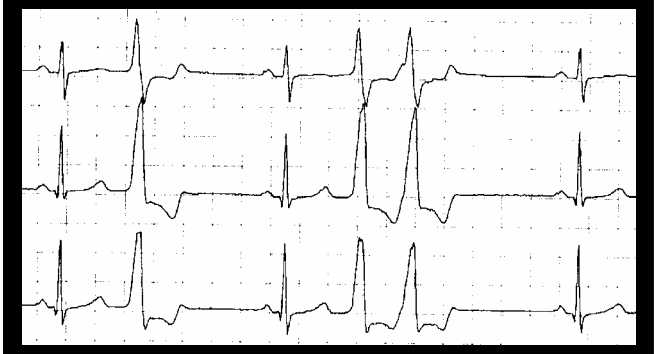
Ventricular Arrhythmias in Patients Without Structural Heart Disease.
Evaluating Risk.

Sami Viskin.
Tel Aviv Medical Center, Israel.

NASPE, Boston 2001.
Mexico City, Mexico 2002.
Zfat, Israel 2004.

Ventricular ectopy in clinically healthy adults



NSVT in Holter = 4%

Kennedy *N Engl J Med 1985*

The New England Journal of Medicine

73 asymptomatic healthy subjects.
- Age 40 ± 13 years.
- 560 ± 50 PVCs/hour, NSVT 26%
- Normal exercise stress test.
- 20% had coronary narrowing !
- 50% received beta-blockers !

Follow-up = 6.5 ± 2 years
➔ 1 (1.3%) sudden death.

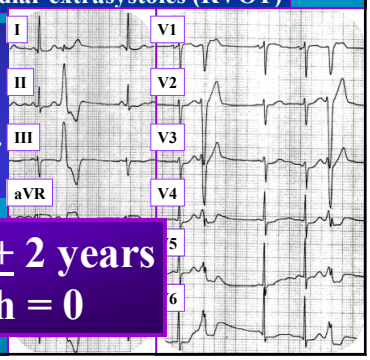
Long-Term Follow-Up of Right Ventricular Monomorphic Extrasystoles

Fiorenzo Gaita, MD,* Carla Giustetto, MD,† Paolo Di Donna, MD,* Elena Richiardi, MD,* Luigi Libero, MD,† Maria C. Rosa Brusin, MD,† Giuseppe Molinari, MD,* Giampaolo Trevi, MD†
Asti and Torino, Italy

J Am Coll Cardiol 2001

61 patients: right-ventricular extrasystoles (RVOT)

- *Age = 44 ± 15 years*
- *Normal ECG*
- *Normal echocardiogram*
- *Holter 60–2000 PVCs/hr*
- *Mean 400 PVCs/hr*



Follow-up 15 ± 2 years
• Sudden death = 0

The New England Journal of Medicine

VOLUME 343 SEPTEMBER 21, 2000 NUMBER 12

LONG-TERM OUTCOME IN ASYMPTOMATIC MEN WITH EXERCISE-INDUCED PREMATURE VENTRICULAR DEPOLARIZATIONS

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 27, 2003

Frequent Ventricular Ecto… as a Predictor… se

Joseph P. Frolkis, M.D., Ph.D., Claire E. Pothier, M.S., … M.D., and Michael S. Lauer, M.D.

Prior myocardial infarction
16% - 34%.

Are exercise induced ventricular arrhythmias really benign?

- > 6000 men from the Paris Civil Service.
- No clinical evidence of heart disease.
- Normal electrocardiogram.
- ➔Submaximal exercise testing.

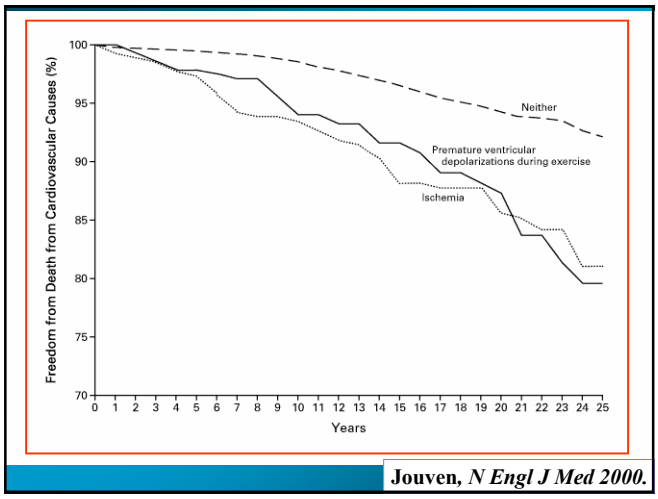
Age 40 –50 y.
Max rate 160

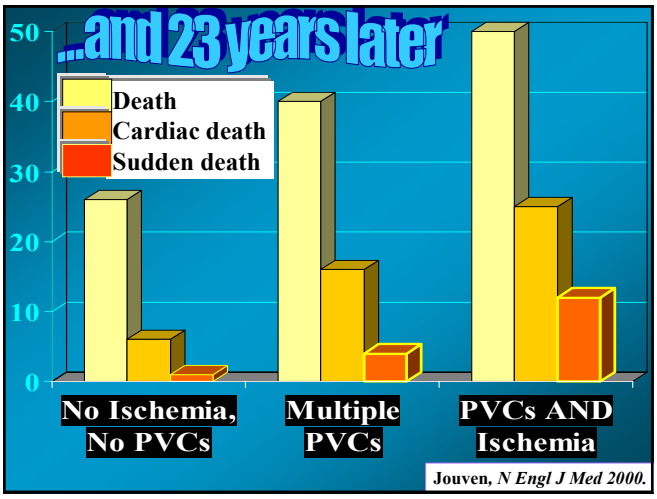
Frequent PVCs with exercise*

Before	During	After
1%	2%	3%

*>10% of QRS per ECG trace

Jouven, *N Engl J Med 2000.*





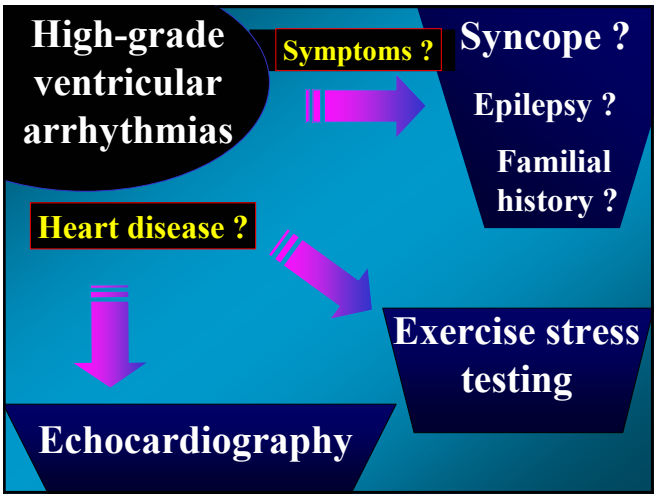
Patients with ventricular arrhythmias.

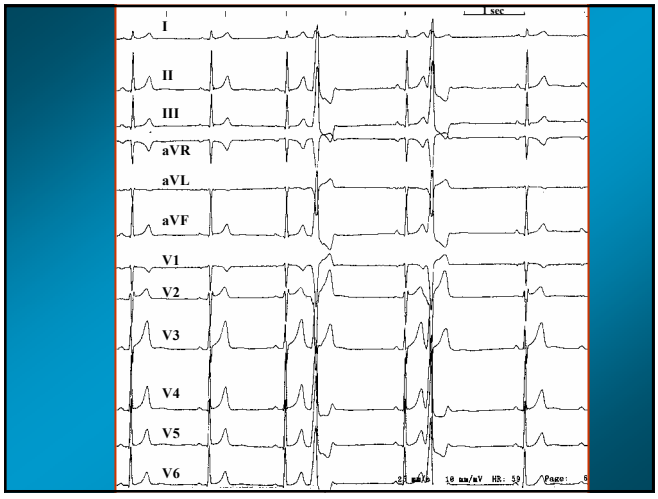
If symptoms do *NOT* suggest sustained arrhythmias.

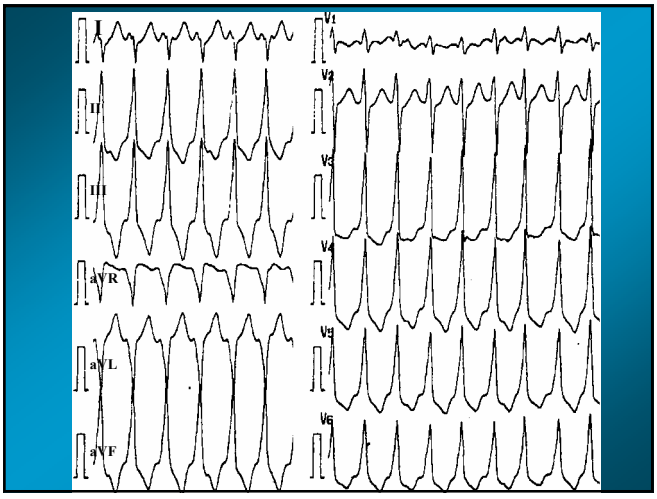
If baseline *ECG* and *echocardiogram* are normal.

