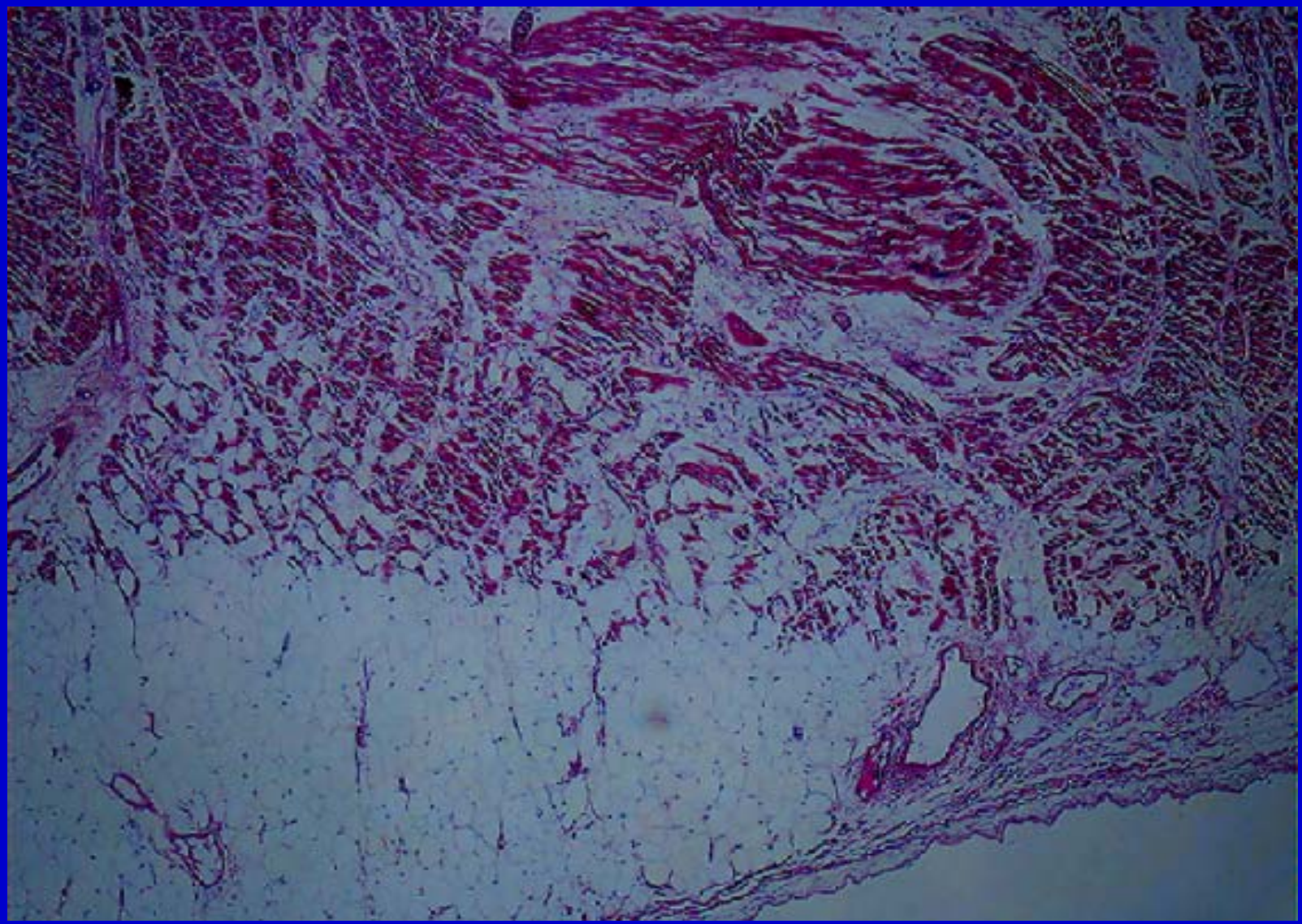
ARVD/C

Arrhythmogenic RV Dysplasia/Cardiomyopathy

경북의대 조용근

돌연사, 여자 19세



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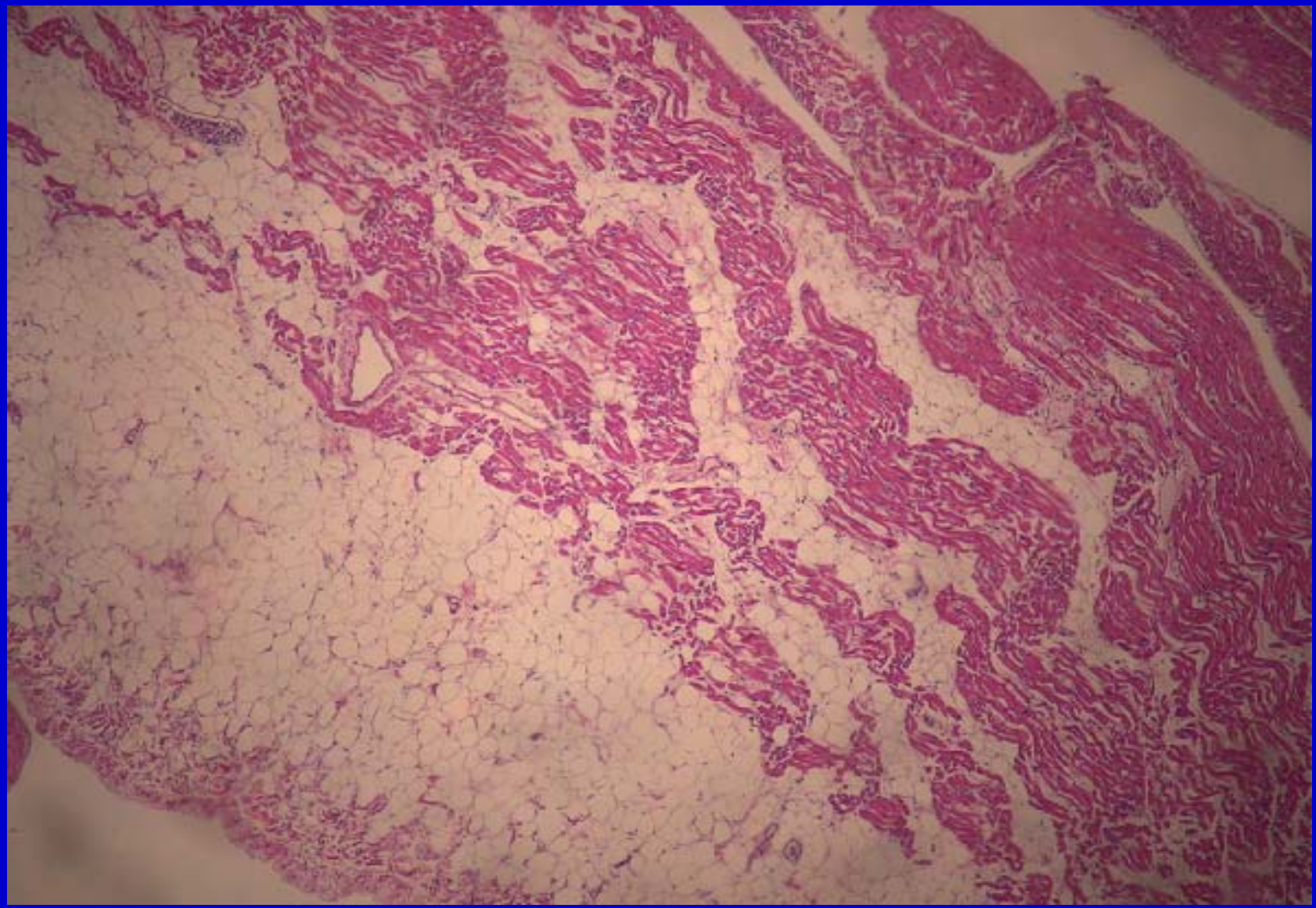

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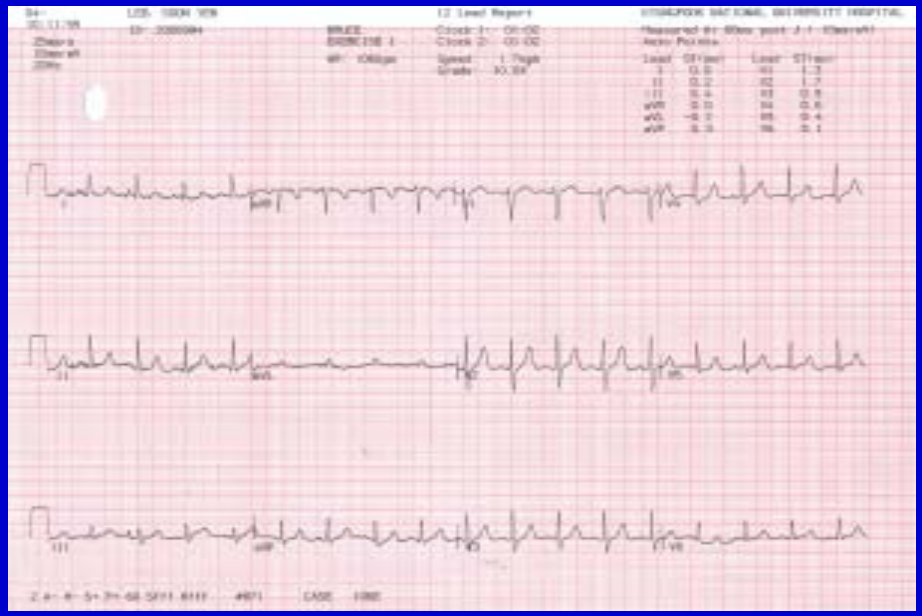

