

Fisiología y fisiopatología de los canales iónicos y farmacología de los anti arrítmicos

Primera parte

Rafael Porcile

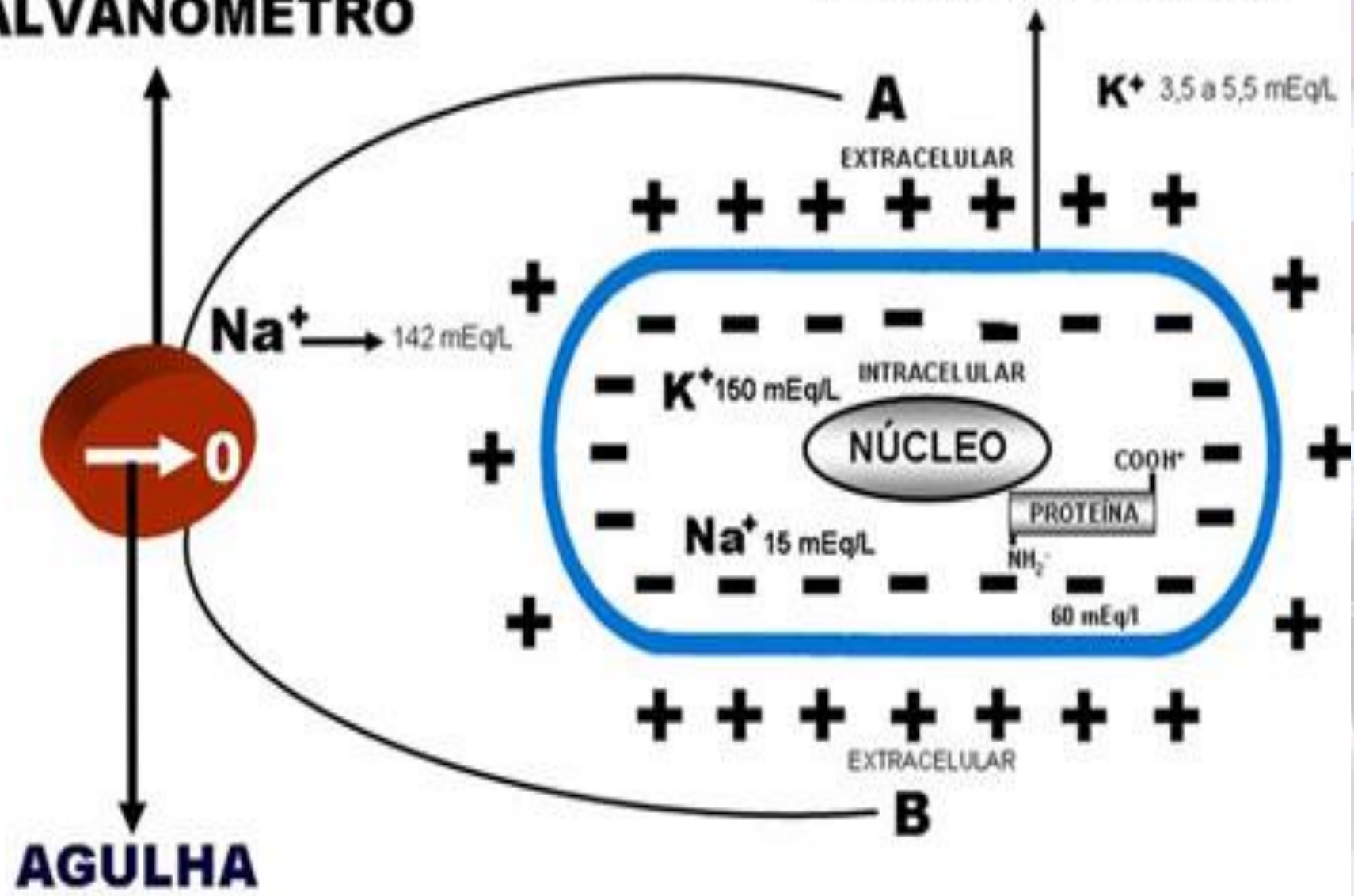
rafael.porcile@vaneduc.edu.ar

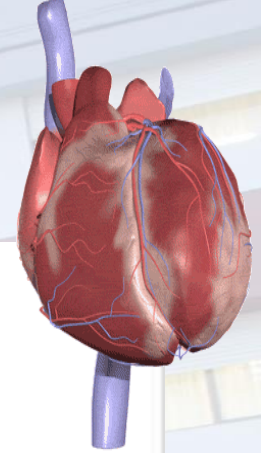
**DEPARTAMENTO DE CARDIOLOGIA
CATEDRA DE FISILOGÍA**

