Gaetano Thiene. Top Ital. sci. j. 2025;2(1)
https://www.doi.org/10.62684/IYMY6207

Top Italian Scientists Journal

Open Access | Review | Biomedical Sciences

ISSN 3033-5132

Cardiovascular Aging: a Pathologist overview

Gaetano Thiene

Department of Cardiac, Thoracic, Vascular Sciences and Public Health

University of Padua Medical School, Padova, Italy

Corresponding author:

Gaetano Thiene, MD

Emeritus Professor

Via A. Gabelli 61 - 35121 Padova, Italy

e-mail: gaetano.thiene@unipd.it

Mobile phone: +39 337386756

Keywords: Aging; Cardiovascular Disease, Elderly, Epidemiology; Longevity; Pathology; Prevention

Published: 2 Jan 2025

Abstract

Cardiovascular diseases are the main cause of death in the elderly, much more than neoplasms. Atherosclerosis is the malignancy which affects the blood circulation. Calcification is peculiar of aging. The cardiovascular disease are mostly structural at any components of the cardiovascular system: aorta, arteries, valves, myocardium, conduction system.

The paper covers the complications which threaten the longevity. They need not only of secondary prevention (therapy) but also of primary prevention (early detection by screening) which is mandatory as much as in oncology.

INTRODUCTION

"*Heart disease represents the worst calamity in terms of mortality*". The main cardiac structures (aorta, coronary arteries, valves, myocardium, conduction system) are the target of specific age-related diseases [***Tab. I***]. The purpose and results of this paper is to illustrate:

a) gross and microscopic pathology of the main cardiovascular morbid entities;
b) therapy to increase longevity;
c) the need of early diagnosis;
d) primary and secondary prevention.

AORTA

Atherosclerosis and dissection are the main foes.

The intima is the target of atherosclerosis since childhood with fatty streaks and proliferation of smooth muscle cells. With time plaques grow up, complicated by ulceration and fibrous cap rupture, followed by thombosis and marked deposits of calcification [***Fig. 1***]. The smooth aorta of children [***Fig. 2***] turns out into a rigid tube with aging.

The stiffness of the aorta increases arterial resistance and gives origin to onset of hypertension, which precipitates a series of severe complications [***Tab. II***] as follows:

Left ventricular hypertrophy [***Fig. 3***], which impairs diastole and dilates left atrium, which triggers atrial fibrillation with thrombosis inside the left appendage [***Fig. 4a***] and systemic embolism with stroke [***Fig. 4b***]. Occlusion device like umbrella is now a way to close the opening of the appendage and to prevent embolism.

Aortic atherosclerotic aneurysm [***Fig. 5***] develops because of progressive wall thinning by release of metalloproteinases from macrophages of the atherosclerotic plaques. The intimal release of metalloproteinase creates rupture of plaque fibrous cap with platelets and fibrin deposition, whereas the release on the other side disrupts the elastic lamellae of the tunica media, with weakening and thinning of the wall and onset of dilatation [***Fig. 5***]. Thus the disease is not only degenerative, but also inflammatory from the beginning. It occurs more frequently in abdominal aorta [***Fig. 5a,b***], where normally the elastic fibers are much less than in thoracic aorta. The abdominal atherosclerotic aneurysm is at high risk of rupture when the diameter exceeds 5 cm. Surgical replacement with implant of vascular prosthesis by laparotomy under deep anaesthesia or endovascular prosthesis via femoral artery without laparotomy are both effective and lifesaving.

Another frequent complication of hypertension in aged patients is aortic dissection [***Fig. 6***]. During a hypertensive attack an intimal tear develops [***Fig. 7***] with blood entering into the tunica media, upstream and downstream, at risk of external rupture and death. A degenerative phenomenon of the tunica media is present, with elastic disruption, necrosis of smooth cells within the lamellar units and accumulation of ground substance (so called cystic medionecrosis) [***Fig. 8***]. It may facilitate the onset and propagation of the dissection [***Fig. 9***], which may involve the whole aorta (Type A) [***Fig. 6a***] or be limited to the descending thoracic aorta (Type B) [***Fig. 6b***].

A high peak of arterial hypertension stretches the intima and creates a tear [***Fig. 7***] and the blood enters into the tunica media with distal and proximal dissection [***Fig. 9***], involving collateral arterial branches. A spontaneous re-entry may occur, especially in iliac arteries, giving origin to self-healing. A double lane develops: chronic dissection with so called “double barrel” [***Fig. 10***].

When the dissection of the ascending aorta (type A) propagates proximally, it may involve the sinusal aorta and the aortic valve apparatus, developing valve incompetence and coronary ostia occlusion with myocardial infarction. Moreover, blood infiltration of the atrial septum may interrupt internodal connections with av block. Prompt cardiac surgery saves life through sternotomy with extracorporeal circulation and replacement of the dissected aorta with prosthetic tube. As far as type B [***Fig. 6b***], endovascular prosthetic tube, implanted via femoral artery without thoracotomy, is nowadays feasible with rewarding results.

CORONARY ARTERIES

Ischemic heart disease is the most frequent cause of death in the elderly, much more than oncology [***Fig. 11***] (1). The culprit disease is obstructive coronary artery atherosclerosis [***Fig. 12***]. Acute myocardial infarction [***Fig. 13***], mostly occurring after 70 years of age, both in men and women, is precipitated by thrombotic occlusion of a subepicardial coronary artery by atherosclerotic fibrous cap rupture [***Fig. 14***]. The amount of myocardial ischemic necrosis may be limited by prompt revascularization (so called "primary angioplasty"), with reopening of the occluded coronary segment through a catheter with balloon and implanting a prosthetic stent to maintain the patency for ever. If not, the necrosis may become transmural at risk of cardiac rupture and hemopericardium with tamponade [***Fig. 13***]. Establishment of coronary units by Desmond Julian [***Fig. 15***] and then primary angioplasty for revascularization contributed to reduce hospital death by acute infarction from 30% to less than 10% [***Fig. 16***]. As far as chronic ischemic heart disease, scarring of previous infarct is a potential substrate of ventricular tachyarrhythmia at risk of ventricular fibrillation and cardiac arrest. Implant of defibrillator [***Fig. 17***] and external defibrillator availability, even at home, are lifesaving.

Cardiac valves: AORTIC VALVE

The most typical cardiac valve disease of aging is aortic stenosis by dystrophic calcification [***Fig. 18***], known in the past as "atherosclerotic stenosis of the aortic valve", because regularly associated to severe atherosclerosis of the aorta. It might be a transfer of calcium from the bones to the heart, in the setting of elderly osteoporosis.

Rheumatic valve disease, an inflammatory immune morbid entity, is disappearing in west countries, whereas it is still a nightmare in third world. Degenerative valve diseases are nowadays the protagonists [***Fig. 19***]. Therapy is accomplished by surgical valve replacement, in extracorporeal circulation and through thoracotomy, with mechanical or biological valve prostheses, in keeping with patient age (less or over 65 yrs respectively). A transcutaneous arterial valve implantation (TAVI) has been invented with competitive results, requiring neither thoracotomy nor extracorporeal circulation.

As far as aortic incompetence in aged patients, Dominique Corrigan [***Fig. 20***], Irish cardiologist from Dublin, discovered a new entity, beyond rheumatism, bacterial endocarditis and syphilis. The aortic regurgitation of this new entity is due to aortopathy with aneurysmatic dilatation of ascending aorta, particularly the sinus portion which holds the aortic valve [***Figs. 21***]. The challenge for the surgeon is to replace the dilated aorta and preserve the cusps which are frequently normal, being the

regurgitation due to enlargement of the aorta to which the cusps are attached. Erdeim' medionecrosisis of the aortic wall is regularly present as microscopic degenerative feature of an aortopathy [***Fig. 21b***].

MITRAL VALVE

As far as mitral valve is concerned, a peculiar pathology occurring with time in the natural history is dystrophic calcification of the annulus [***Fig. 22***], frequently associated with calcific aortic valve stenosis. Oddly enough, mineralization involves the cusps at the aortic but not at the mitral level. Clearly it is not due to mechanical stress, which is less at the aortic level since the aortic valve close in diastole and mitral valve in systole. The involvement of the mitral annulus by calcification hinders the sphincteric contraction and causes per se' mitral regurgitation (20% of mitral orifice closure is due to sphyncteric action) [***Fig. 23***].

Mitral valve leaflets with aging undergo a different pathology, namely mitral valve prolapse with a progressive accumulation of mucoid extracellular matrix in spongiosa and fibrosa layers with balloon remodelling and regurgitation [***Fig. 24***]. In this case chronic mechanical stress is a plausible explanation of degeneration, considering the billions of systolic closures of the mitral leaflets with undergo during life. The edge-to-edge repair with double orifice technique is nowadays available to treat incompetence, both by invasive cardiology with catheter and surgery without extracorporeal circulation.

Also mitral papillary muscles and the ventricular myocardium, on which they are implanted, substain stress with myocyte death. The inherent fibrotic scarring becomes an arrhythmic substrate for life threatening ventricular tachyarrhythmia and cardiac arrest. Sudden death is a "Damocle' sword" during natural history of patients, affected by mitral valve prolapse.

TRICUSPID VALVE

As far normal tricuspid valve, myocardial attachment at the ring is such to be poorly capable to cope with pulmonary hypertension. Moreover, a congenital defect known as Ebstein anomaly may develop incompetence late in the elderly [***Fig. 25***].

