HEART DISEASES
Myocarditis, cardiomyopathy

Pavel Maruna
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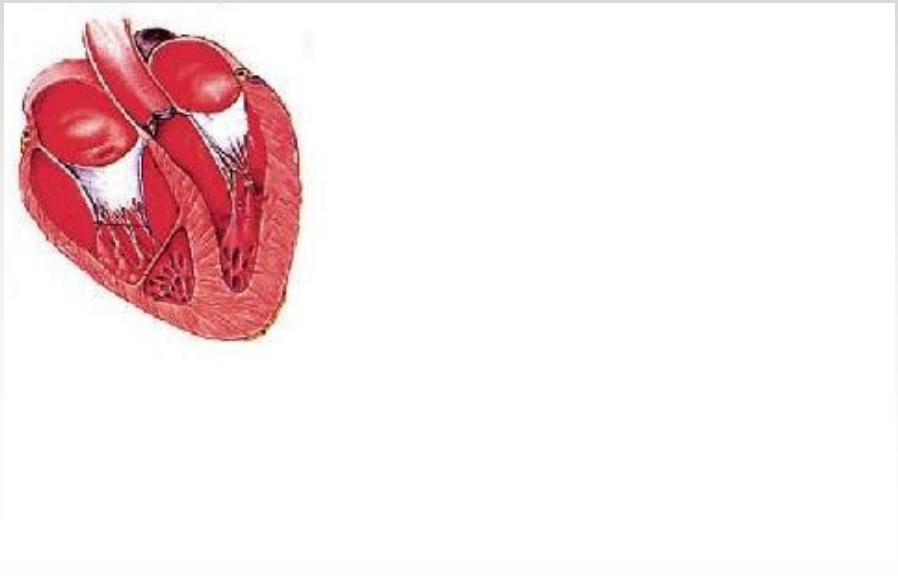


Cardiomyopathy

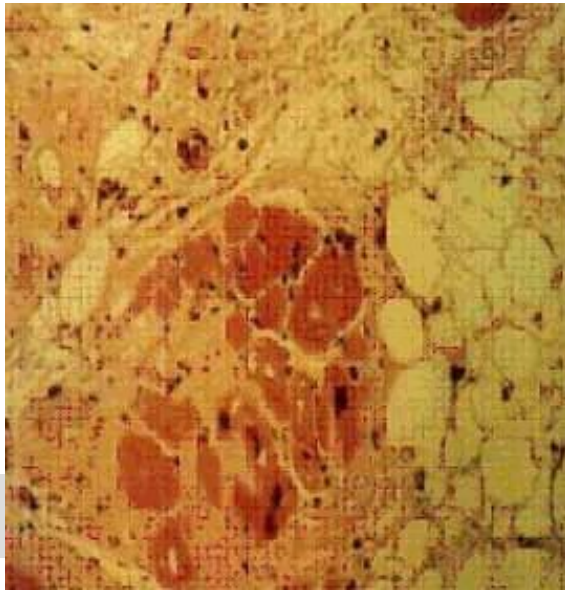
Definition:

= chronic disorder of myocardium with abnormal ventricular both function and morphology
weakening of the heart muscle or a change in heart muscle structure
prolonged course, slow progression

Pathogenesis:

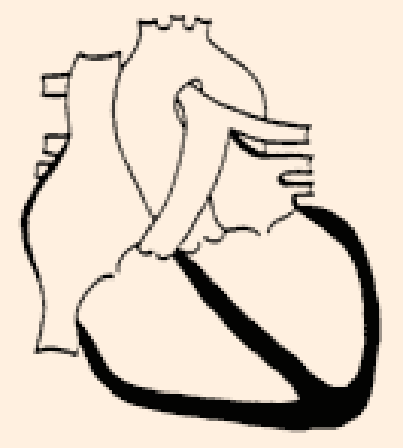
“universal” reaction of cardiac muscle on various noxa

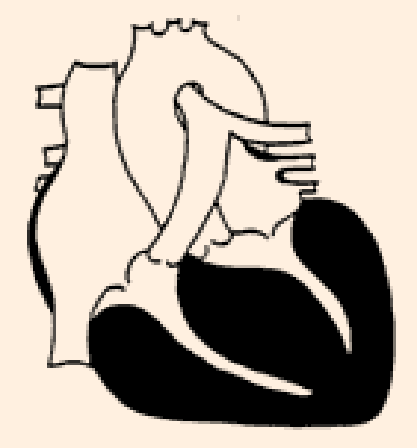
→ inflammation, hypertrophy, degeneration, necrosis, fibrosis
→ accumulation of lipids, glycogen, amyloid

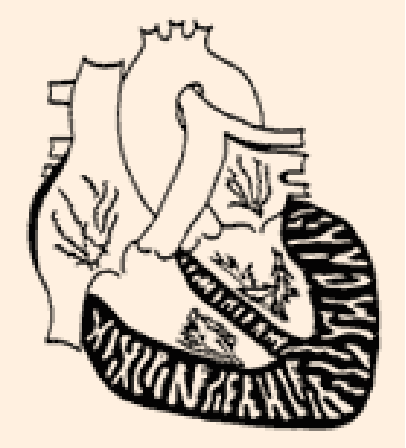


Lipoid deposits in myocardium

Cardiomyopathy



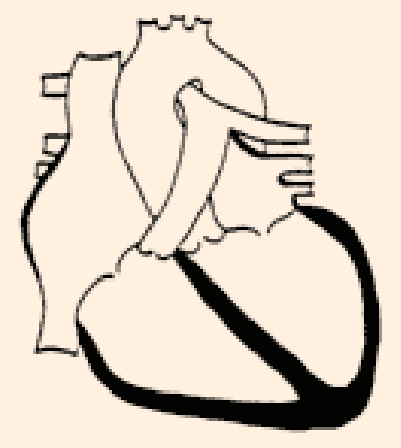


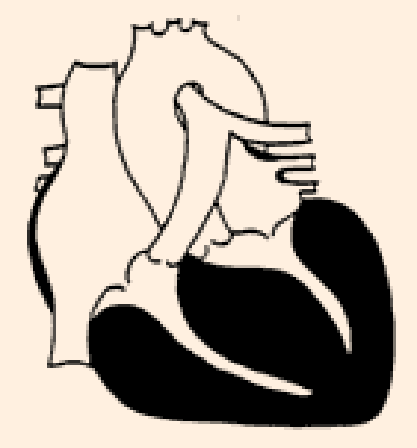


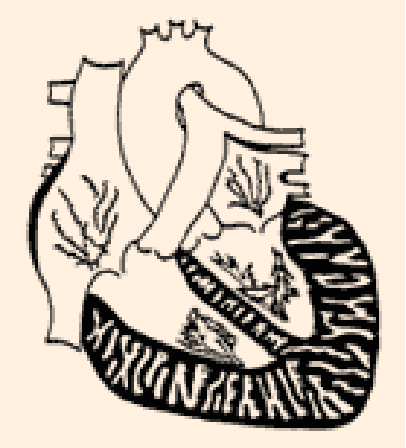
Dilated CM

- destruction of muscle fibers
- dilatation without hypertrophy

Cardiomyopathy



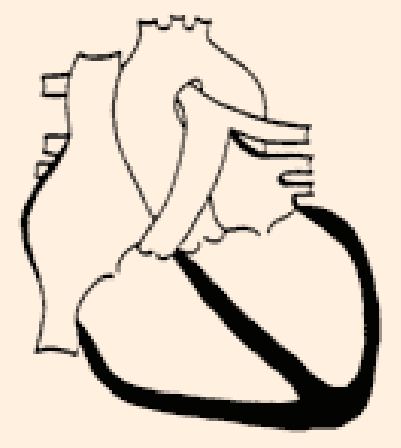


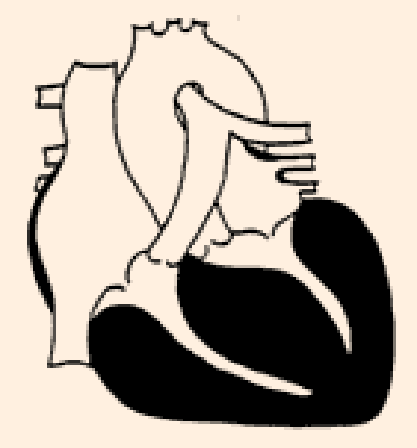


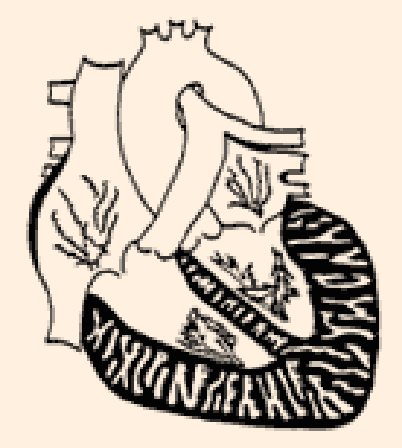
Hypertrophic CM

- **asymmetric hypertrophy**
- **obstruction of LV offtake**

Cardiomyopathy







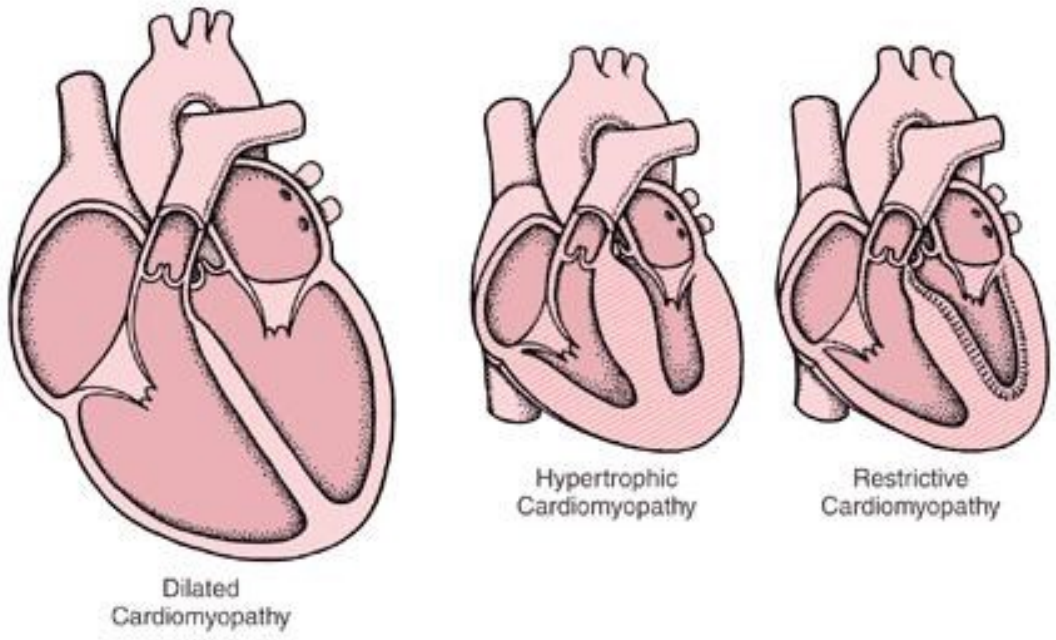
Restrictive CM

- **subendocard. fibrosis**
- **arrhythmia**

Cardiomyopathy

Primary:

Genetic factors, worse prognosis
(must be excluded ischemia, hypertension, congenital + acquired cardiac defects)



Cardiomyopathy

Secondary:

infectious

- **bacterial**
- **viral (coxsackie)**
- **ricketsia**
- **mycosis**
- **parasitic (Chagas dis.)**

toxic (alcohol, Co, narcotics, psychofarmacs, adriamycin, prokainamid)

endocrine / metabolic (↓T4, ↑T4, ↑GH, uremia, ↓vit.B1, K, Mg)

allergy, autoimmunity (immunocomplex., SLE, sarkoidosis…)

Myocardial changes

DO NOT result from the hemodynamic changes (e.g. those which react as a compensation of the heart failure)