Universidad Abierta Interamericana

GALVANÔMETRO

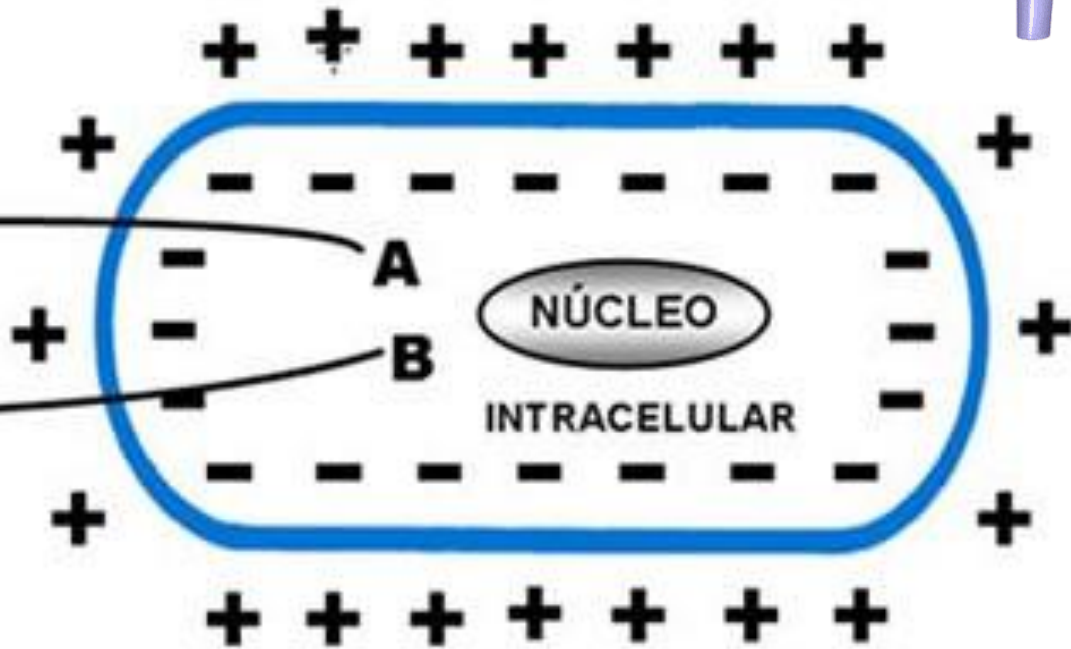
SARCOLEMA OU MEMBRANA CELULAR





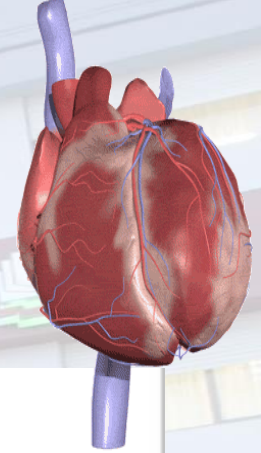
GALVANÔMETRO

EXTRACELULAR

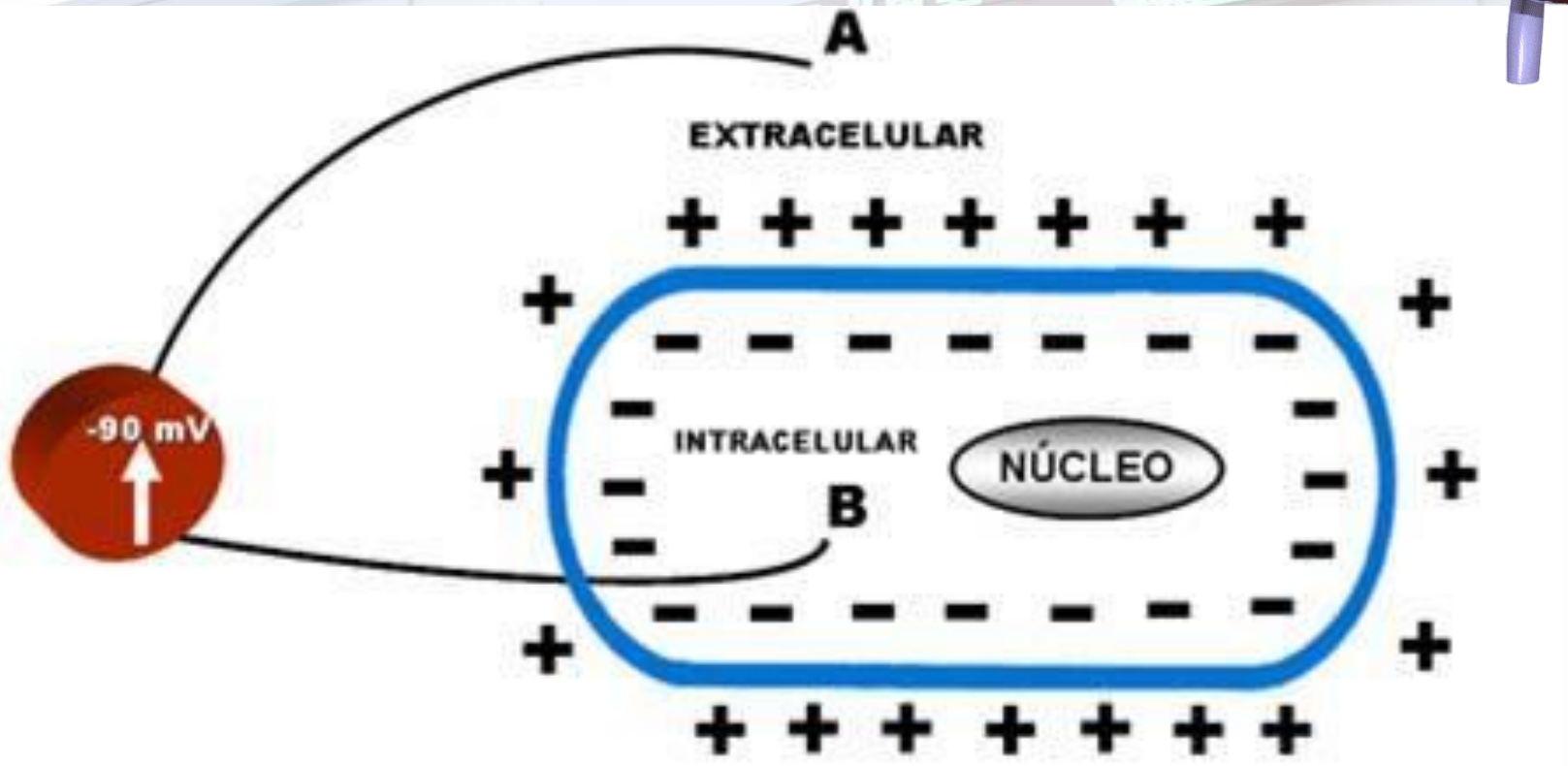


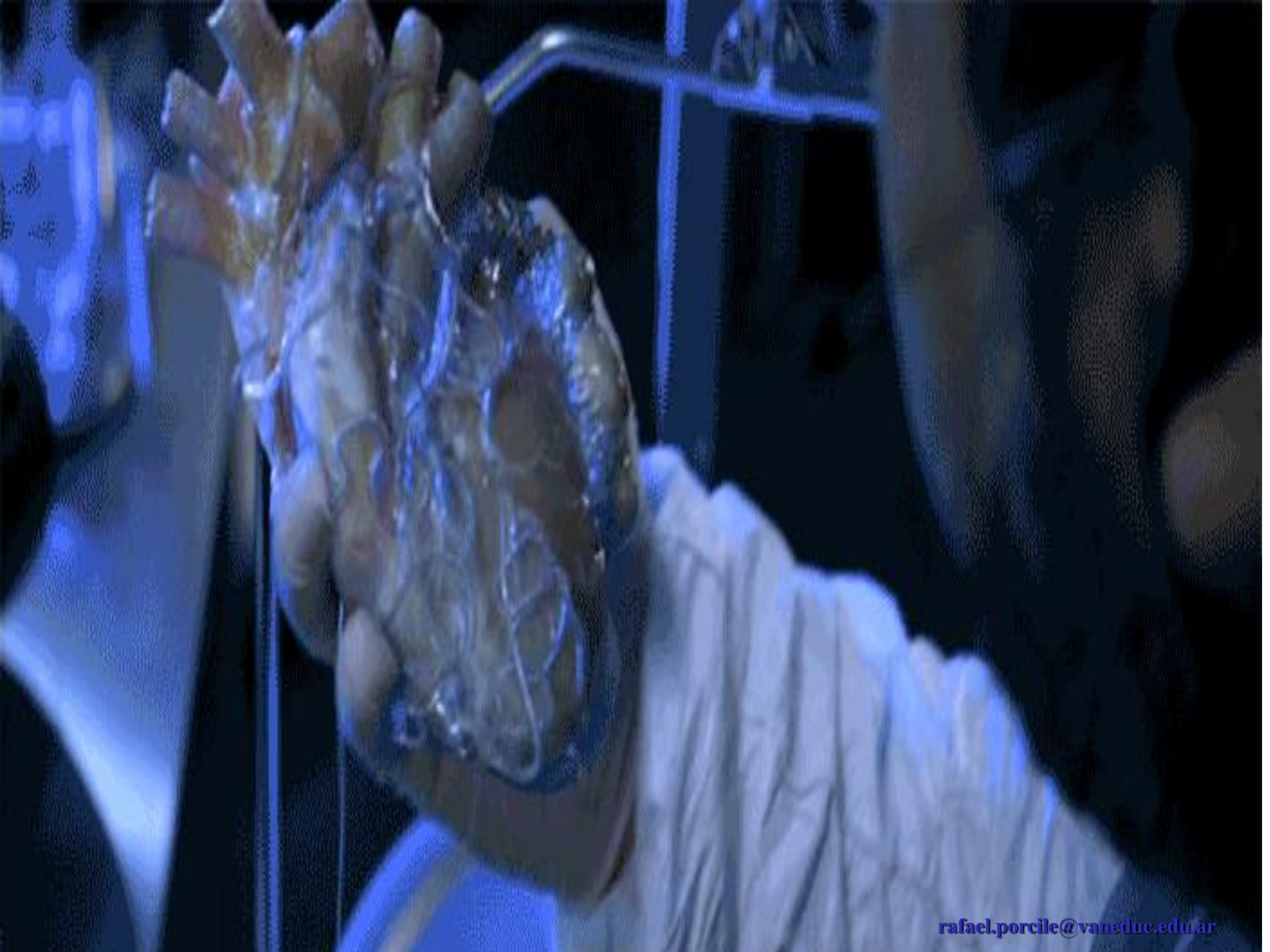
AGULHA

EXTRACELULAR



Diferencia de potencial





Propiedades eléctrica del músculo cardíaco