MYOCARDIUM

Aside genetically determined cardiomyopathies and ischemic heart disease (see the latter under coronary arteries subchapter), lipofuscin deposits are visible inside cardiomyocytes. They are metabolic debris and intracellular deposits which displace the sarcomer apparatus [***Fig. 26a***] and

impair contractility. Haemochromatosis of the myocardium occurs in old patients undergoing chronic blood transfusion [***Fig. 26b***].

Amiloidosis is an interstitial infiltration of amyloid immunoprotein which hinders the transfer of oxigen and nutrition from capillary blood to parenchyma, comparing myocardial contractility and relaxation [***Fig. 27a***]. Amyloidosis is a secondary restrictive cardiomyopathy, since ventricular walls become so stiff as to compromise the diastole [***Fig. 27b***]. Myeloma, a frequent neoplasm of aged people, is the main source of the amyloid immunoprotein. There is also amyloidosis genetic in origin, like transthyretin produced by liver. Amyloidosis of the atria may trigger atrial fibrillation. Since amyloid deposits in the brain are the cause of Alzheimer, atrial fibrillation amyloidosis of the heart might be named "Cardiac Alzheimer".

CONDUCTION SYSTEM

The heart is equipped by an electrical unit, consisting by specialized myocardial tissue (not nerves), which takes care of origin (sinoatrial node) and transmission of the electrical impulse to the ventricles via a atrioventricular axis (Tawara system) [***Fig. 28a,b***]. The conduction system may undergo to progressive wear and tear with fibrosis, discontinuing the conduction pathways at various levels [***Fig. 28c***]. The phenotype is a progressive av block of variuos degrees (from partial to complete). The av block is cured by implant of a pacemaker.

The disease, named Lev-Lenègre disease, is considered an exaggerate aging change with progressive fibrosis and even calcium deposits of the His bundle bifurcation and proximal left and right branches [***Fig. 29***]. Other causes [***Tab. III***] may account of av block in the elderly: ischemic damage involving the conduction system, dissection of the aorta with retrograde blood propagation, separating the av node from internodal connections, neoplasm of the av node known as Tawarioma or coelothelioma. Genetically determined av block was proved to be due a missense mutation of Sn5 channel in the sarcolemma, by making molecular investigation of the original affected families studied by the French cardiologist Lenègre.

DISCUSSION AND CONCLUSIONS

In 2007 Jonas (2) reported that life expectancy increased in USA from 50 to 80 average years in the time interval 1900-2000 [***Fig. 30***]. Data from the Center of Disease Control and Prevention in Atlanta (USA) showed in 1997 that life expectancy in the previous 30 years increased 6 years, 39% of which thanks to decrease of cardiovascular death and only 0.3% to decrease of cancer death [***Tab. IV***] (3).

This supremacy was due to invention of diagnosis and therapy tools (surgery and invasive cardiology), together with drugs (β-blockers, ACE inhibitors, Statins and anticoagulants), worth of Nobel Prizes [***Fig. 31***].

Even in the past prevention played a fundamental role to increase life span: heating, food, hygiene (4).

Primary prevention is currently the main measure to postpone the onset of the disease, thus increasing longevity: vaccination, life style, behaviour and screening for early diagnosis before the disease manifestation (5).

William Kannel in 1961, starting a demographic investigation program, identified risk factors in the population of Framingham [***Tab. V***], a study the resulted in a significant postponed death by coronary artery disease [***Tab. VI***]. Decrease in death could happen more through reduction of risk factors than treatment.

As predicted by Eugene Braunwald (6), prevention in the next 50 years will prevail to therapy [***Fig. 32***] (7).

Food in Medicine [***Fig. 33***] (8) and Mediterranean Diet (9) will be the winner. Centenary heart is not so far (10).

Declarations

Conflict of Interest

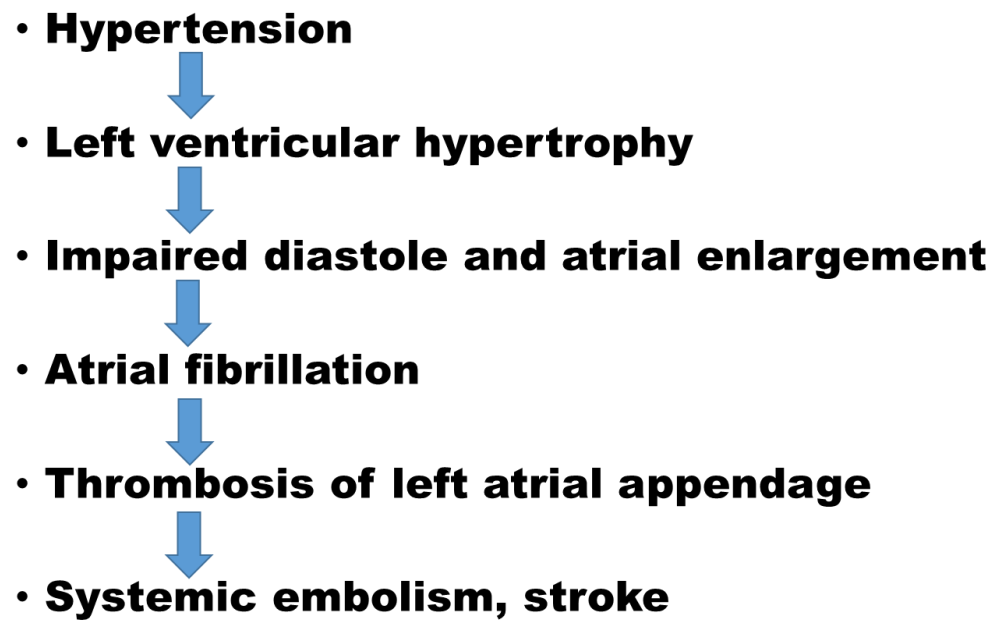
The Author declares that there is no conflict of interest.

Tab. I

Cardiovascular Structures affected by age-related disease	
Aorta	aterosclerosis, dissection
Coronary arteries	atherosclerosis
Valves	senile aortic valve stenosis, anuloaortic ectasia with valve incompetence, calcification of the mitral anulus, mitral valve prolapse
Myocardium	lipofuscin deposits, senile amyloidosis, hemochromatosis
Conduction System	AV Block

Tab II

Complications cascade by calcification of the aorta



Tab. III

Causes of AV block. The main is the idiopatic one

PATHOLOGY OF CHRONIC AV BLOCK (Total N. 177 cases)		
Idiopathic bilateral bundle branch fibrosis	69	39%
Ischaemic (CAD)	30	16,9%
Calcific AV block	17	9,6%
Cardiomyopathy	25	14,1%
Other causes, including tumors	36	20,3%

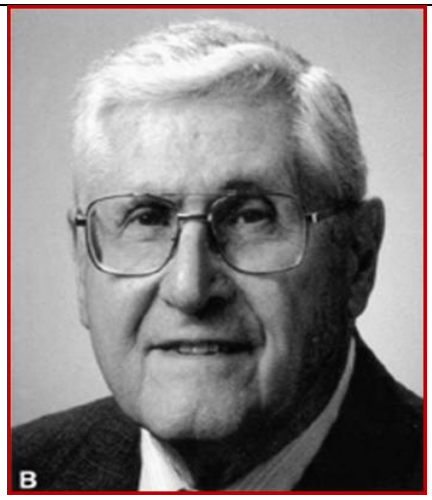
[From Davies MJ, Acta Cardiologica 1976]

Tab. IV

Gains of Life Expectancy by eliminated deaths from various morbidities in the last 30 years	
Cardiovascular Disease	+3.9 yrs
Perinatal disease	+0.5 yrs
Injuries	+0.7 yrs
Cancer	+0.3 yrs
Other causes	+0.9 yrs
Chronic obstructive pulmonary disease	-0.2 yrs
AIDS	-0.1 yrs

Tab. V

William Kannel with the Framingham Study identified the coronary risk factors

William Kannel, 1961 Framingham Study on coronary risk factors	
	Smoking
	Hypertension
	Hypercholesterolemia
	Diabetes
	Obesity

Tab. VI

Rate of deaths from coronary artery diseases prevented or postponed thanks changes of risk factors

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%

LEGENDS

Fig. 1 – Gross view of open thoracic aorta in the elderly, with ulcerated atherosclerotic plaques, thrombus deposits and calcification

Fig. 2 – Gross view of aorta in a child, from distance (a), and close up (b). Note the smooth intima, only a few fatty streaks are visible. (c) Histologic section showing intact intima and parallel elastic lamellae in the tunica media

Fig. 3 – Hypertensive cardiopathy, with left ventricular hypertrophy and dilated left atrium, prone to atrial fibrillation

Fig. 4 – Thrombosis within the left atrial appendage (a) and brain infarct (stroke) (b) in a patient with aortic fibrillation

Fig. 5 – Abdominal atherosclerotic aortic aneurysm. (a) drawing; (b) view of a gross specimen; (c) histology of the aortic wall, with atherosclerotic plaque in the intima, full of cholesterol needles, and the tunica media with disruption of elastic lamellae by the release of metalloproteinases by macrophages

Fig. 6 – Drawings of aortic dissection. Type A (a). The dissection starts in ascending aorta with intimal tear and extend to descending thoracic and abdominal aorta; Type B (b). The dissection starts with intimal tear in the aortic arch and involve only the descending thoracic aorta

Fig. 7 – Mechanism of intimal tear onset. (a) hypertensive peak stretches the intima and gives origin to a tear, with blood entering in the tunica media; (b) view of intimal tear under scanning electron microscopy