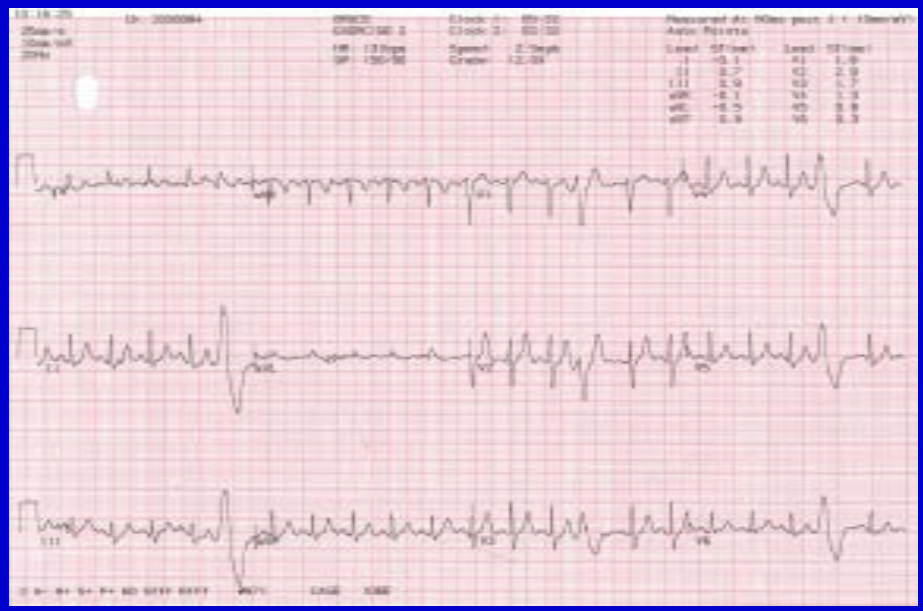

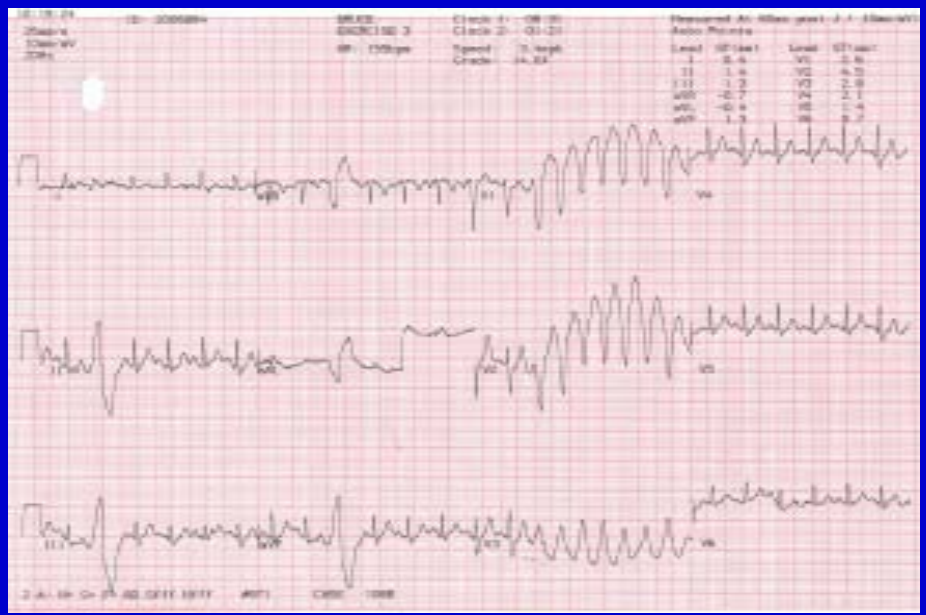

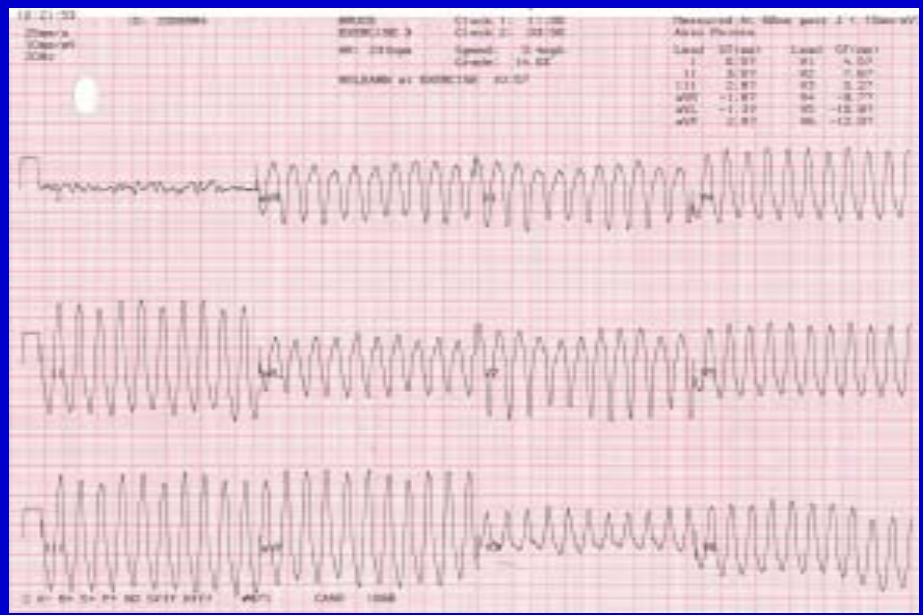

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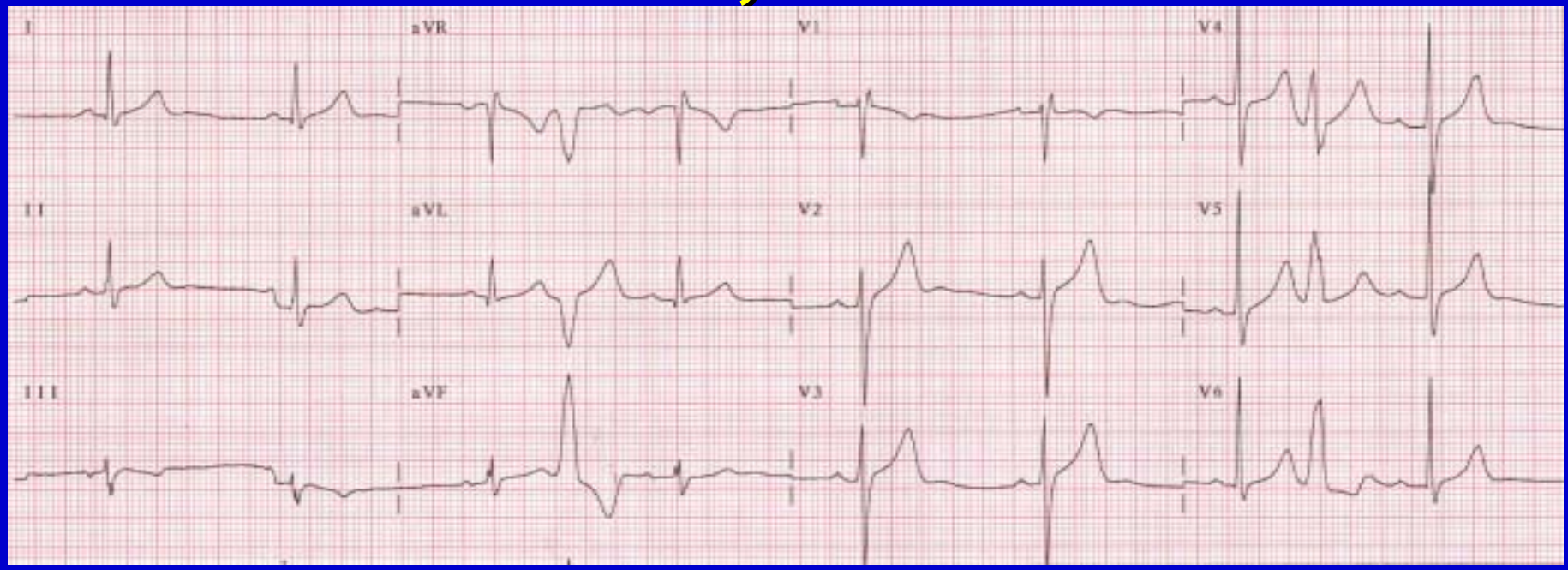
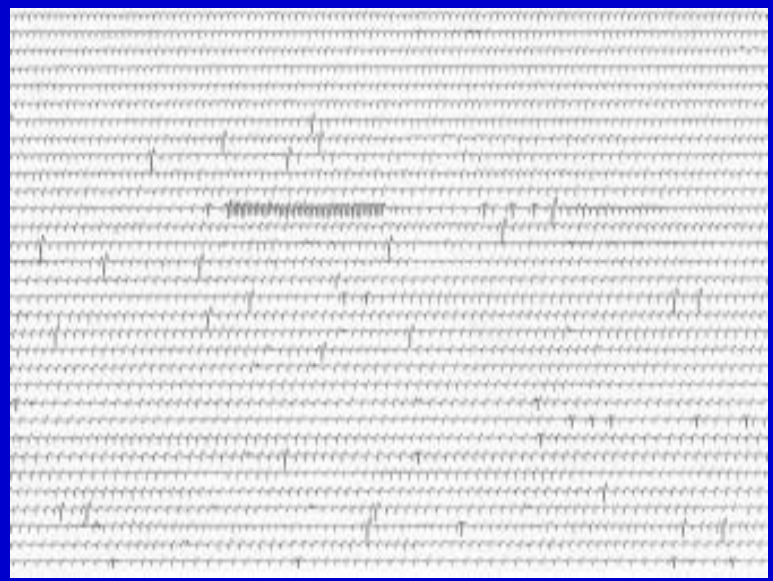
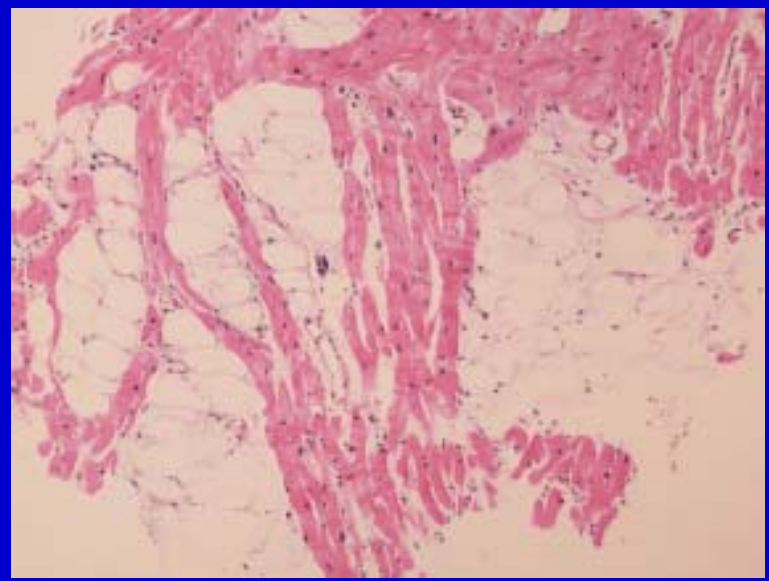






ARVD

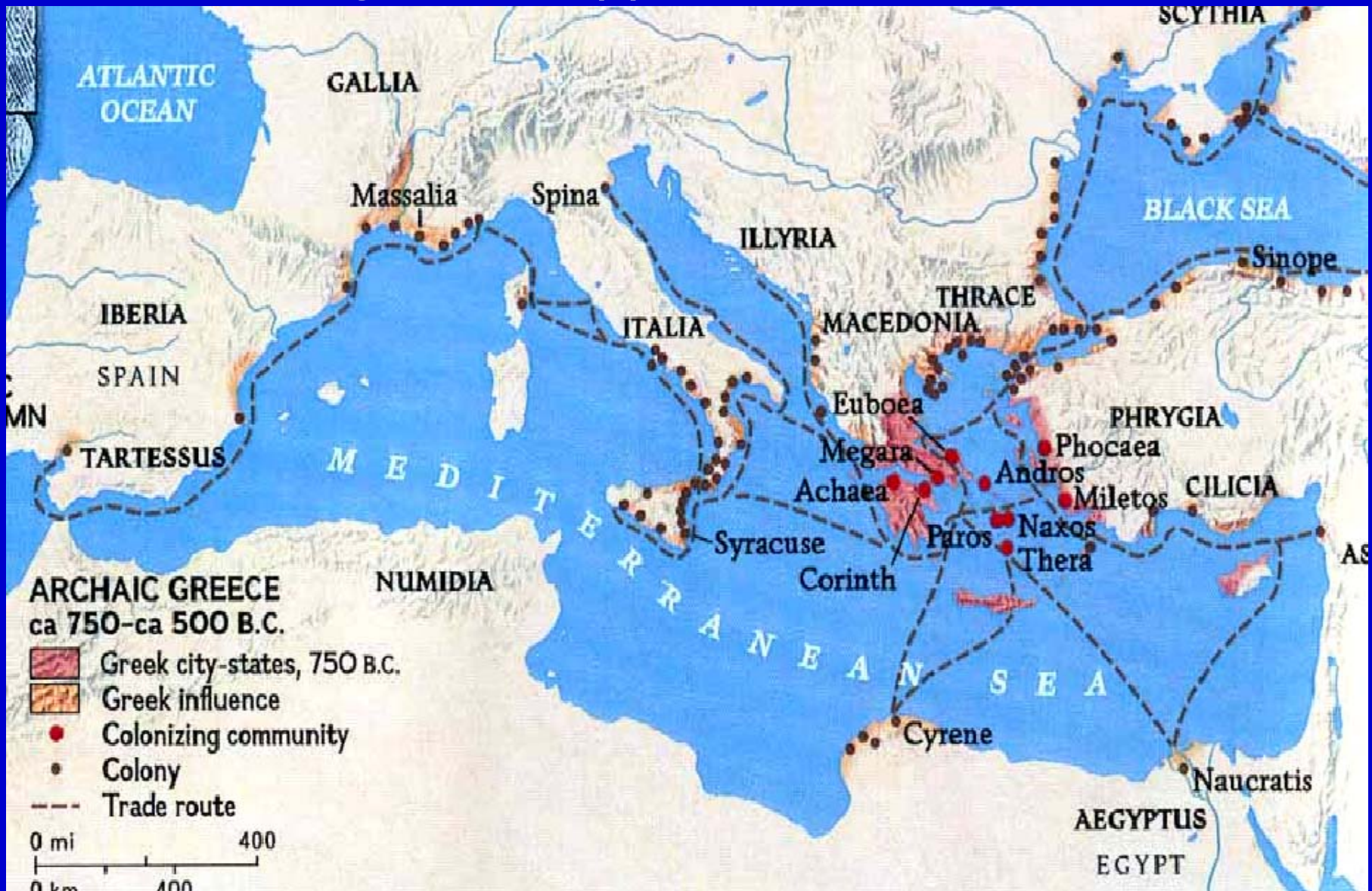
- Fibrofatty infiltration
- Right ventricle
- Sudden death, Ventricular arrhythmia, Right heart failure, Asymptomatic

- Concealed phase
- Overt electrical phase
- (Bi)ventricular failure

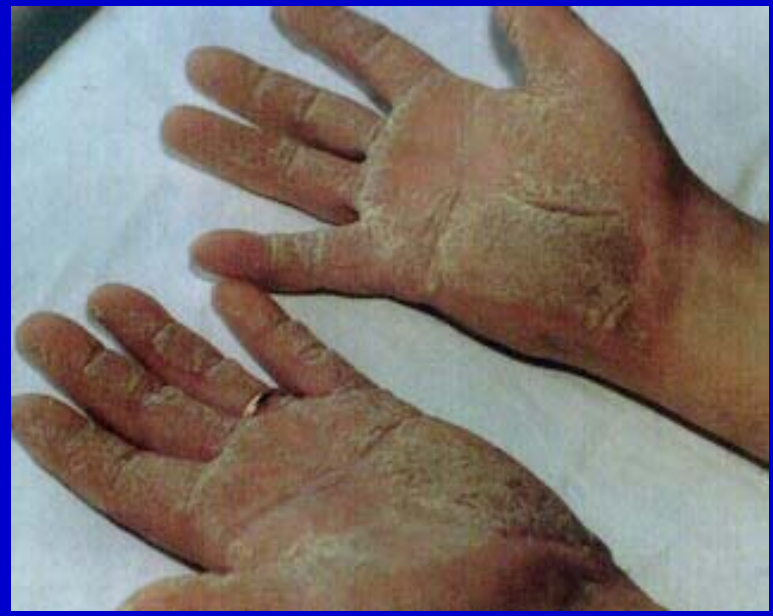
- Acute and active cell death $\Rightarrow$ VF & SD
- Fibrosis and Reentry $\Rightarrow$ VT