Potencial de reposo de -90 mv

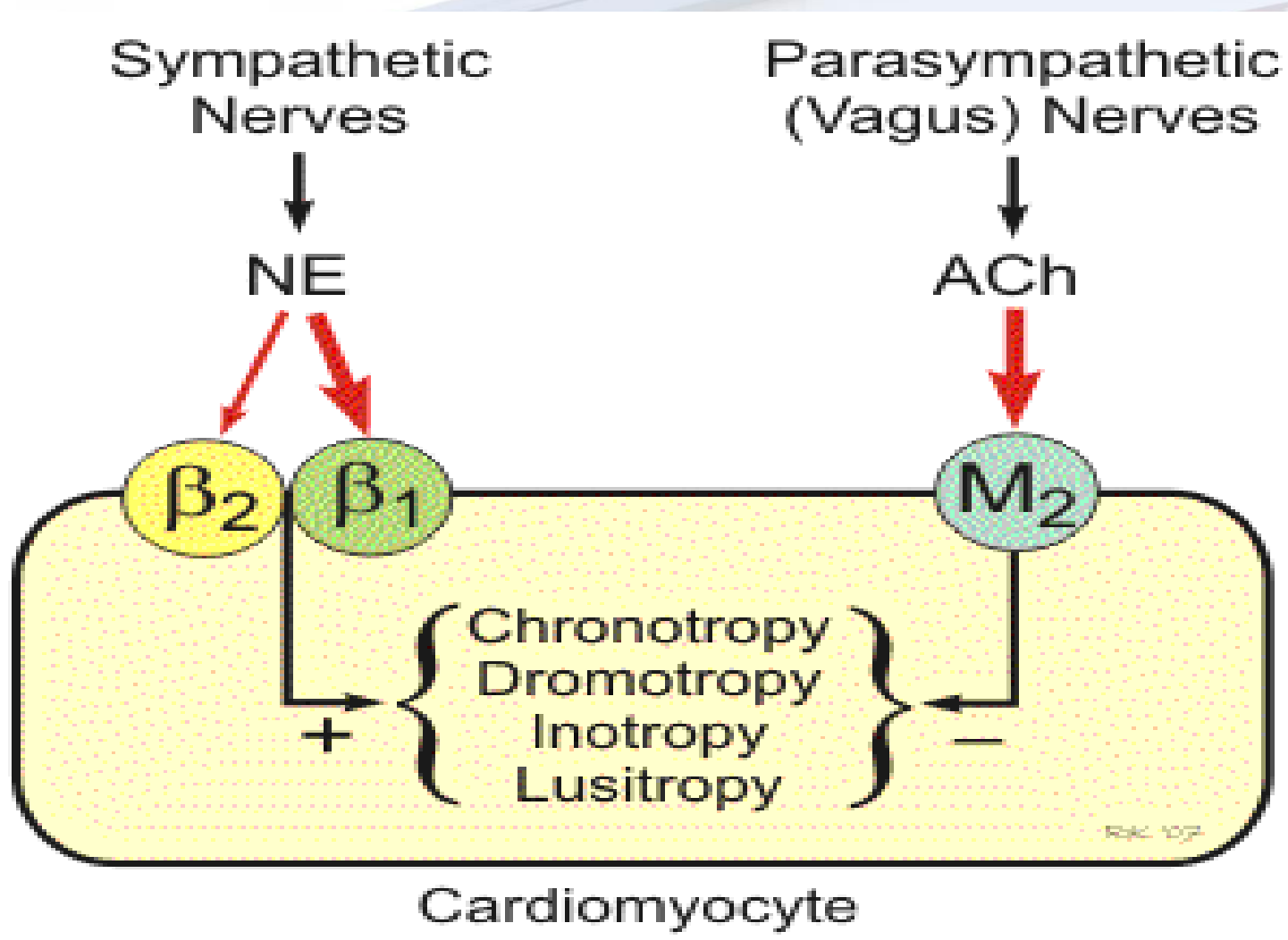
Interior negativo

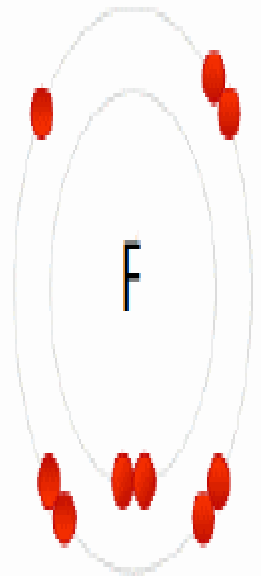
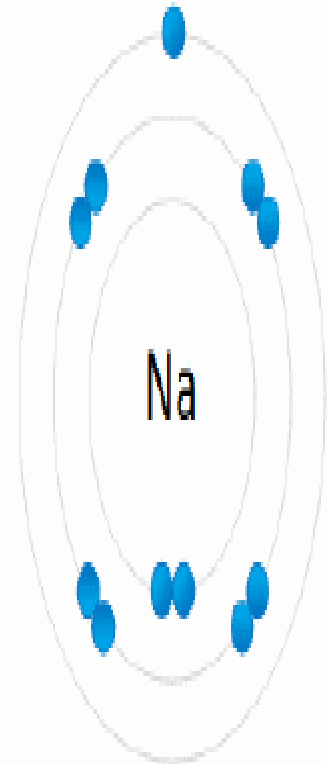
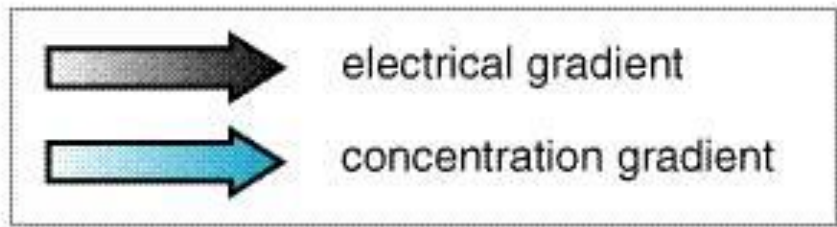
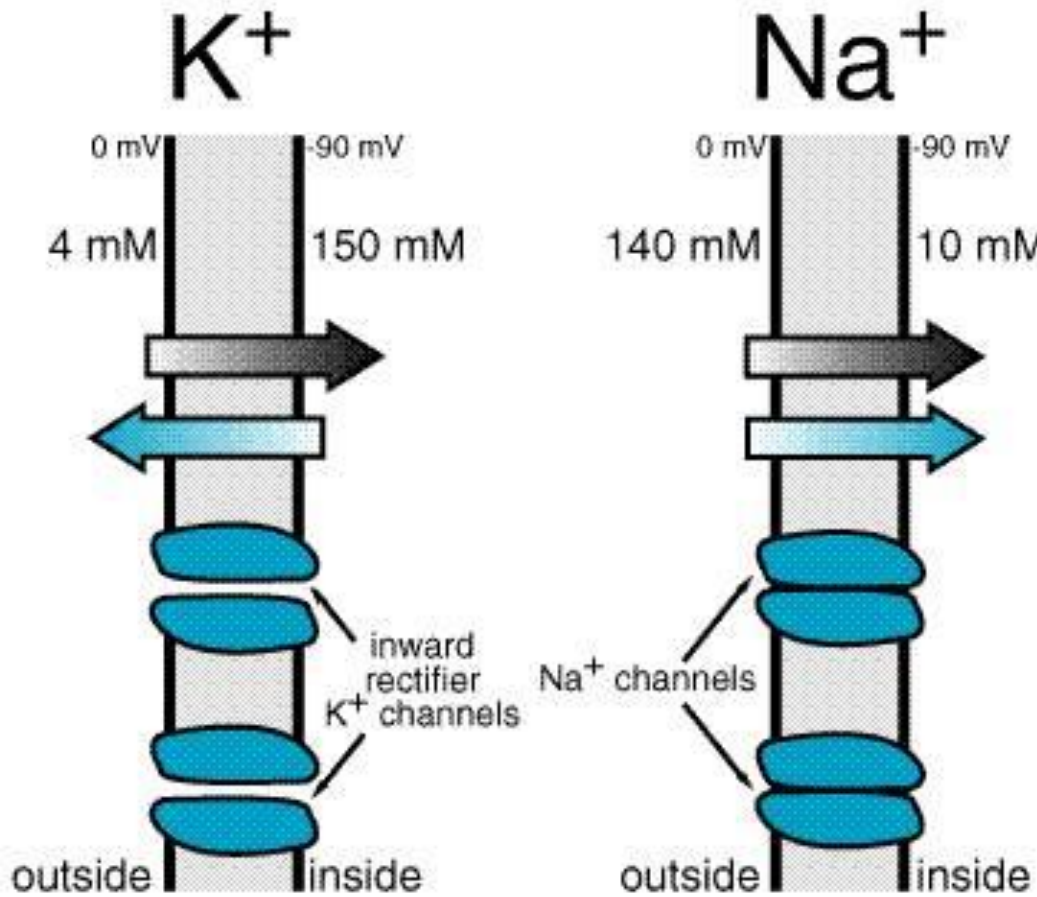
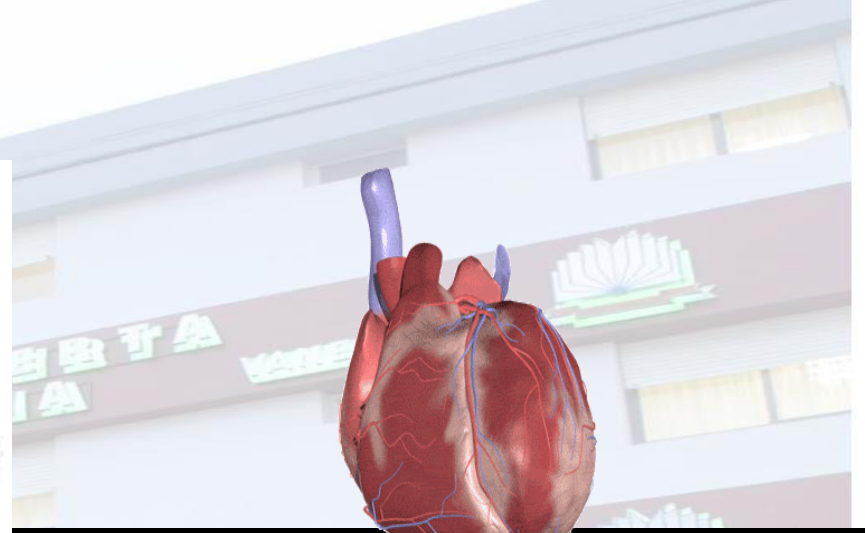
Se invierte el potencial con meseta antes de la repolarización