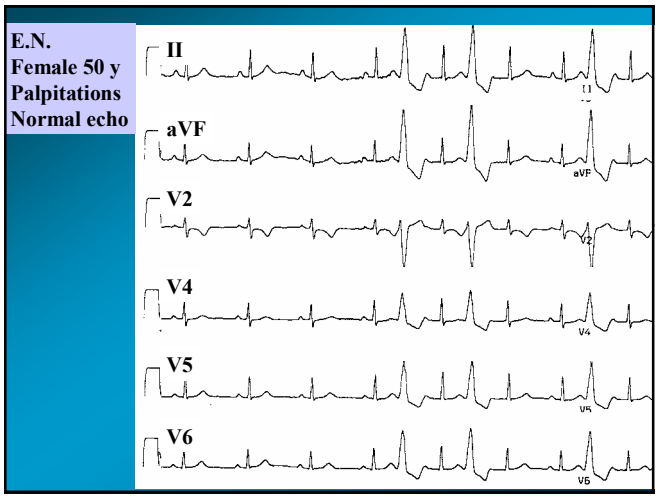
The risk for sudden death *should be* small, but the evidence supporting this statement is limited.

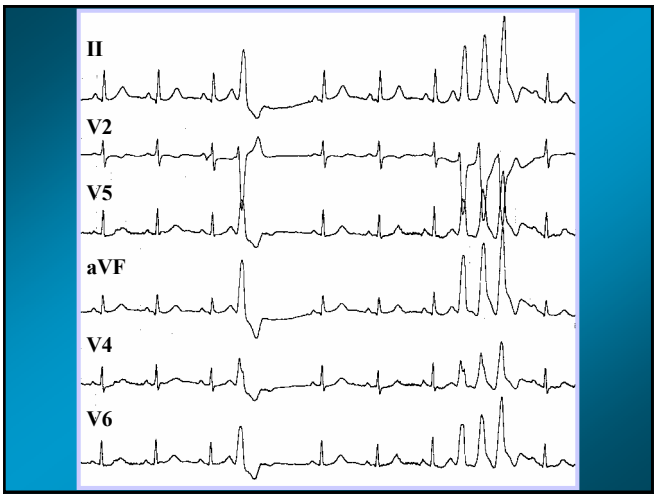
There is *NO EVIDENCE* to support aggressive approach or antiarrhythmic therapy.

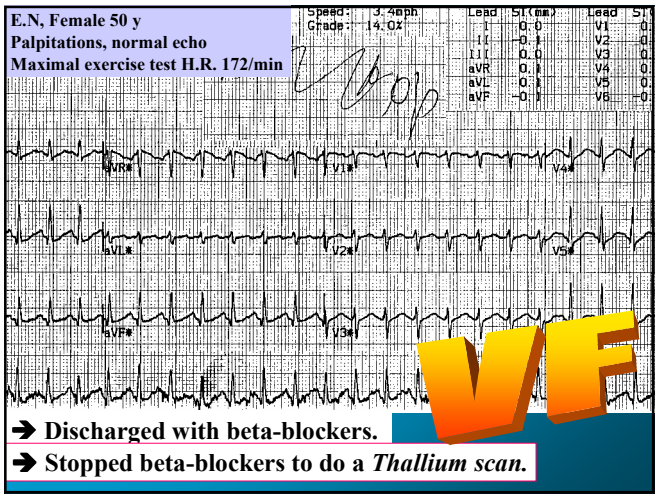


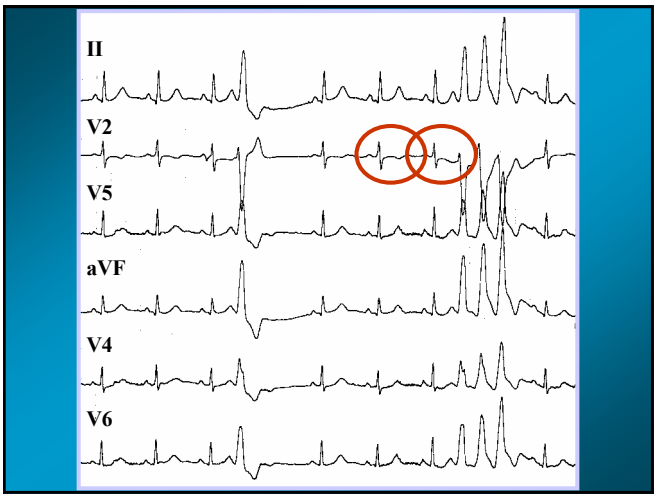


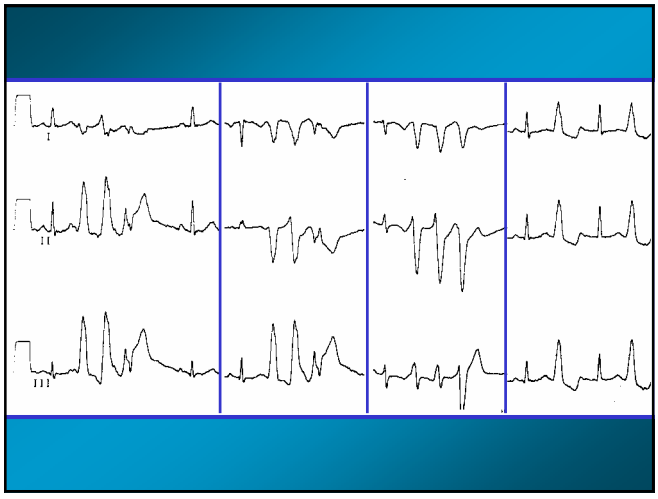


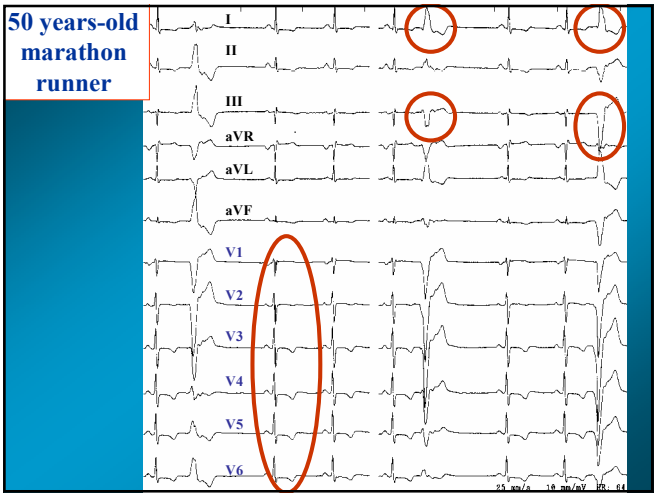

E.N.
Female 50 y
Palpitations
Normal echo
II
aVF
V2
V4
V5
V6

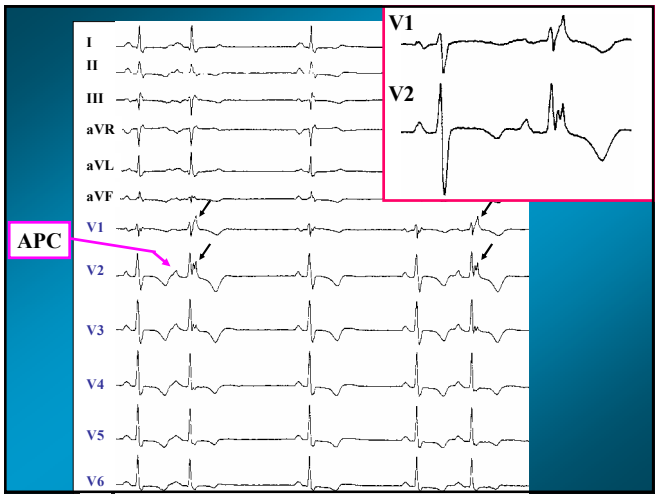

II
V2
V5
aVF
V4
V6

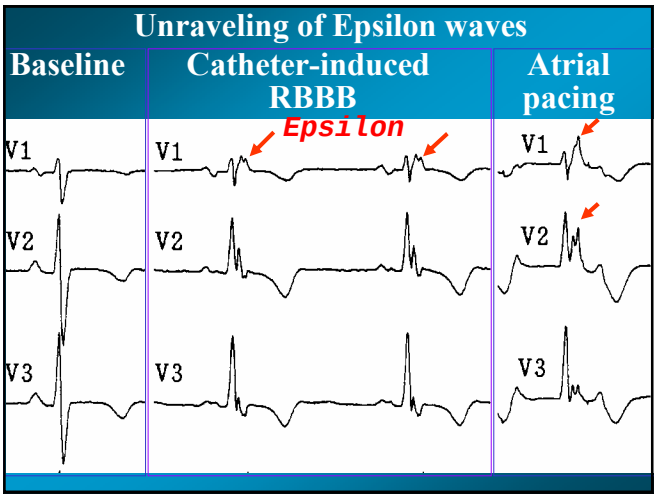

E.N, Female 50 y
Palpitations, normal echo
Maximal exercise test H.R. 172/min
VF
➔ Discharged with beta-blockers.
➔ Stopped beta-blockers to do a *Thallium scan.*