Fig. 8 – Medionecrosis of the aortic tunica media. (a) disappearance of smooth muscle cells in the tunica media; (b) fragmentation of elastic lamellae; (c) spots of mucoid substance

Fig. 9 – Slamination of the tunica media by aortic dissection: (a) gross and (b,c) histological view. The dissection is close to the adventitia

Fig. 10 – Healing chronic dissection. (a) Gross view with “double barrel”; (b) histology of the aortic wall with loss elastic lamellae in the tunica media

Fig. 11 – Mortality in USA in 2005: cardiac cause of death much higher than oncological one

Fig. 12 – Obstructive coronary artery with concentric atherosclerotic plaque

Fig. 13 – Post myocardial infarction rupture of the left ventricle with haemopericardium

Fig. 14 – Occlusive thrombosis of the anterior descending coronary artery by fibrous cap rupture of an atherosclerotic plaque

Fig. 15 – Desmond Julian, the outstanding Scottish cardiologist who set up the Coronary Care Unit in 1961

Fig. 16 – A sharp decrease of short-term mortality by myocardial infarction, thanks to Coronary Care introduction defibrillator and Reperfusion Era

Fig. 17 – Electric shock by implanted defibrillator, turning ventricular fibrillation into sinus above, with the picture of the inventor Michel Mirowski (1924-1990)

Fig. 18 – Senile aortic valve stenosis by dystrophic calcification. (a) intrinsic nodular deposits of calcium, whitin the cusps

Fig. 19 – Current sharp decline of inflammatory vs degenerative valve disease

Fig. 20 – Dott. Dominic Corrigan (1802-1880), the Irish cardiologist that discovered a new cause of aortic valve incompetence by a degenerative aortopathy

Fig. 21 – A marked dilatation of the aortic root, seen at angiography, by severe aortopathy at histology, with atrophy of the tunica media and aortic valve incompetence

Fig. 22 – Huge deposit of calcium at the posterior ring of mitral valve at gross examination. (a) low magnification; (b) close-up

Fig. 23 – (a) Dystrophic calcification of the mitral annulus at X-ray, (b) gross view of the specimen and (c) histology of the ring with calcific deposits, reducing sphincter contraction

Fig. 24 – Mitral valve prolapse. (a) drawing which shows regurgitation with prolapse in the left atrium of the posterior leaflet; (b) balloon deformation of the leaflets; (c) histology with massive infiltration of mucoid substance into spongiosa and fibrosa

Fig. 25 – Ebstein malformation of the tricuspid valve. (a) Drawing showing the downward displacement of the leaflets and an interatrial communication through a patent foramen ovale. (b) Heart specimen of Ebstein's anomaly: a congenital stenosis of the tricuspid valve

Fig. 26 – (a) Lipofuscin deposits disarranging the sarcomeres (transmission electromicroscopy). (b,c) Haemochromatosis of the cardiomyocites by chronic blood transfusion. Endomyocardial biopsy with Haematoxilin-eosin stain (b) and iron stain (c)

Fig. 27 – Cardiac amyloidosis. (a) interstitial deposits of amyloid, stained with kongo red; (b) Stiff heart specimen

Fig. 28 – The atrioventricular conduction system, outlined in a heart specimen from the right (a) and left (b) sides. Sites of block: His bundle bifurcation is the most frequent (c)

Fig. 29 – AV block by fibrotic interruption of His bundle bundle branches. (a) Almost interruption of the left bundle branch with still tiny connexions and (b) fibrotic right bundle branch

Fig. 30 – Increase of life expectancy in USA from 1900 to 2000

Fig. 31 – Invention of drugs has been a great deal to increase longevity. The discovers became Nobel Prize winners

Fig. 32 – In the next future, Prevention Medicine will be much more effective than Treatment Medicine

Fig. 33 – Mediterranean Diet is a great means to prevent atherosclerosis

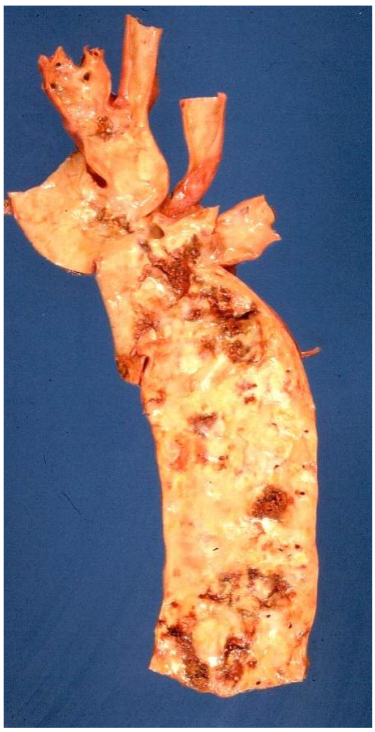
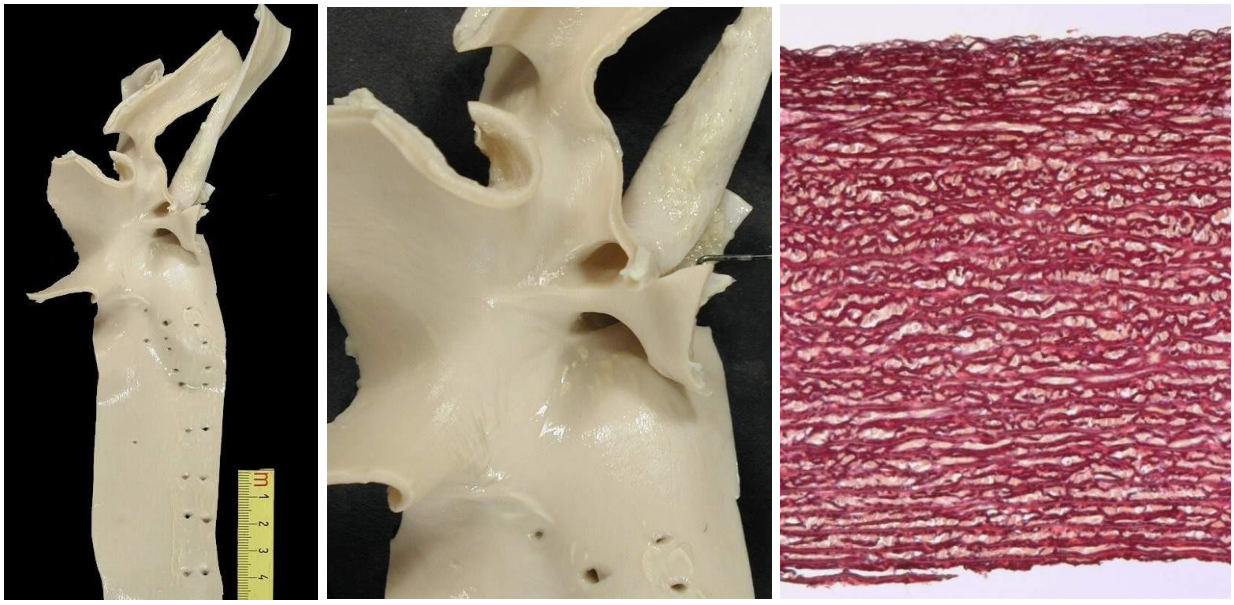