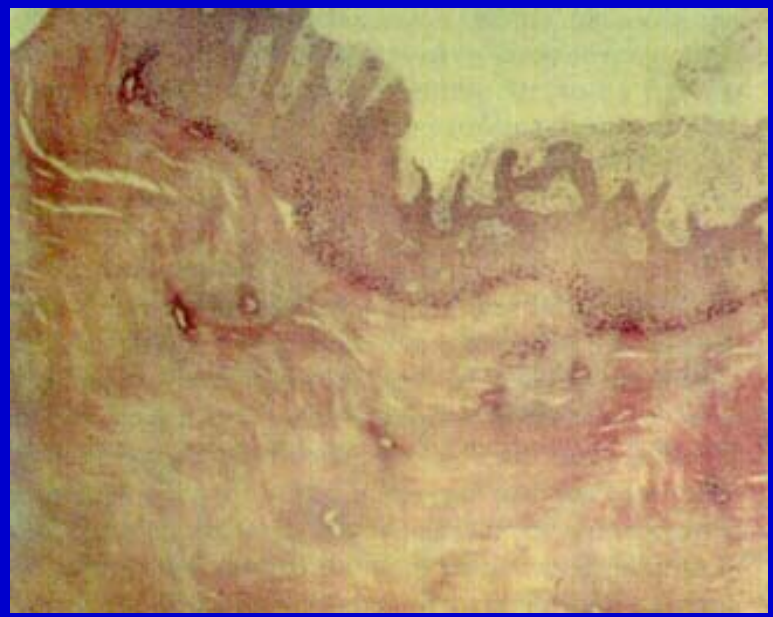
History of ARVD

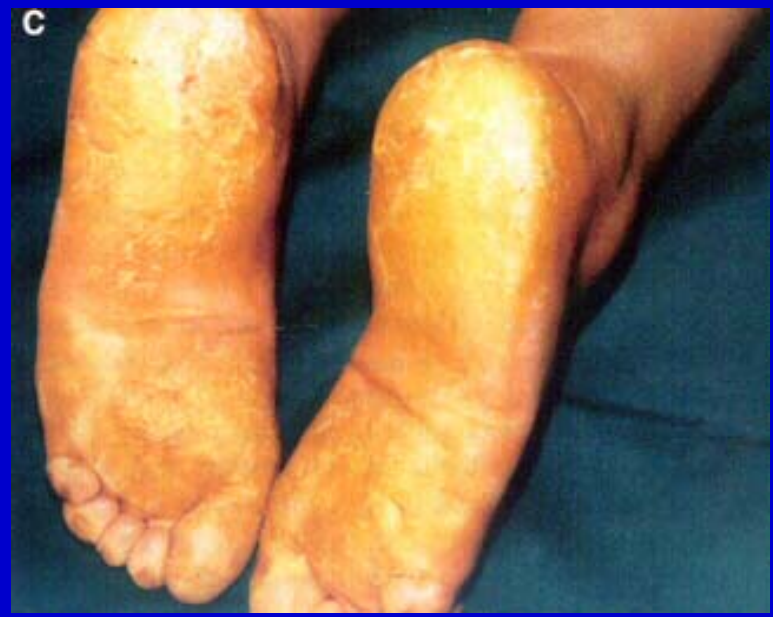
- Greek legend Philippides

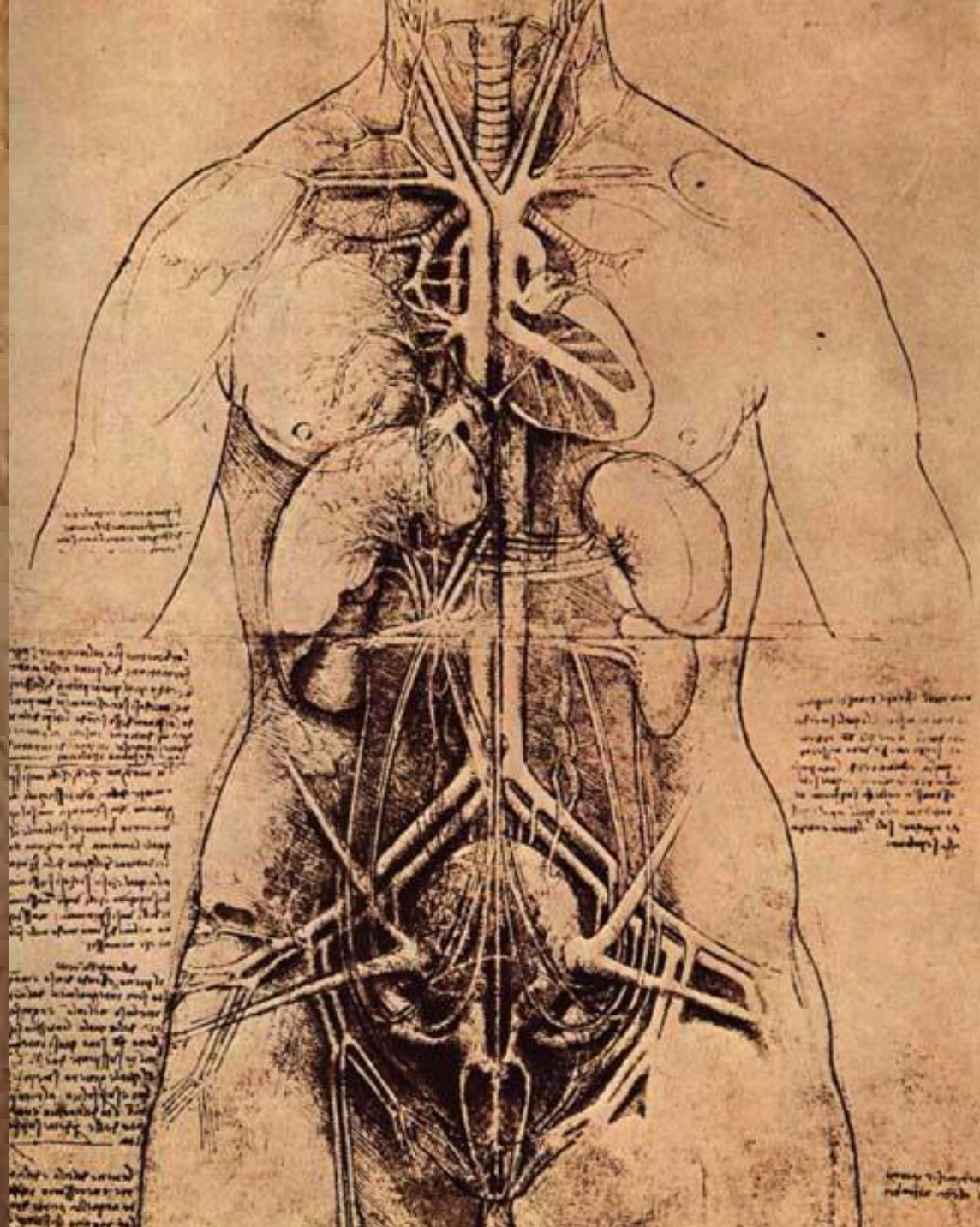


Naxos Disease









THE PRINCIPLES AND PRACTICE OF MEDICINE

DESIGNED FOR THE USE OF PRACTITIONERS AND STUDENTS OF MEDICINE

BY

WILLIAM OSLER, M. D.

Fellow of the Royal Society; Fellow of the Royal College of Physicians, London; Professor of Medicine in the Johns Hopkins University and Physician-in-chief to the Johns Hopkins Hospital, Baltimore; formerly Professor of the Institutes of Medicine, McGill University, Montreal; and Professor of Clinical Medicine in the University of Pennsylvania, Philadelphia

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with in cases of typhoid, typhus, small-pox, and other infectious diseases, particularly when the course is protracted. There is no definite relation between it and the high temperature.

5. **Fatty Heart.**—Under this term are embraced fatty degeneration and fatty overgrowth.

(*a*) *Fatty degeneration* is a very common condition, and mild grades are met with in many diseases. It is found in the failing nutrition of old age, of wasting diseases, and of cachectic states; in prolonged infectious fevers, in which it may follow or accompany the parenchymatous change; associated with acute and chronic anæmias. Certain poisons, such as phosphorus, produce an intense fatty degeneration. Local causes: Pericarditis is usually associated with fatty or parenchymatous changes in the superficial layers of the myocardium. Disease of the coronary arteries is a much more common cause of fibroid degeneration than of fatty heart. Lastly, in the hypertrophied ventricular wall in chronic heart-disease fatty change is by no means infrequent. This degeneration may be limited to the heart or it may be more or less general in the solid viscera. The diaphragm may also be involved, even when the other muscles show no special changes. There appears to be a special proneness to fatty degeneration in the heart-muscle, which may perhaps be connected with its incessant activity. So great is its need of an abundant oxygen supply that it feels at once any deficiency, and is in consequence the first muscle to show nutritional changes.

Anatomically the condition may be local or general. The left ventricle is most frequently affected. If the process is advanced and general, the heart looks large and is flabby and relaxed. It has a light yellowish-brown tint, or, as it is called, a faded-leaf color. Its consistence is reduced and the substance tears easily. In the left ventricle the papillary columns and the muscle beneath the endocardium show a streaked or patchy appearance. Microscopically, the fibres are seen to be occupied by minute globules distributed in rows along the line of the primitive fibres (Welch). In advanced grades the fibres seem completely occupied by the minute globules.

(*b*) *Fatty Overgrowth.*—This is usually a simple excess of the normal subpericardial fat, to which the term *cor adiposum* was given by the older writers. In pronounced instances the fat infiltrates between the muscular substance and, separating the strands, may reach even to the endocardium. In corpulent persons there is always much pericardial fat. It forms part of the general obesity, and occasionally leads to dangerous or even fatal impairment of the contractile power of the heart. Of 122 cases analyzed by Forchheimer there were 88 males and 34 females. Over 80 per cent occurred between the fortieth and seventieth years.

The entire heart may be enveloped in a thick sheeting of fat through which not a trace of muscle substance can be seen. On section, the fat infiltrates the muscle, separating the fibres, and in extreme cases—particularly in the right ventricle—reaches the endocardium. In some places there may be even complete substitution of fat for the muscle substance. In rare instances the fat may be in the papillary muscles. The heart is usually much relaxed and the chambers are dilated. Microscopically the muscle fibres may show, in addition to the atrophy, marked fatty degeneration.

Ventricule droit papyracé * du jeune adulte par dystrophie congénitale [1]

A propos de 2 cas anatomo-cliniques et de 3 cas cliniques

Par R. FROMENT, A. PERRIN, R. LOIRE et Cl. DALLOZ

avec la collaboration de C. AGE, P. CAHEN, P. ARNAUD, G. PERRAS, G. PLAUCHU et A. SAINT-PIERRE **

1° C'est en 1952 qu'Henry Uhl (de Baltimore) rapporta un cas anatomique bien particulier d'insuffisance cardiaque du *nourrisson :* caractérisé par une « absence presque totale du myocarde du ventricule droit ». Il l'expliquait par un défaut de développement du muscle de cette cavité [17].

Deux cas analogues ont été ensuite publiés par Gasul (1960) [5] et Cumming (de Winnipeg, 1965) [3]. On peut en rapprocher un cas, d'interprétation un peu plus douteuse de Miss Taussig (édition de 1960 de son livre sur les cardiopathies congénitales) [16].

Dans ce petit groupe de cas *purs* du nourrisson, l'origine congénitale des troubles n'est pas discutable. L'absence d'anomalies coronariennes et de signes inflammatoires a d'autre part conduit logiquement les auteurs sus-nommés à invoquer une extrême hypoplasie ventriculaire droite, élective : pouvant s'expliquer embryologiquement dans le cadre de la théorie de Davis.

2° Toujours chez le nourrisson, quelques cas d'aspect ventriculaire droit identique, mais *associé* à d'autres anomalies congénitales, ont été rapprochés des précédents : forme avec atrésie pulmonaire et agénésie tricuspidienne (Mouquin-Lepoix, 1958 [8]; Neimann, 1965 [9]), forme avec tricuspide du type Ebstein (Taussig, 1960 [16]; Cumming, 1965 [3]), forme avec fibro-élastose endocardique diffuse (Arcilla-Gasul, 1961 [1]).

3° Quelques cas anatomiquement similaires, et de nature congénitale apparemment certaine, ont été également observés chez *l'adulte:* l'exemple le plus typique en étant probablement celui relaté par Castleman (1952) chez une jeune femme de 24 ans [2]. On en a rapproché quelques autres observations d'interprétation plus discutable : celle de Reeve par exemple (1964), concernant une femme morte à 47 ans, mais porteuse d'une large communication interauriculaire [13], ou celle de Gould (1967) concernant un homme mort à 66 ans d'une leucémie myéloïde, mais dont l'aspect anatomique « d'absence partielle de la musculature ventriculaire droite » était, il faut l'avouer, vraiment très particulier [6].