La despolarización dura 2 mseg

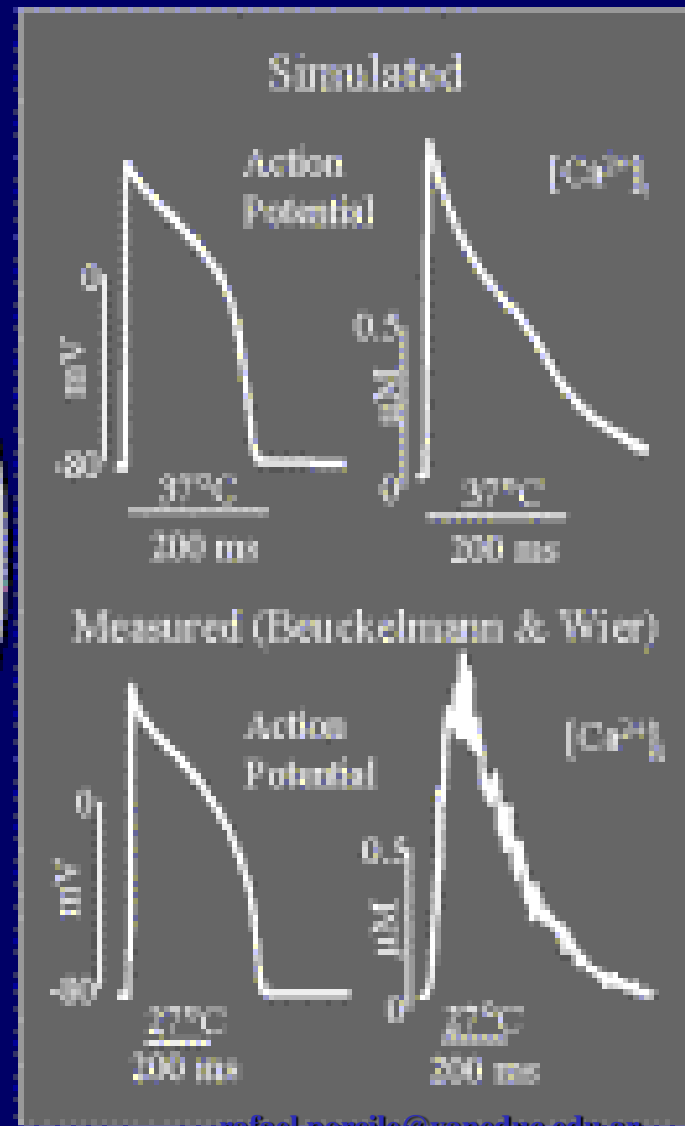
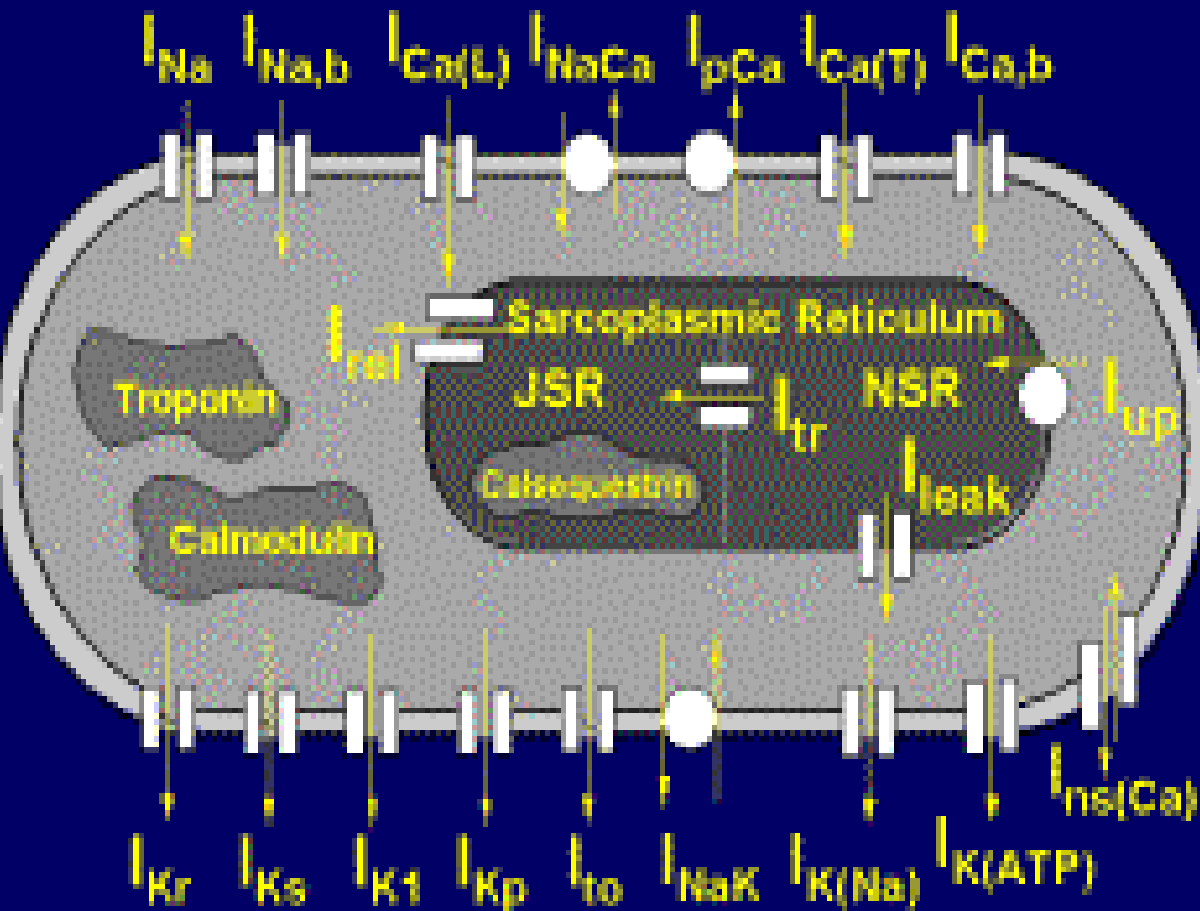
La meseta dura 200 mseg

Los cambios de la concentración externa de k afecta los potenciales de reposo mientras que la concentración externa de Sodio modifica la magnitud de la respuesta





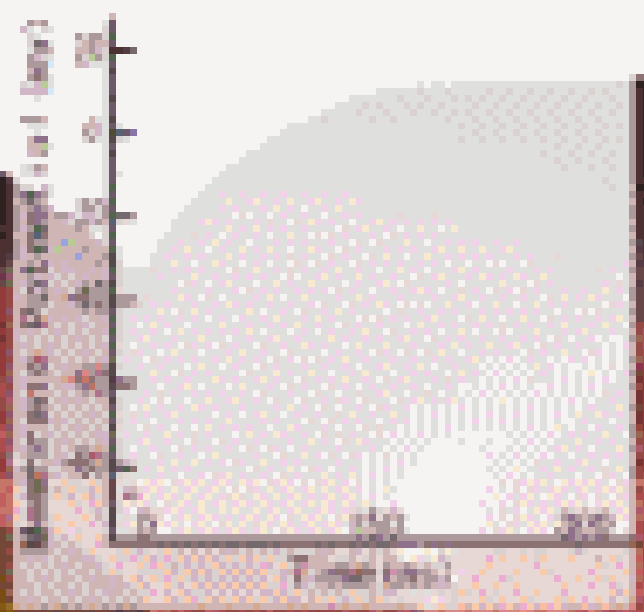
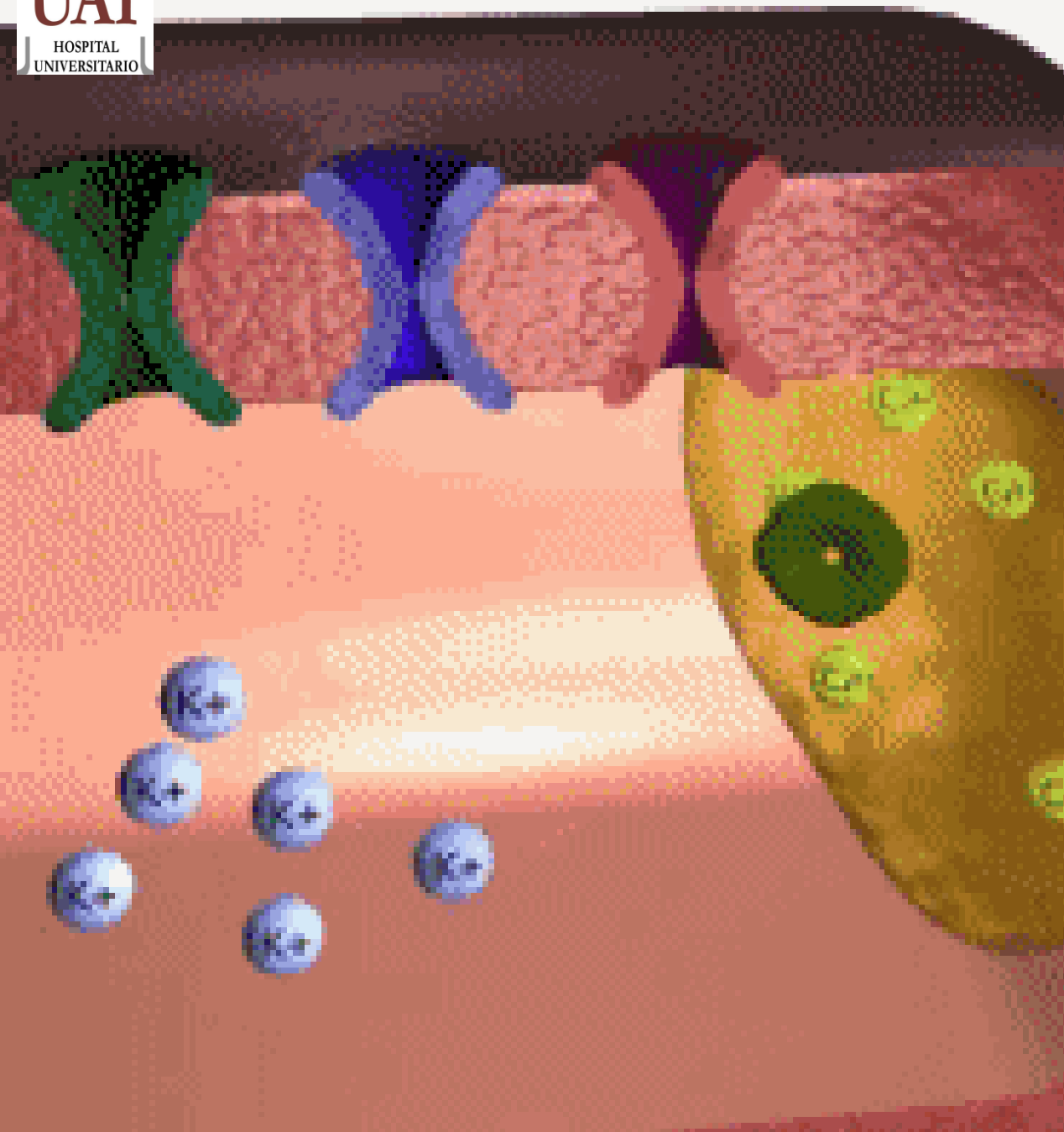
Cardiac Cell Model





