Coronary Heart Disease



from Ford ES & Capewell S. *The Journal of the American College of Cardiology*  
Volume 50, No. 22, November 2007, Pages 2128-2130



# Deaths from Coronary Heart Disease, Prevented or Postponed by Medical or Surgical Treatments in USA, 2000

	Number	%
Acute myocardial infarction – Unstable angina	35,145	10%
Secondary prevention after myocardial infarction	28,565	8%
Chronic angina	17,730	5%
Secondary prevention after CABG or PTCA	7,435	3%
Heart failure	30,235	9%
Hypertension	23,845	7%
Statin for lipid reduction, primary prevention	16,580	5%
Total	159,330	47%



# Deaths from Coronary Heart Disease, Prevented or Postponed as a Result of Changes in Population Risk Factors in USA, 1980 to 2000

	Number	%
Smoking	39,925	12%
Systolic blood pressure	68,800	20%
Cholesterol	82,830	24%
Physical inactivity	17,445	5%
Body mass index	- 25,905	-8%
Diabetes	- 33,465	-10%
Total	149,635	44%