* Ou parcheminé (« *Parchment Right Ventricle* » des auteurs anglo-saxons).

(1) Communication présentée en mai 1967 à la Société Française de Cardiologie.

** Nous remercions les docteurs BRENIER (Grenoble), CHARLEUX (Annemasse), EXBRAYAT (Annonay) et STEFANINI (Chambéry) qui nous ont confié les malades étudiés ici.

Right Ventricular Dysplasia: A Report of 24 Adult Cases

FRANK I. MARCUS, M.D., GUY H. FONTAINE, M.D., GERARD GUIRAUDON, M.D., ROBERT FRANK, M.D., JEAN L. LAURENCEAU, M.D., CHRISTINE MALERGUE, M.D., AND YVES GROSGOGEAT, M.D.

SUMMARY **Right ventricular dysplasia is characterized by an abnormality in the development of part of the right ventricular musculature. Patients with right ventricular dysplasia may present with ventricular tachycardia, supraventricular arrhythmias, right-heart failure or asymptomatic cardiomegaly. Twenty-two adult patients with right ventricular dysplasia who had recurrent ventricular tachycardia were seen during a 7-year period. The male/female ratio was 2.7:1. The mean age at the time of hospitalization was 39 years. All but one of the patients had ventricular tachycardia of a left bundle branch block configuration. With few exceptions, the T waves were inverted over the right precordial leads. The heart was usually enlarged and the pulmonary vasculature was usually normal. In six patients who had two-dimensional echocardiograms, all showed increased right ventricular diastolic dimensions. All patients had right ventricular angiography; the diagnosis of right ventricular dysplasia was substantiated during surgery in 12 patients and at autopsy in another. Two other patients who did not have arrhythmias had right ventricular dysplasia diagnosed by right- and left-heart angiography.**

Our unique experience, when combined with a literature review of 34 adult cases, permits a composite clinical profile of this condition in the adult.

The New England
Journal of Medicine

Volume 318 JANUARY 21, 1988 Number 3

RIGHT VENTRICULAR CARDIOMYOPATHY AND SUDDEN DEATH IN YOUNG PEOPLE

GAETANO THIENE, M.D., ANDREA NAVA, M.D., DOMENICO CORRADO, M.D., LINO ROSSI, M.D., AND NATALE PENNELLI, M.D.

Abstract From 1979 to 1986, we conducted postmortem studies of 60 persons under 35 years of age who had died suddenly in the Veneto Region of northeastern Italy. Unexpectedly, we found that 12 subjects — 7 males and 5 females ranging in age from 13 to 30 years — had morphologic features of right ventricular cardiomyopathy. This disorder had not been diagnosed or suspected before the subjects died. In five cases, sudden death was the first sign of disease; the remaining seven subjects had a history of palpitations, syncopal episodes, or both, and in five of those seven, ventricular arrhythmias had previously been recorded on electrocardiographic examination. Ten of the subjects had died during exertion.

At autopsy, the subjects' heart weights were normal or moderately increased. Two main histologic patterns were identified — a lipomatous transformation or a fibrolipomatous transformation of the right ventricular free wall (6 cases each); in all cases, the left ventricle was substantially spared. Signs of myocardial degeneration and necrosis, with or without inflammatory infiltrates, were occasionally observed.

These findings indicate that right ventricular cardiomyopathy, the cause of which is still unknown, may be more frequent than previously thought. At least in this area of Italy, it may represent an important cause of sudden death among young people. (N Engl J Med 1988; 318:129-33.)

ARVD in Animal

Spontaneously Occurring Arrhythmogenic Right Ventricular Cardiomyopathy in the Domestic Cat

A New Animal Model Similar to the Human Disease

Philip R. Fox, DVM; Barry J. Maron, MD; Cristina Basso, MD, PhD;
Si-Kwang Liu, DVM, PhD; Gaetano Thiene, MD

Background—Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a primary myocardial disease of incompletely resolved pathogenesis and is a largely unappreciated cause of sudden death in the young.

Methods and Results—Clinical features of 12 domestic cats with ARVC (7 male; 1 to 20 years old, mean 7.3±5.2 years) were right-sided congo (n=3), polymorphic ve 8 cats examined with ec regurgitation. Eight die were characterized gros formation (n=6). Histo injury (myocyte death in the left ventricle (LV cats. Apoptosis was d ventricular septum) but

Conclusions—In the com in humans. This uniqu mechanisms responsibl

Key W

Arrhythmogenic Right Ventricular Cardiomyopathy Causing Sudden Cardiac Death in Boxer Dogs

A New Animal Model of Human Disease

Cristina Basso, MD, PhD; Philip R. Fox, DVM; Kathryn M. Meurs, DVM, PhD; Jeffrey A. Towbin, MD;
Alan W. Spier, DVM, PhD; Fiorella Calabrese, MD; Barry J. Maron, MD; Gaetano Thiene, MD

Background—Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a primary familial heart muscle disease associated with substantial cardiovascular morbidity and risk of sudden death. Efforts to discern relevant pathophysiological mechanisms have been impaired by lack of a suitable animal model.

Methods and Results—ARVC was diagnosed in 23 boxer dogs (12 male; 9.1±2.3 years old). Clinical events alone or in combination included sudden death (n=9; 39%), ventricular arrhythmias of suspected right ventricular (RV) origin (n=19; 83%), syncope (n=12, 52%), and heart failure (n=3; 13%). Right ventricular enlargement or aneurysms occurred in 10 (43%). Striking histopathological abnormalities were present in each boxer dog but not in controls, including severe RV myocyte loss with replacement by fatty (n=15, 65%) or fibrofatty (n=8, 35%) tissue. Focal fibrofatty lesions were also present in both atria (n=8) and the left ventricle (LV) (n=11). Fatty replacement occupied substantially greater RV wall area in ARVC dogs than controls (40.4±18.8% versus 13.8±3.4%, respectively) ($P<0.001$); residual myocardium was correspondingly reduced (56.6±19.2% versus 84.8±3.8% in controls) ($P<0.001$). MRI demonstrated bright anterolateral and/or infundibular RV myocardial signals, confirmed as fat by histopathology. Myocarditis appeared in the RV (n=14, 61%) and LV (n=16, 70%) and in each dog with sudden death, but not in controls. Familial transmission was evident in 10 of the 23.

Conclusions—We describe a novel, spontaneous, and genetically transmitted animal model of ARVC associated with sudden death in the boxer dog, closely resembling the human disease. This model may aid in understanding the pathogenic mechanisms of ARVC. (***Circulation***. **2004;109:1180-1185.**)

Key Words: models, animal ■ cardiomyopathy ■ pathology ■ death, sudden

Sudden Unexpected Perioperative Death

Table 1. Clinico-pathological data

Age/ Sex	Operation	Timing of cardiac arrest	Primary lesion	Associated lesions
44/M	Thyoid adenoma (el)	Maintenance	Dilated cardiomyopathy	MVP
32/F	Caesarean (em)	Maintenance	Dilated cardiomyopathy	His bundle fibrosis + MVP
47/M	Inguinal hernia (el)	Maintenance	Dilated cardiomyopathy	
33/M	Ungis incarnatus (el)	Maintenance	Hypertrophic cardimyopathy	His bundle fibrosis + MVP
16/M	Halux valgus (el)	Maintenance	Hypertrophic cardiomyopathy	Myocardial bridging of LAD + MVP
14/M	Tonsillectomy (el)	Maintenance	Hypertrophic cardiomyopathy	His bundle fibrosis
46/M	Fracture rotula(el)	Maintenance	Hypertrophic cardiomyopathyi	
23/M	Acetabulum prosth (el)	Induction	Hypertrophic cardiomyopathy	
14/M	Appendicectomy (em)	Maintenance	Acute myocarditis	
29/M	Lithotripsy (el)	Maintenance	CAD + thrombosis	
65/M	Prostatectomy (el)	Maintenance	CAD	Right ventricle hypertrophy
55/M	Prostatectomy (el)	Maintenance	CAD	Right ventricle hypertrophy
44/M	Intest. obstruction (em)	Maintenance	CAD	His bundle fib + MVP
21/F	Tibial fracture (em)	Post op	Coronary emboli	Mitral marentic endocarditis
9/M	Appendicectomy (em)	Induction	Abnormal pathway of coronary A	
62/M	Intest. obstruction (em)	Induction	Abnormal pathway of coronary A	
41/F	Buttock wound (el)	Induction	Myocardial bridging of LADC	His bundle fib + MVP
35/F	Ovarian cyst (el)	Induction	Myocardial bridging of LADC	
38M	Cholecystectomy (el)	Induction	Myocardial bridging of LADC	
3/M	Tonsillectomy (el)	Maintenance	His bundle fibrosis	
6/F	Adenectomy (el)	Maintenance	His bundle fibrosis	
36/F	Laparoscopy (el)	Maintenance	His bundle fibrosis	
38/M	Parotidectomy (el)	Maintenance	His bundle fibrosis + myomatosis	
44/F	Hysterectomy (el)	Induction	His bundle fibrosis + vasc. lesions	
43/F	Mastectomy (el)	2-h post op.	His bundle fibrosis + vasc. lesions	
64/F	Hysteroscopy (el)	Maintenance	His bundle fibrosis + vasc. lesions	
40/F	Hysterectomy (el)	Induction	His bundle fibrosis + vasc. lesions	
17/F	Halux valgus (el)	Induction	His bundle fibrosis + vasc. lesions	MVP
59/F	Hysterectomy (el)	Maintenance	Mitral valve prolaps	
42/F	Neurinoma of VIII (el)	Maintenance	ARVC	
32/F	Caesarean (em)	End	ARVC	
21/F	Appendicectomy (em)	End	ARVC	
38/F	Ligation of fallopian tube (el)	Maintenance	ARVC	
9/M	Fractured thumb (el)	Maintenance	ARVC	
8/M	Eye foreign body (em)	1-h post op.	ARVC	His bundle fibrosis
18/M	Laminectomy (el)	Maintenance	ARVC	
11/M	Tongue debridement (el)	2-h post op.	ARVC	
32/M	Cocised abcess (el)	Maintenance	ARVC	
10/F	Appendicectomy (em)	Maintenance	ARVC	
29/F	Varicose veins (el)	Induction	ARVC	Myocardial bridging of LAD
49/F	Cholecyctectomy (el)	Maintenance	ARVC	His bundle fibrosis
66/F	Hip joint prosthesis (el)	Induction	ARVC	
37/F	Caesarean (em)	Maintenance	ARVC	
44/M	Epistaxis (em)	Maintenance	ARVC	
40/M	Tonsillectomy (el)	Induction	ARVC	Right ventricle hypertrophy
22/M	Nasal polyp (el)	Induction	ARVC	Right ventricle hypertrophy
27/M	Pharyngeal foreign body (em)	End	ARVC	
8/M	Trigger thumb (el)	1-h post op.	Not any	
42/F	Ovarian cyst (el)	End	Not any	
60/M	Inguinal hernia (el)	1-h post op.	Not any	

em, emergency; el, elective; His bundle fibrosis + vasc. lesion, His bundle fibrosis plus intramural small coronary lesions, CAD, coronary artery disease; LAD, left descending anterior coronary artery; MVP, mitral valve prolapse; ARVC, arrhythmogenic right ventricle cardiomyopathy.

 European Journal of Anaesthesiology, 17, 230–235

Diagnosis of ARVC

- Diverse etiology of ventricular arrhythmias with a LBBB morphology
- Nonspecific ECG findings
- Interpretation of endomyocardial biopsy
- Assessment of RV structure and function
  - Thin walled structure
  - Irregular shape, highly trabeculated
  - No standard view
  - Technically unfamiliar
  - Physician inexperience

Diagnostic Tools

Noninvasive

- ECG
- Echo
- SAECG
- Holter ECG
- Exercise ECG
- CT/MRI

Invasive

- RV angio
- Biopsy
- EP study

Genetic

Diagnostic Criteria

I Global and/or regional dysfunction and structural alterations

MAJOR

Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment

Localised right ventricular aneurysms (akinetic or dyskinetic areas with diastolic bulging)

Severe segmental dilatation of the right ventricle

MINOR

Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle

Mild segmental dilatation of the right ventricle

Regional right ventricular hypokinesia

II Tissue characterisation of walls

MAJOR

Fibrofatty replacement of myocardium on endomyocardial biopsy

III Repolarisation abnormalities

MINOR

Inverted T waves in right precordial leads (V2 and V3) (people aged more than 12 yr; in absence of right bundle branch block)

IV Depolarisation/conduction abnormalities

MAJOR

Epsilon waves or localised prolongation (>110 ms) of the QRS complex in right precordial leads (V1–V3)

MINOR

Late potentials (signal averaged ECG)

V Arrhythmias

MINOR

Left bundle branch block type ventricular tachycardia (sustained and non-sustained) (ECG, Holter, exercise testing).