ARE THEMSELVES a cause of the hemodynamic disturbances and of the heart failure

TABLE 1

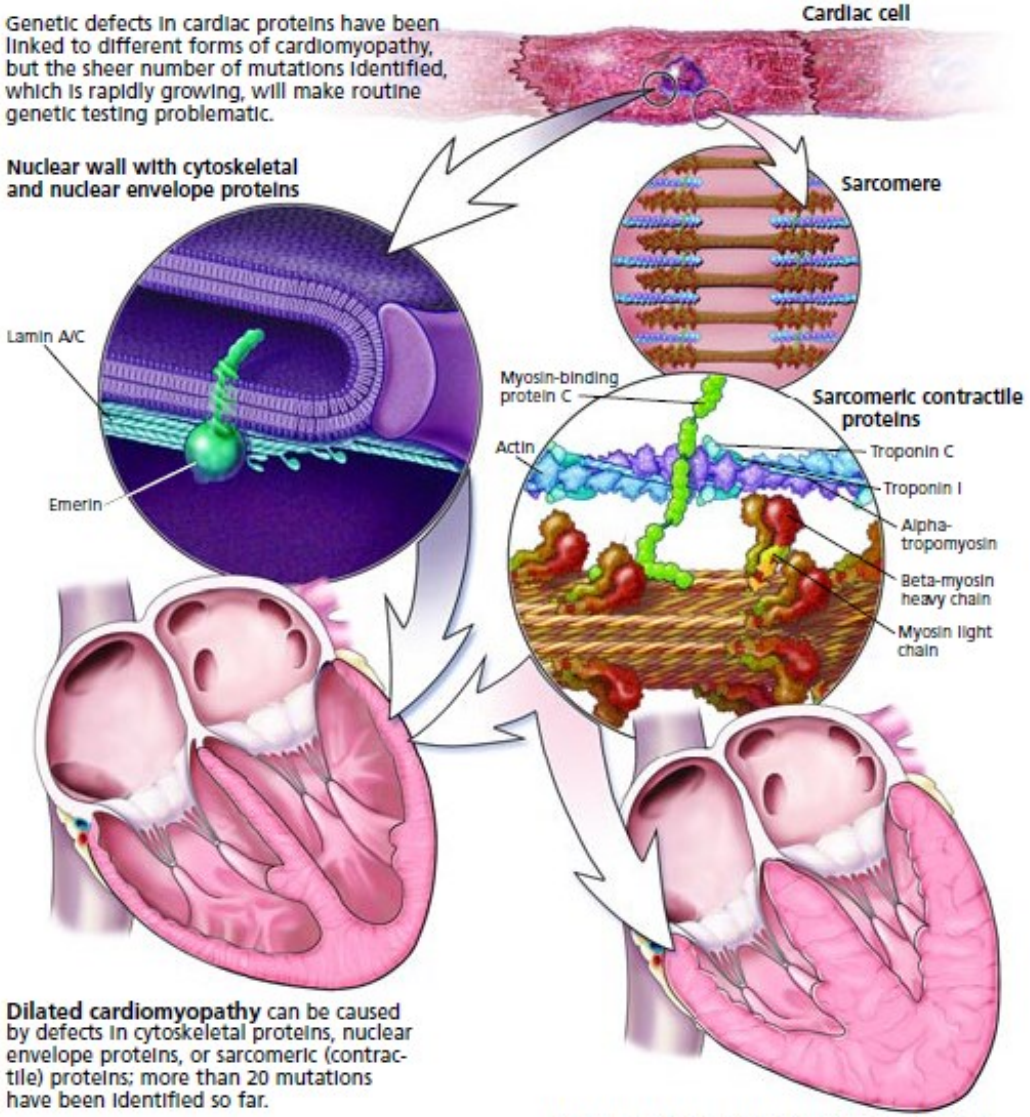
Characteristics and prevalence of the cardiomyopathies vs hypertension, a common cardiovascular condition

DISORDER	PRESENTING SYMPTOMS	ECHOCARDIOGRAPHIC FINDINGS	PREVALENCE	GENE IDENTIFIED
Hypertrophic cardiomyopathy	Chest pain Arrhythmias Dyspnea	LV hypertrophy	1:500	10 genes, > 200 mutations
Dilated cardiomyopathy	Heart failure Arrhythmias	RV or LV dilatation	1:2,500	15 genes, > 20 mutations
Arrhythmogenic RV cardiomyopathy	Arrhythmias Heart failure	RV dilatation and dysfunction	1:1,000 to 1:5,000?	3 genes, > 8 mutations
Restrictive cardiomyopathy	Dyspnea Heart failure	LV stiffness Enlarged atria	Unknown	1 gene, 5 mutations
Systemic hypertension	Hypertension Dyspnea	Can cause LV hypertrophy	1:4	Mostly complex traits

LV = left ventricular, RV = right ventricular

The molecular basis of cardiomyopathy

Genetic defects in cardiac proteins have been linked to different forms of cardiomyopathy, but the sheer number of mutations identified, which is rapidly growing, will make routine genetic testing problematic.



Dilated cardiomyopathy can be caused by defects in cytoskeletal proteins, nuclear envelope proteins, or sarcomeric (contractile) proteins; more than 20 mutations have been identified so far.

Hypertrophic cardiomyopathy is caused by defects in sarcomeric contractile proteins; more than 200 mutations have been identified so far.

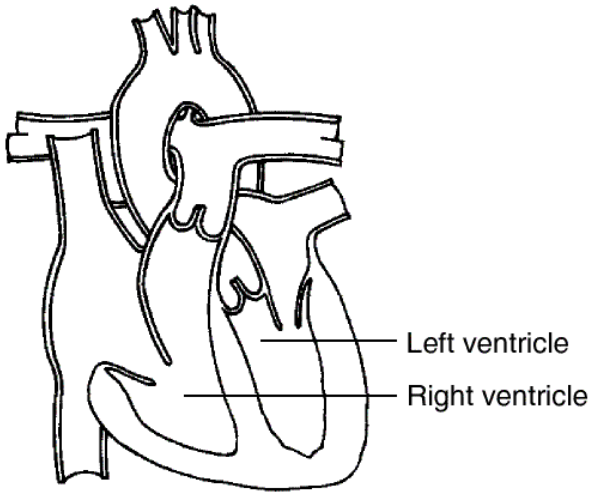
FIGURE 1

Dilated (congestive) CM

Characteristics:

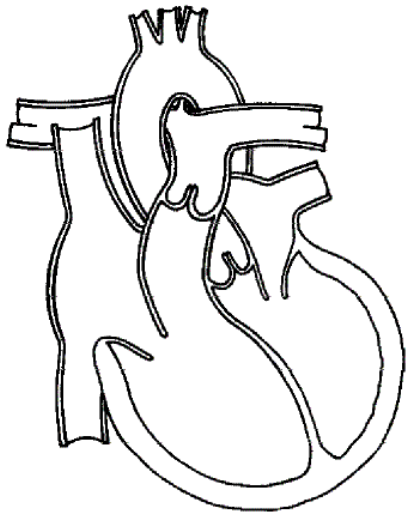
- **heart dilation (without hypertrophy), diffuse hypokinesis (systolic + diastolic dysfunction)**
- **(passive) pulmonary hypertension, right heart failure**
- **arrhythmia, blocks**

Normal Heart



Heart chambers relax and fill, then contract and pump.

Heart with Dilated Cardiomyopathy



Muscle fibers have stretched. Heart chamber enlarges

Dilated CMP

dilatation **of all heart with decreased contractility**
Decreased *systolic* function

low EF
high residual volume in the ventricle
increased EDV and lung congestion
decreased systolic volume and pressure

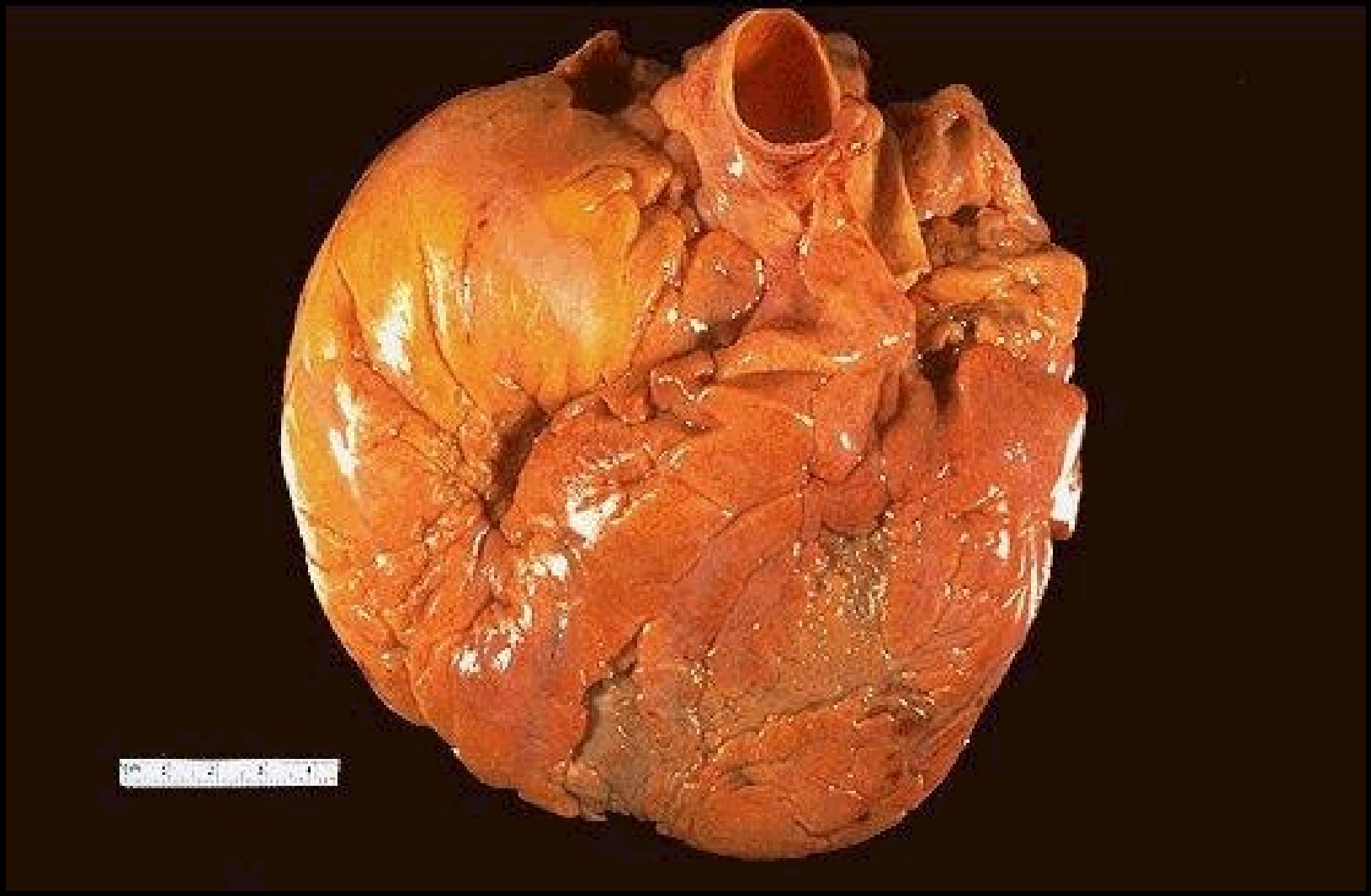
Dilated CMP

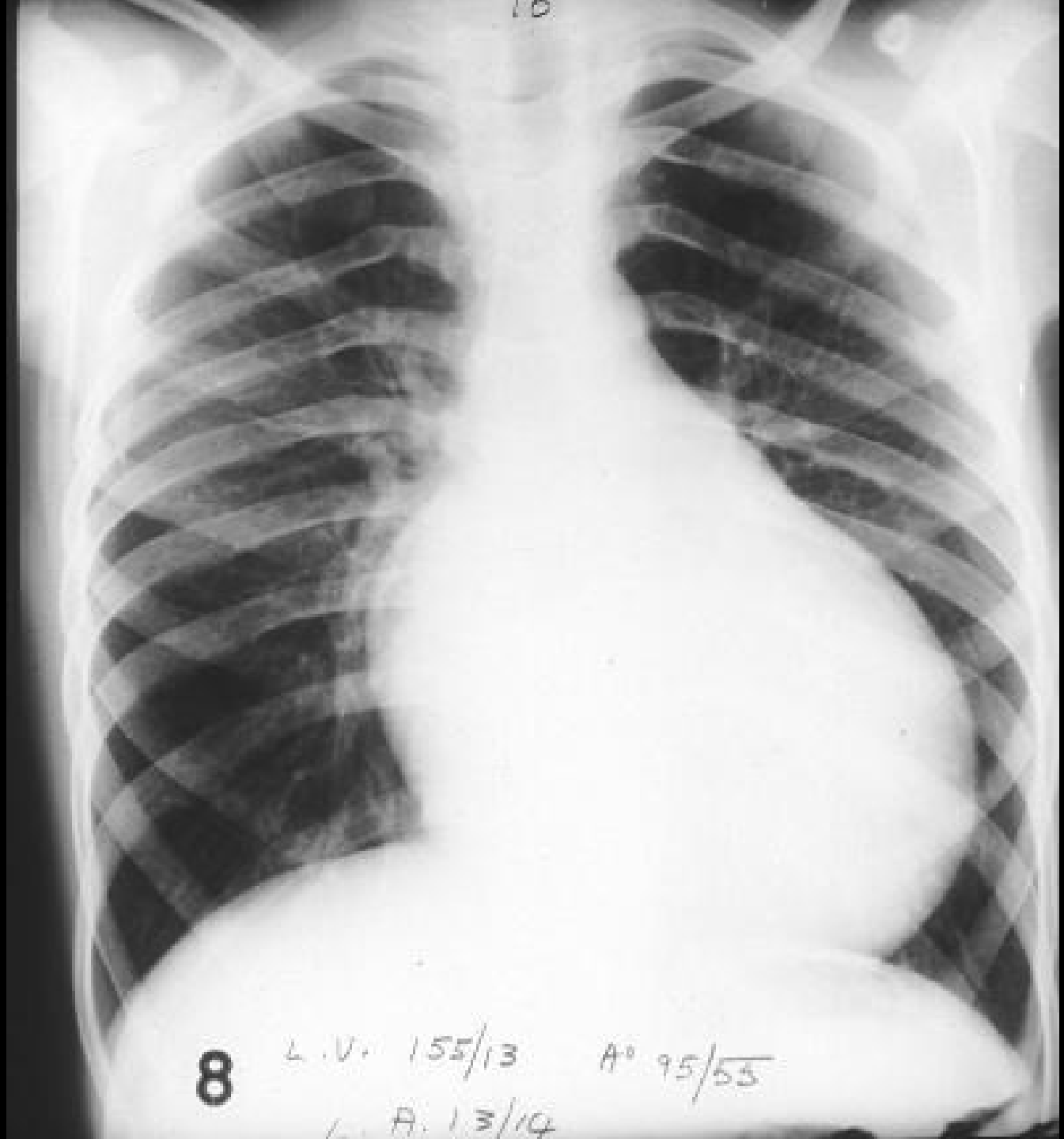
Symptoms typical for heart failure, symptoms both of
low cardiac output*, and *congestion