Fig. 1



a b c

Fig. 2

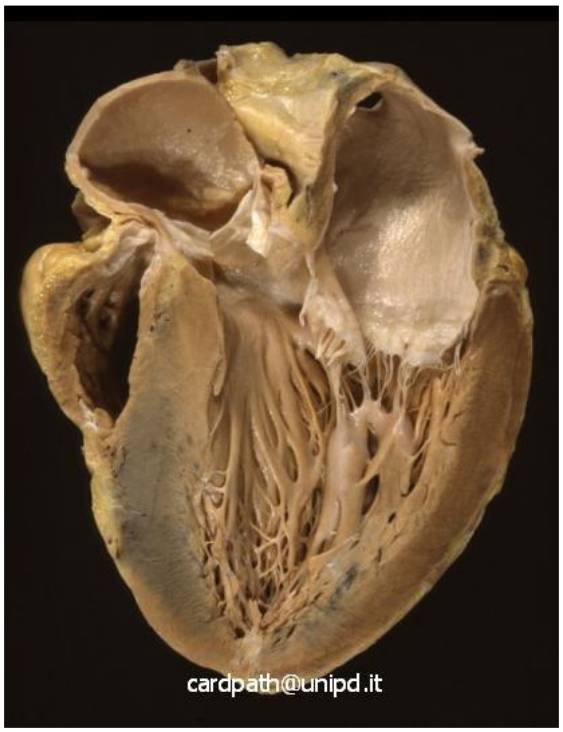
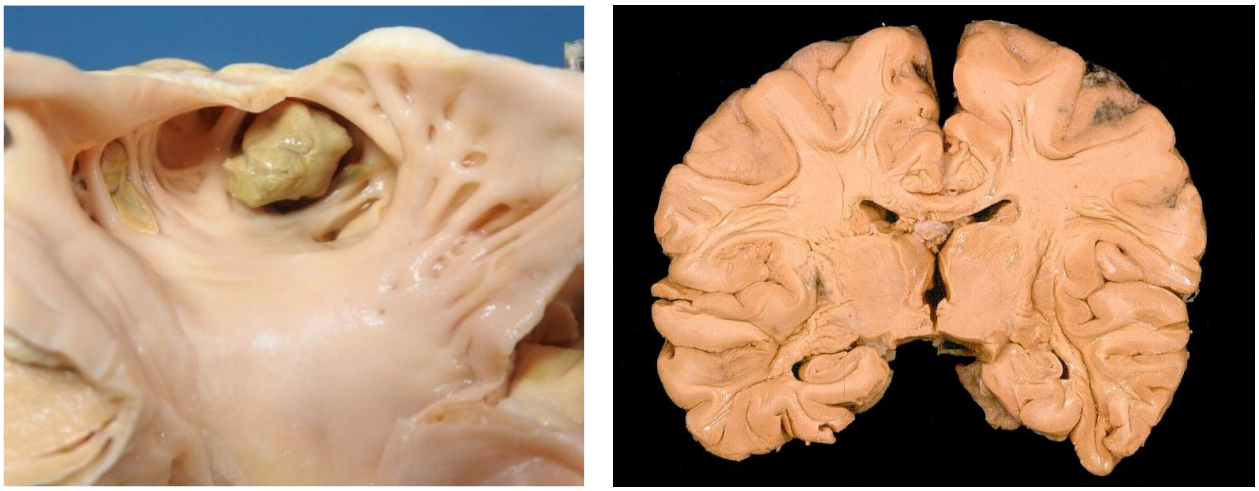
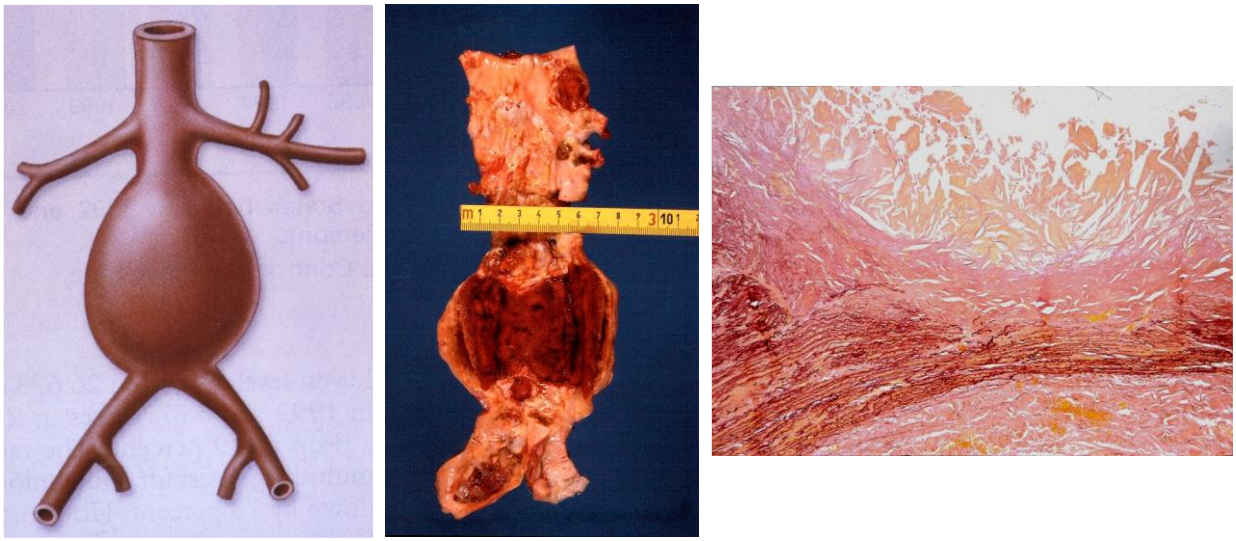


Fig. 3



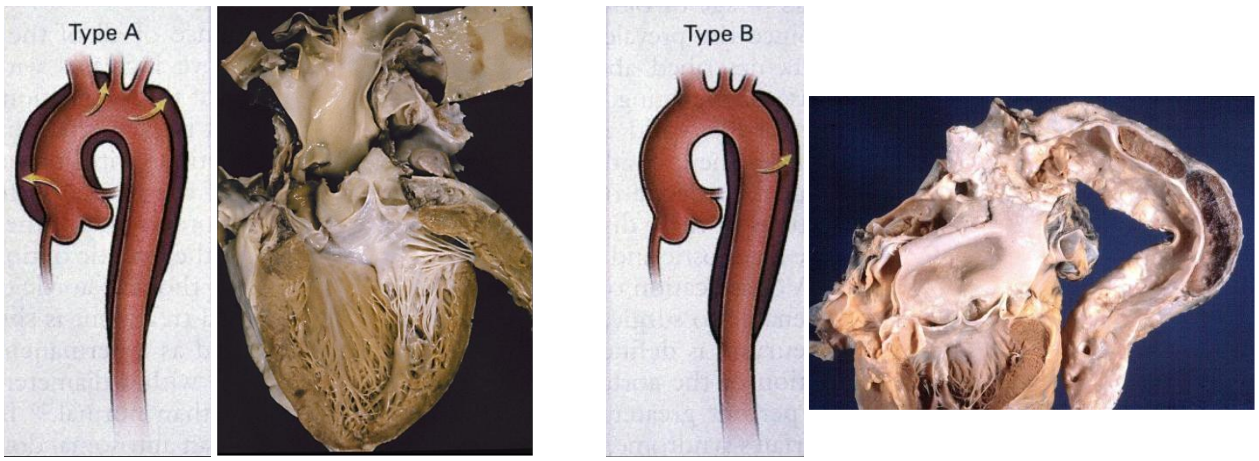
a b

Fig. 4



a b c

Fig. 5



a b

Fig. 6

a

b

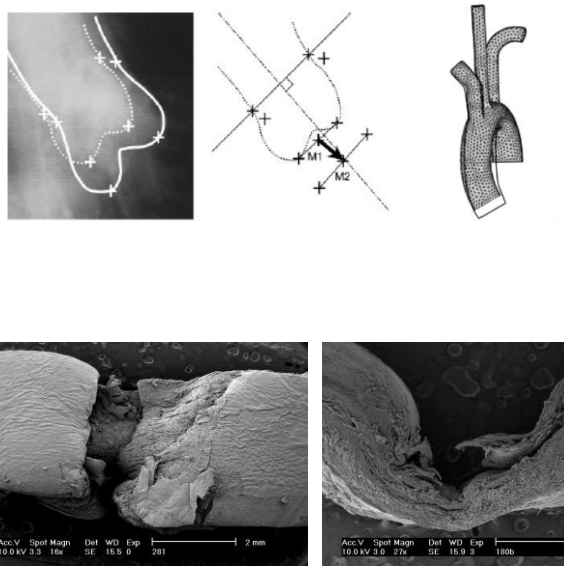


Fig. 7

Erdheim's Medial Necrosis

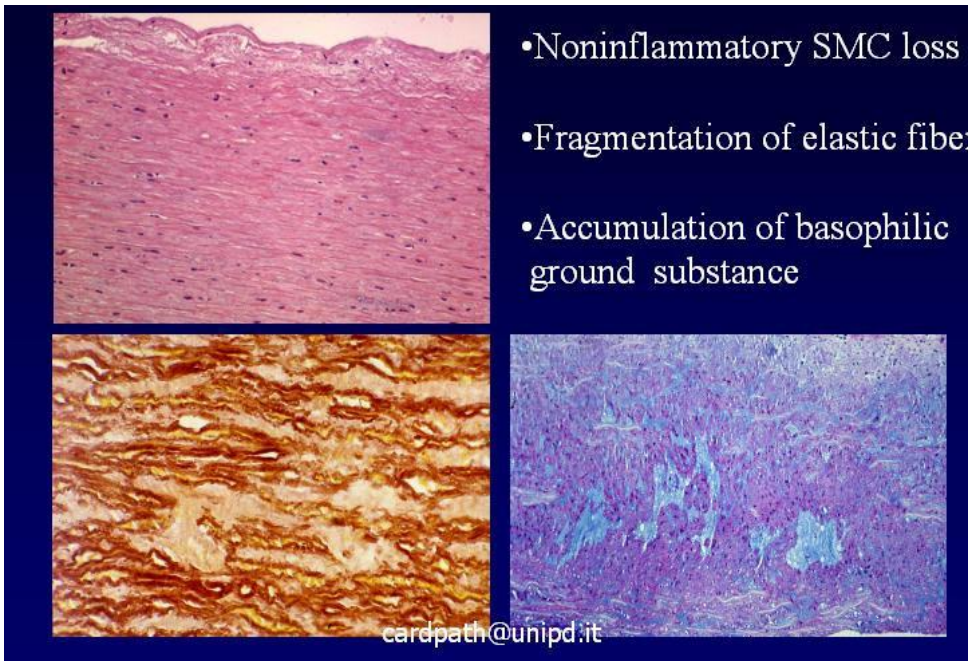
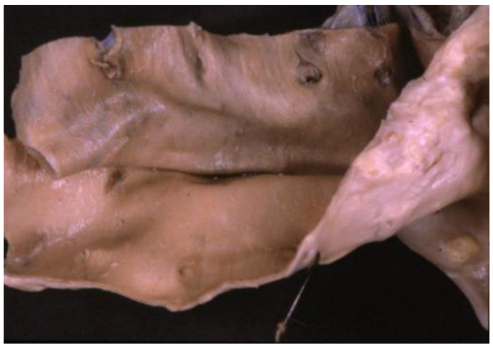
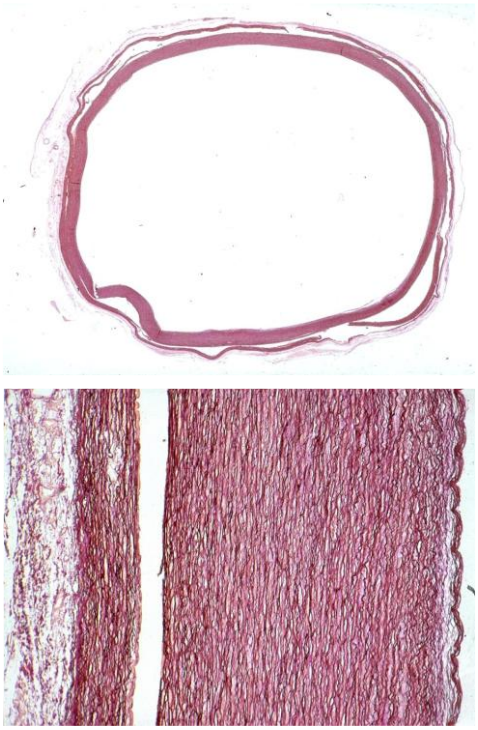