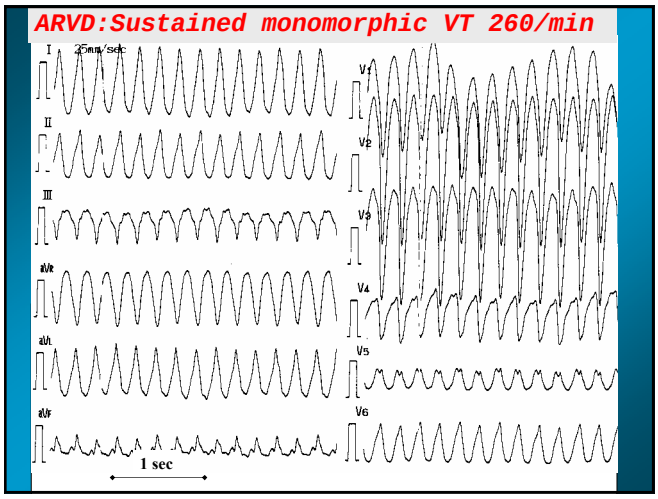

II
V2
V5
aVF
V4
V6




50 years-old
marathon
runner
I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6







Polymorphic ventricular arrhythmias without organic heart disease

Catecholaminergic polymorphic VT

Congenital long QT syndromes

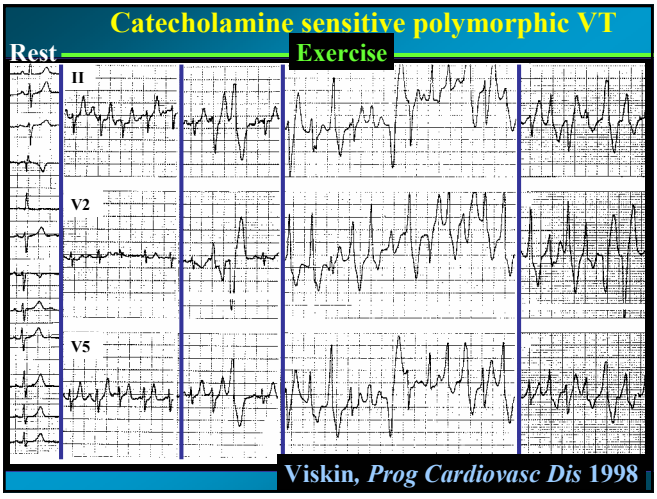
Idiopathic ventricular fibrillation
- with RBBB and ST
- with normal ECG

Catecholamine-dependent polymorphic VT

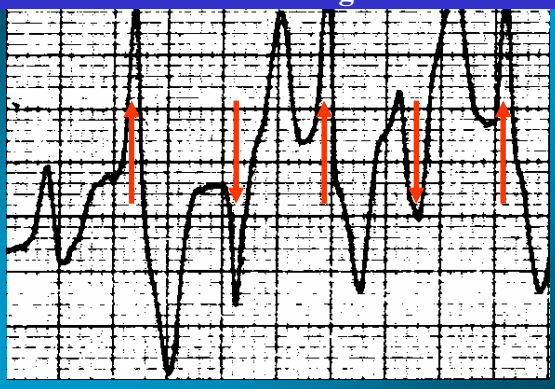
- Age: 8 ± 4 years.
- Male/female = 1.3/1
- Family history ++
- Stress related symptoms +++

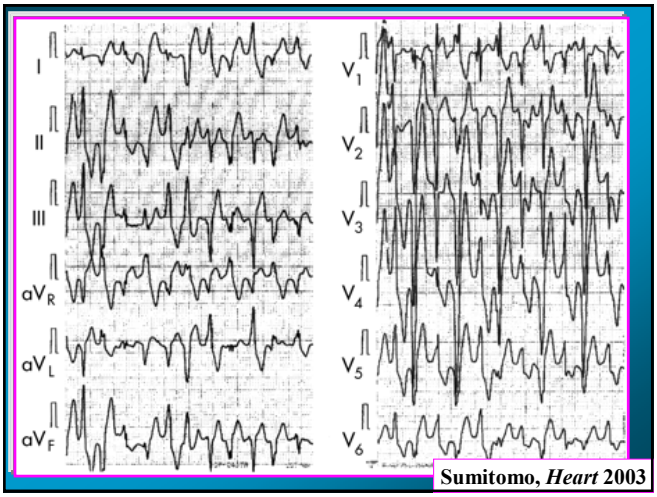
Coumel. *Br Heart J* 1978. Leenhardt. *Circulation* 1995.

- Autosomal dominant: 2 families (33 ± 15 years) linked to chromosome 1q42-q43. Swan, *JACC* 1999
- RyR2 (the gene responsible for calcium release from sarcoplasmic reticulum). Priori, *Circulation* 2000
- CASQ2 (the gene for calsequestrin, the calcium reservoir in sarcoplasmic reticulum). Lahat, *Circulation* 2001



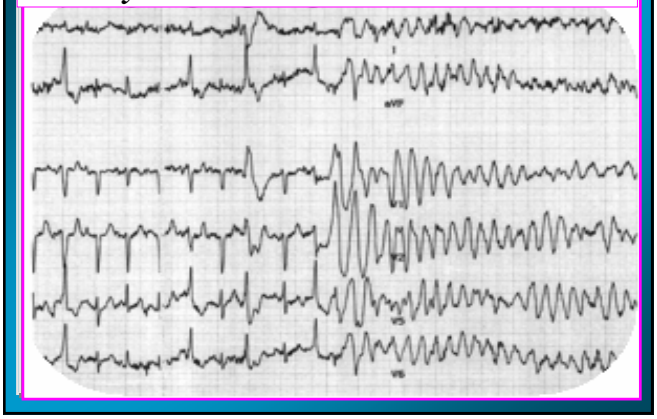
Bidirectional tachycardia in catecholaminergic VT



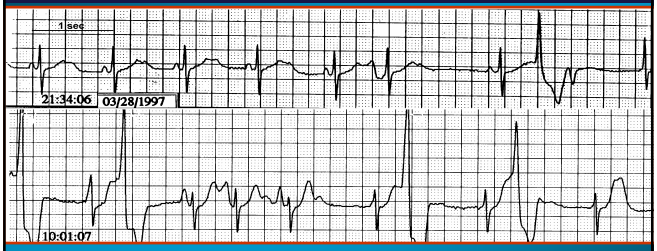


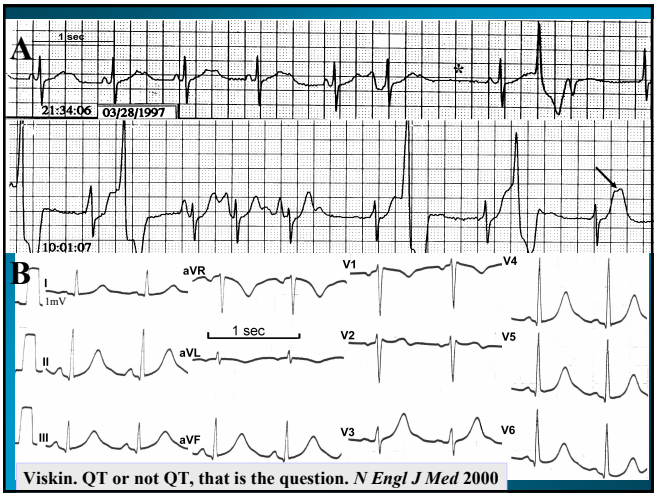
Sumitomo, *Heart* 2003

Evaluation of exercise-induced syncope…
don't try this at home



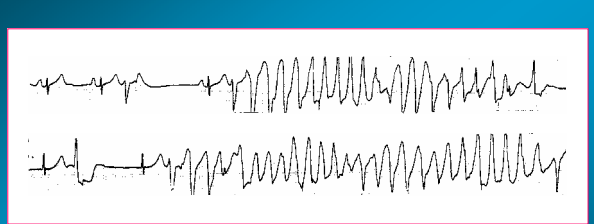
Female, age 32.
Referred for "asymptomatic arrhythmias"

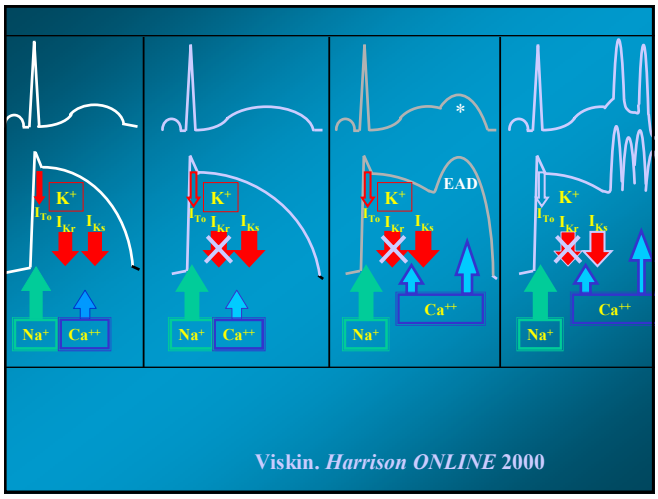


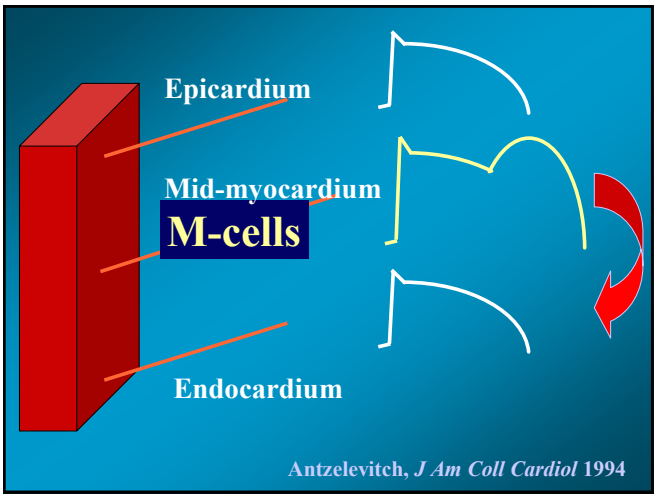


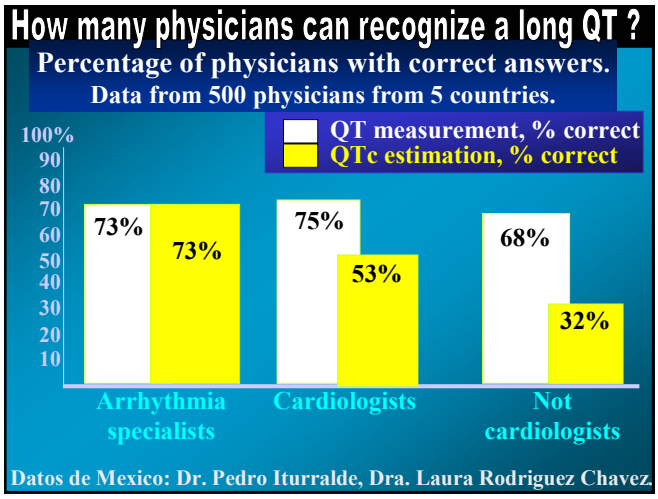
Viskin. QT or not QT, that is the question. *N Engl J Med* 2000