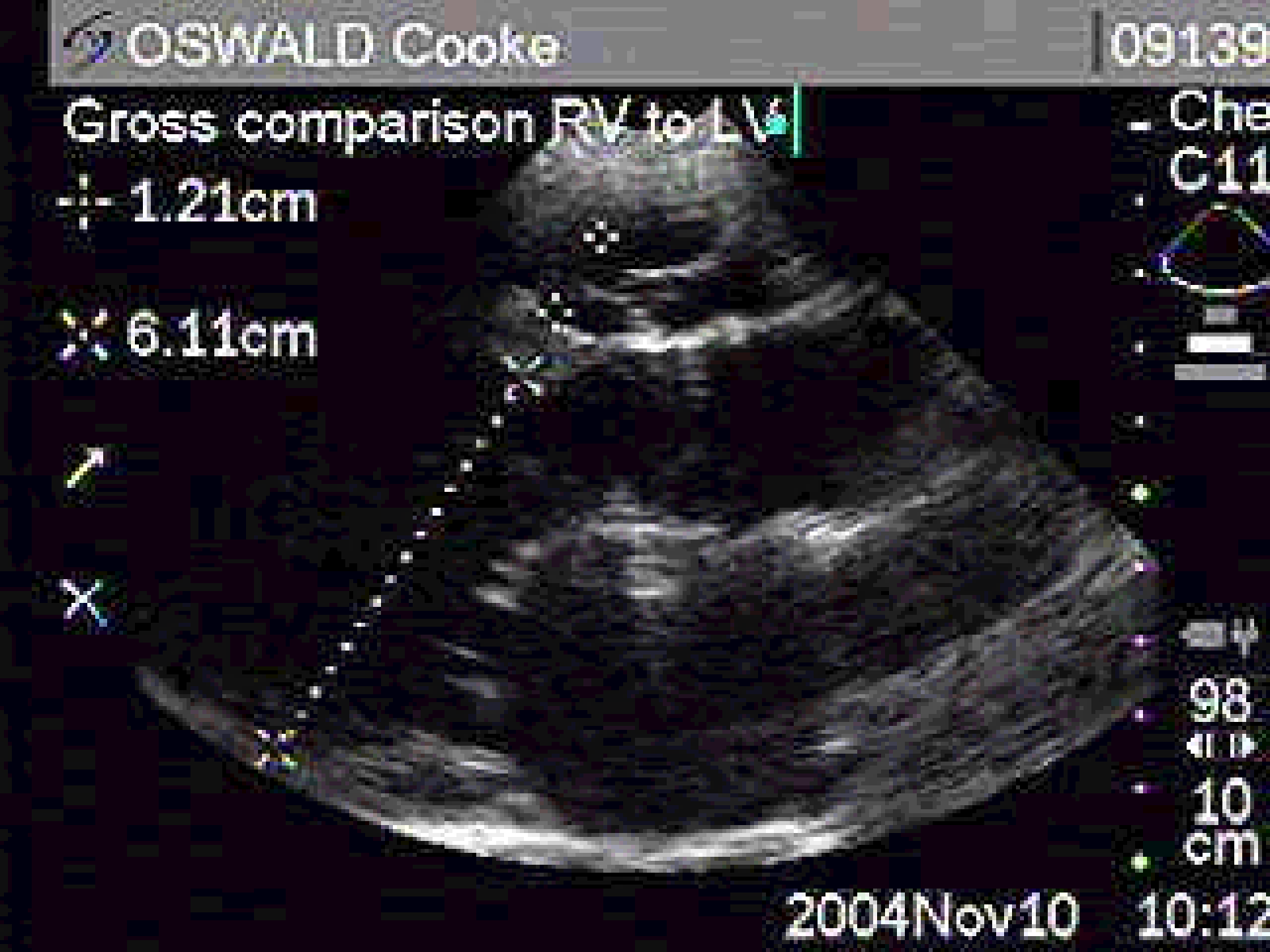
Frequent *arrhytmias* and
***thromboembolic* complications**

Relative valvular *regurgitation*

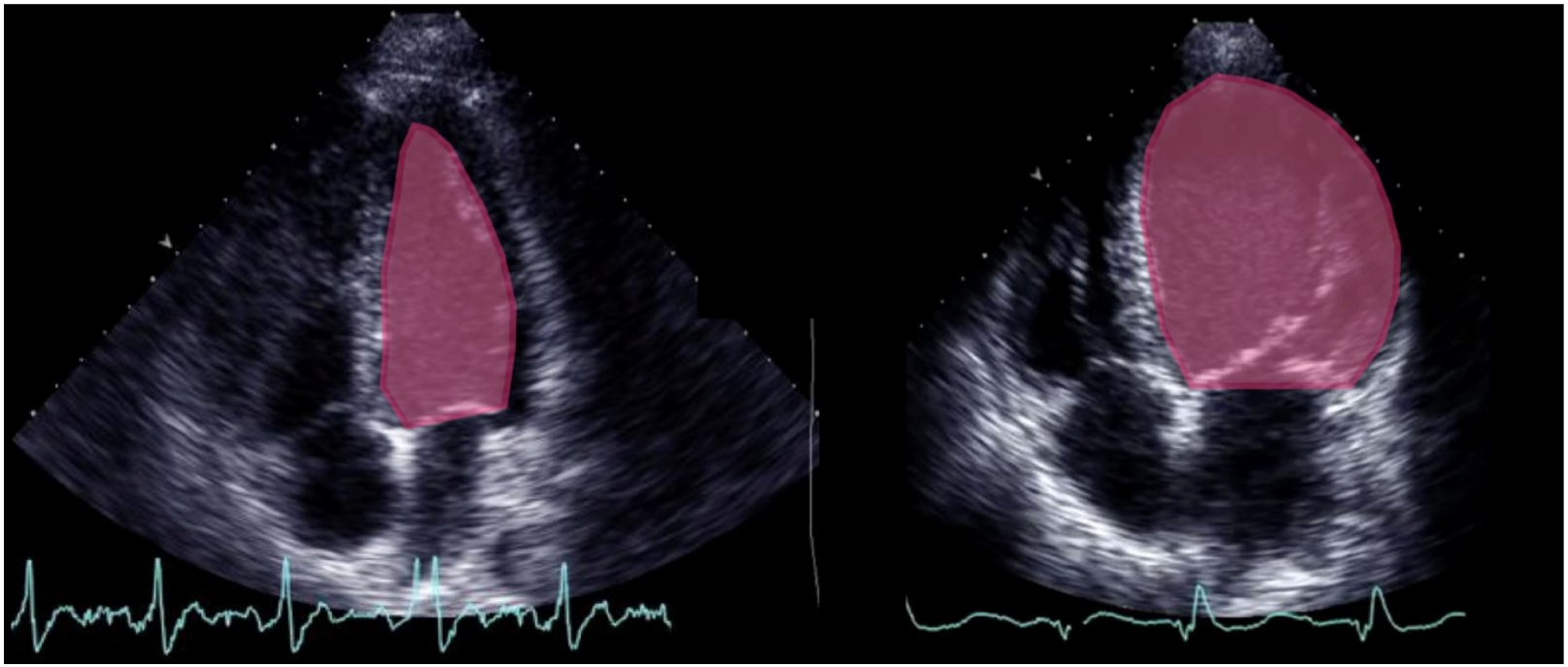
Dilated (congestive) CM




16
8
L.V. 155/13
A° 95/53
A. 13/14


OSWALD Cooke
09139
Gross comparison RV to LV
1.21cm
6.11cm
98
10
cm
2004Nov10
10:12

Echokardiografie



Causes of dilated CMP

*genetic (cytoskeletal proteins, myopathies…) – 30-50 %

- intoxication (alcohol, cytostatics, cobalt, drugs…)
- metabolic diseases
- autoimmune postinfectious mechanisms (sequelae of viral myocarditis, e.g. Coxsackie)
- other…

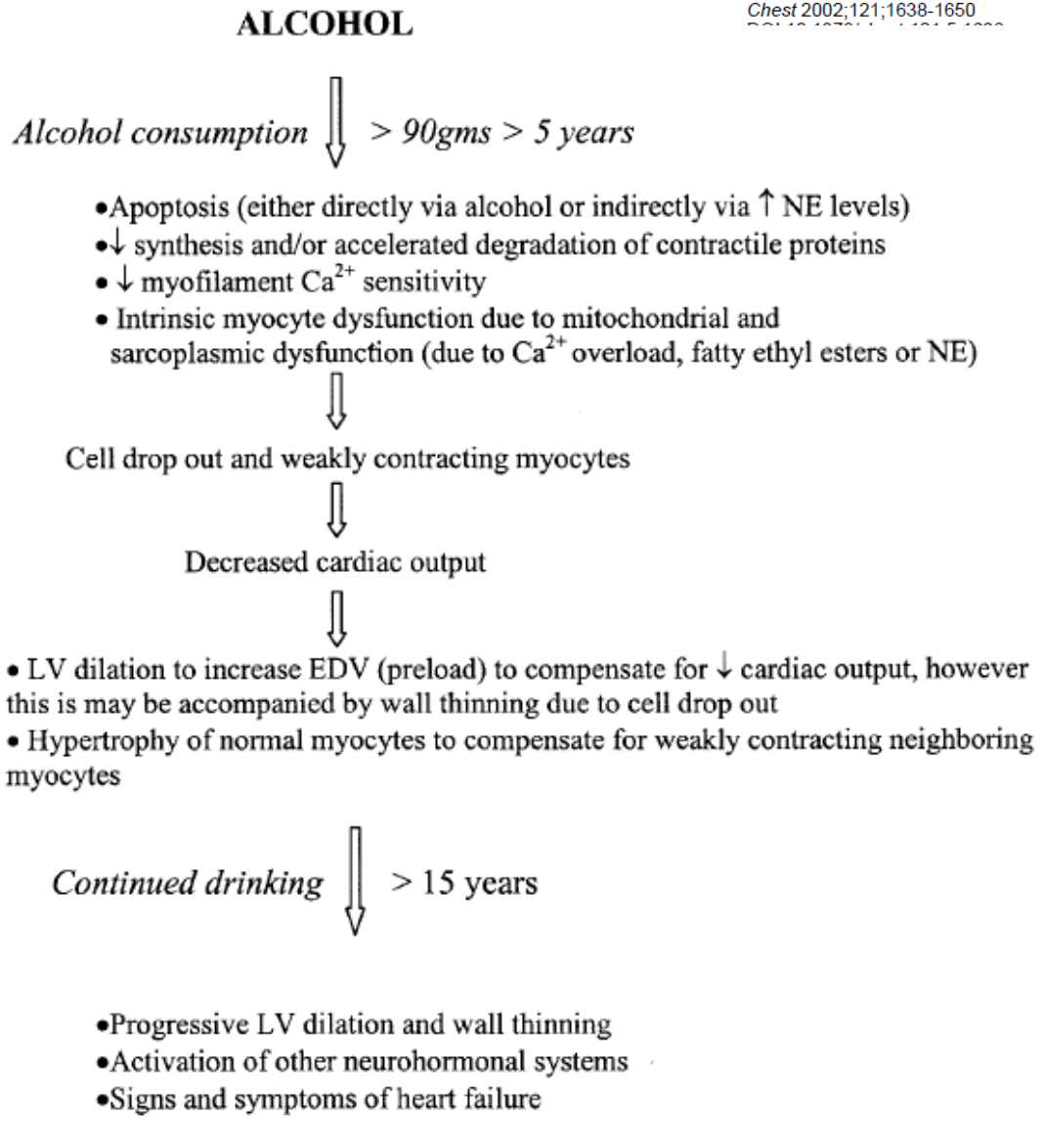


FIGURE 2. Proposed hypothetical schema for the pathogenesis of ACM. gms = grams; NE = norepinephrine.