La despolarización



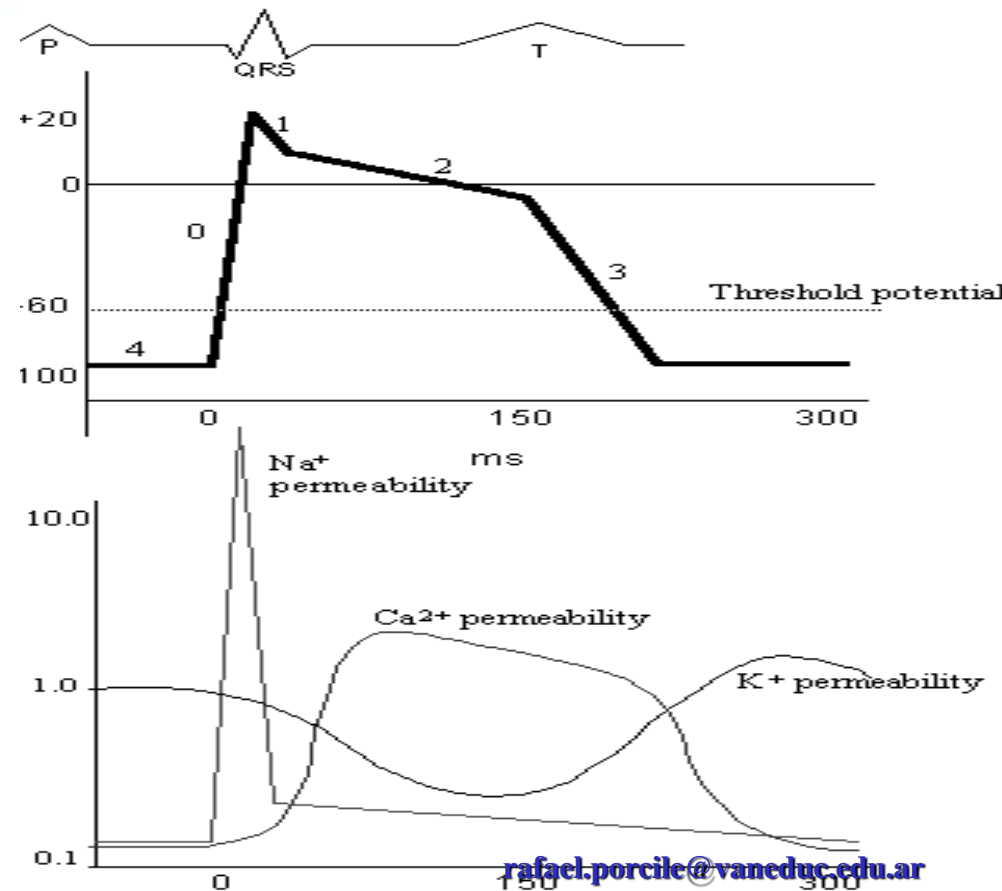
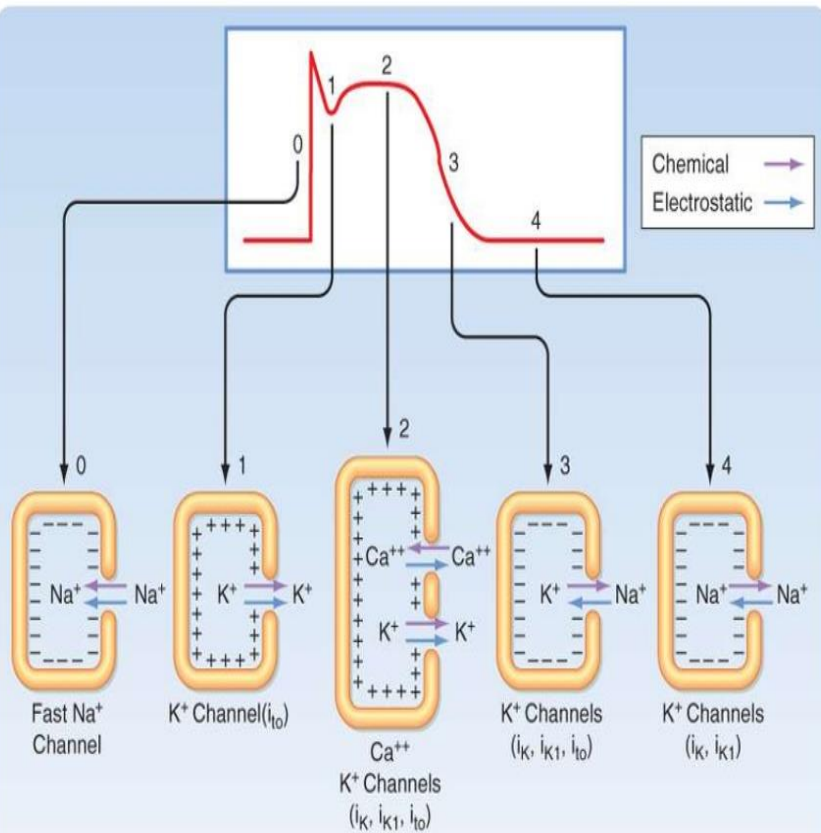


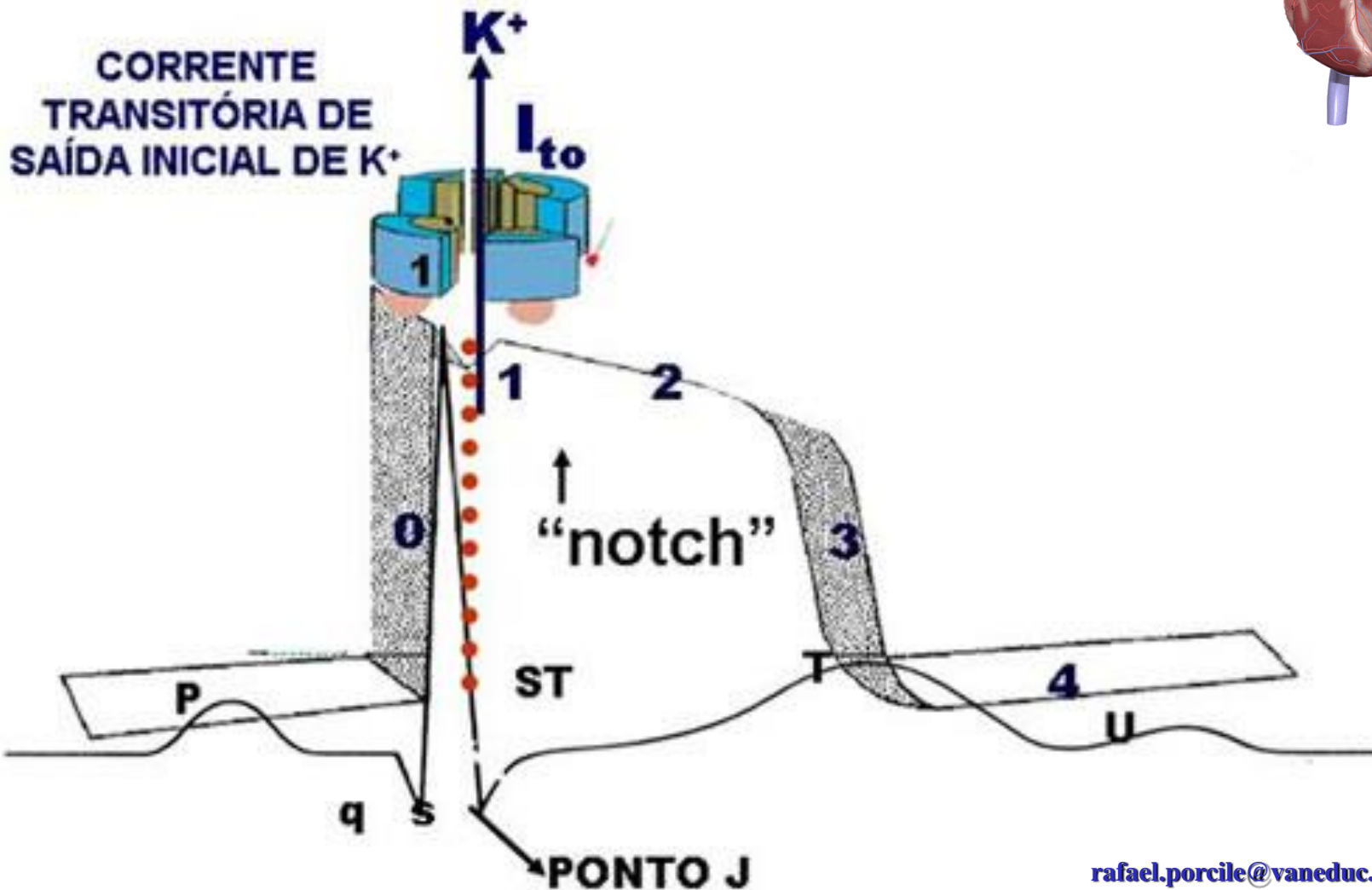
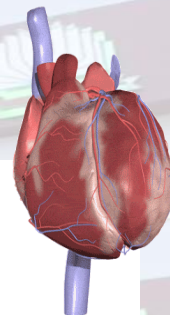
Fase 0: apertura canales de Na activados por voltaje