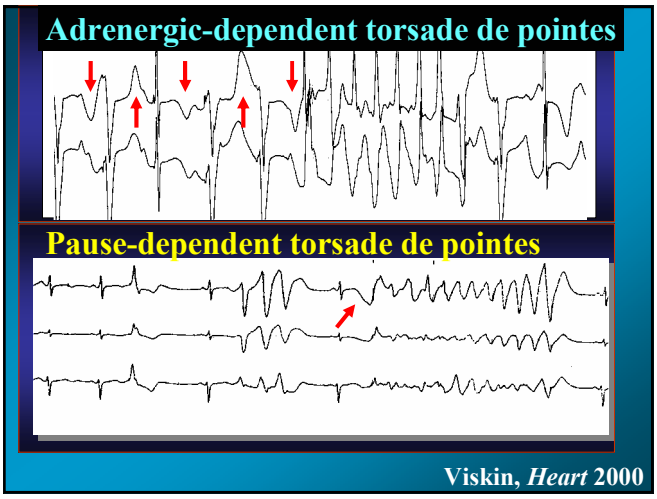
The long QT syndrome and torsade de pointes

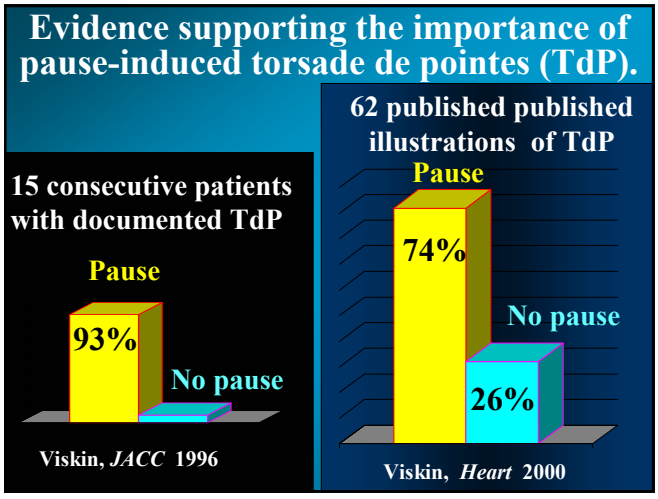


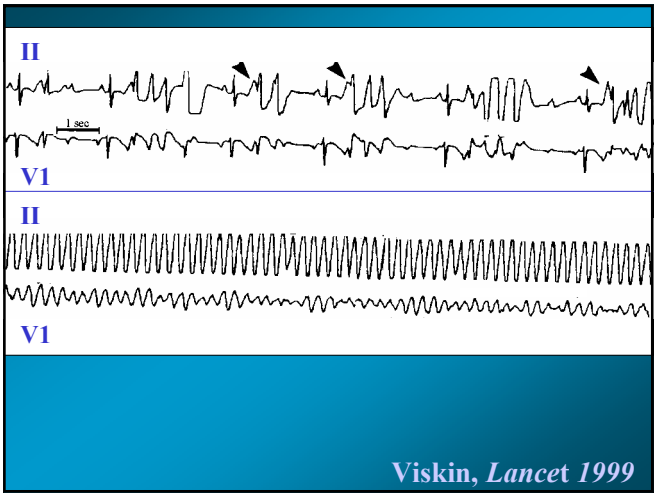

EAD
K+
Na+
Ca++
Viskin. Harrison ONLINE 2000

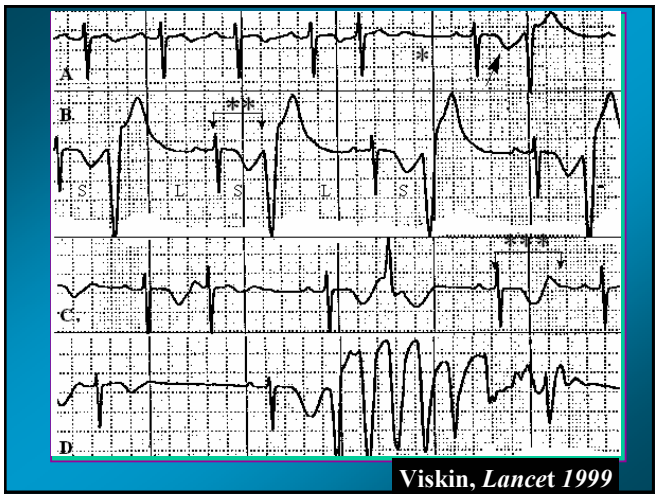

Epicardium
Mid-myocardium
M-cells
Endocardium
Antzelevitch, J Am Coll Cardiol 1994


How many physicians can recognize a long QT ?
Percentage of physicians with correct answers.
Data from 500 physicians from 5 countries.
QT measurement, % correct
QTc estimation, % correct
100%
90
80
70
60
50
40
30
20
10
73%
73%
75%
53%
68%
32%
Arrhythmia specialists
Cardiologists
Not cardiologists
Datos de Mexico: Dr. Pedro Iturralde, Dra. Laura Rodriguez Chavez.

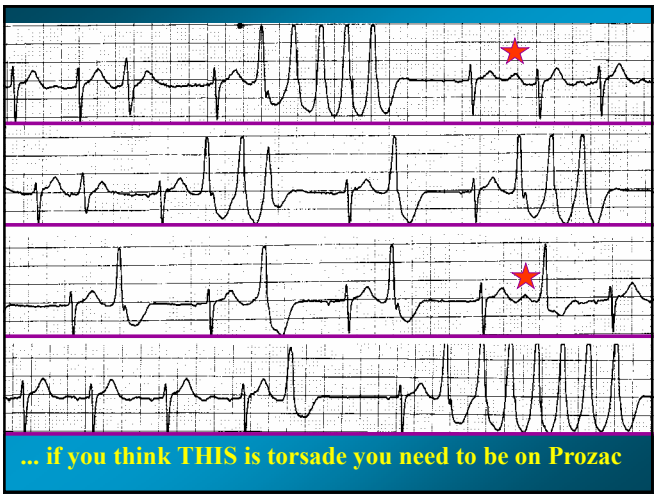

Adrenergic-dependent torsade de pointes
Pause-dependent torsade de pointes
Viskin, Heart 2000

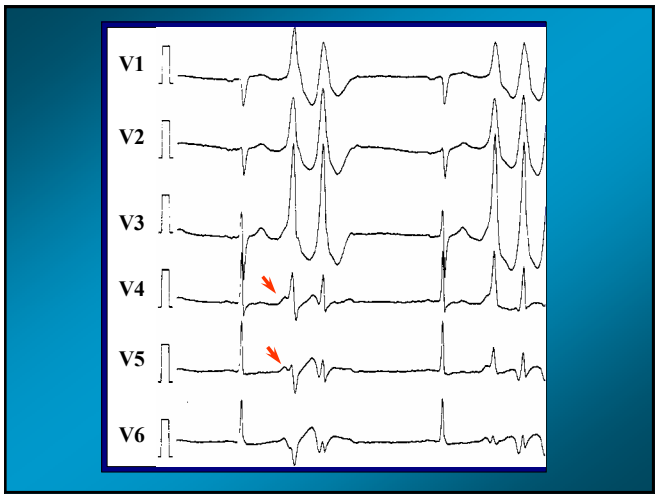

Evidence supporting the importance of pause-induced torsade de pointes (TdP).
15 consecutive patients with documented TdP
Pause
93%
No pause
Viskin, JACC 1996
62 published published illustrations of TdP
Pause
74%
No pause
26%
Viskin, Heart 2000