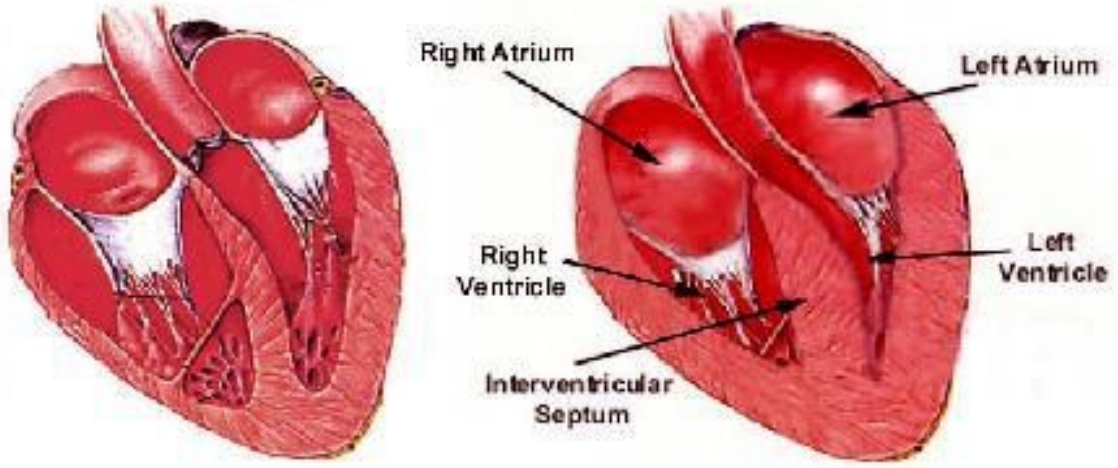
Hypertrophic (obstructive) CM

= subaortic stenosis = subvalvular idiopatic aortic stenosis

Characteristics:

The influence of catecholamines on fetal heart or ↑ catecholamine receptors in fetus

Often AD heredity (to examine relatives)

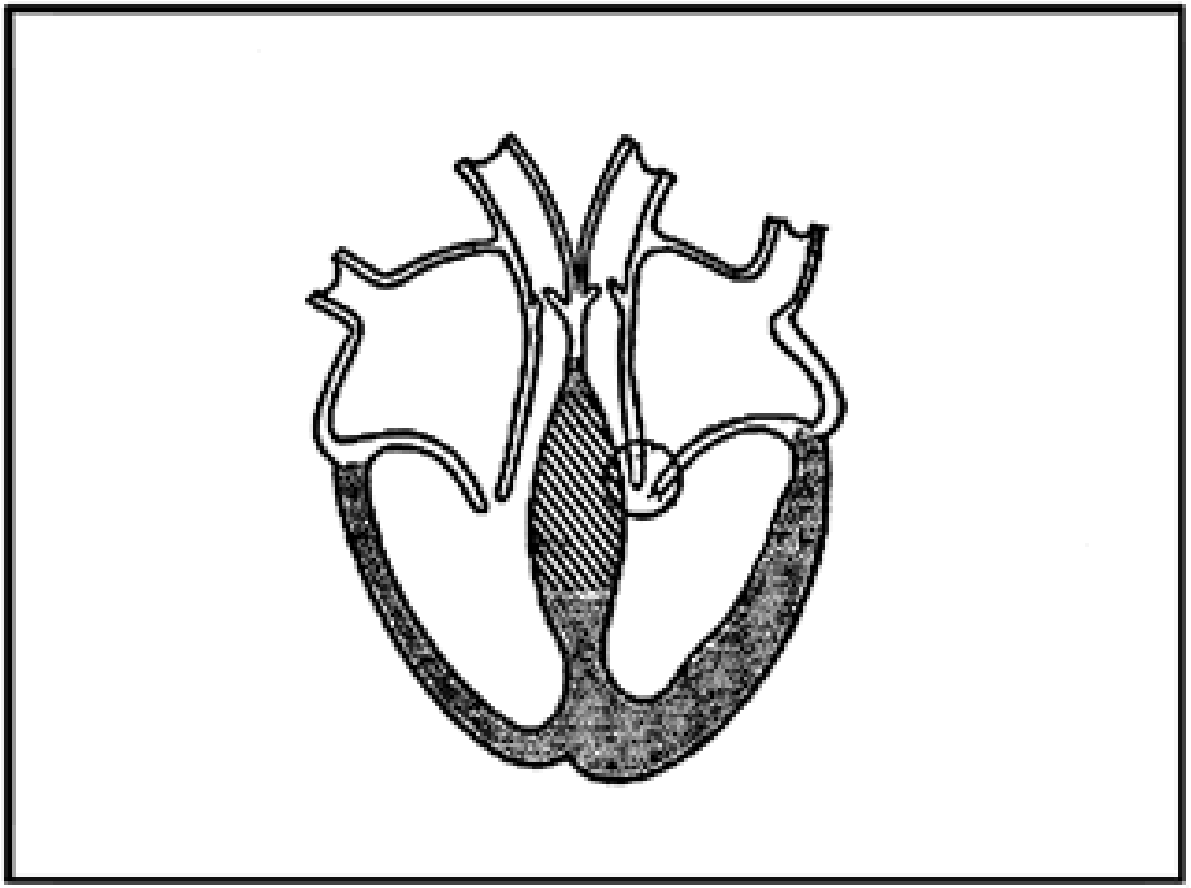


Hypertrophic CMP

abnormal *hypertrophy* of the myocardium, mainly of LV – subaortic stenosis) w/o stimulus

Normal *systolic* function
Impaired ejection of the blood due to the obturation

Disturbed *ventricle filling,* diastolic dysfunction (increase in EDV)



Hypertrophic (obstructive) CM

♥ asymmetric hypertrophy LV > septum > RV (with ECG picture)
♥ microscopy: disorganization of musculature, islets of fibrosis
♥ vault of hypertr. septum >>> obstruction of aortic intake

→ normal systolic function, low diastolic compliance
→ ventricular arrhythmia (risk of sudden death)
→ dizziness, syncope
→ intolerance of strain, dyspnoe
→ palpitation

SUDDEN DEATH

Causes

- various mutation of several genes in the sarcomera – actin, myosin, tropomyosin…
- up to 90 % AD hereditance – test the family!
- incidence up to 1:500

HKMP

Hypertrophic cardiomyopathy

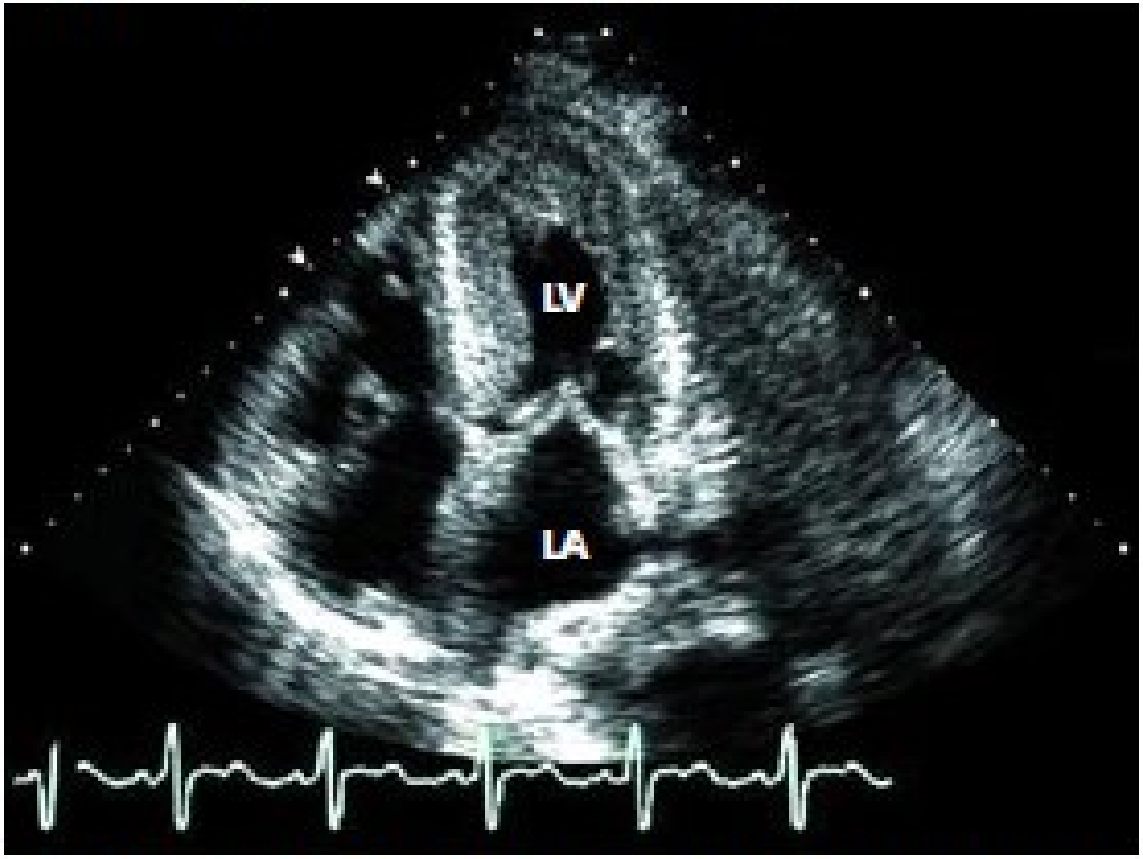
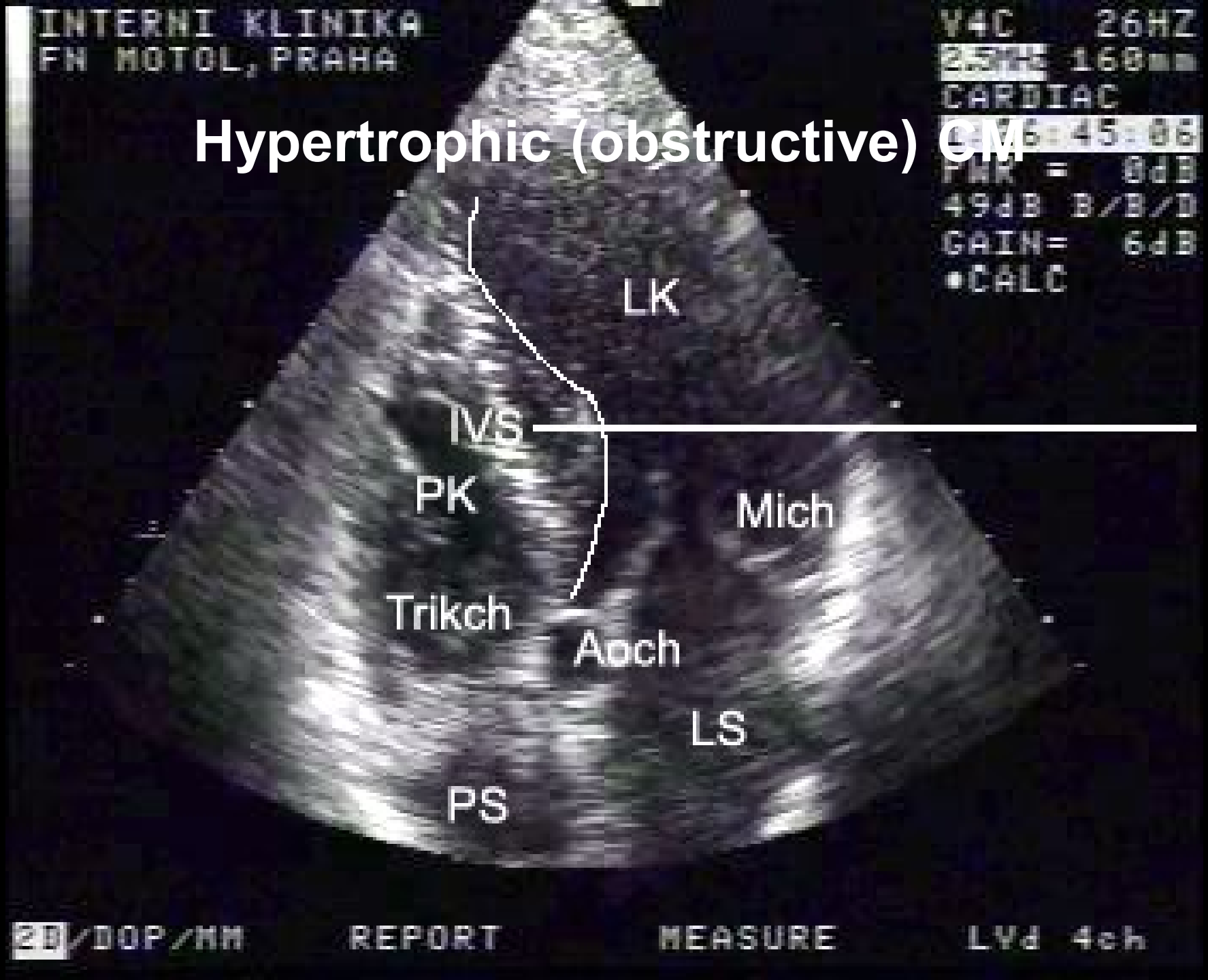


FIGURE 2. Two-dimensional transthoracic echocardiographic image in the apical four-chamber view of a patient with hypertrophic cardiomyopathy showing severe left ventricular hypertrophy. LV = left ventricle, LA = left atrium.

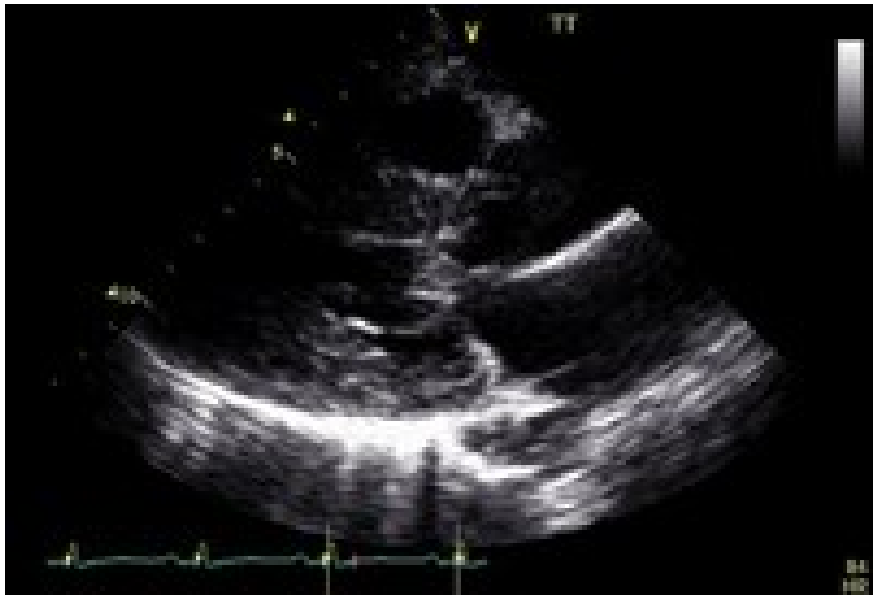
Hypertrophic (obstructive) CM



Case report 1

- 21 year old man suddenly collapsed during jogging. Immediately transported to the hospital.
- He was pronounced dead the autopsy was performed.

Case report 2



30year old mather of 4 children started to suffer from increasing dyspnea. She felt chest pain during physical acitivity and several times she collapsed (syncope).

The symptoms were worsening during several month completely disabling the patient from normal life.