Fig. 8



a

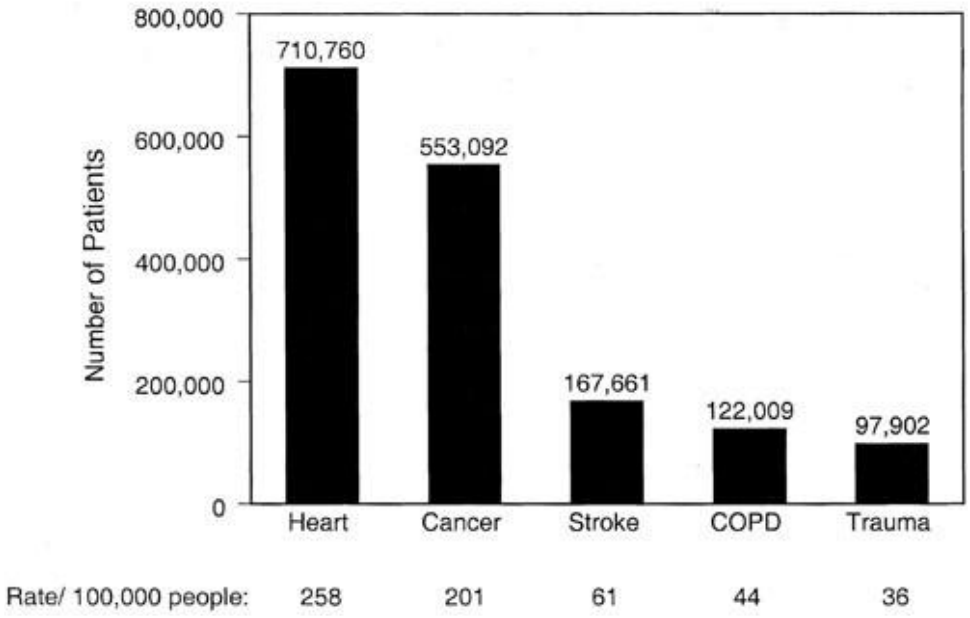


b c

Fig. 9

a b

Fig. 10



from Topol EJ - Circulation 2003;108:III-6-III13

Fig. 11

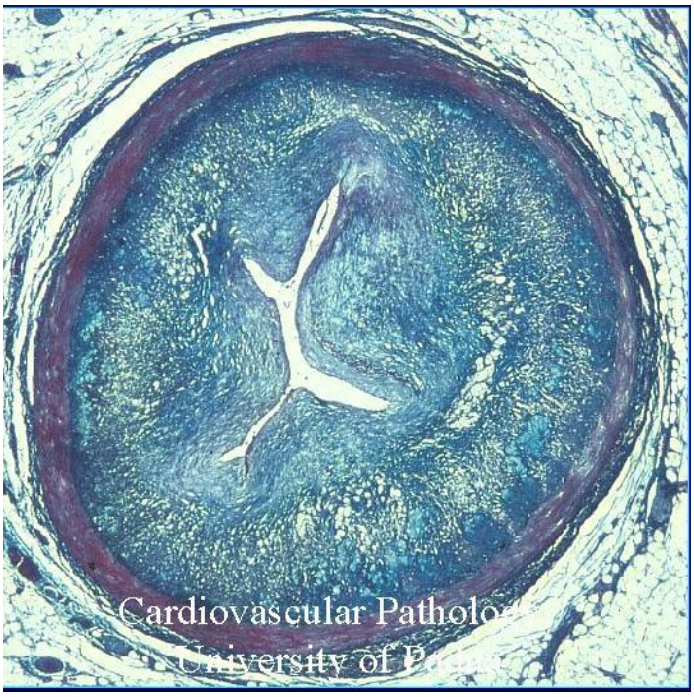
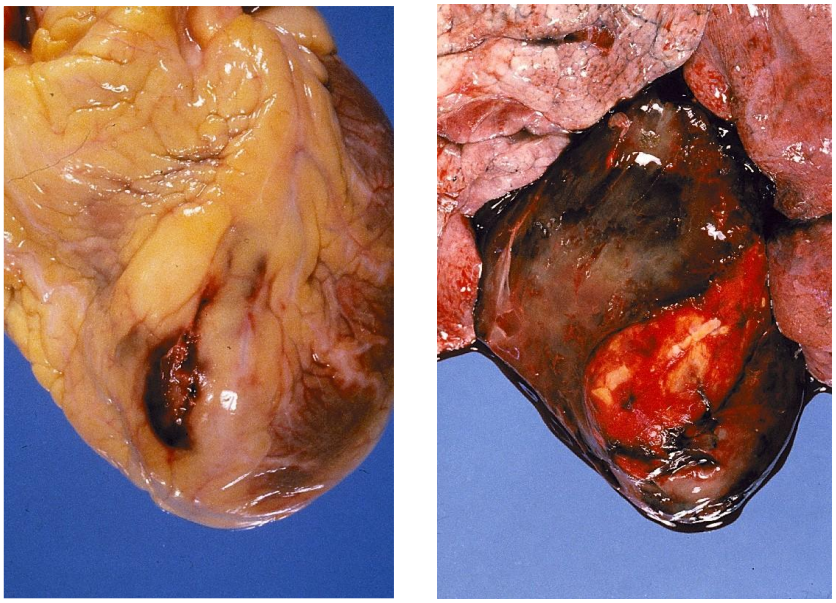
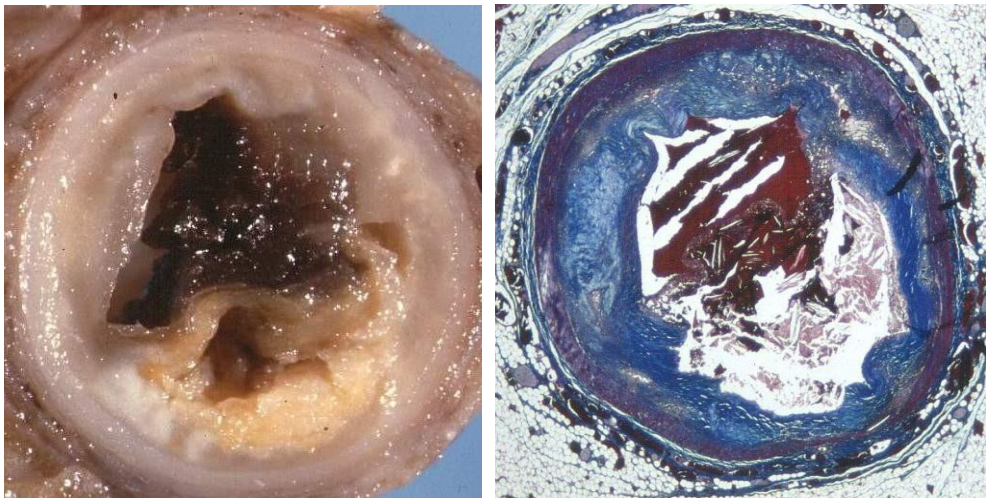