Frequent ventricular extrasystoles (more than 1000/24 h) (Holter)

VI Family history

MAJOR

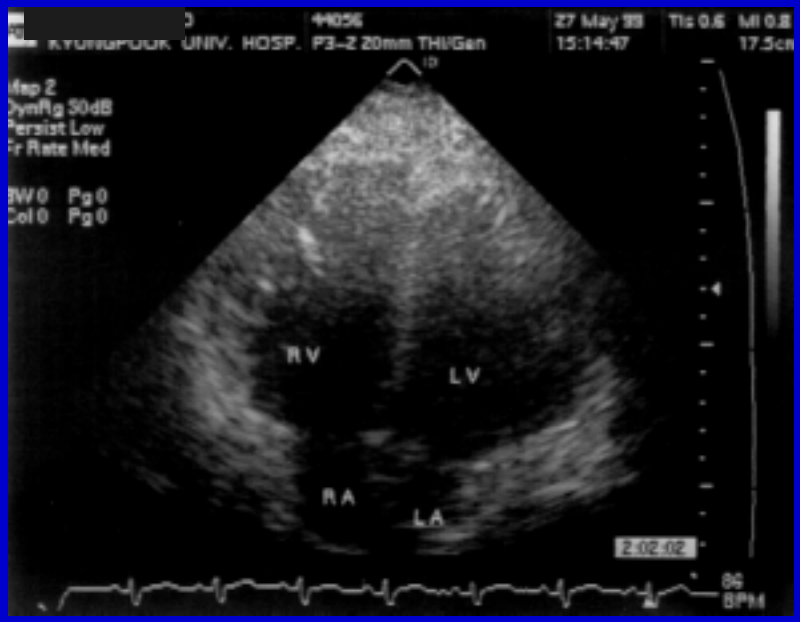
Familial disease confirmed at necropsy or surgery

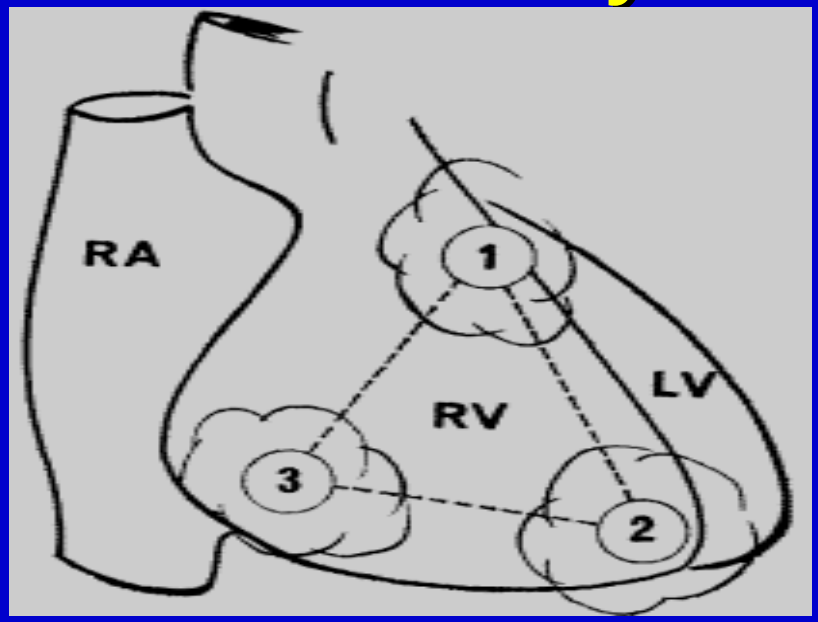
MINOR

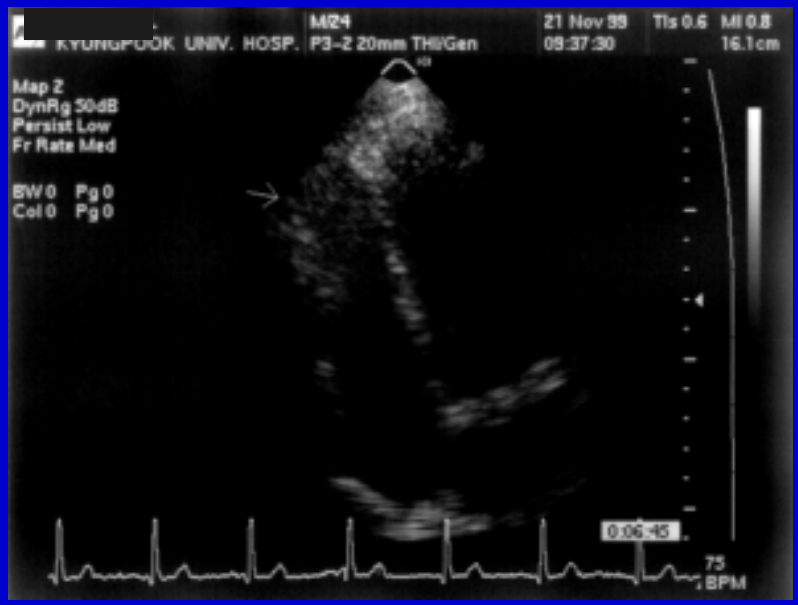
Familial history of premature sudden death (<35 yr) due to suspected right ventricular dysplasia.

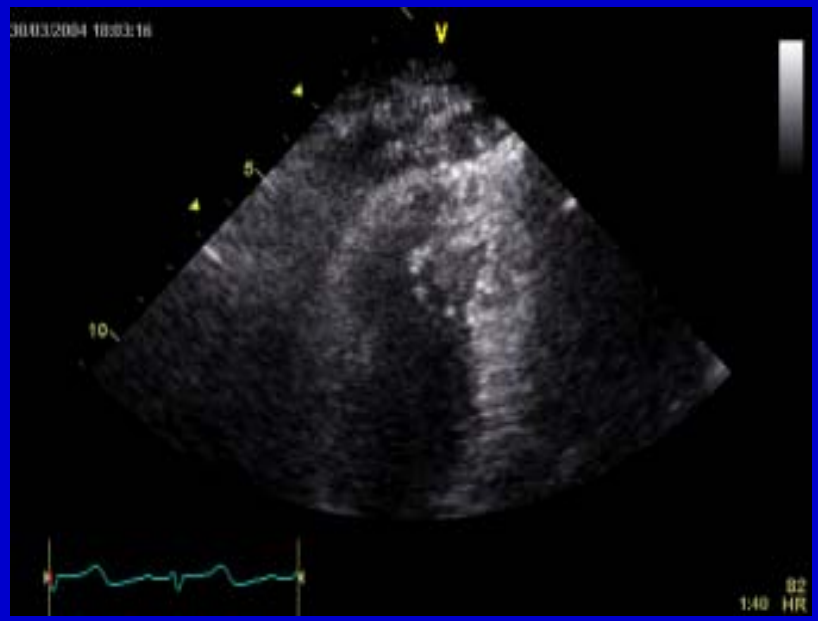
Familial history (clinical diagnosis based on present criteria)