Restrictive CMP

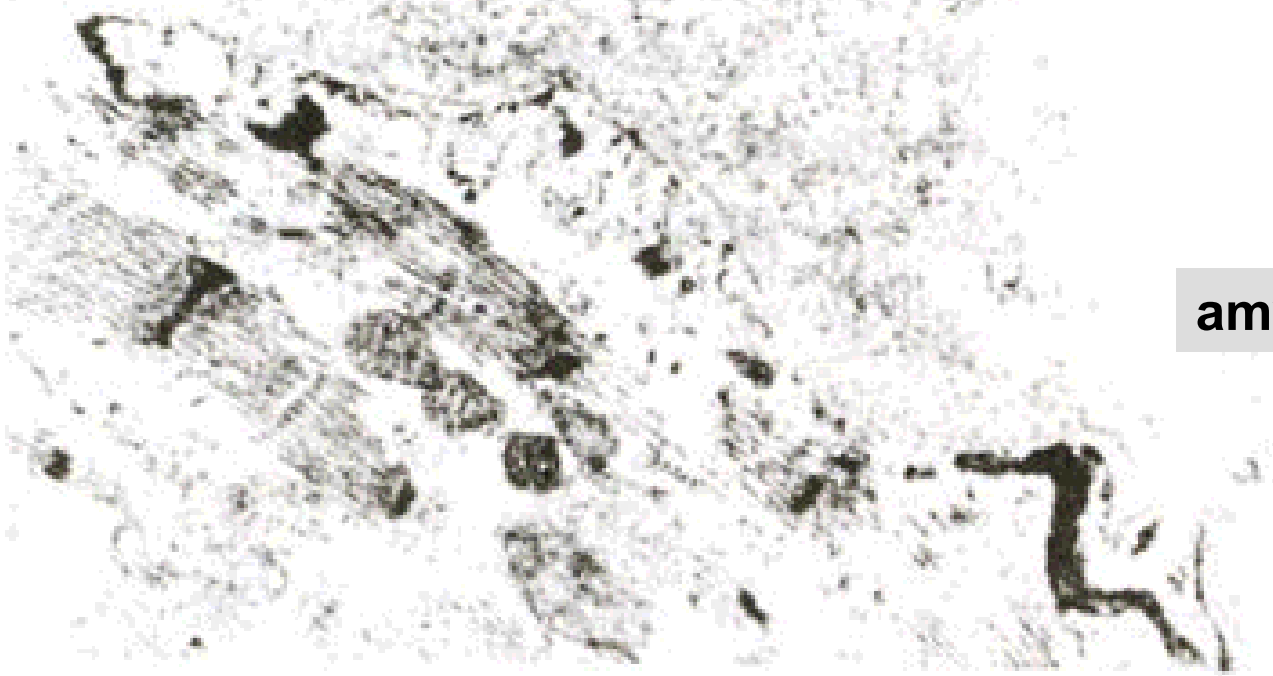
Decreased *compliance* of the heart and impaired dilatation
Decreased filling in the diastole + increased EDP
systolic function and EF are normal

Symptoms:
Both *backward* and *forward* heart failure
congestion + low CO
arrhytmias

Restrictive CM

Characteristics:

- ♥ subendocardial fibrosis (event. eosinophil infiltration)
- ♥ frequent arrhythmia
- ♥ heart is normal in size or only slightly enlarged
- ♥ rare form

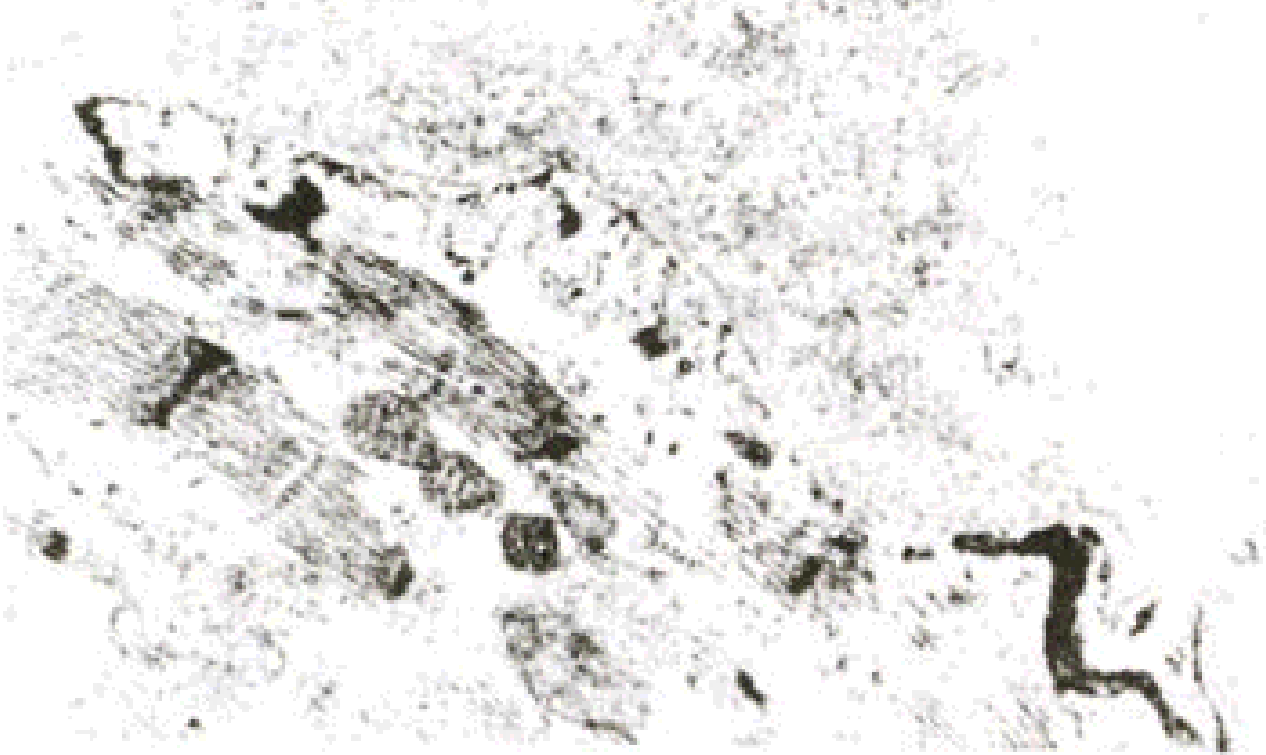


amyloid deposits

Restrictive CM

Symptoms:

- ♥ excessive tiredness (fatigue), poor tolerance of exercise
- ♥ cough - difficulty breathing
- ♥ palpitation, syncope - arrhythmia



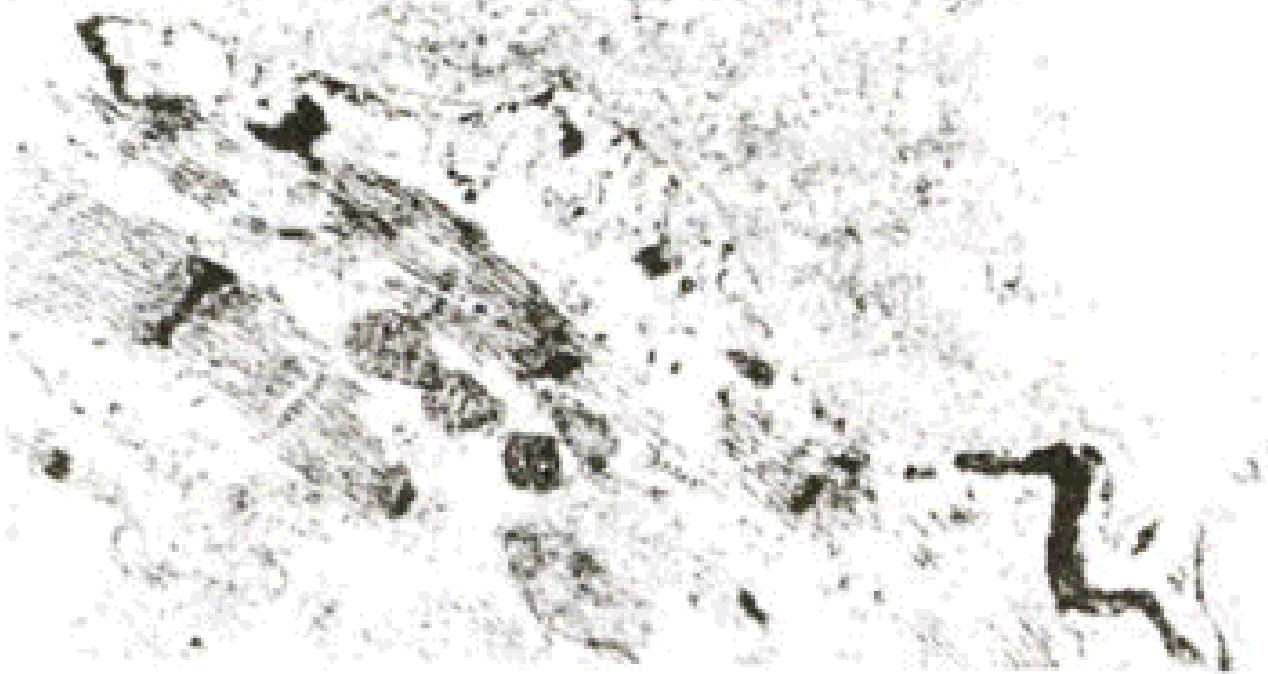
Restrictive CM

Prognosis:

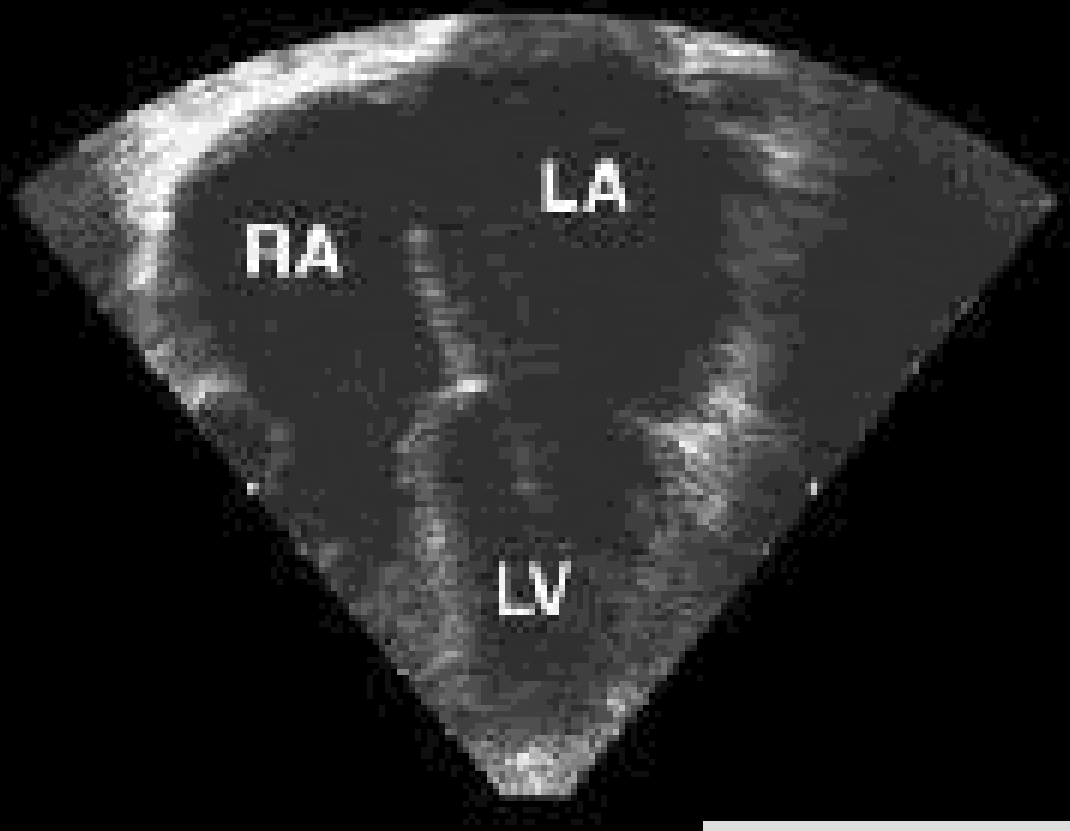
People with restrictive CM may be candidates for heart transplant.

Prognosis is dependent on the underlying cause but it is usually poor.

Average (mean) survival after diagnosis is 9 years.