Fig. 12



a b

Fig. 13



a b

Fig. 14

Desmond Julian (1926-)
***Coronary Care Unit*, 1961**

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

Fig. 15

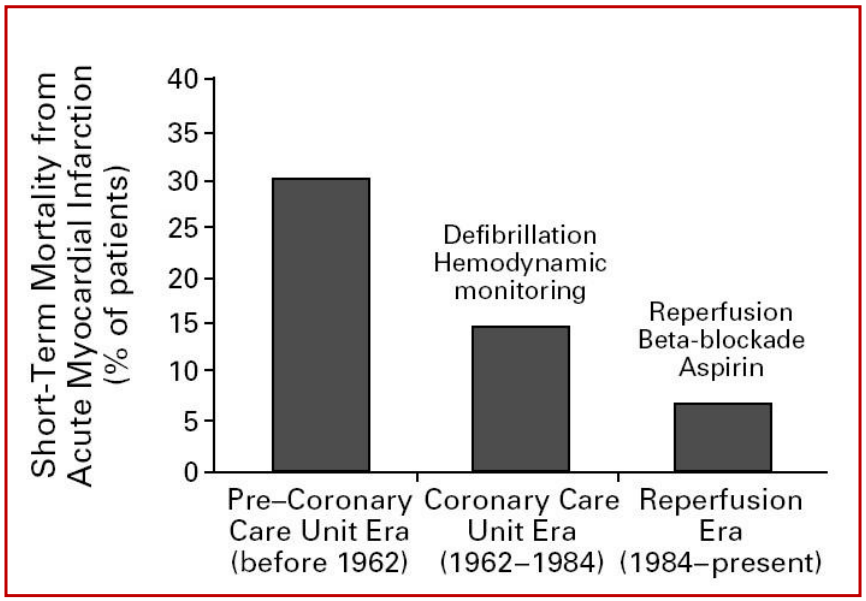


Fig. 16

Michel Mirowski (1924-1990) invents implantable defibirllator in 1980

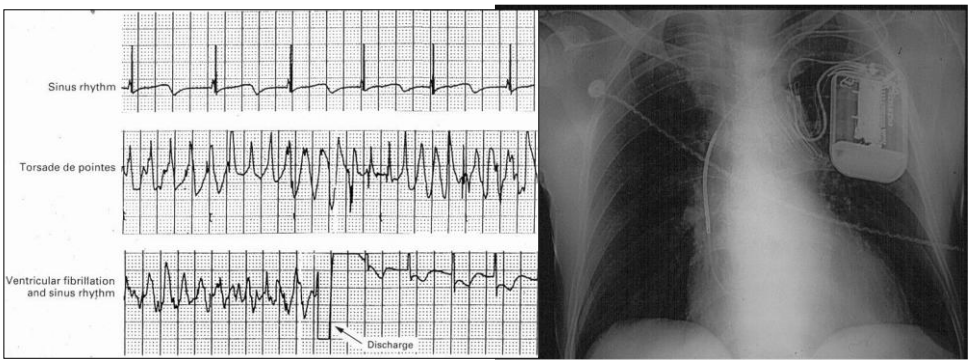
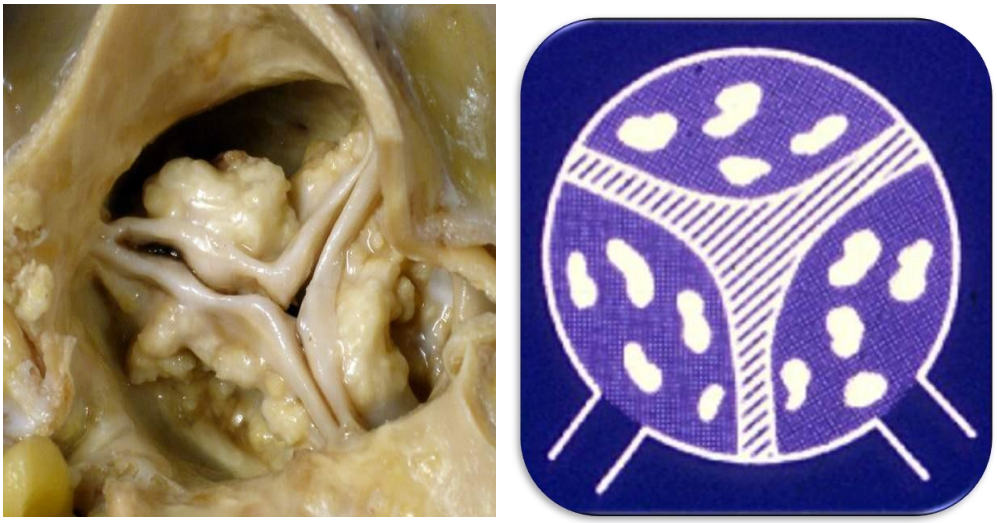
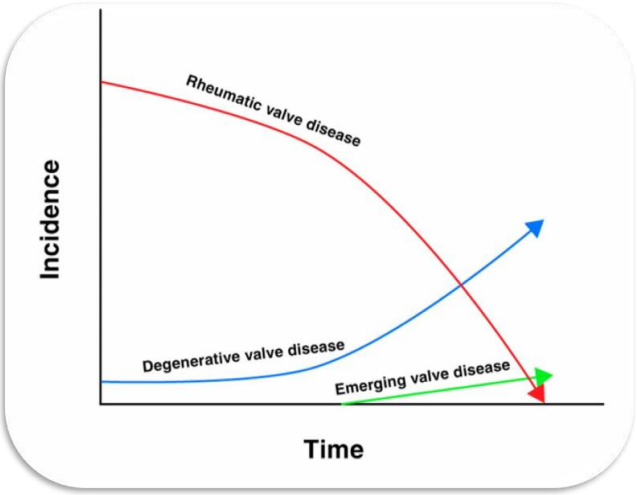


Fig. 17



a b

Fig. 18



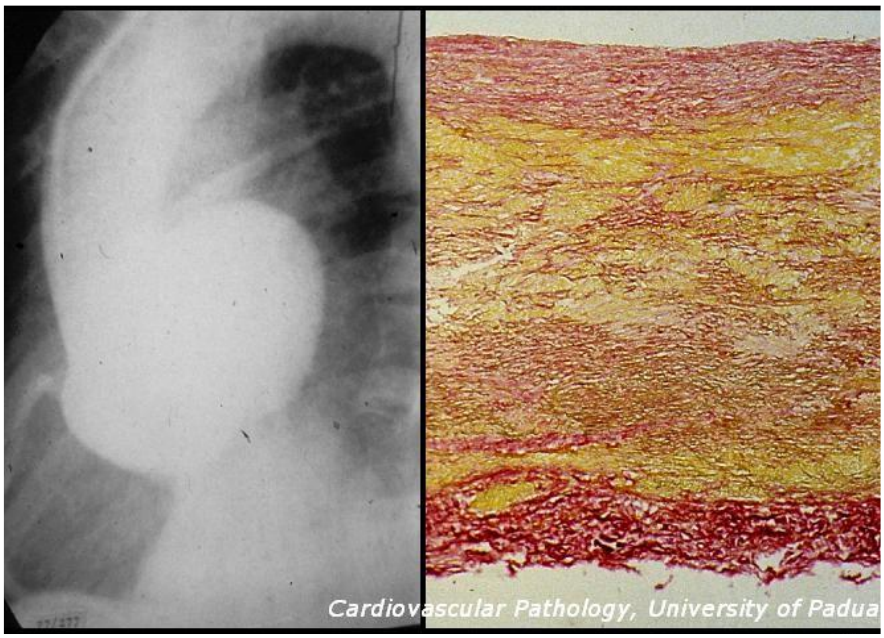
Soler-Soler, Heart 2002

Fig. 19

IN 1832, D. J. Corrigan of Dublin published his article entitled "Permanent Patency of the Mouth of the Aorta."

Frater R.W.M., Circulation 74 (suppl. I), I: 136-141,1986

Fig. 20



a b

Fig. 21

a

b

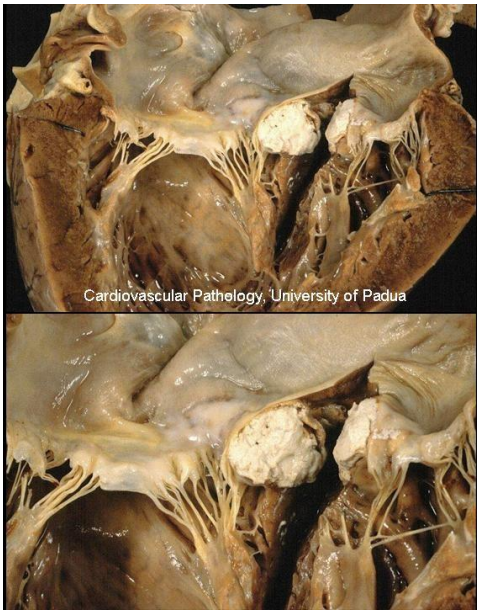
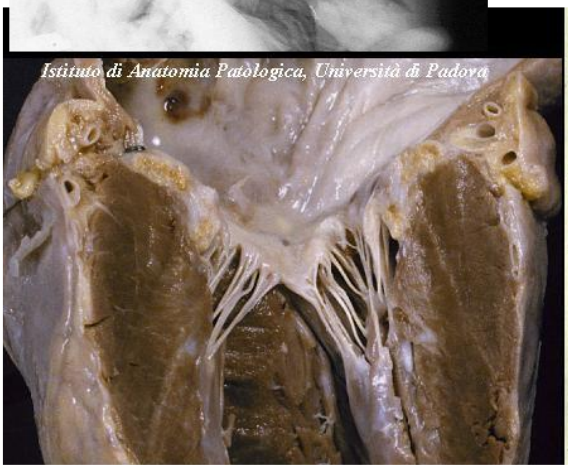