RV Wall Motion Abnormality

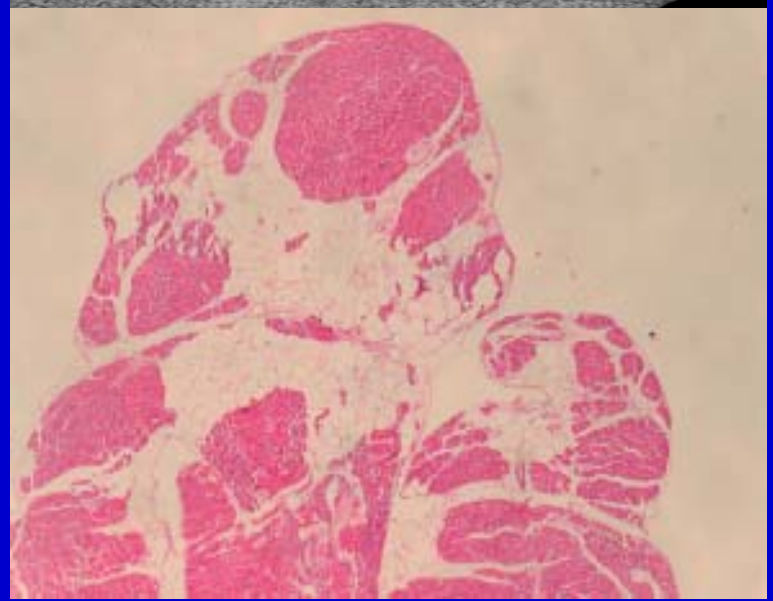


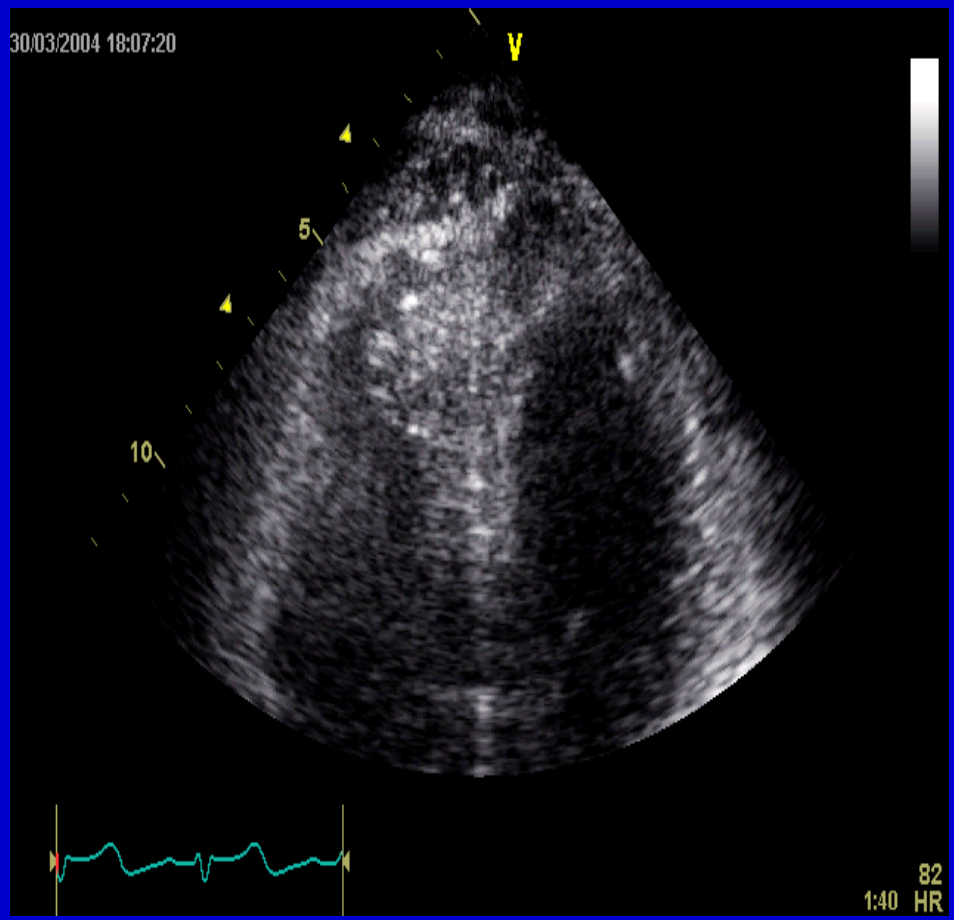




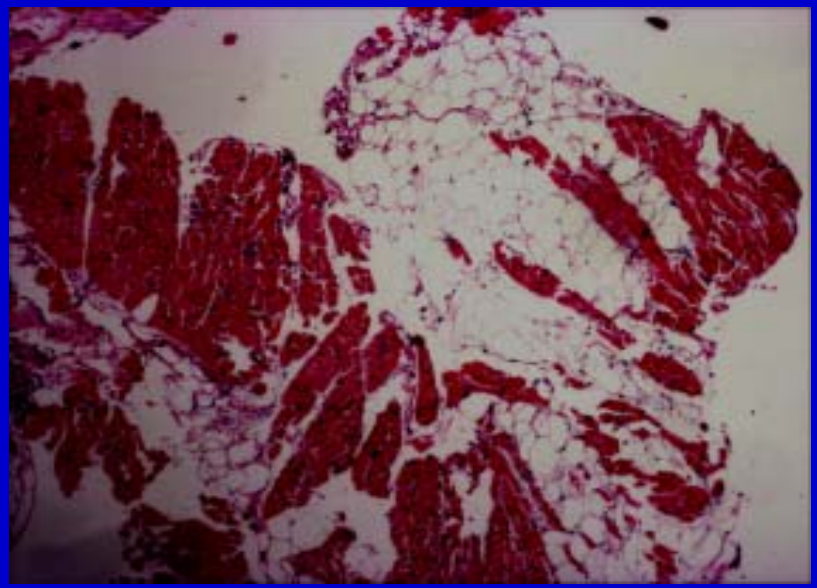


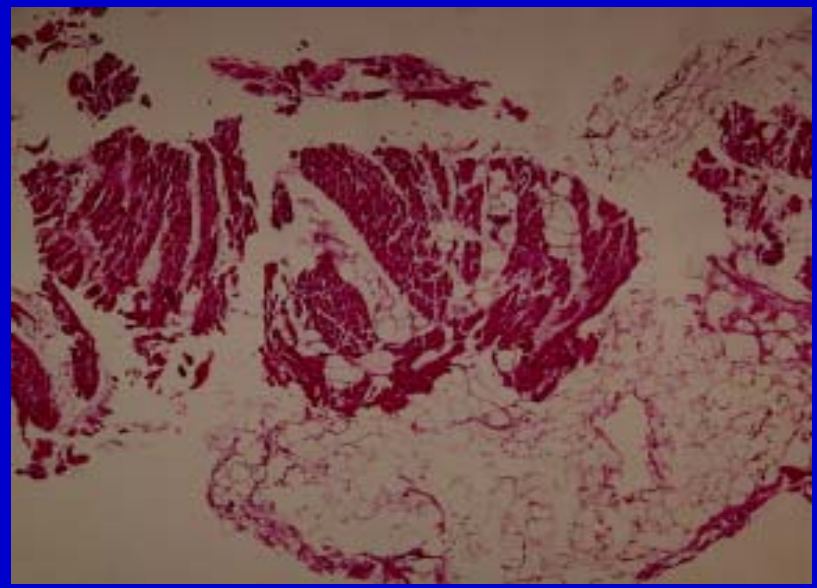
RV versus Bi-Ventricular Disease

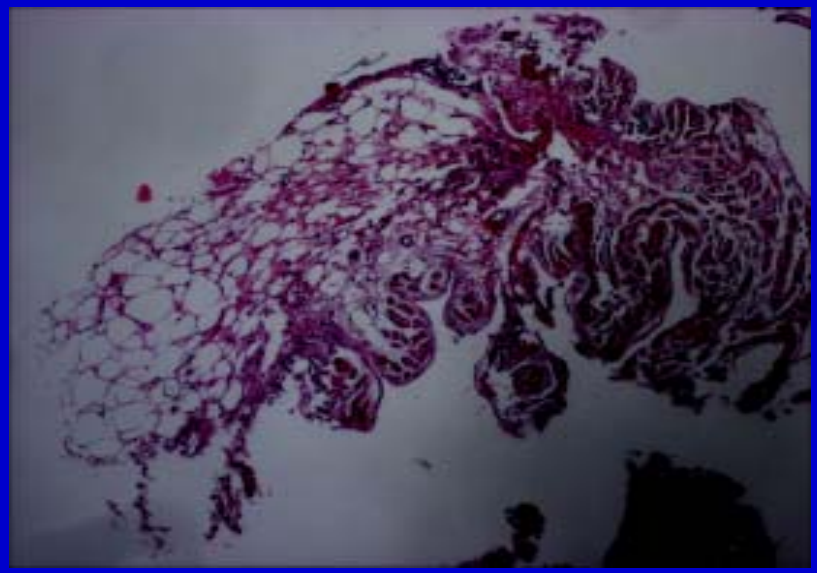


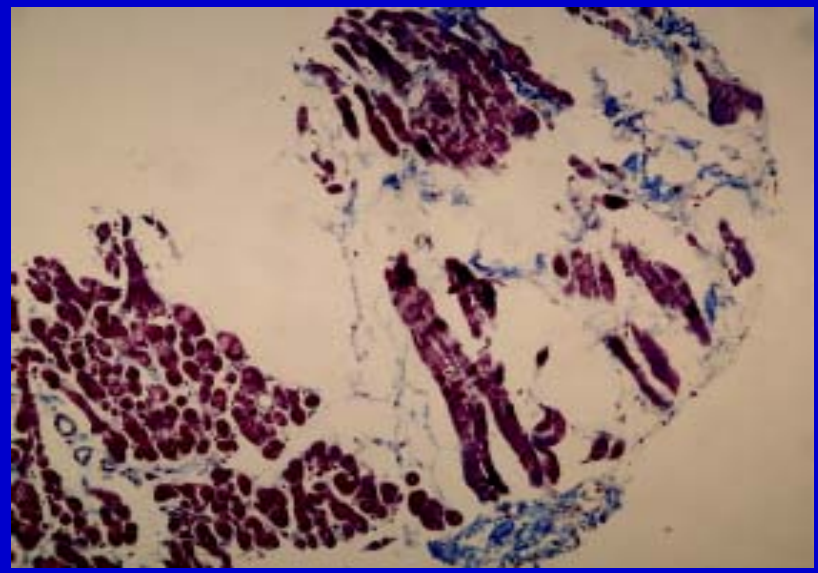


Tissue Characterization

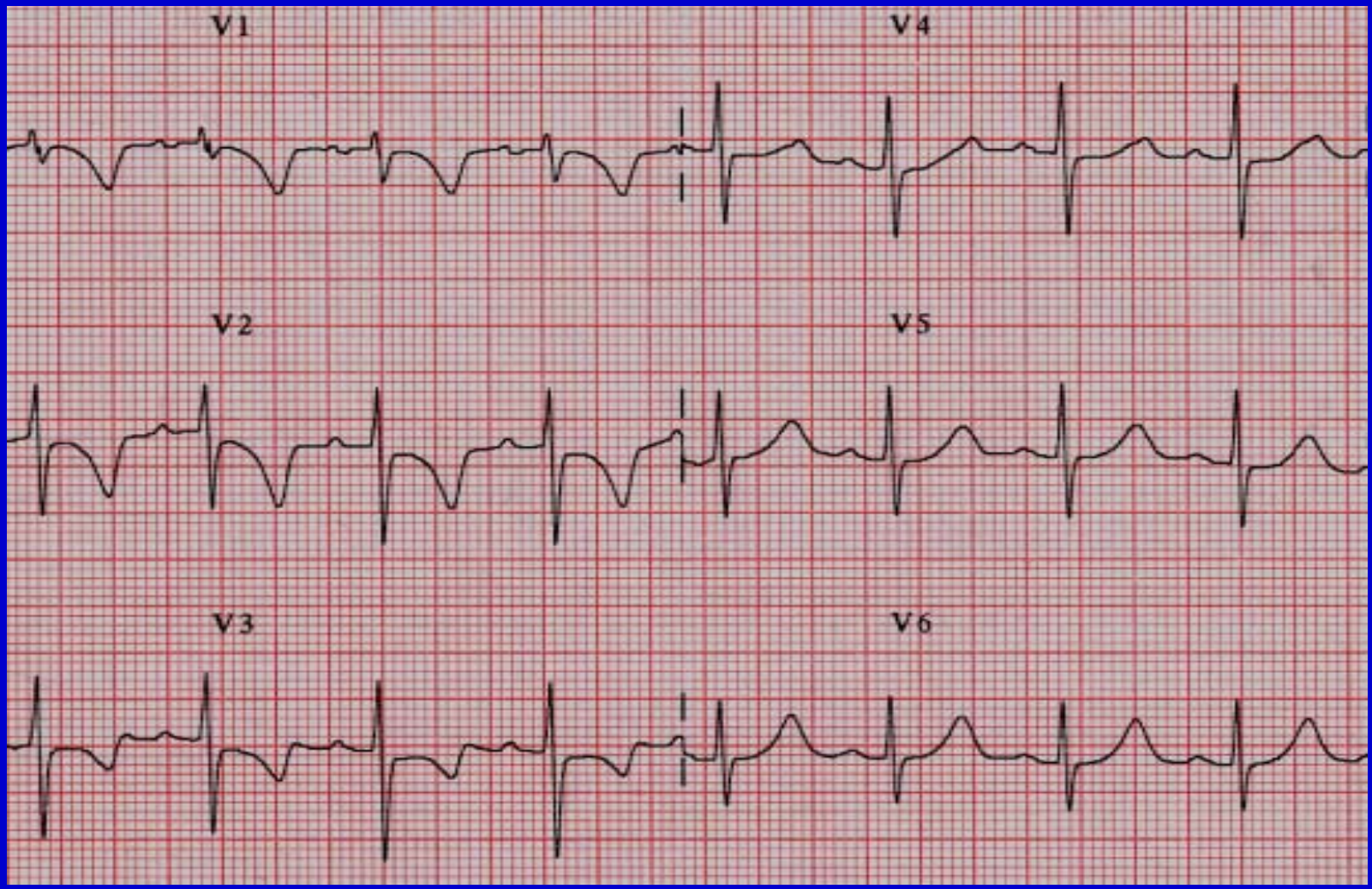






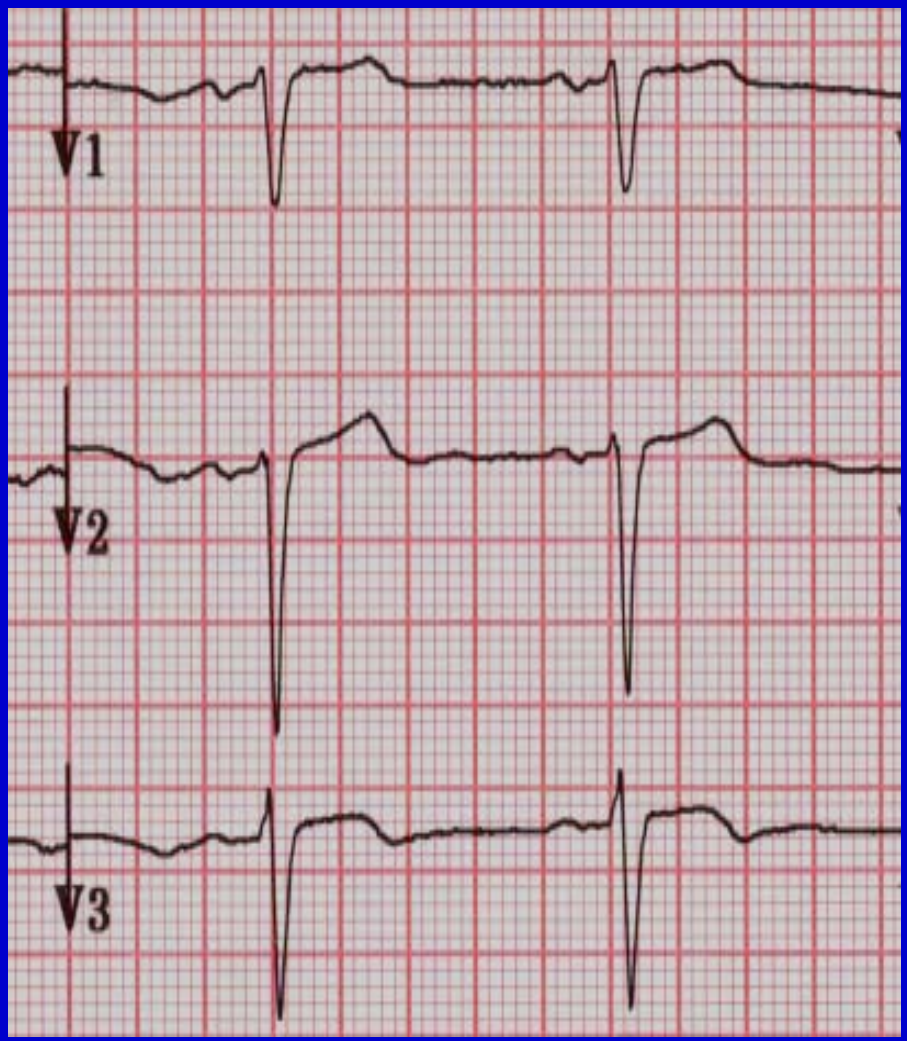


Repolarization Abnormality

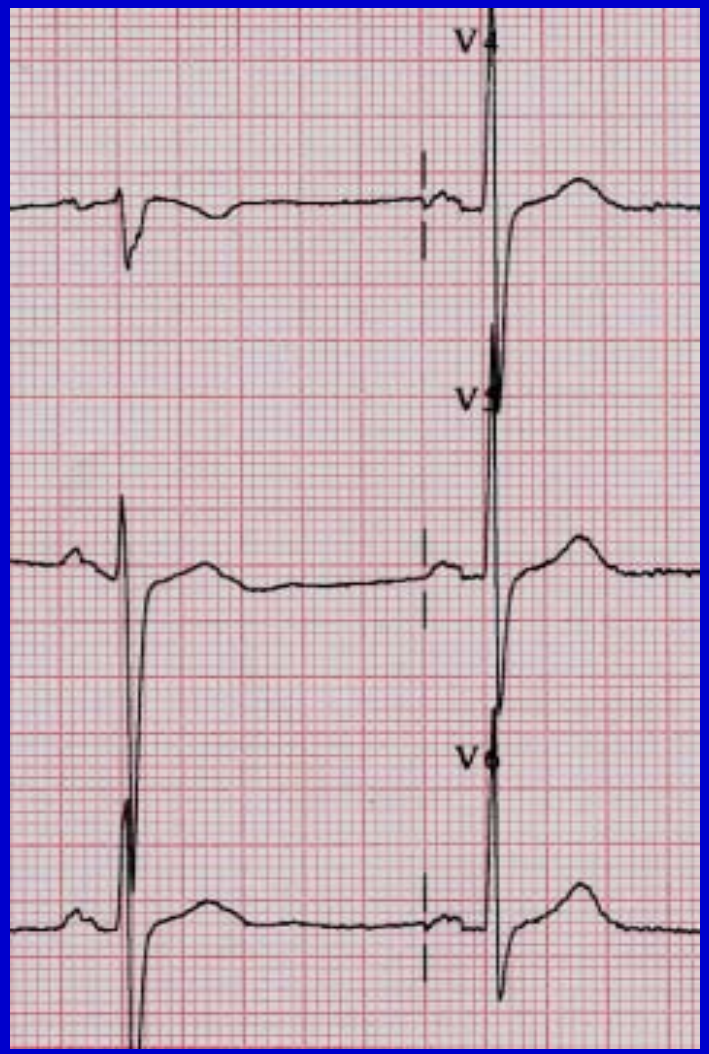


Depolarization/Conduction Abnormality

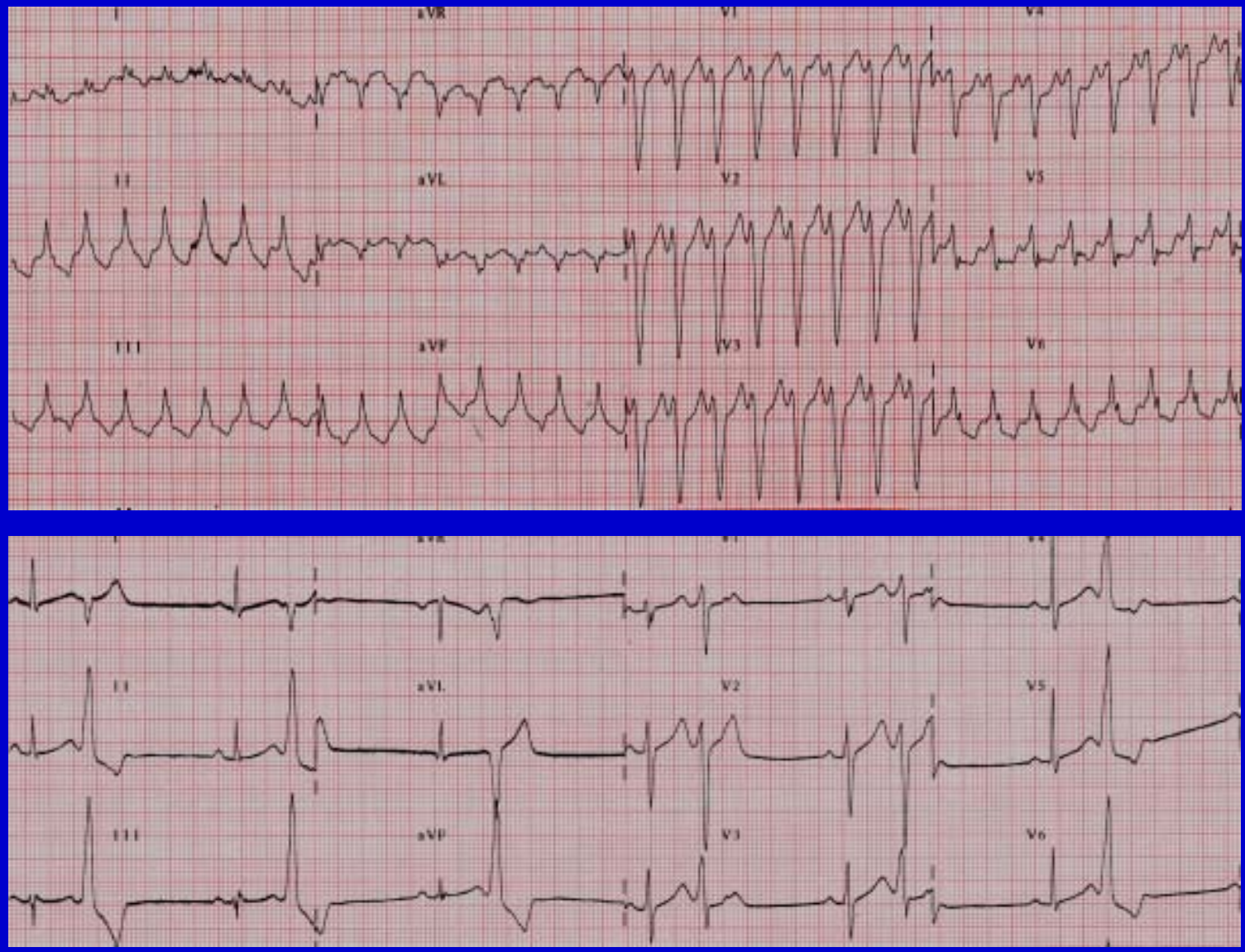
Epsilon Wave



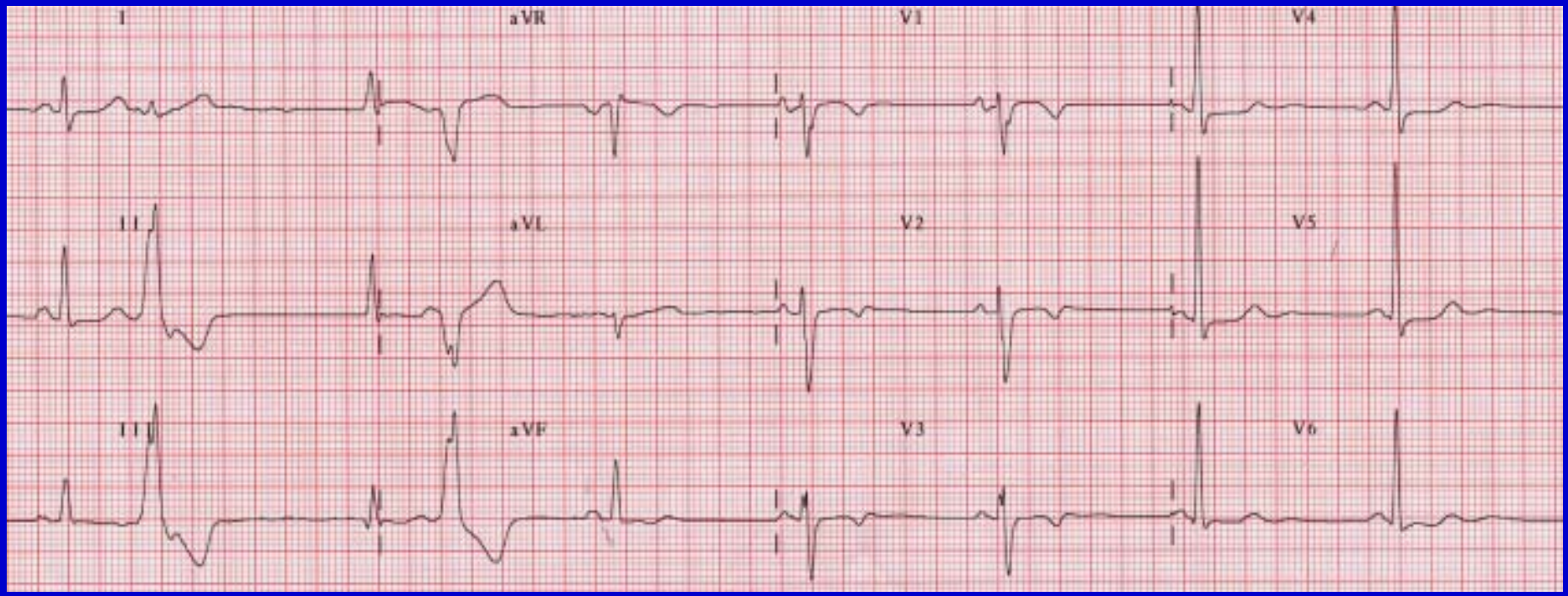