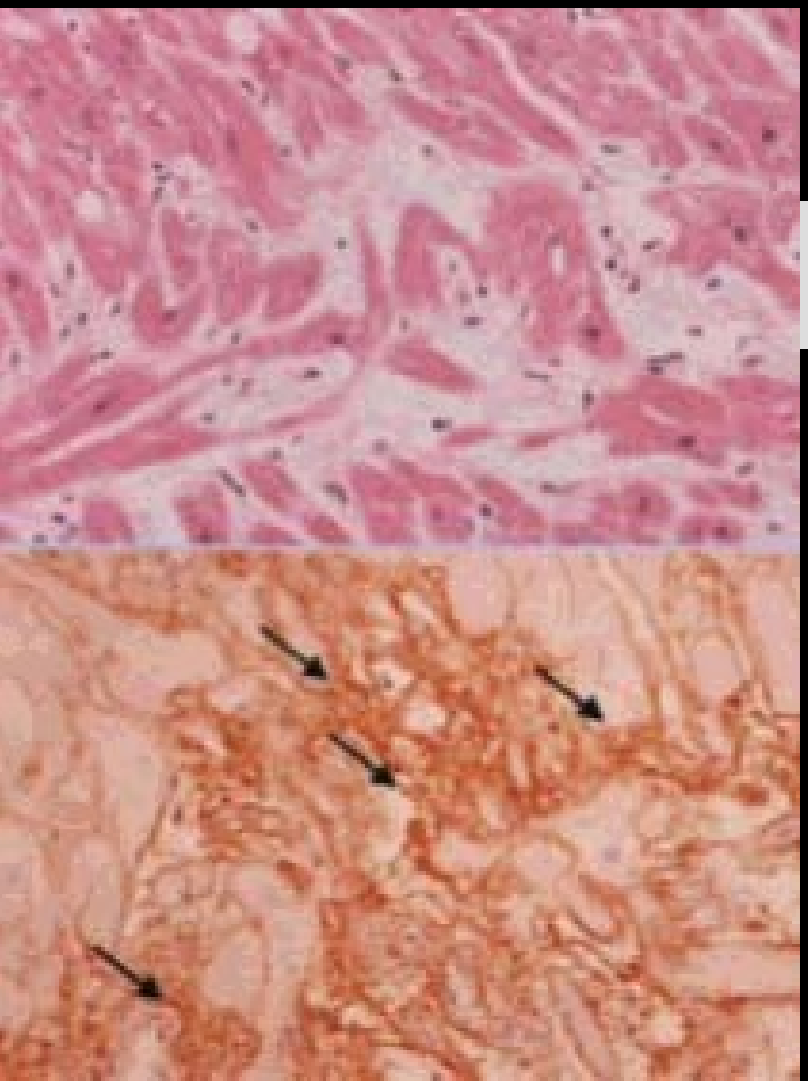


Restrictive CM



Characteristic echo finding:
RA, LA size > LV size

Restrictive CM

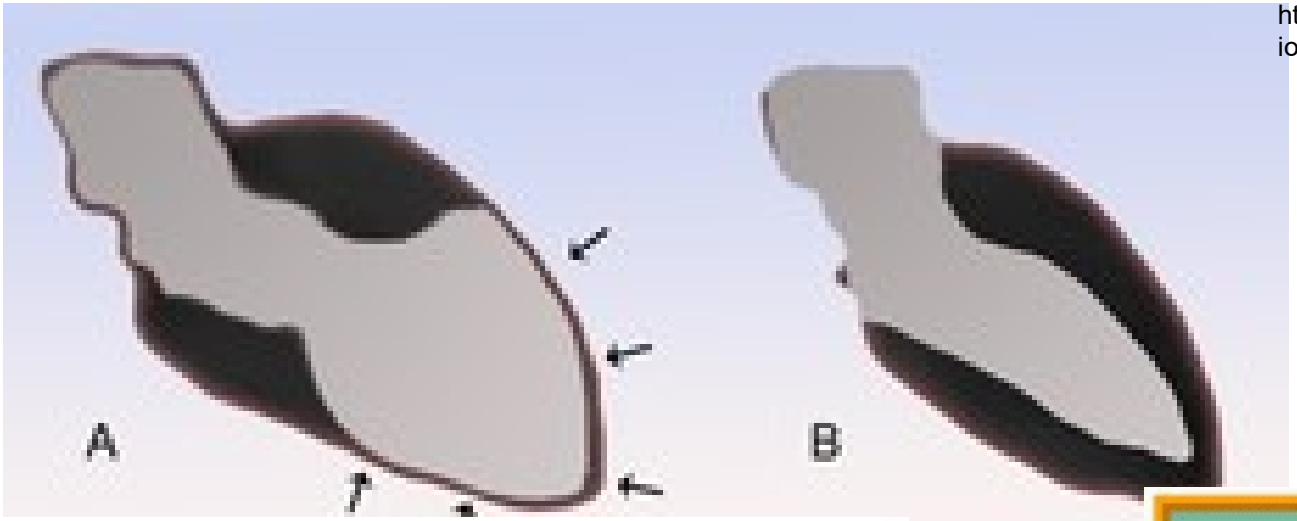


eosinophil fibrillar structures in myocardial interstitium

Stress CMP – broken heart syndrome, tako tsubo

- nonischemic CMP with sudden narrowing of myocardium usually around the apex with contractility disturbance
- **during the contraction the apex area remains akinetic (balloon-like) while the base area contracts normally (narrowing)**
- reminds the octopus trap – tako tsubo
- described first in 1991
- rare, estimated 12 000 in USA/year

Heart changes in stress CMP



http://en.wikipedia.org/wiki/Takotsubo_cardiomyopathy

tako = chobotnice
tsubo = nádoba

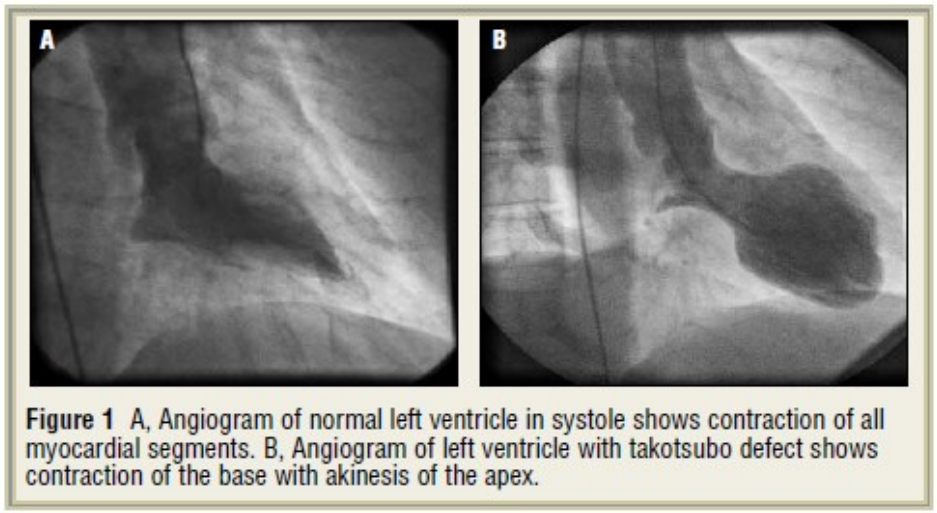


Figure 1 A, Angiogram of normal left ventricle in systole shows contraction of all myocardial segments. B, Angiogram of left ventricle with takotsubo defect shows contraction of the base with akinesis of the apex.

The "Broken Heart Syndrome": Understanding Takotsubo Cardiomyopathy

Clinical picture of stress CMP

- occurs **mainly in postmenopausal women** following emotional or physical stress – „broken heart“
- acute, severe symptoms – dyspnea, lung edema, ecg changes, arrhytmia, chest pain… - **resembles acute heart attack (infarction)**
- no signs of coronary arteries narrowing and/or CHD risk factors
- risk of heart rupture
- **usually has tendency for spontaneuous improvement** in days or weeks

Table 2 Emotional and physical stressors associated with takotsubo cardiomyopathy

Emotional stressors
Unexpected death of relative or friend[1,7]
Domestic abuse[1]
Confrontational argument[1,7]
Catastrophic medical diagnosis[1]
Devastating business[1]
Armed robbery[7]
Gambling losses[1]
Surprise party[7]
Surprise reunion[7]
Car accident[7]
Fear of procedure[7]
Fear of choking[7]
Court appearance[7]
Public performance[7]
Physical stressors
Exacerbated systemic disorders[1]
Noncardiac invasive procedures[1,13]
Exhausting physical effort[1,5]
Asthma attack[1]
Pneumothorax[5]
Ventricular fibrillation[5]
Cold exposure[5]

Theories of the pathogenesis

- too much catecholamines
- temporary multiple vasospasms
- why mainly women ?
  why mainly the apex ?

Case report

- 65 year old lady participating at the funeral
- Sudden onset of the strong retrosternal pain (8/10), w/o irradiation, dyspnea
- **BP 106/50** with the tendency to decrease
- **Saturation of** Hb 89%, auscultation and X-ray singns of lung congestion, increased filling of the neck veins (**L and R failure**)
- HR 112/min, changes in ST segment on **ECG**
- **Laboratory** exams – increase of myocardial enzymes

Diagnosis ??

Case report

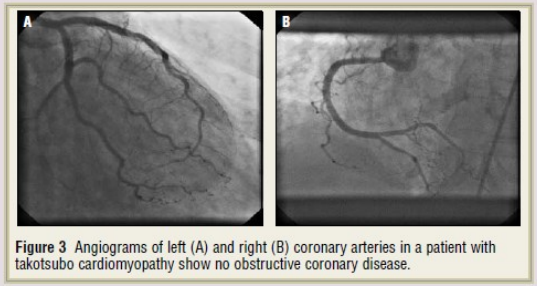


Figure 3 Angiograms of left (A) and right (B) coronary arteries in a patient with takotsubo cardiomyopathy show no obstructive coronary disease.

- **catheterization** of the coronary arteries – without narrowing or occlusion
- Pulmonary wedge pressure – 19 mm Hg
- Mean pressure in AP – 25 mm hg
- Pressure in the right atrium – 9 mm Hg
- **echocardiography** – extensive hypokinesis anterolaterally, apically and diaphragmatically, EF 25 %

Arythmogenic right vetricular dysplasia (ARVD)

- progressive loss of the myocytes with the replacement by the fat and fibrous tissue
- Mainly RV (dilatition or aneurysm, hypokinesis and decreased EF), but some changes also in LV
- Mutations in desmosomal proteins, AD inheritance with incomplete penetration
- Ventricular arrhytmias, loss of consciousness, sudden death of young people

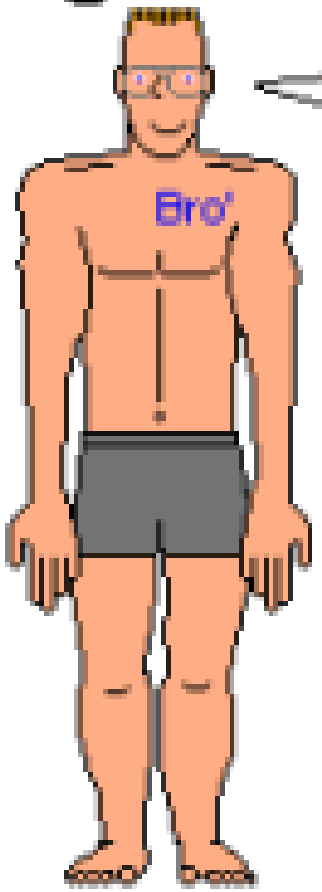
Arrhythmogenic Right Ventricular Cardiomyopathy

Much of the right ventricle is replaced by a chaotic mix of heart muscle, fibrous tissue, and fat.

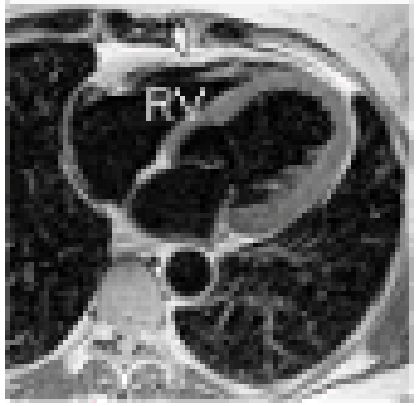
"Epsilon wave" -- slow RV

Flipped T's in V2-V3

Don't miss this common killer.



My jock brother just died in his sleep. Could I be next?

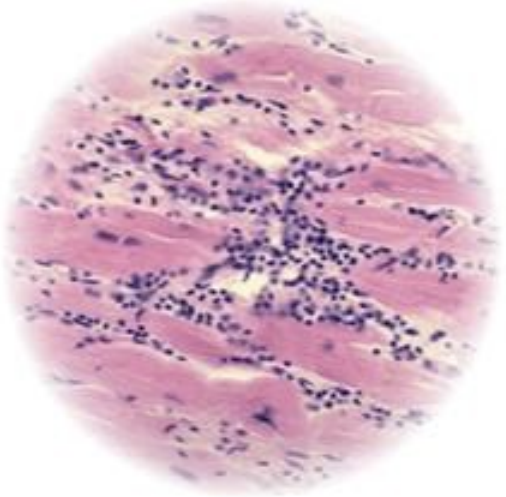


The key is loss of movement, and maybe fat, seen on imaging.