II
1 sec
V1
II
V1
Viskin, Lancet 1999

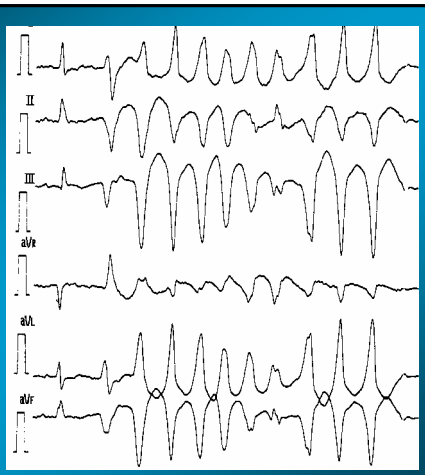


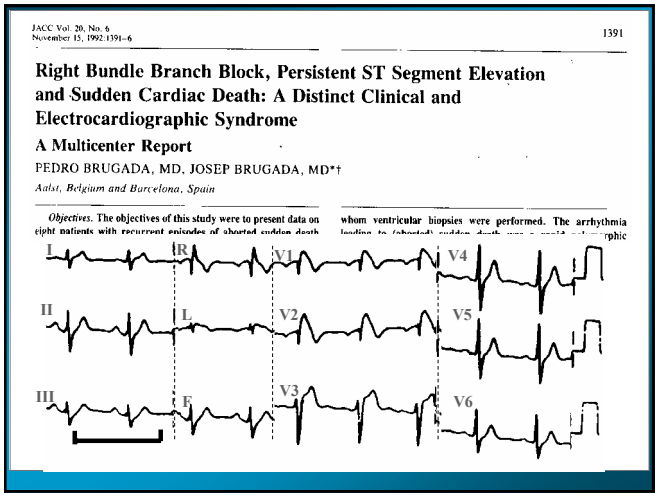
Viskin, *Lancet 1999*


... if you think THIS is torsade you need to be on Prozac



And some time later…




JACC Vol. 20, No. 6
November 15, 1992:1391–6

1391

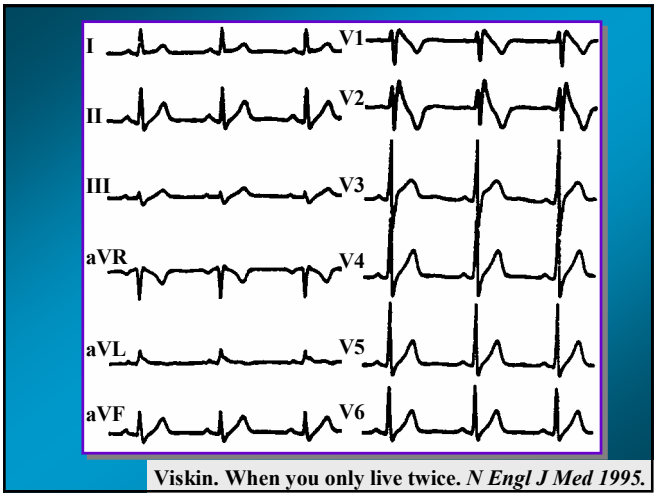
Right Bundle Branch Block, Persistent ST Segment Elevation and Sudden Cardiac Death: A Distinct Clinical and Electrocardiographic Syndrome

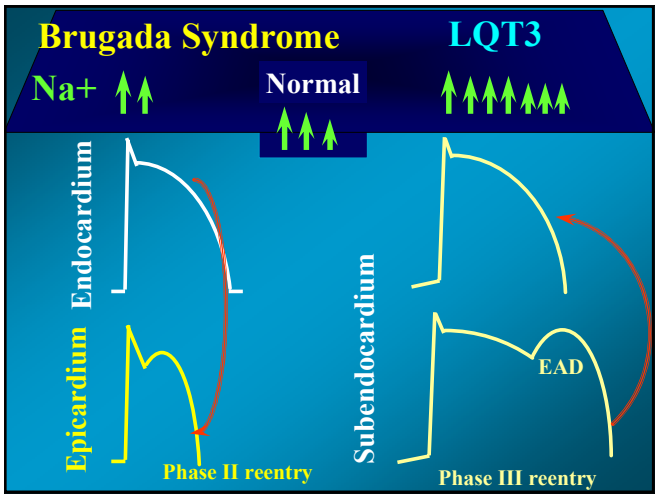
A Multicenter Report

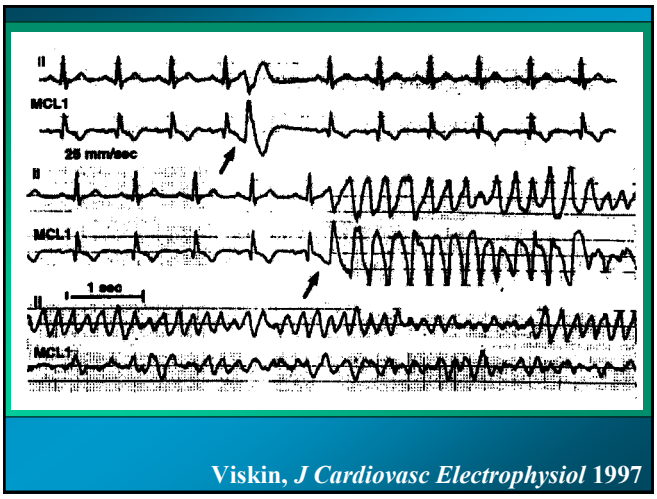
PEDRO BRUGADA, MD, JOSEP BRUGADA, MD*†

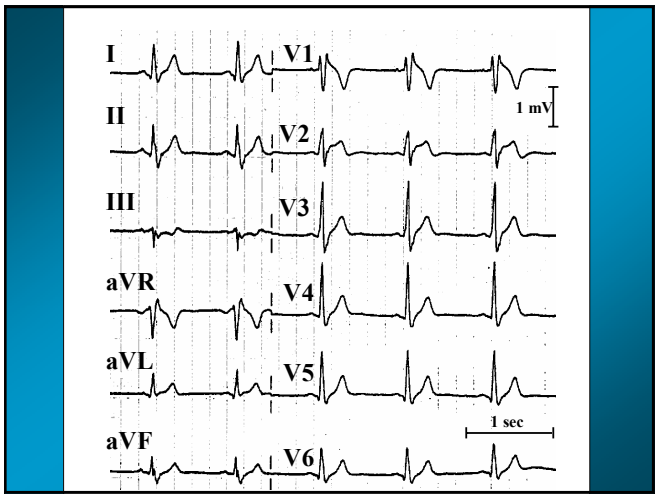
Aalst, Belgium and Barcelona, Spain

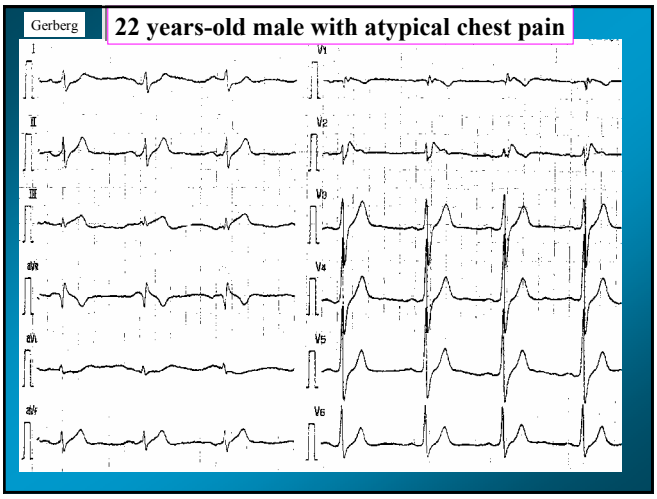
Objectives. The objectives of this study were to present data on eight patients with recurrent episodes of aborted sudden death whom ventricular biopsies were performed. The arrhythmia

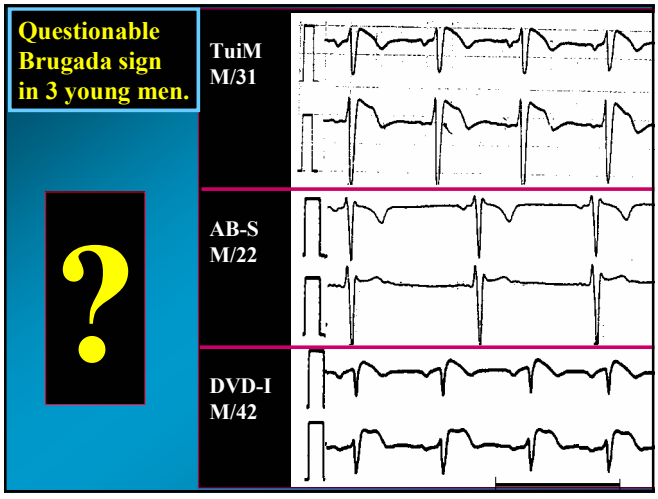

Viskin. When you only live twice. *N Engl J Med 1995.*

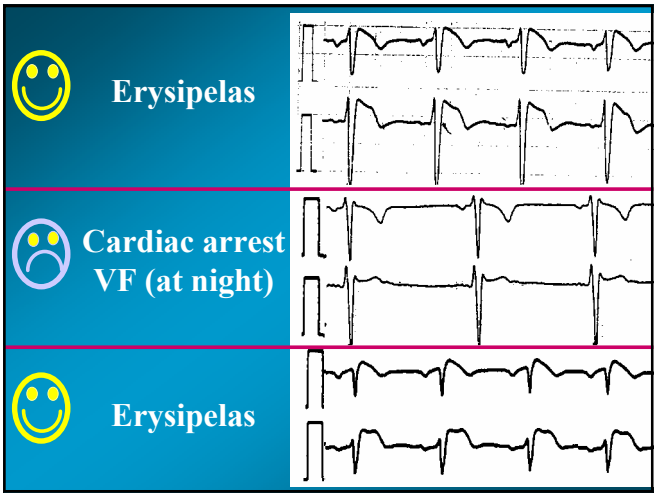

Brugada Syndrome
LQT3
Na+
Normal
Endocardium
Epicardium
Subendocardium
EAD
Phase II reentry
Phase III reentry