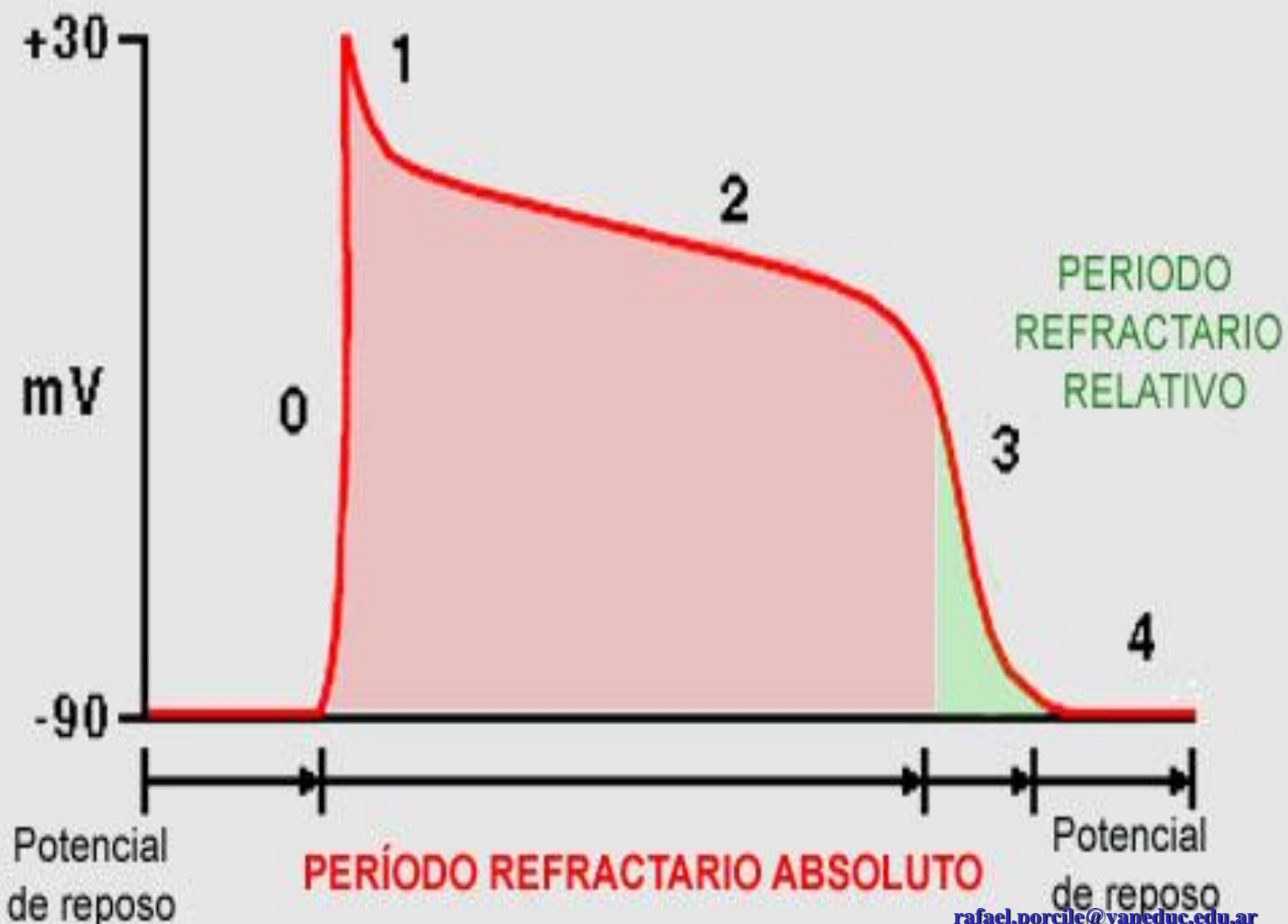
Fase 1: Cierre de canales de Na y Apertura de Cloro

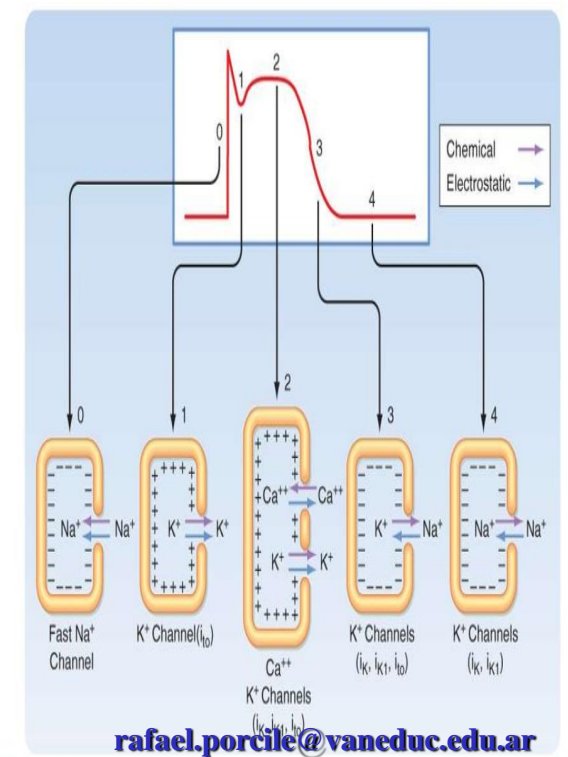
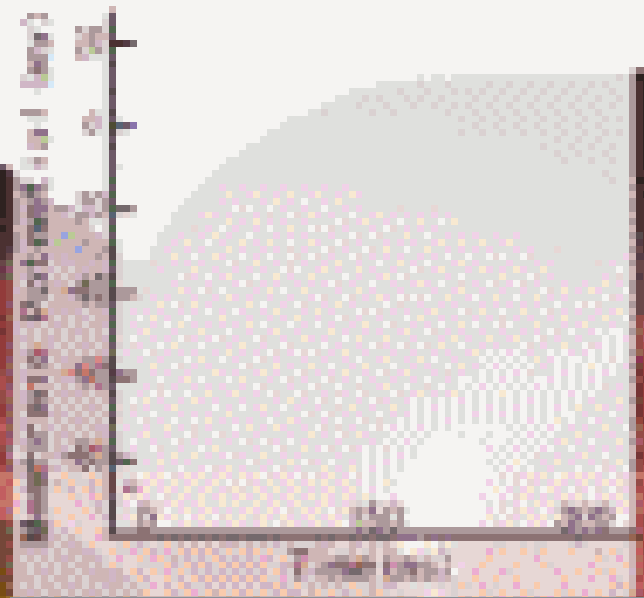
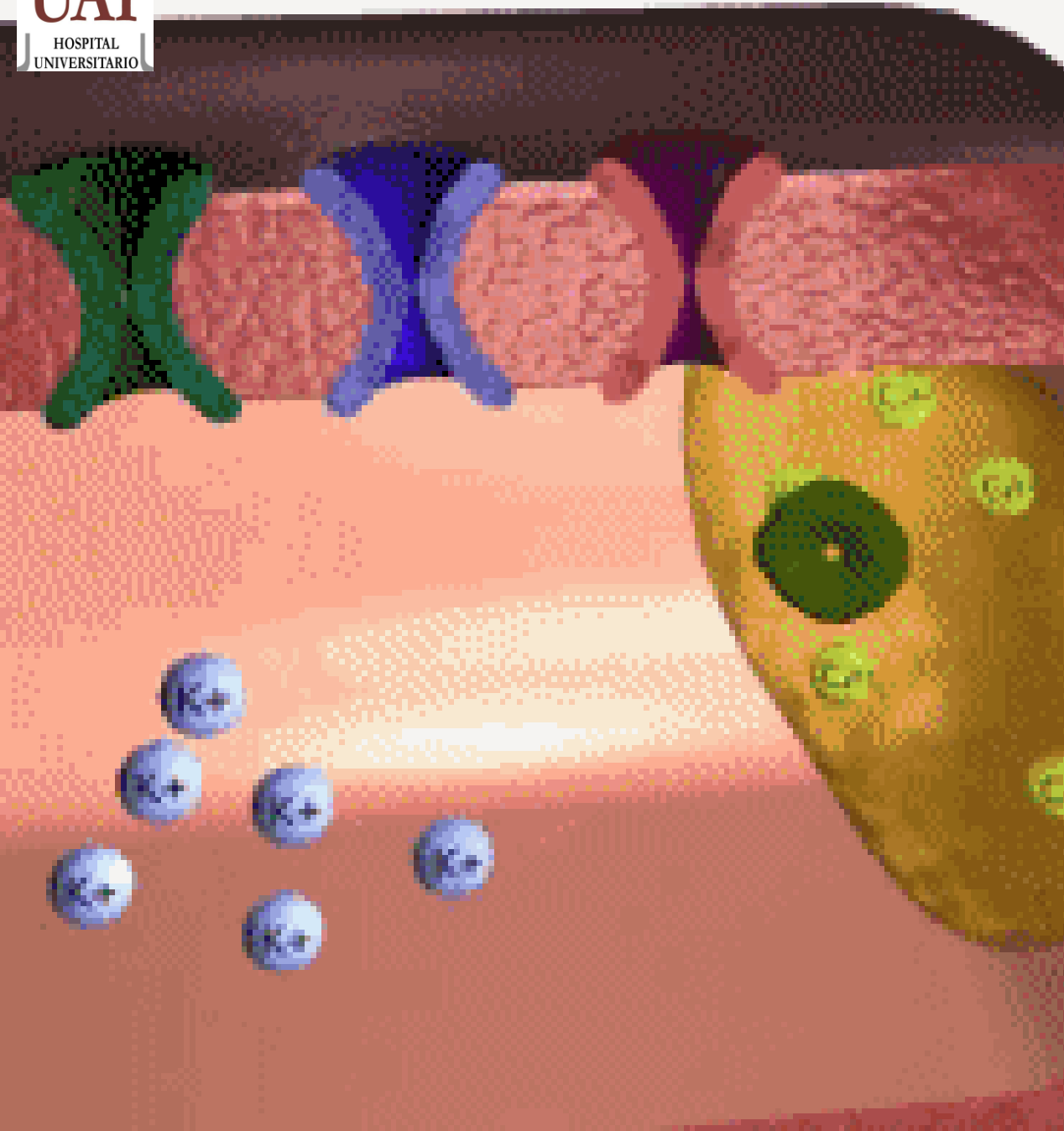
Fase 2: Apertura lenta y prolongada de canales de Calcio