Localized QRS prolongation in Right Precordial Leads



LBBB Type VT/PVC



ECG Features of ARVD



- T wave inversions in V_1 through V_3.
- Prolonged S-wave upstroke in V_1 through V_3 $\geq$55 ms.

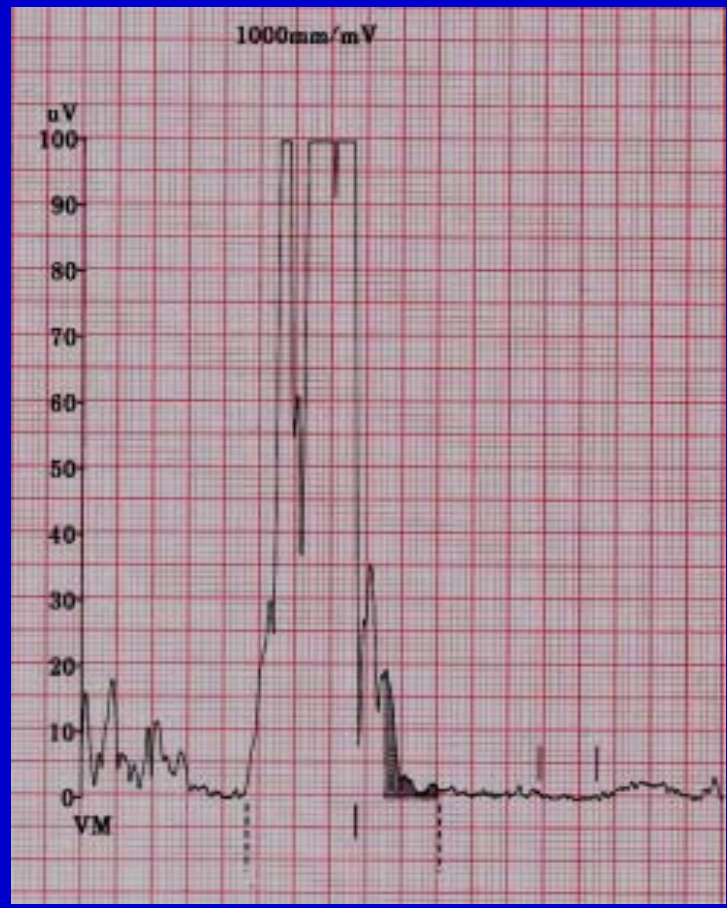
(Nasir 2004)

Late Potential

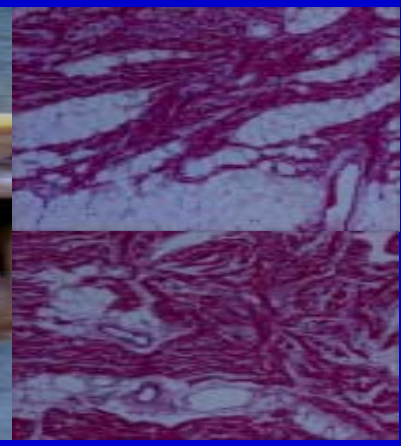
- Correlation between the SAECG and extent of disease than with the presence of ventricular arrhythmias (Nava 2000).

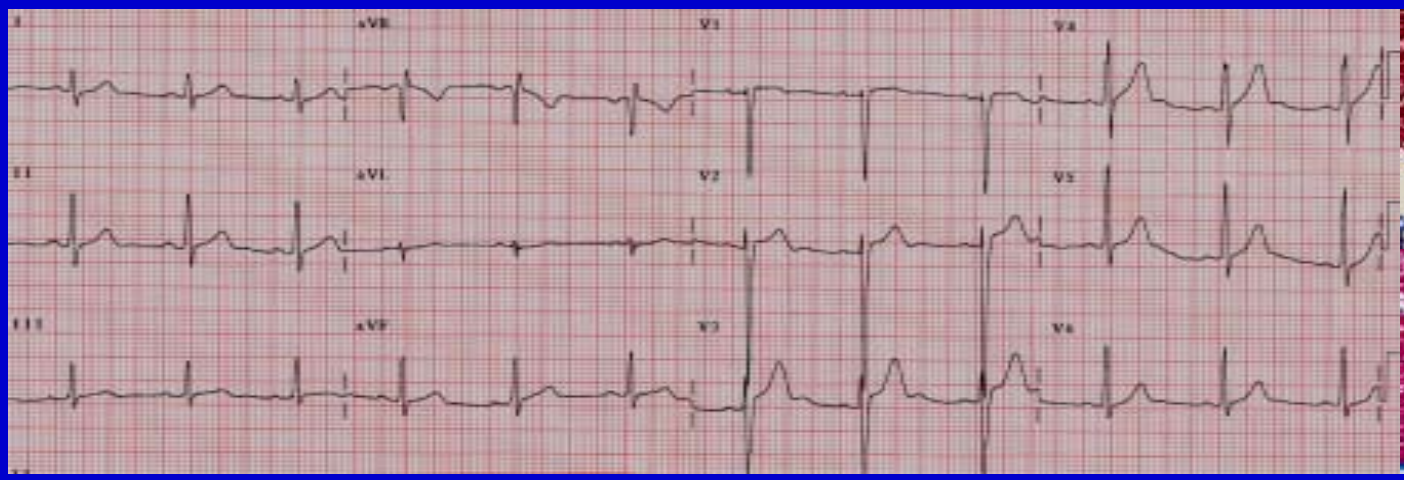
VERSUS

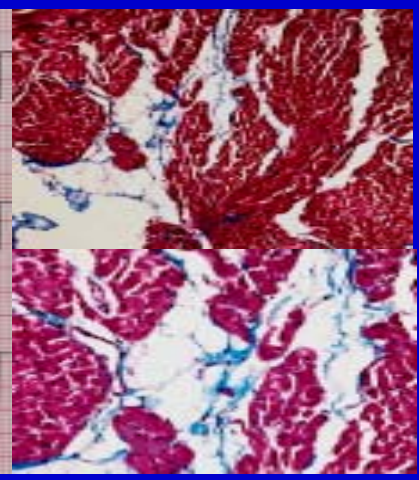
- Filtered QRS duration on SAECG predicts inducibility of sustained VT (Nasir 2003).