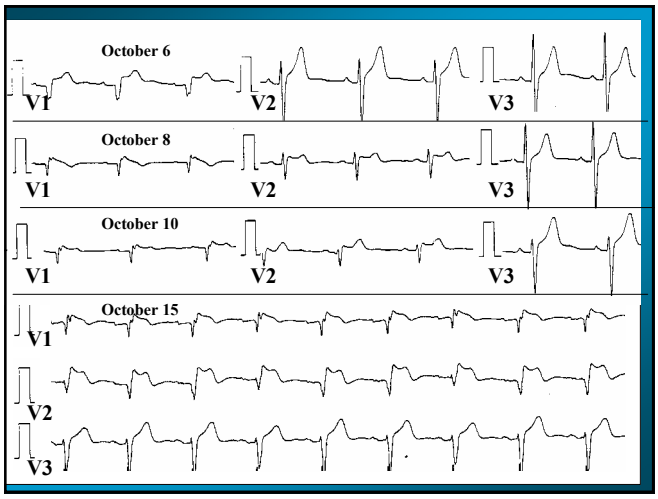

II
MCL1
25 mm/sec
1 sec
Viskin, J Cardiovasc Electrophysiol 1997


I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
1 mV
1 sec


Gerberg
22 years-old male with atypical chest pain

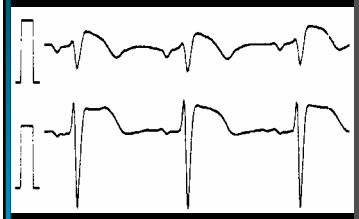

Questionable Brugada sign in 3 young men.
?
TuiM M/31
AB-S M/22
DVD-I M/42


Erysipelas
Cardiac arrest VF (at night)
Erysipelas



Prevalence of the Brugada sign in idiopathic VF and in healthy controls

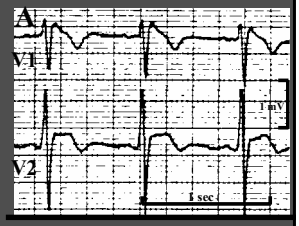
Major Brugada sign



Idiopathic VF 15%

Control 0 (95% C.I. <0.5%)

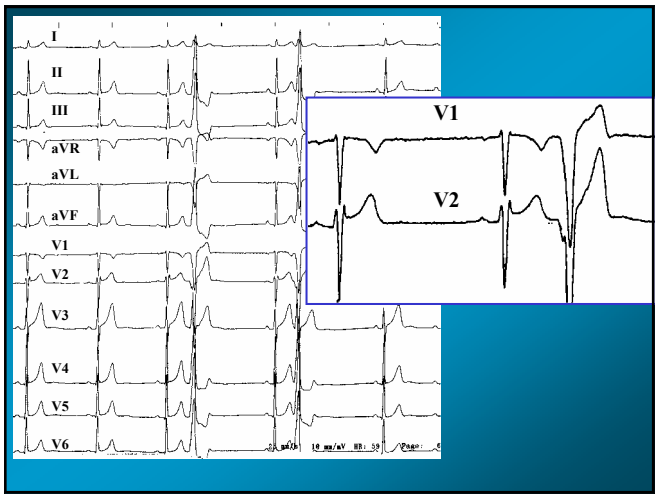
Minor Brugada sign



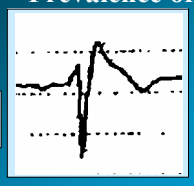
Idiopathic VF 5%

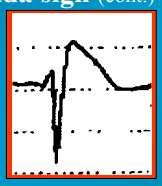
Control 1%

Viskin, *Heart* 2000



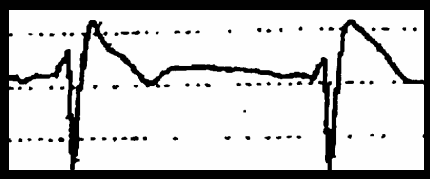
Prevalence of the Brugada sign (cont.)

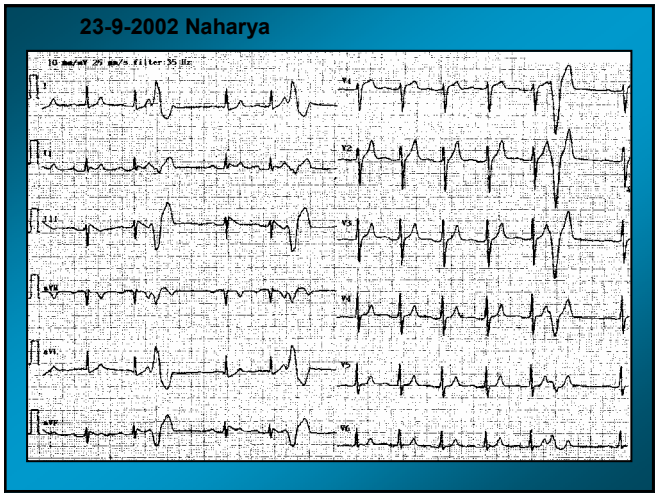


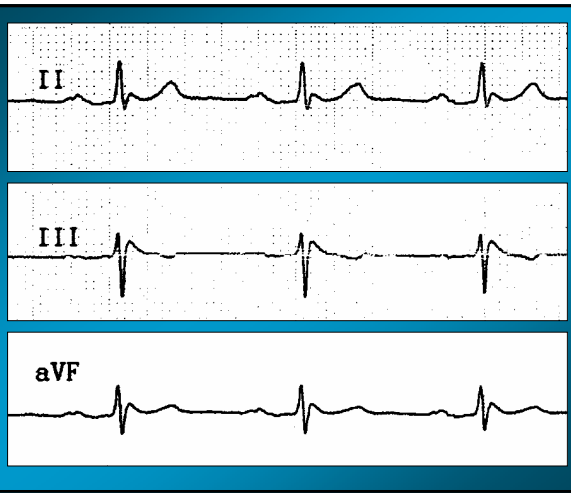


Saddle back pattern:
the common thing?

Coved pattern:
the real thing?







Questionable Brugada syndrome: Diagnostic approach

1. History: syncope?, epilepsy?, familial history?

2. ECG:
   - Repeated traces.
   - ECG with high V1-V2.

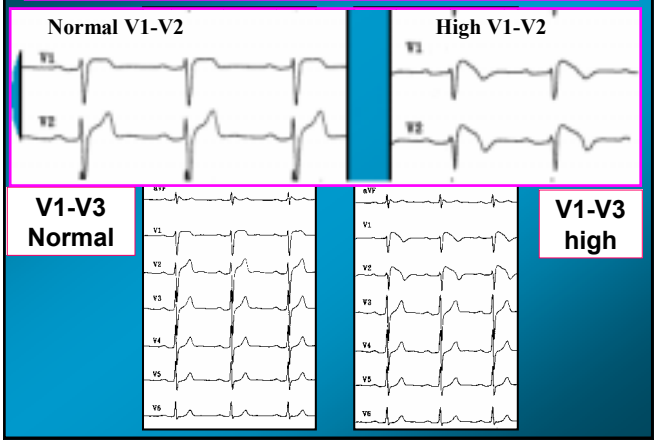
2. Holter:
   - Short-coupled PVCs

3. Flecainide test.

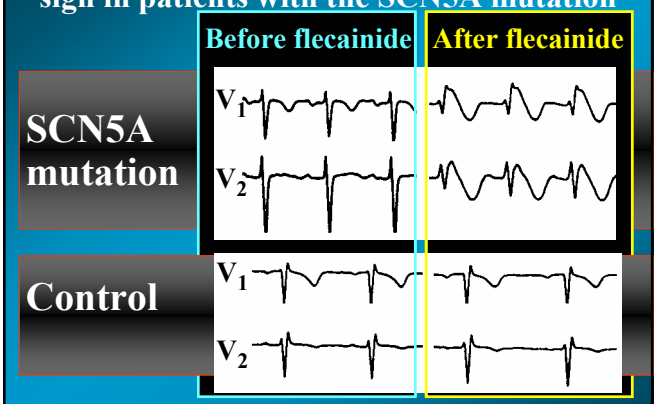
4. Genetic screening.

5. Electrophysiologic study.

Effects of precordial electrode position on Brugada sign

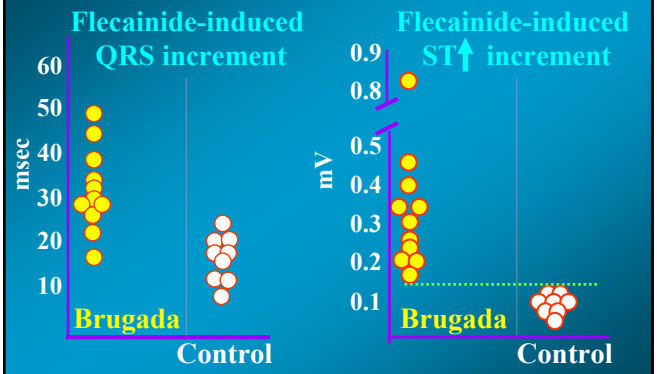


Sodium channel blockers unmask a Brugada sign in patients with the SCN5A mutation



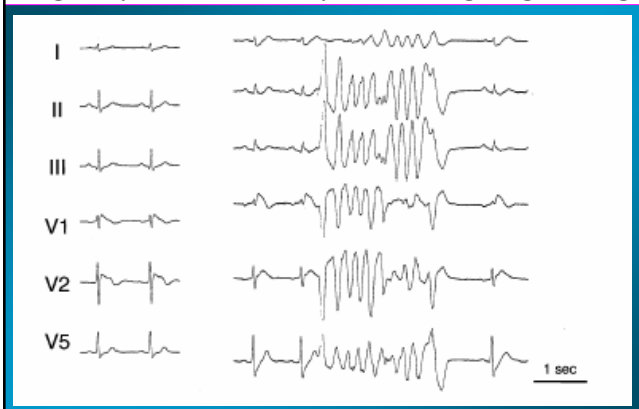
Brugada, *Circulation* 2000

Drug –induced changes in 12 patients with Brugada syndrome (VF) and 10 healthy controls.