Fig. 22

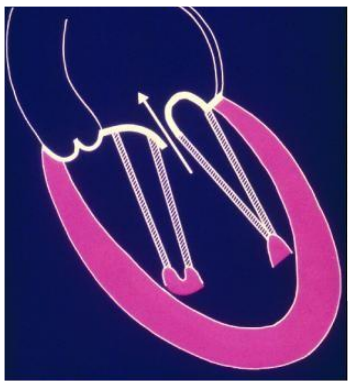
a

b

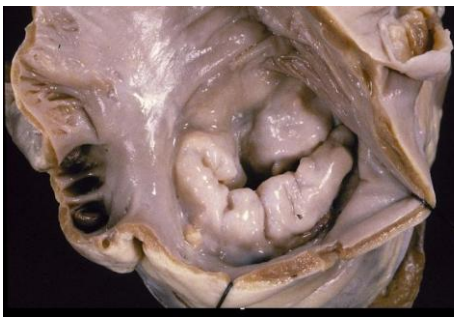


c

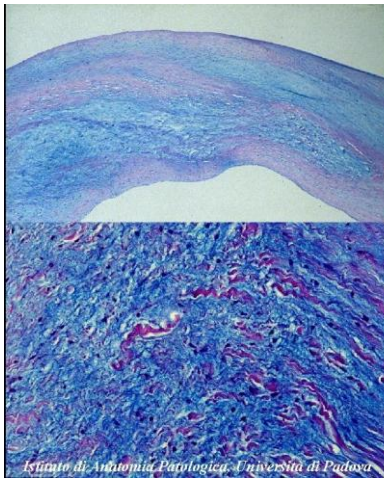
Fig. 23



a

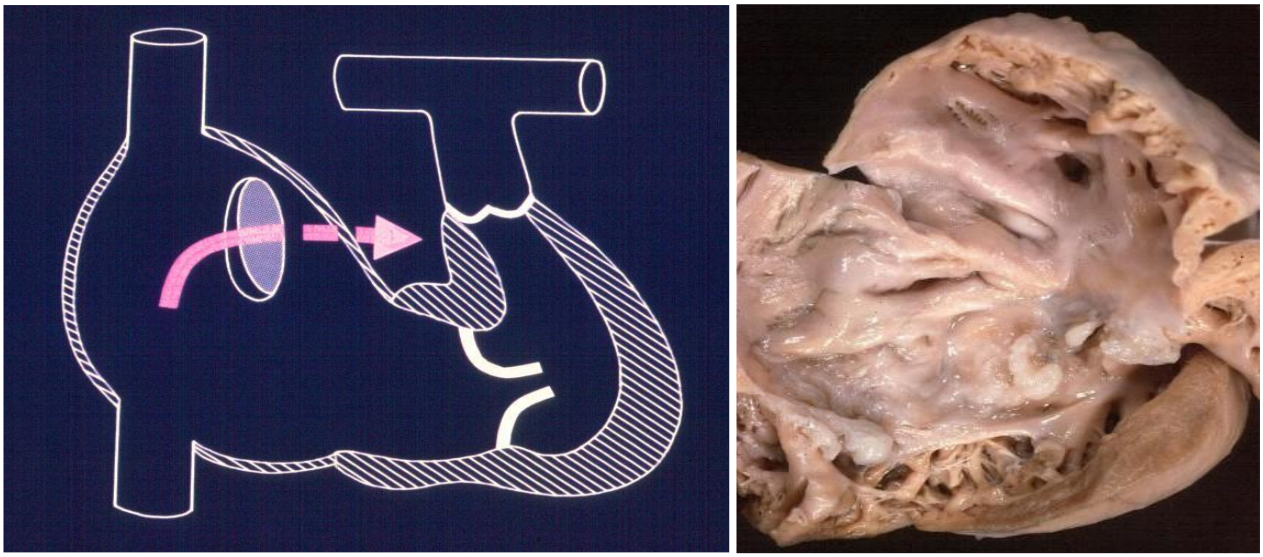


b



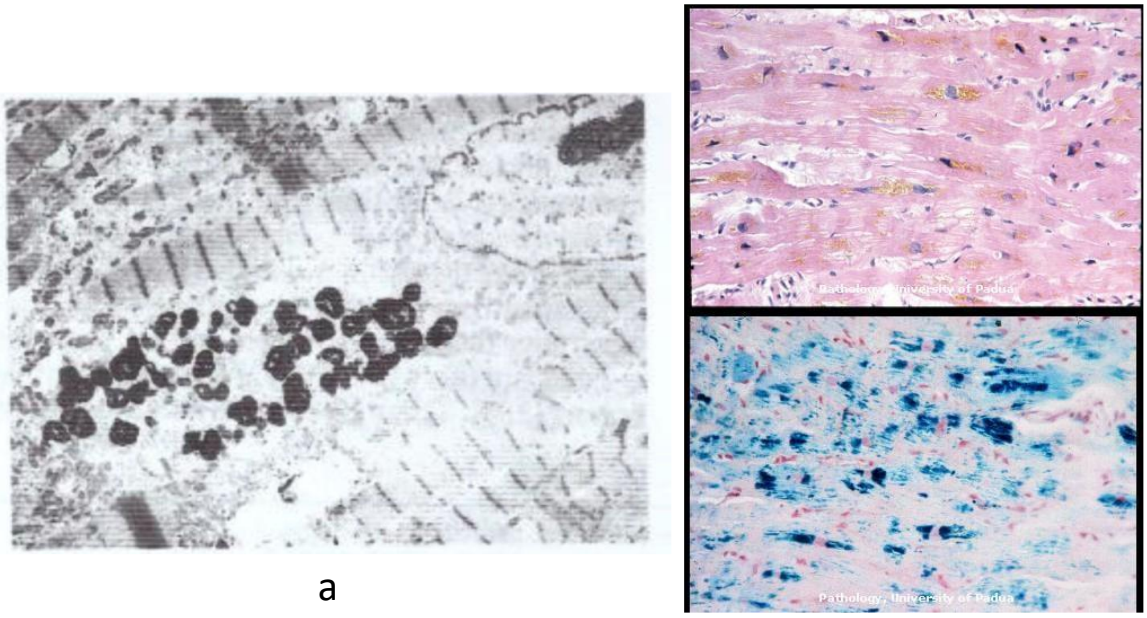
c

Fig. 24



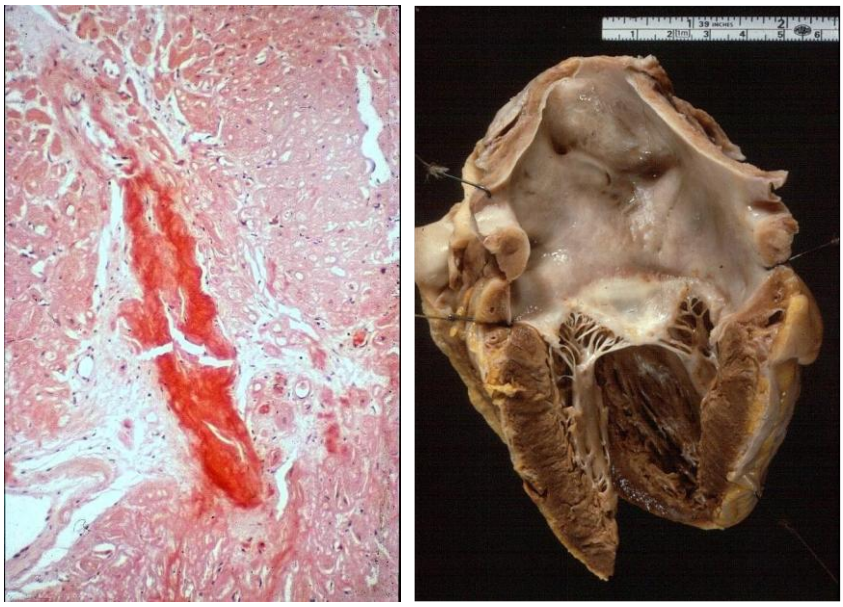
a b

Fig. 25



a b

Fig. 26

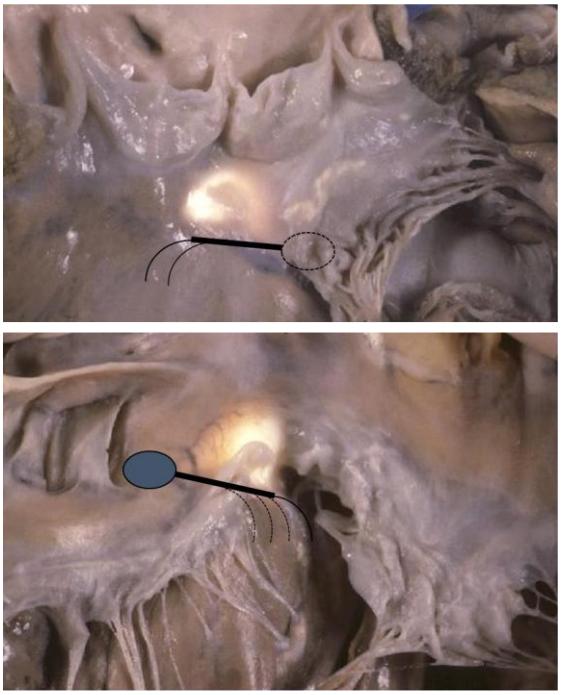


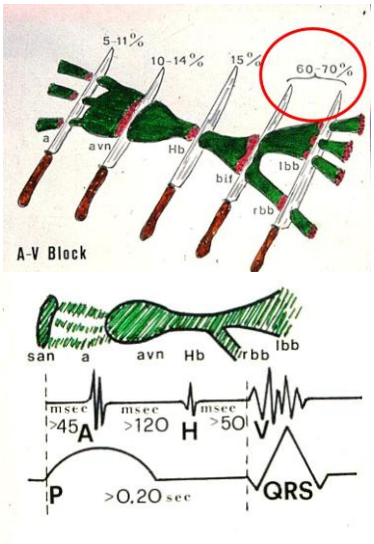
a b

Fig. 27

a

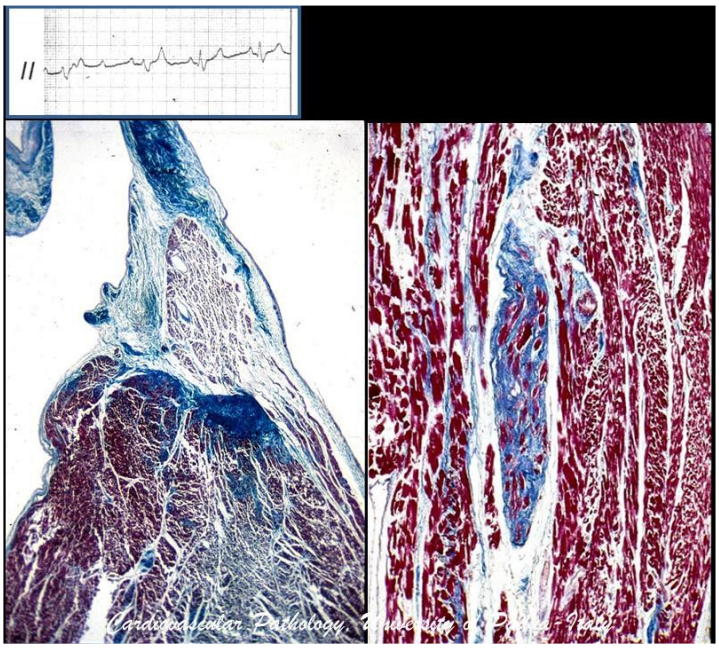
b





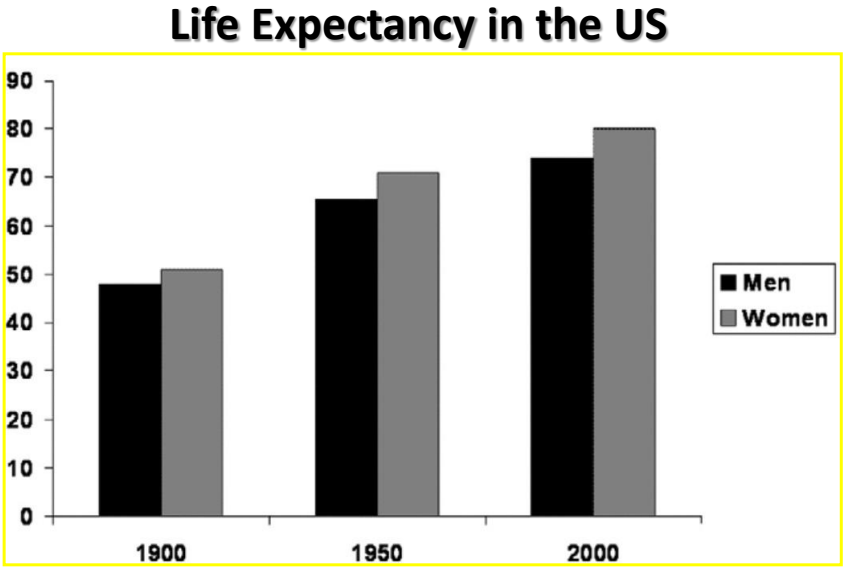
c

Fig. 28



a b

Fig. 29



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

Fig. 30

JW Black DW Cushman MA Ondetti A.Endo

Cardiovascular Pharmacology: a mine of Nobel prizes

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

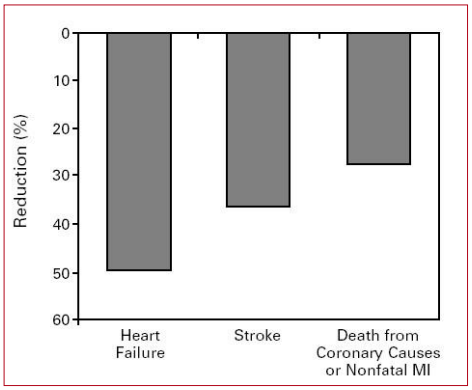


Fig. 31

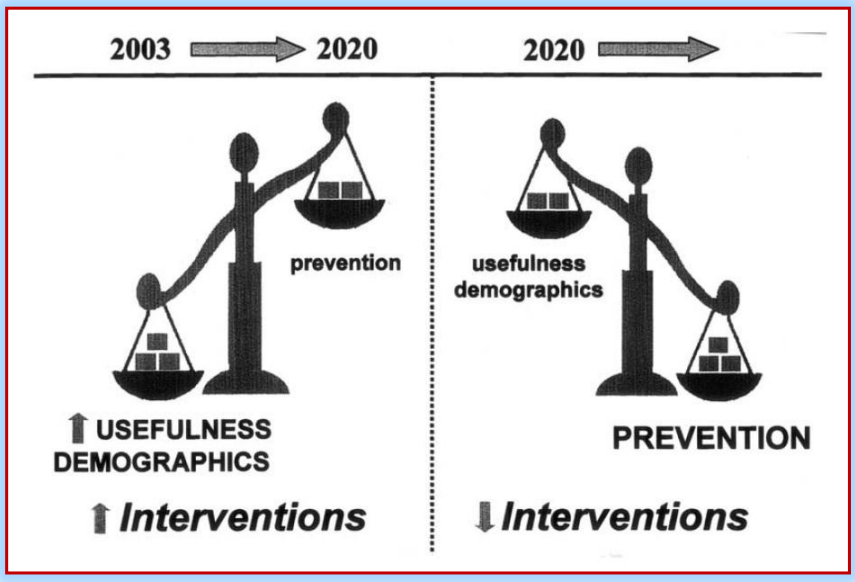
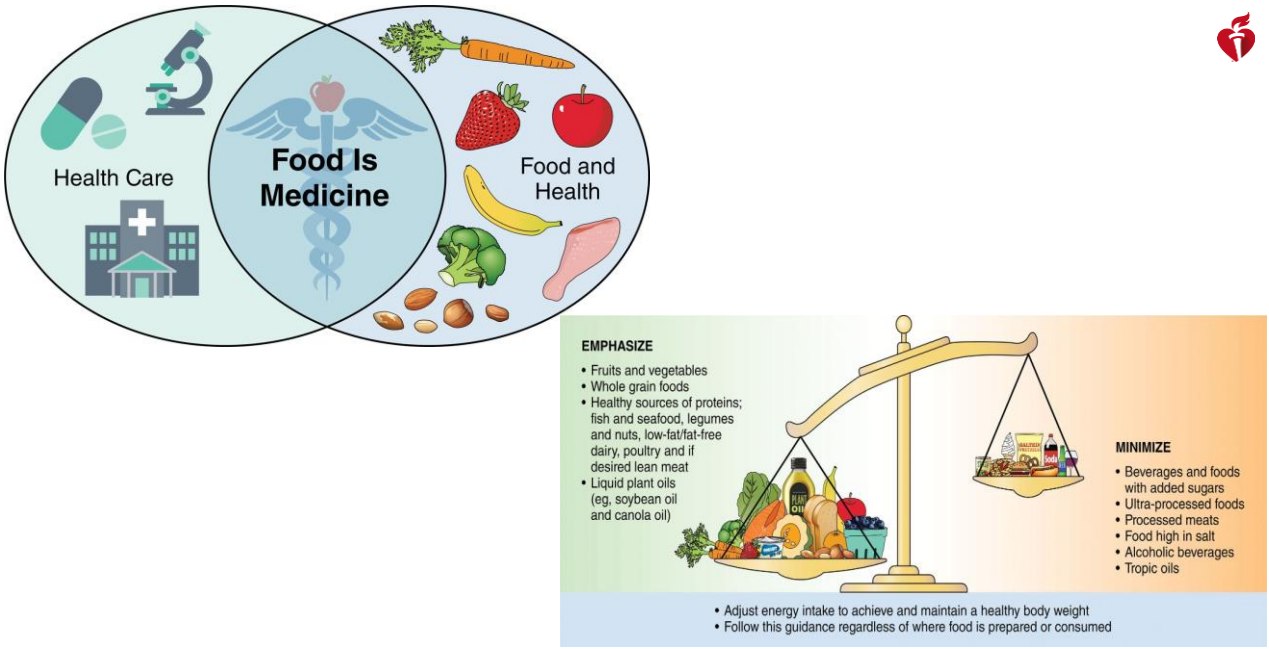


Fig. 32



Kevin G. Volpp . Circulation. Food Is Medicine: A Presidential Advisory From the American Heart Association, Volume: 148, Issue: 18, Pages: 1417-1439, DOI: (10.1161/CIR.0000000000001182)

Fig. 33

REFERENCES

1. Topol EJ. Current status and future prospects for acute myocardial infarction therapy. Circulation. 2003 Oct 21;108(16 Suppl 1):III6-13.
2. Jonas RA. Rewards, risks, and responsibilities of globalization for the cardiothoracic surgeon. J Thorac Cardiovasc Surg. 2007 Jul;134(1):1-14.