Family History

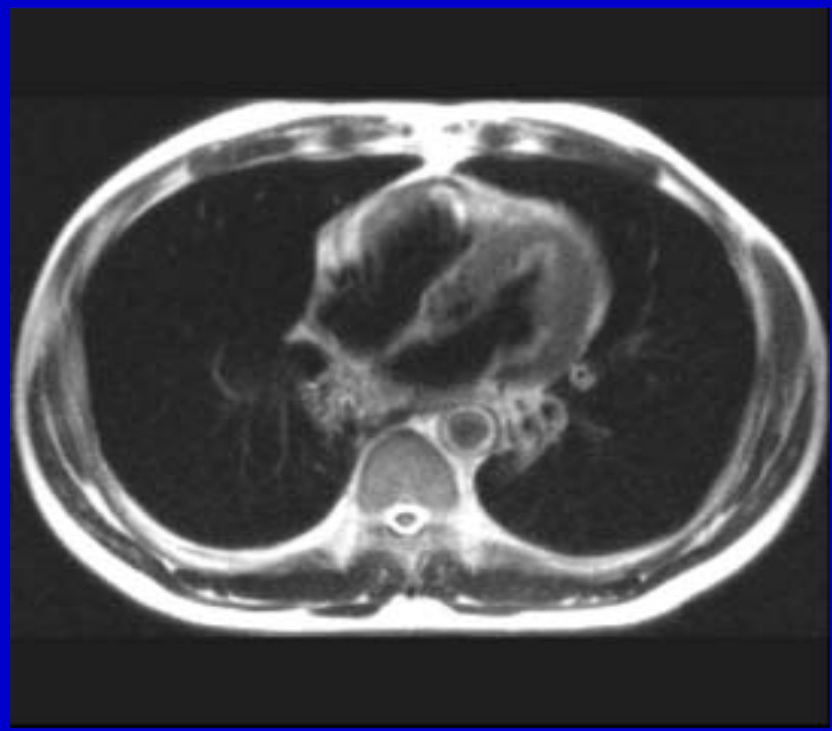






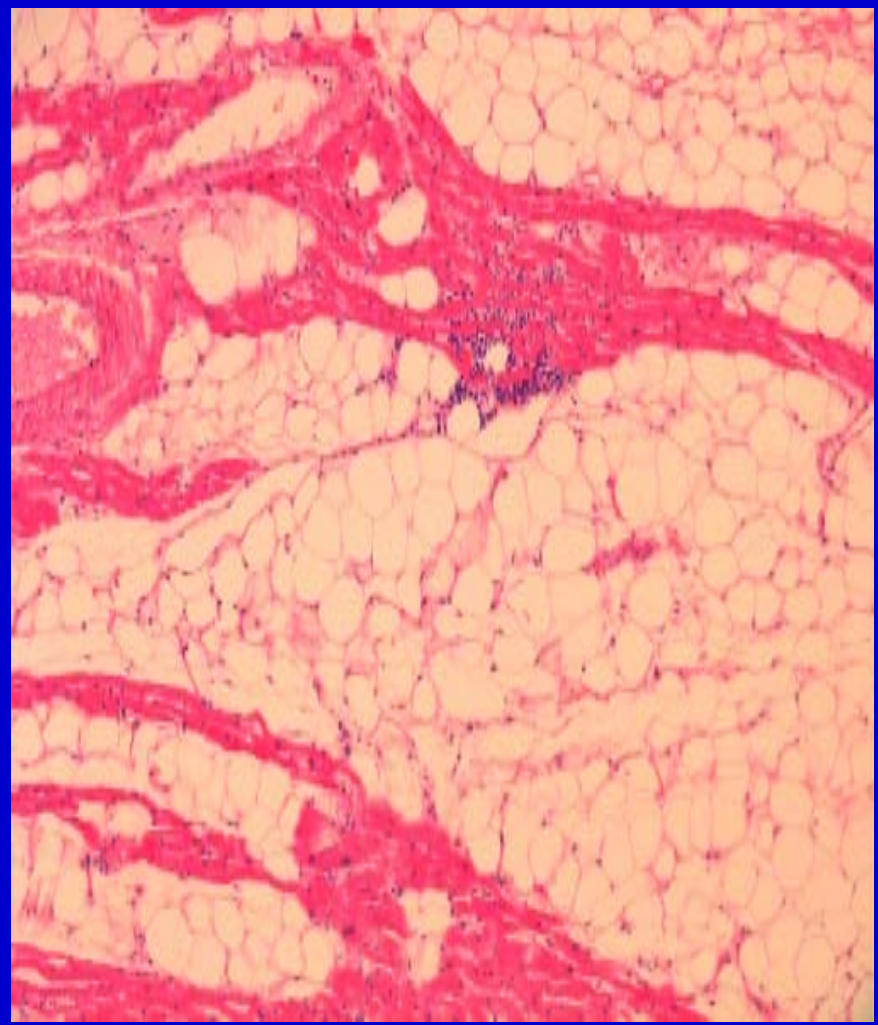
Misdiagnosis of ARVC

- Incomplete diagnostic testing.
- Lack of awareness of the Task Force criteria.
- Over-reliance on the presence of intramyocardial fat/wall thinning on MRI (Bomma 2004).
- MRI did not differentiate patients with ARVD from patients with localized myocarditis (Chimenti 2004).



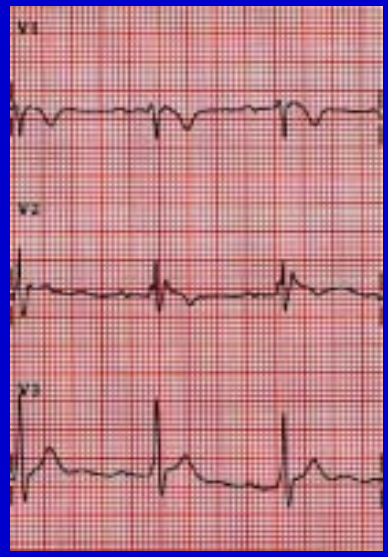
Cardiomyopathy versus Myocarditis

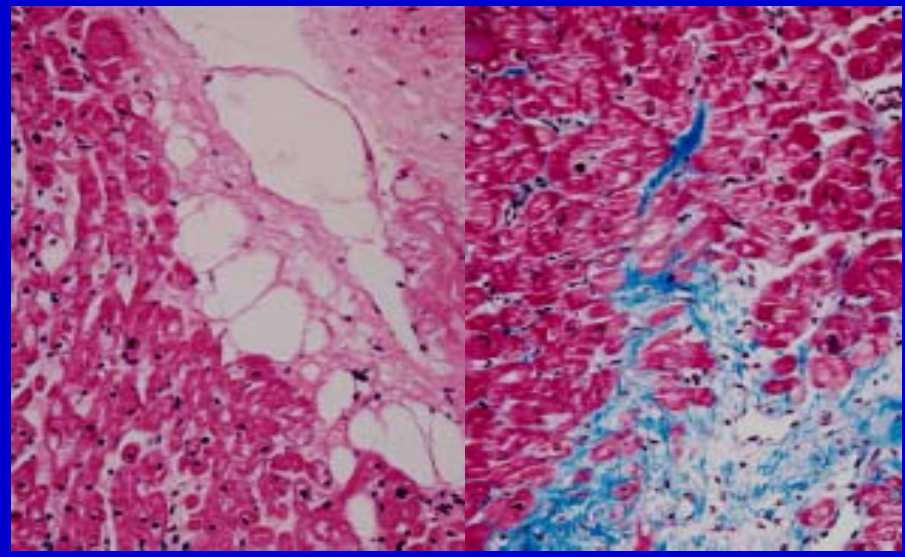
- High prevalence of myocarditis (80%)
- Myocardial inflammation was more prevalent in younger patients with fibrofatty ARVC
- Younger patients dying with fibrofatty ARVC may have a more lethal or aggressive form of the disease characterized by myocardial inflammation



ARVD and Brugada Syndrome

- RV morphologic and histologic abnormalities (Tada 1998 and Takagi 2001)
- Brugada ECG in 14% of victims of ARVC and available ECG (Corrado 2001).
- RV hypertrophy, fat infiltration and fibrosis in the RVOT (Coronel 2004).
- Coved ST segment elevation after ajmaline test in some ARVD patients (Peters2004).





Sports/Exercise

- Most SD or severe symptoms occurred during sports activity or exertion (Thiene 1988, Furlanello 1989, Corrado 1990). Prevalence of ARVC among athletes with CA or SD is high (23 and 25%). All CA were athletic activity related (Furlanello 1998).

VERSUS

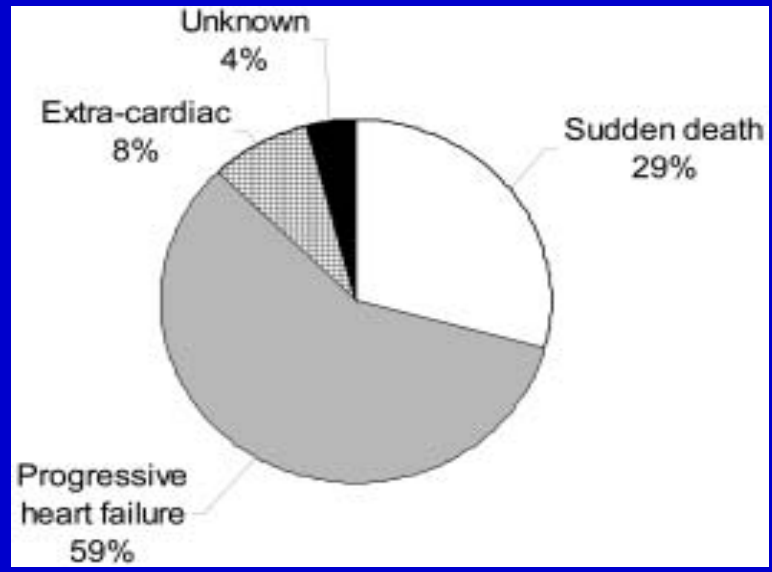
- Most SD occurred during everyday life events. Only 4% developed during sports activity (Tabib 2003). All sudden death was not related to vigorous physical or competitive activity (Cho 2003).

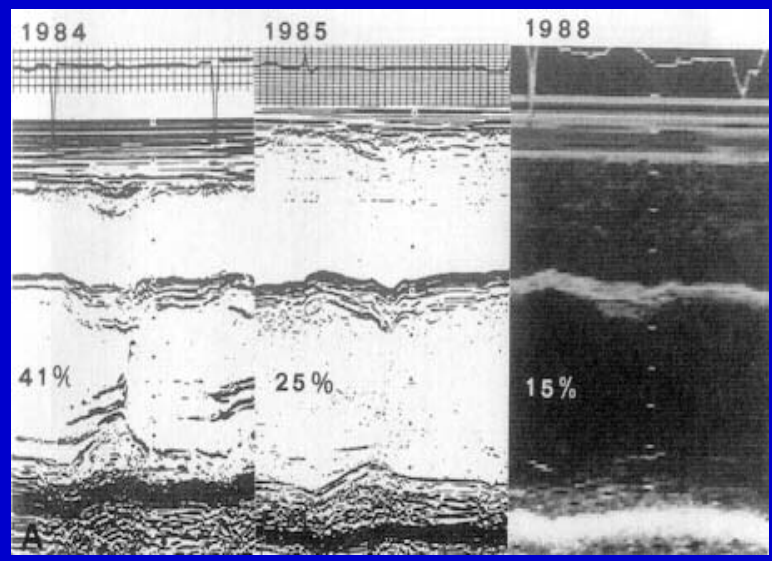
Risk of Cardiac Events

- History of syncope/cardiac arrest
- Younger age
- RV dysfunction
- LV involvement
- T inversion beyond V_1
- QRS dispersion ≥40 msec
- QT dispersion >65 msec
- Programmed Electrical Stimulation

versus

- RV failure and LV dysfunction
- Ventricular tachycardia (Hulot 2004)





Family Screening

- Minor ECG and echocardiographic abnormalities may diagnostic.
  - SAECG and standard ECG recordings showed abnormal findings in 38% (Hermida 1997).
  - 41% of family members were affected. During a follow-up of 8.5±4.6 years, 10% of unaffected at initial examination developed as an overt form of ARVC (Nava 2000).
  - Familial disease was present in 28% of index patients. A further 11% of their relatives had minor cardiac abnormalities (Hamid 2002).

Treatments of ARVC

- Beta blocker, Sotalol
- Catheter ablation
- Surgery
- ICD
- Heart transplantation?