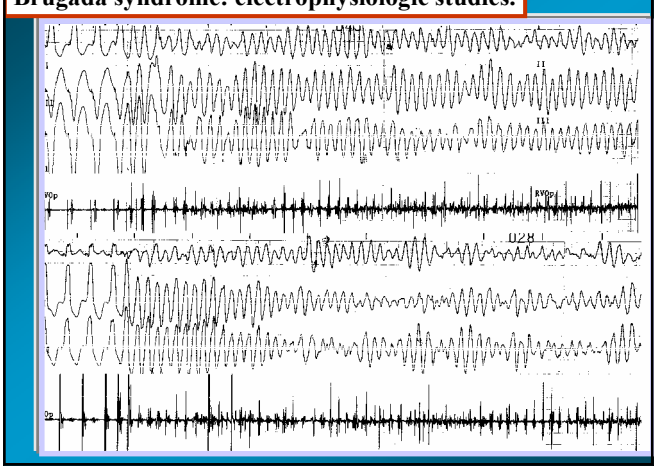
Shimizu, *JCE* 2000

Brugada syndrome: Proarrhythmia during drug challenge

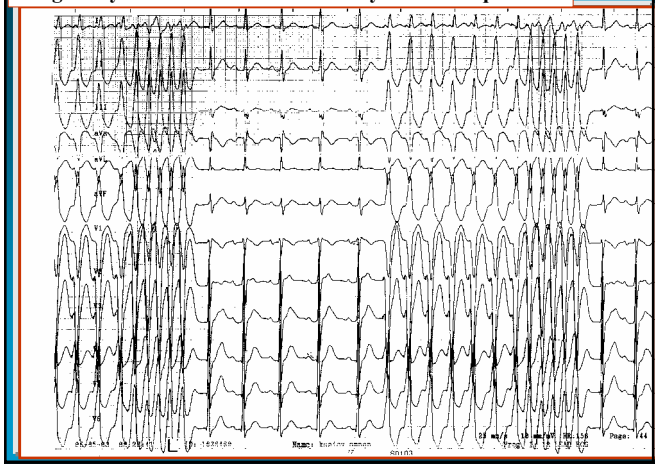


Morita, *JACC* 2003.

Brugada syndrome: electrophysiologic studies.

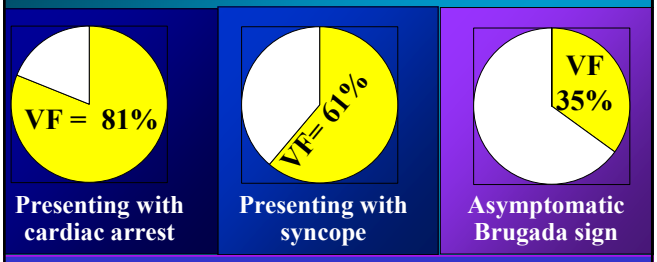


Brugada syndrome: No inducible arrhythmias on quinidine



Role of EPS in Brugada syndrome (Brugada *JCE 2003*).

1. Percentage of Brugada patients with inducible VF



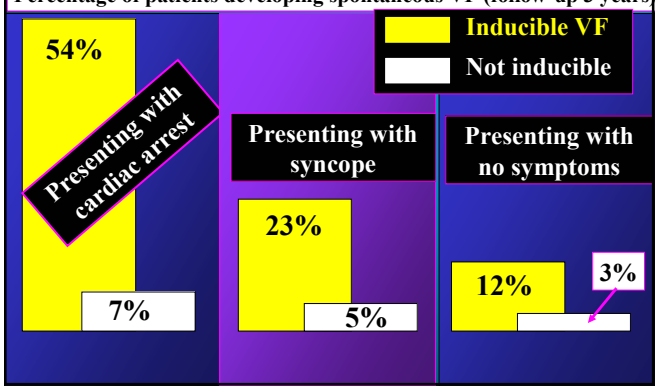
2. What is the percentage of healthy individuals who have inducible VF ?

- Inducible VF with aggressive protocols: ***At least*** 9%
- Inducible non-sustained polymorphic VT: 45%

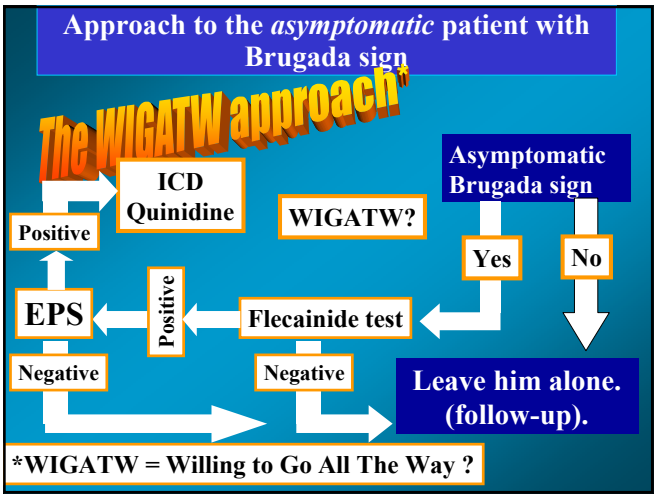
Role of EPS in Brugada syndrome (Brugada *JCE 2003*).

2. Prognostic value of inducible VF.

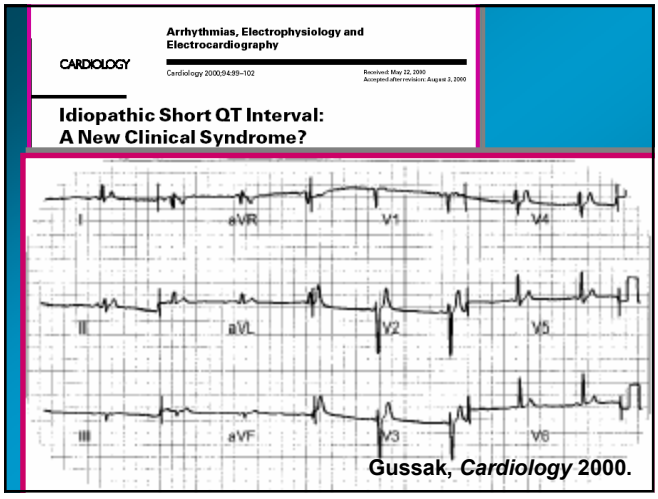
Percentage of patients developing spontaneous VF (follow-up 3 years)

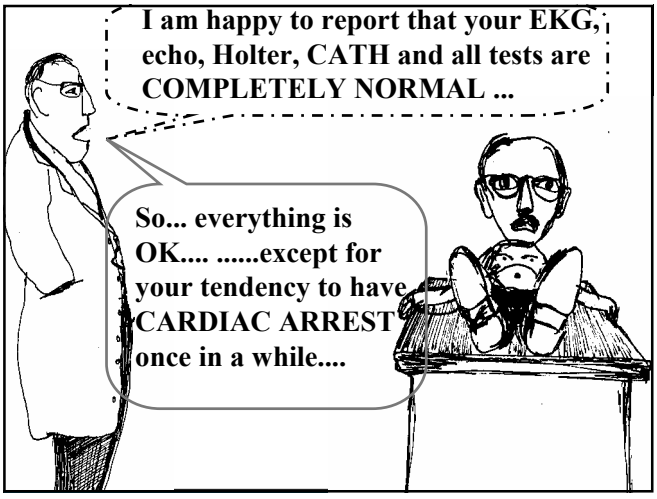


Approach to the *asymptomatic* patient with Brugada sign

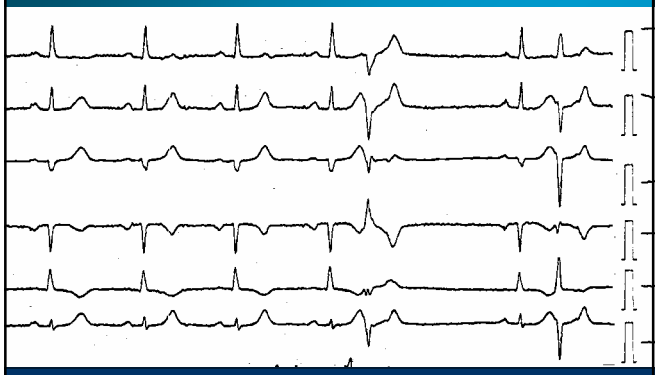


*WIGATW = Willing to Go All The Way ?