Myocarditis

Etiology: infection + (auto)immunity

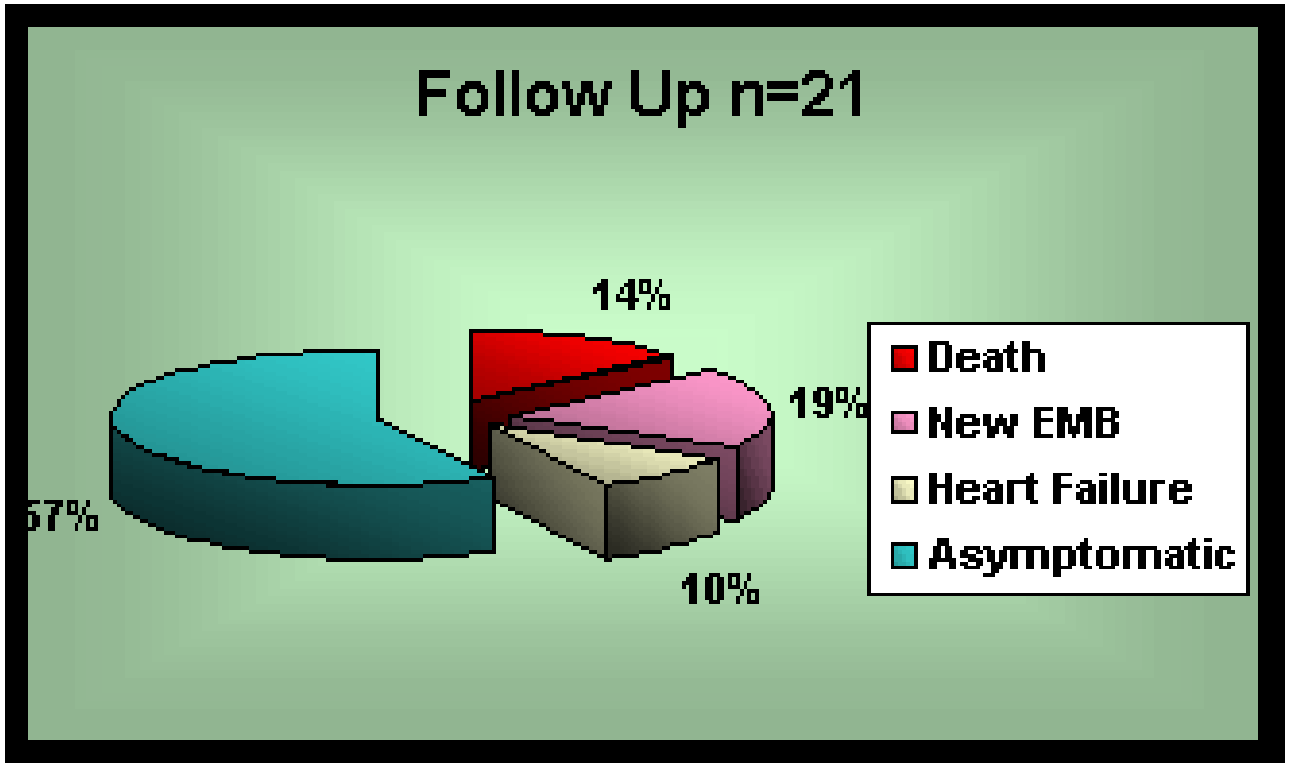
- rheumatoid fever
- diphteria
- streptococcal infection
- mycoplasma
- salmonelosis
- Weil dis. (leptospirosis)
- ricketsia
- influensa, polio, parotitis, CMV
- Chagas dis. (trp. crusii)
- systemic dis. of connective tissue
- immunocomplex. vasculititis
- Fiedler idiopatic myocarditis (virosis ?)



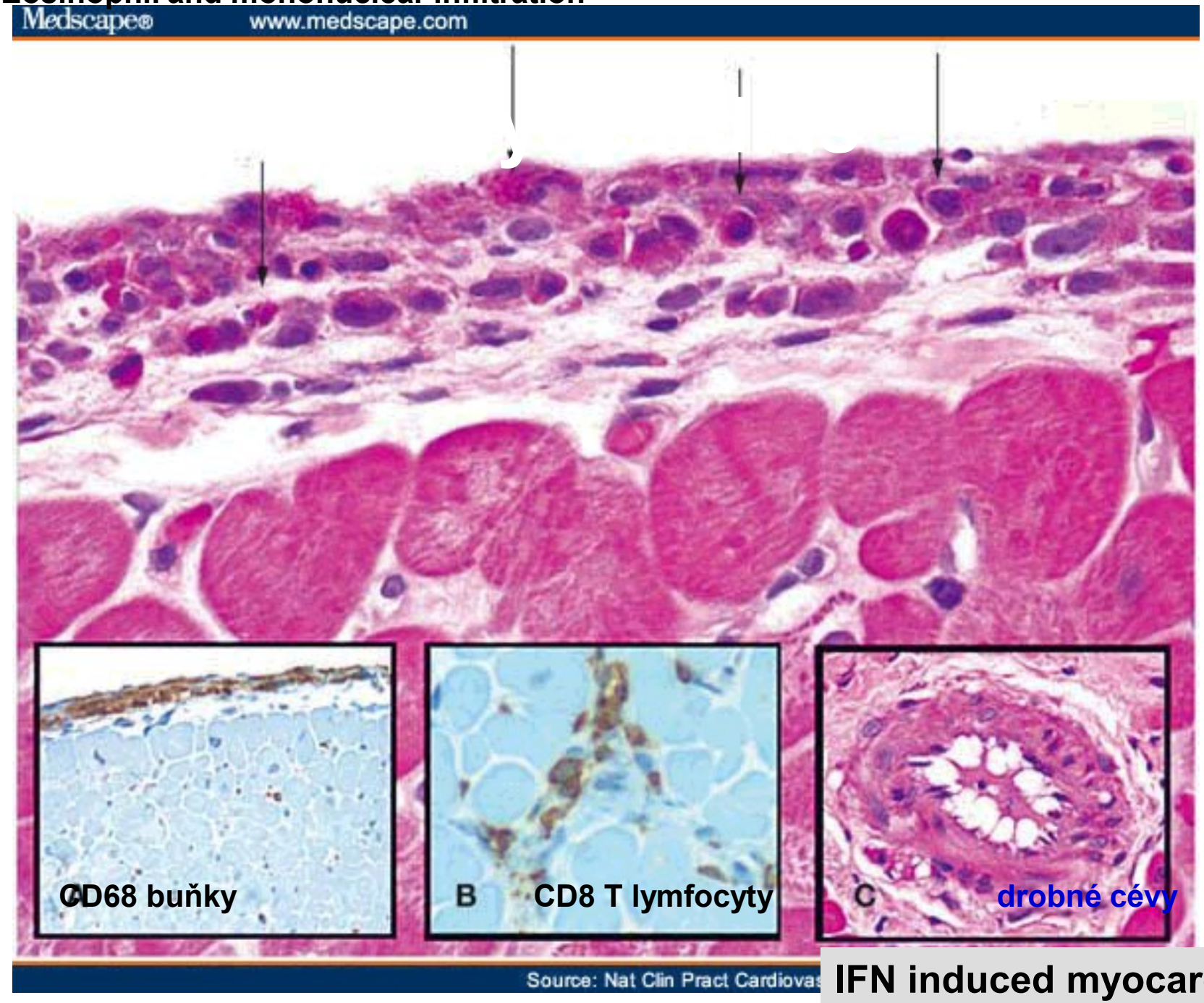
Myocarditis

Prognosis:

recovery / cardiac failure / latent development of dilated CM

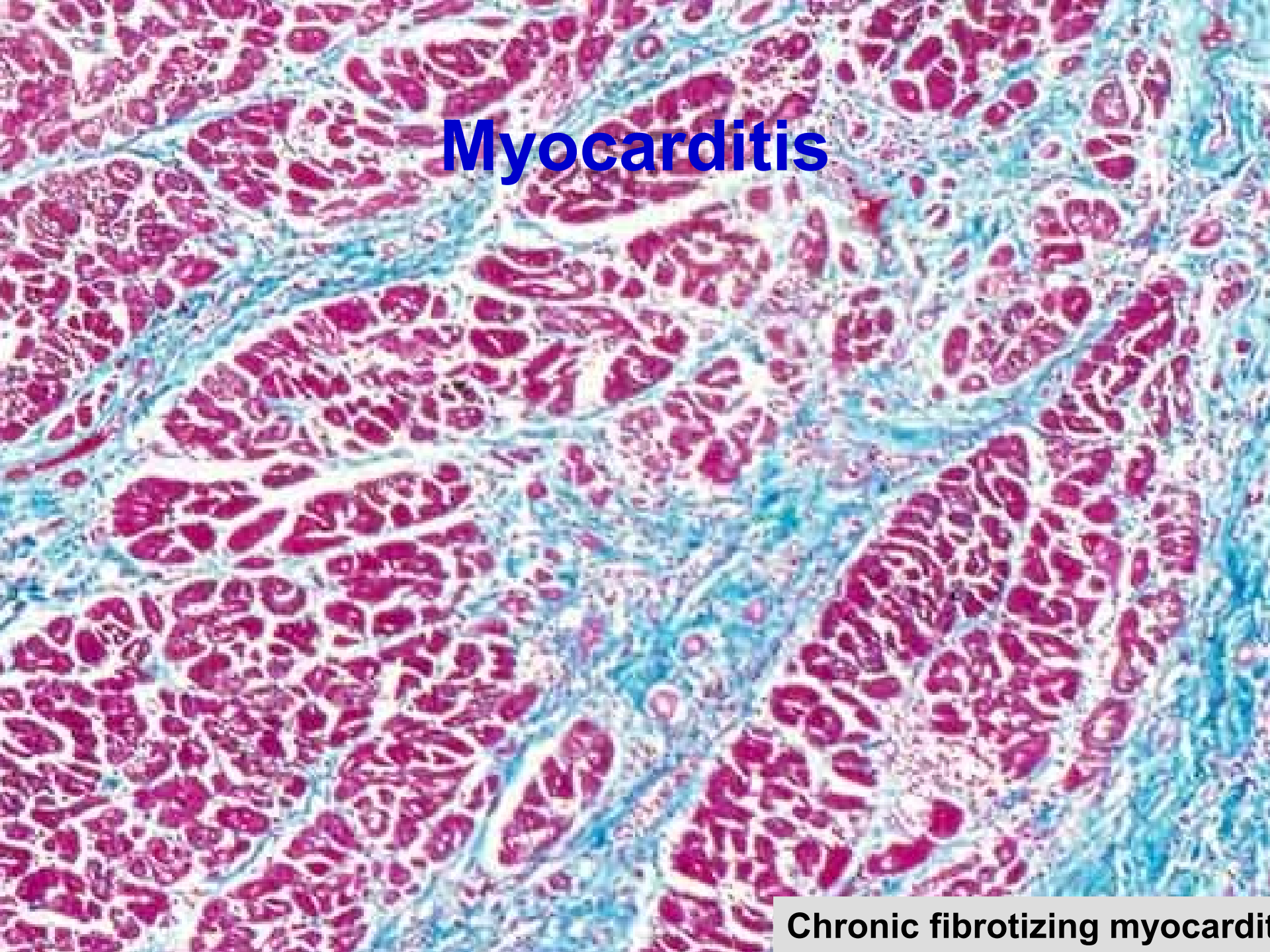


Eosinophil and mononuclear infiltration



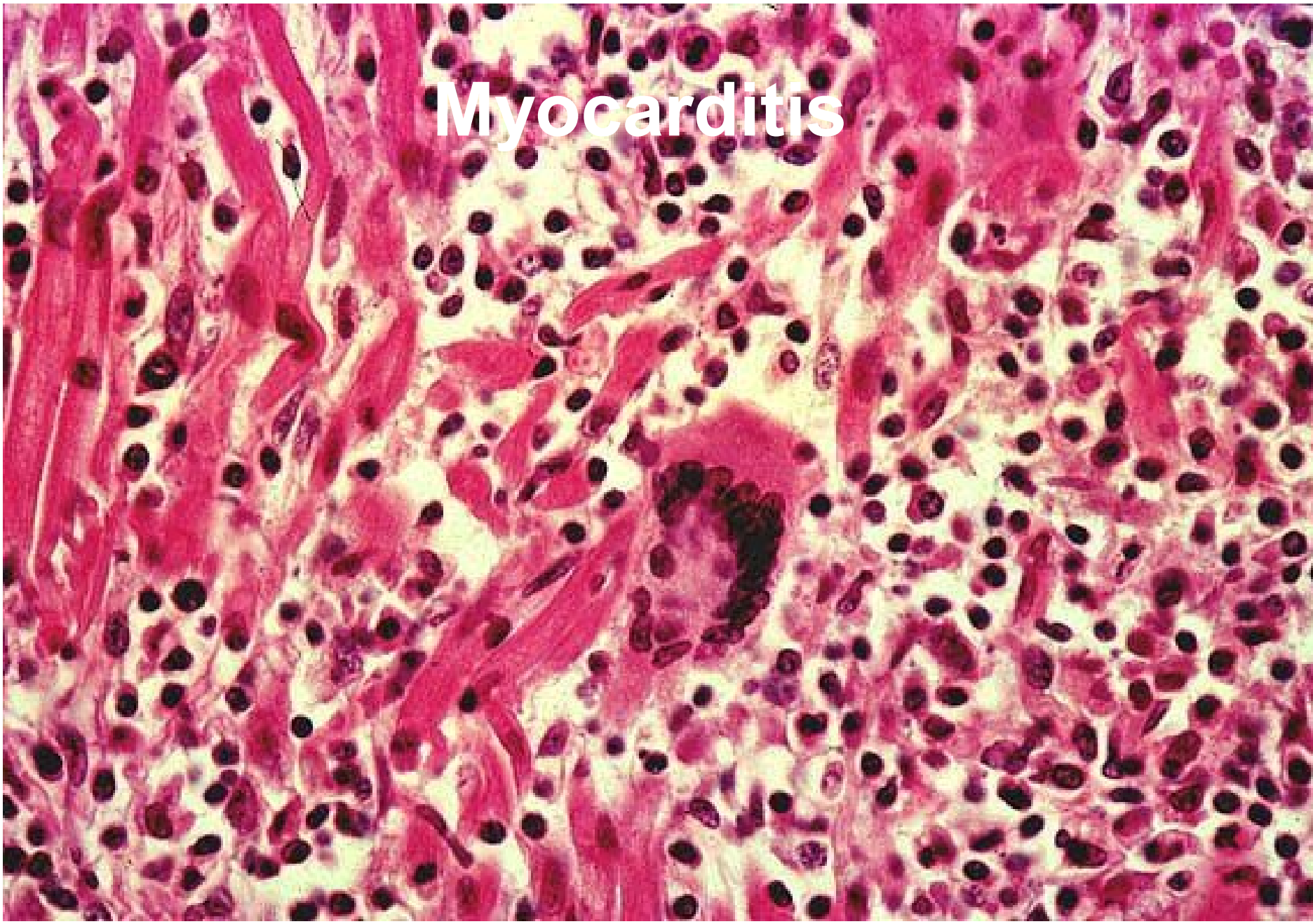
IFN induced myocarditis

Myocarditis



Chronic fibrotizing myocardit

Myocarditis

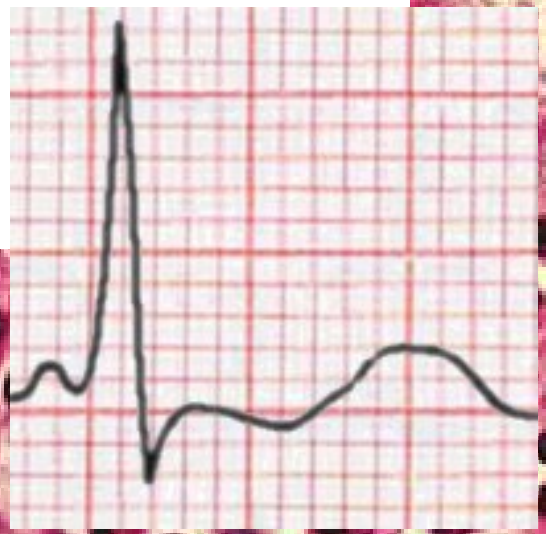


Giant cell myoc

Myocarditis

Manifestation:

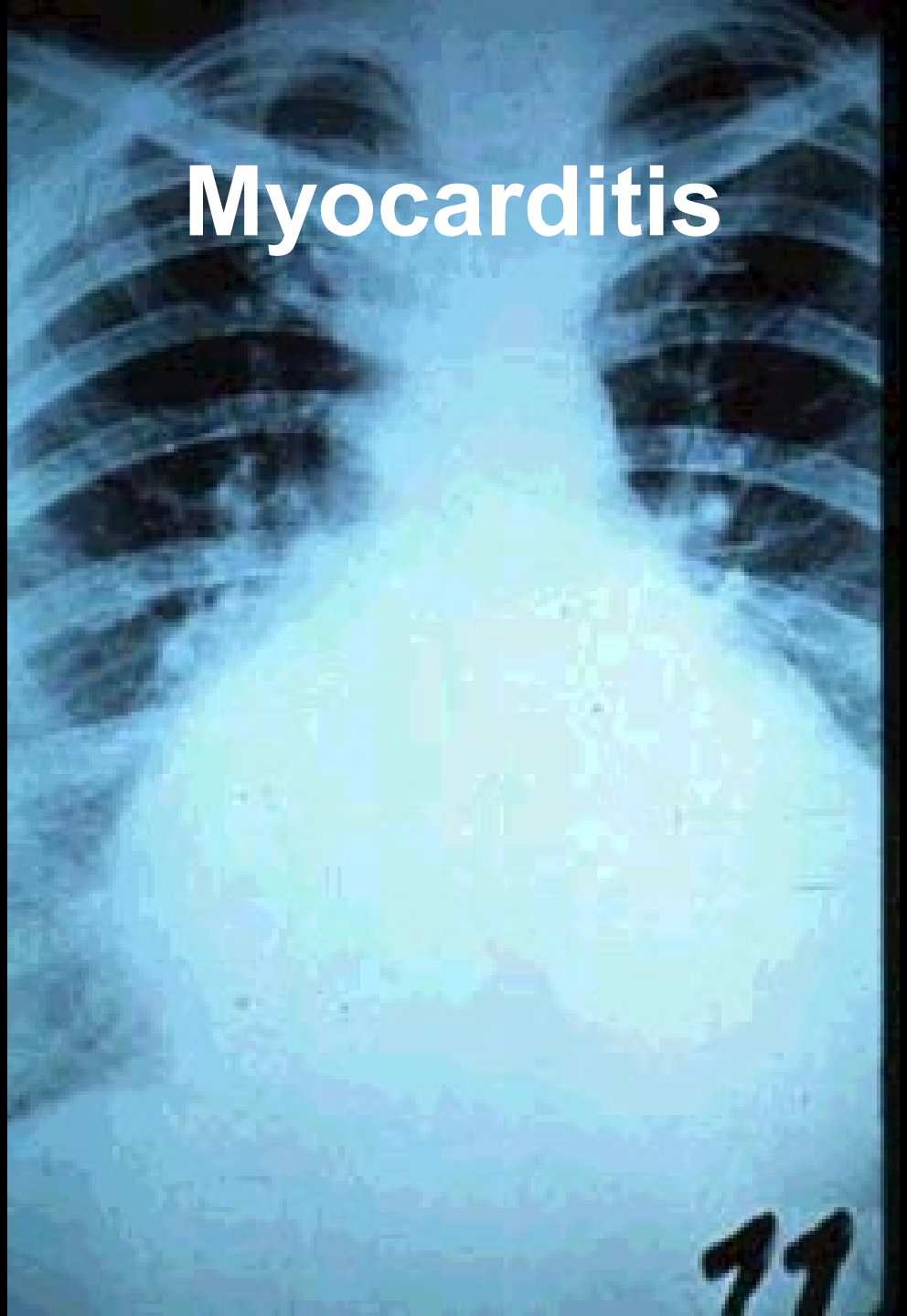
- ♥ asymptotic
- ♥ chest pain, dyspnoe, palpitation
- ♥ arrhythmia
- ♥ cardiac failure
- ♥ ECG: variable finding (PQ int., ST-T, blocks), "myocarditic curve"



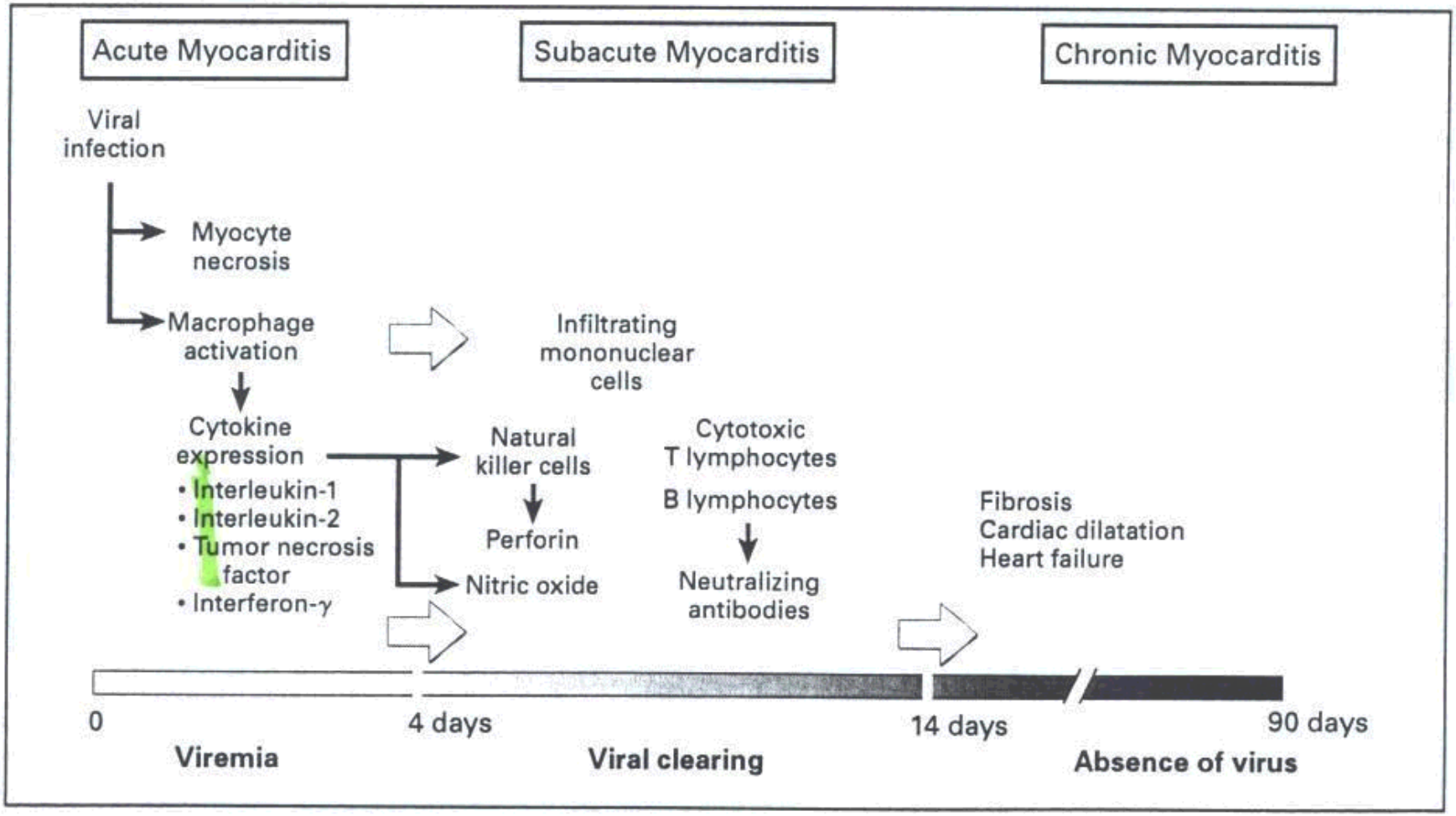
Diagnosis:

difficult – echocardiography

Myocarditis



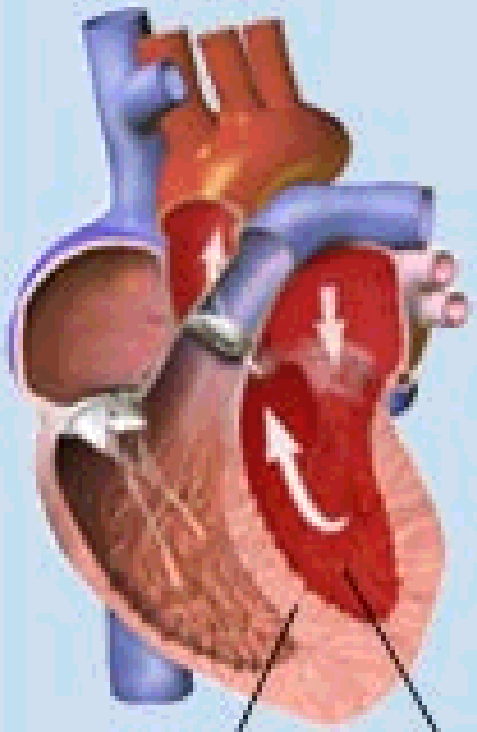
Myocarditis



Time Course of Experimental Viral Myocarditis in Mice.
Adapted from Kawai[11] with the permission of the publisher. The timeline is not drawn to scale.

The End

Normal

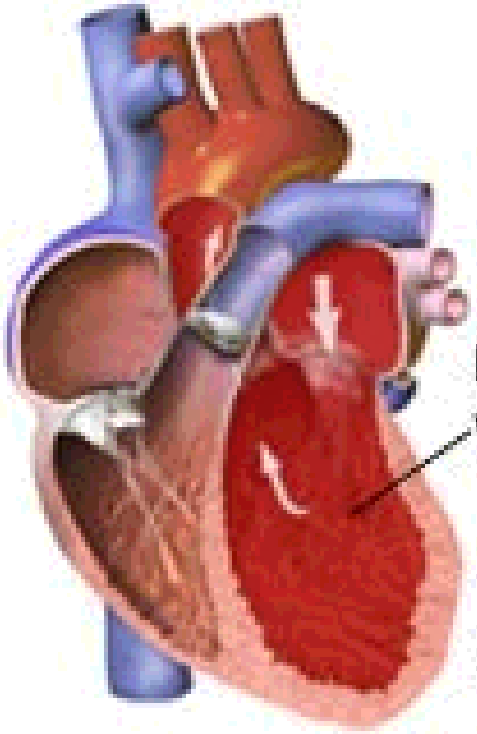


A healthy left ventricle pumps enough oxygenated blood to meet the body's needs.

Cardiomyopathy

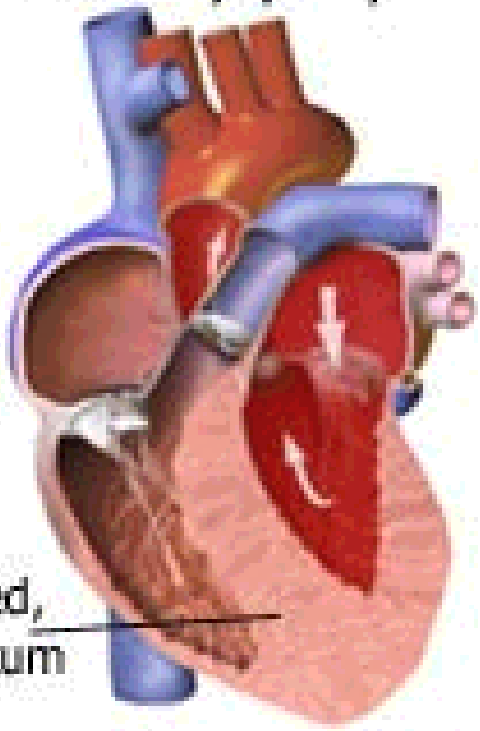
A condition in which a ventricle has become enlarged, thickened and/or stiffened. As a result, the heart's ability to pump is reduced. Two types of cardiomyopathy include:

Dilated cardiomyopathy



An enlarged, weakened left ventricle struggles to pump enough blood to meet the body's needs.

Hypertrophic cardiomyopathy



Left ventricle cannot fully relax between heartbeats, resulting in less blood flow.

Dilated (congestive) CM

Links:

- **alcoholism (+ malnutrition, ↓vitamin., hepatopathy…)**
- **coxsackie B (e.g. intrauterine infection)**
- **hereditary factors (...to examine relatives)**
- **drug factors (ATB, sympathomimetics)**

Cardiomyopathy

ECG:

SVES, VES, atrial fibrillation
RBBB, LBBB
T wave aplanation / inversion
LV hypertrophy (♂ > 400 g, ♀ > 385 g)

It is unusual for patients with cardiomyopathy to have a normal ECG