Fase 3: bomba Na /K, cierre canales de Ca

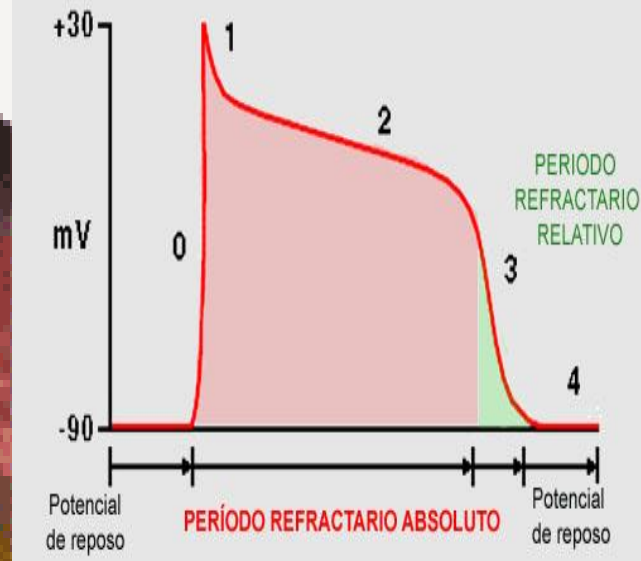




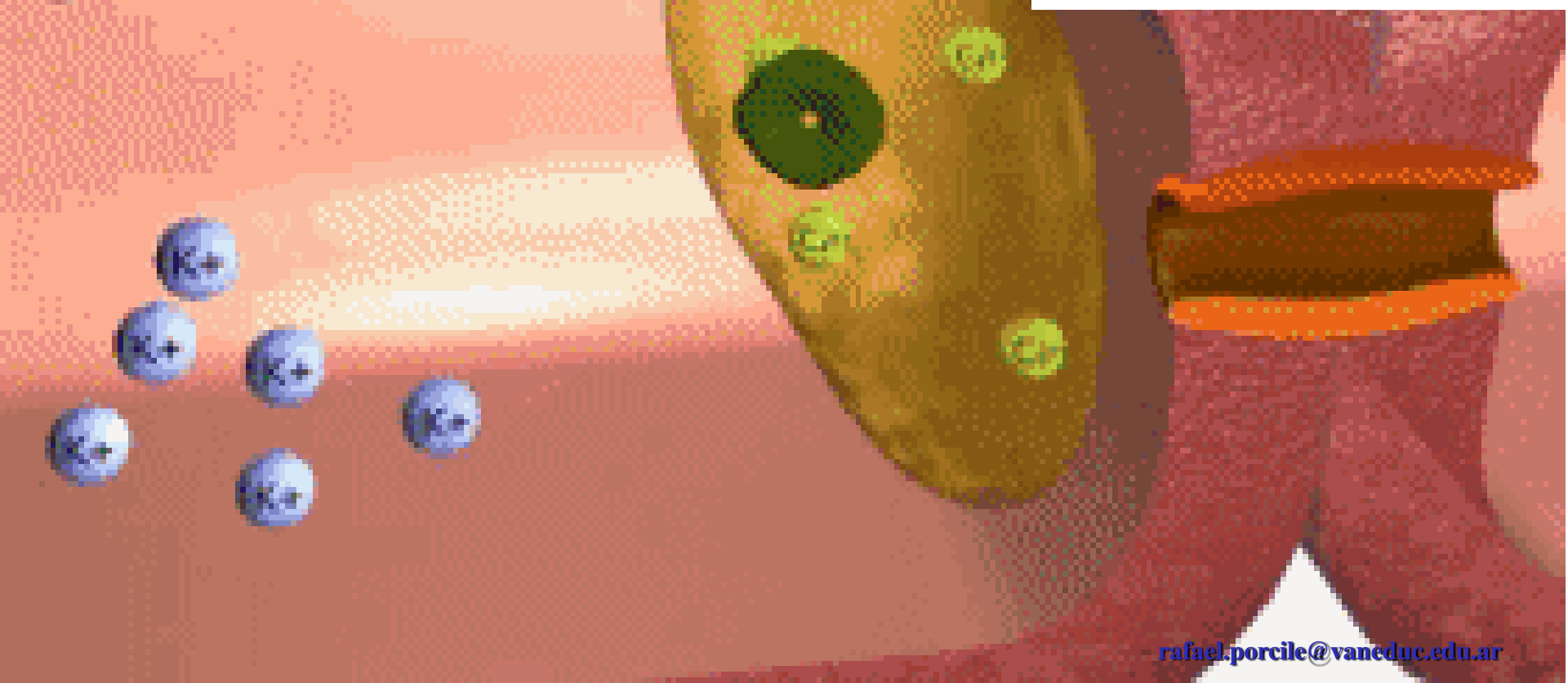
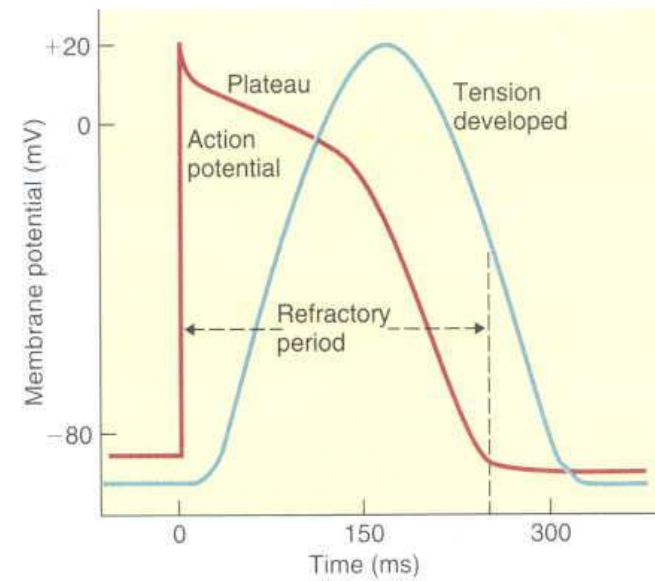