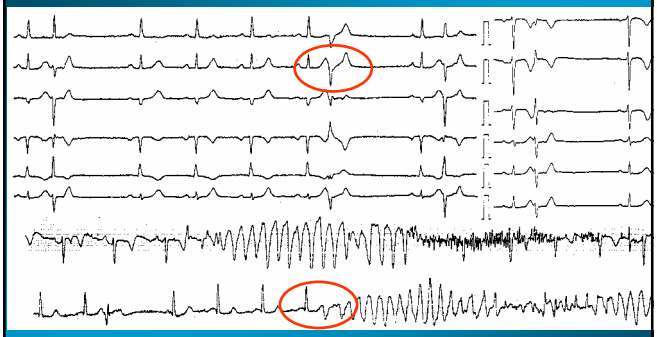




50 year old woman referred for neurological evaluation

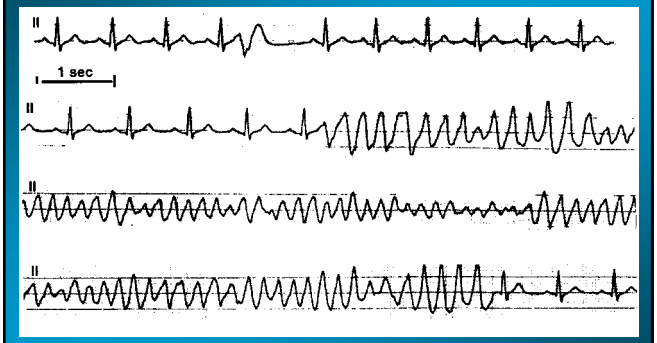


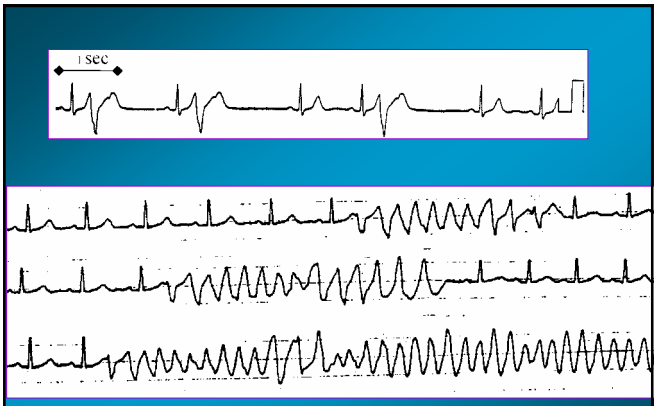
50 year old woman referred for neurological evaluation



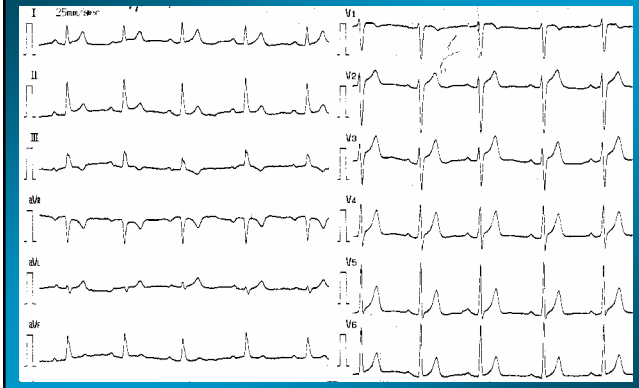
Viskin, *Prog Cardiovasc Dis* 1998.

Syncope in idiopathic VF:
Self-terminating polymorphic VT or non-sustained VF

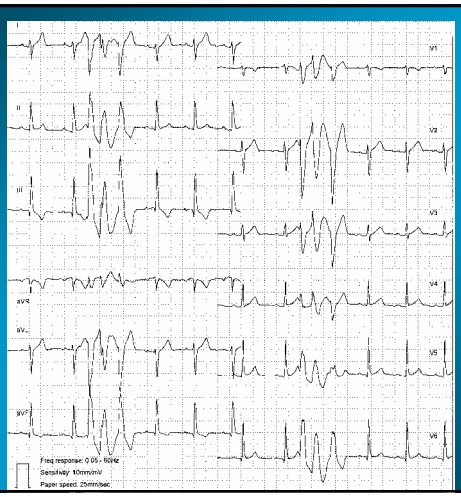


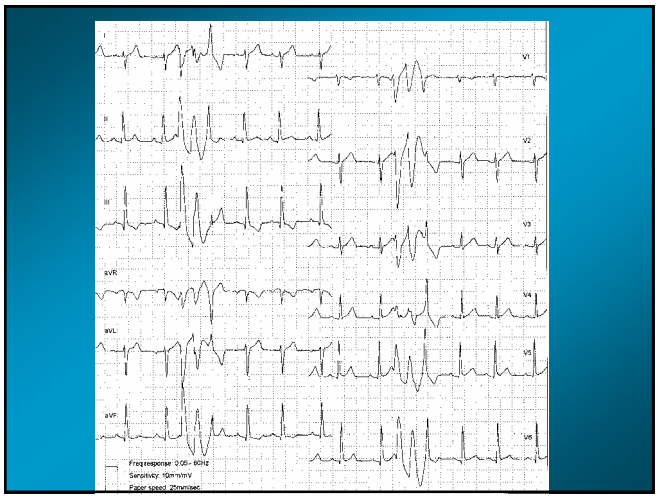


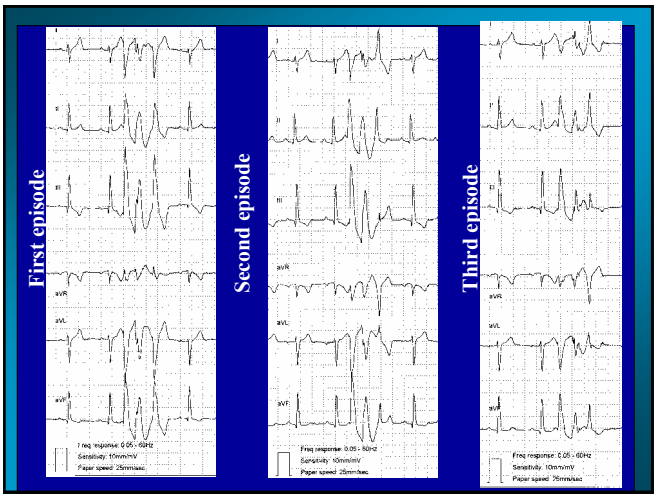
Shukrun Alroi

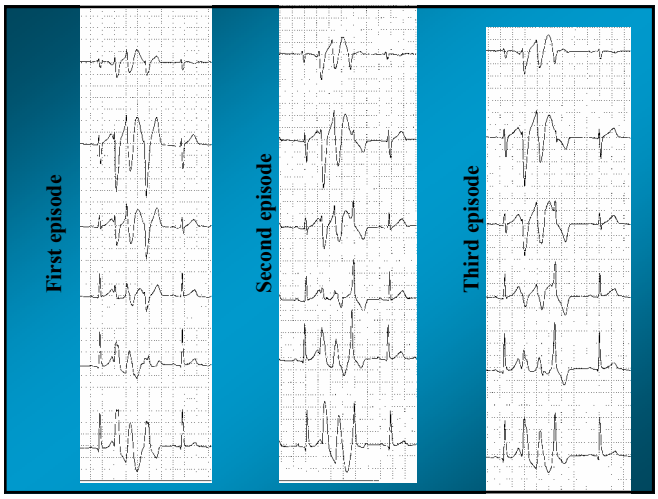


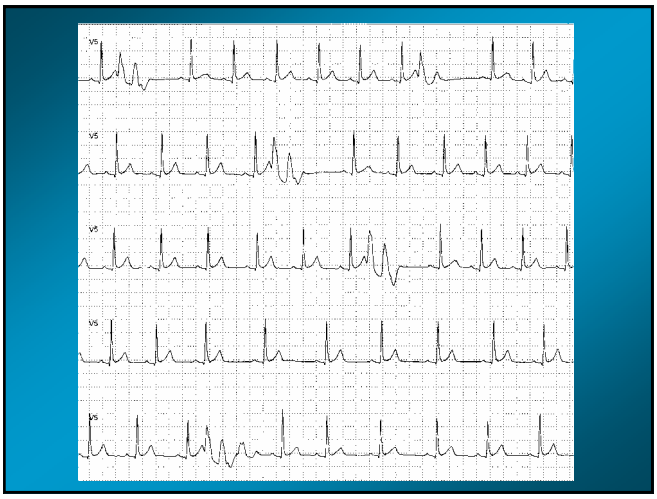
QT= 300 msec, R-R= 760 msec, QTc = 340 msec.

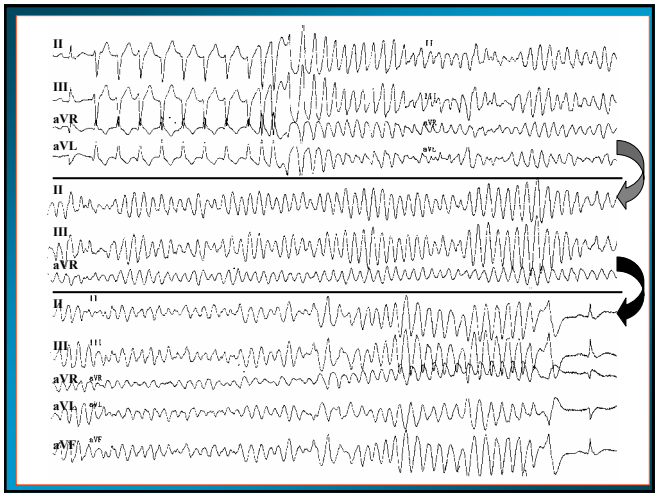





First episode
Second episode
Third episode


First episode
Second episode
Third episode




II
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