3. Braunwald E. Shattuck lecture--cardiovascular medicine at the turn of the millennium: triumphs, concerns, and opportunities. N Engl J Med. 1997 Nov 6;337(19):1360-9.
4. Schroeder SA. Shattuck Lecture. We can do better--improving the health of the American people. N Engl J Med. 2007 Sep 20;357(12):1221-8.
5. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, Giles WH, Capewell S. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med. 2007 Jun 7;356(23):2388-98.
6. Braunwald E. Will primordial prevention change cardiology? Eur Heart J. 2023 Sep 14;44(35):3307-3308.
7. Kuehn BM. Novel Approaches Expand Access to Cardiovascular Preventive Care. Circulation. 2021;143(16):1629-1630.
8. Wang DD, Li Y, Bhupathiraju SN, et al. Fruit and Vegetable Intake and Mortality: Results From 2 Prospective Cohort Studies of US Men and Women and a Meta-Analysis of 26 Cohort Studies. Circulation. 2021;143(17):1642-1654.
9. Subirana MT, Juan-Babot JO, Puig T, Lucena J, Rico A, Salguero M, Borondo JC, Ordóñez J, Arimany J, Vázquez R, Badimon L, Thiene G, de Luna AB. Specific characteristics of sudden death in a mediterranean Spanish population. Am J Cardiol. 2011 Feb 15;107(4):622-7.
10. Thiene G. Longevity and Prevention: Can the Heart Become Centenary? Bulletin of the European Association of Professors Emeriti. Pp. 89-93. ISSN 2945-0381