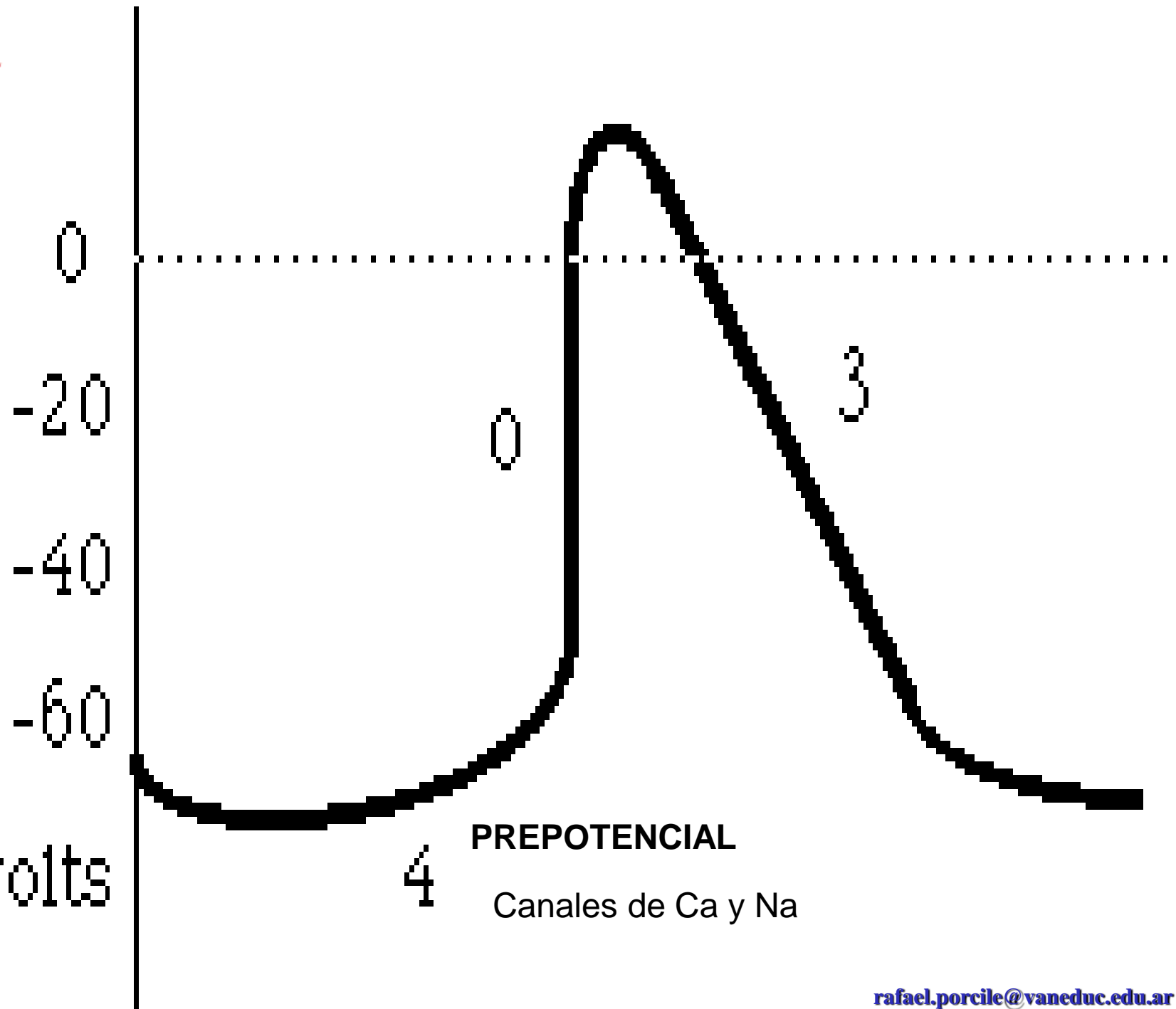
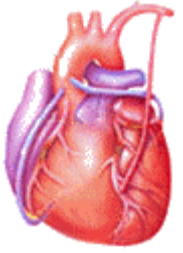


Los Periodos refractarios



Los Periodos refractarios



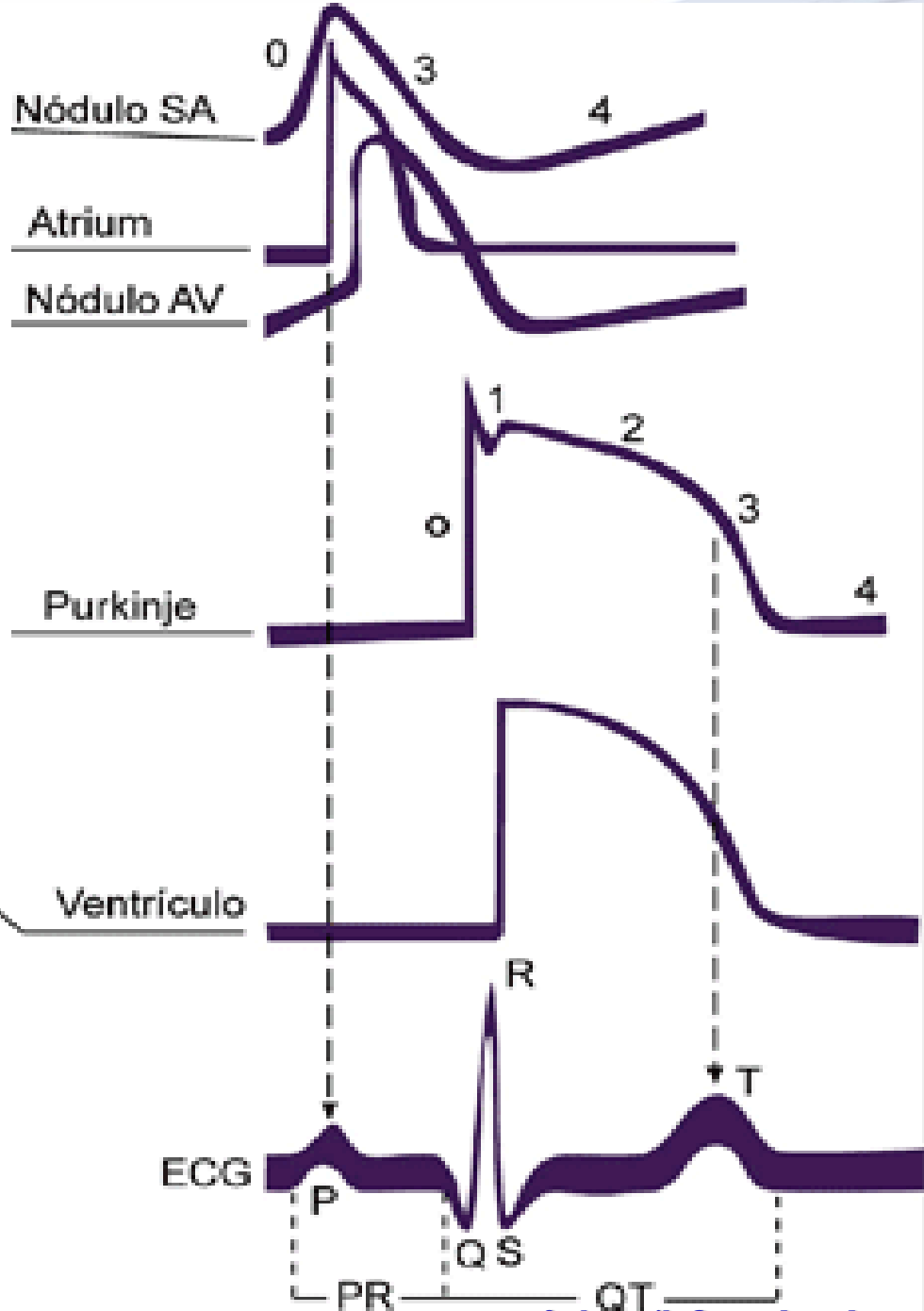
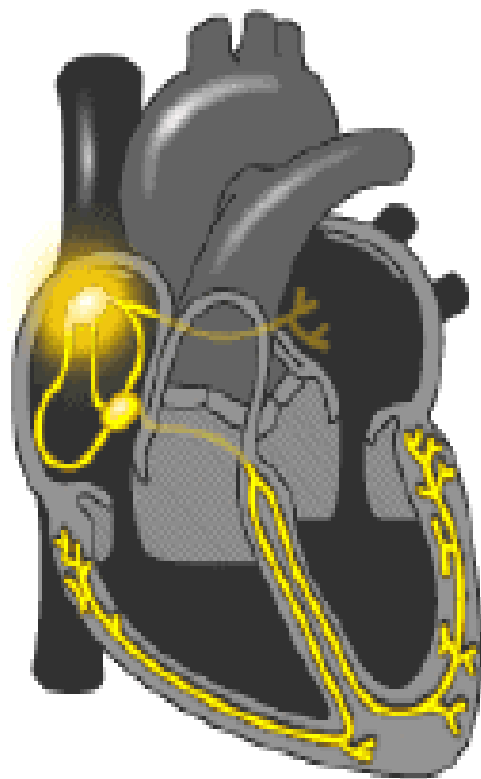


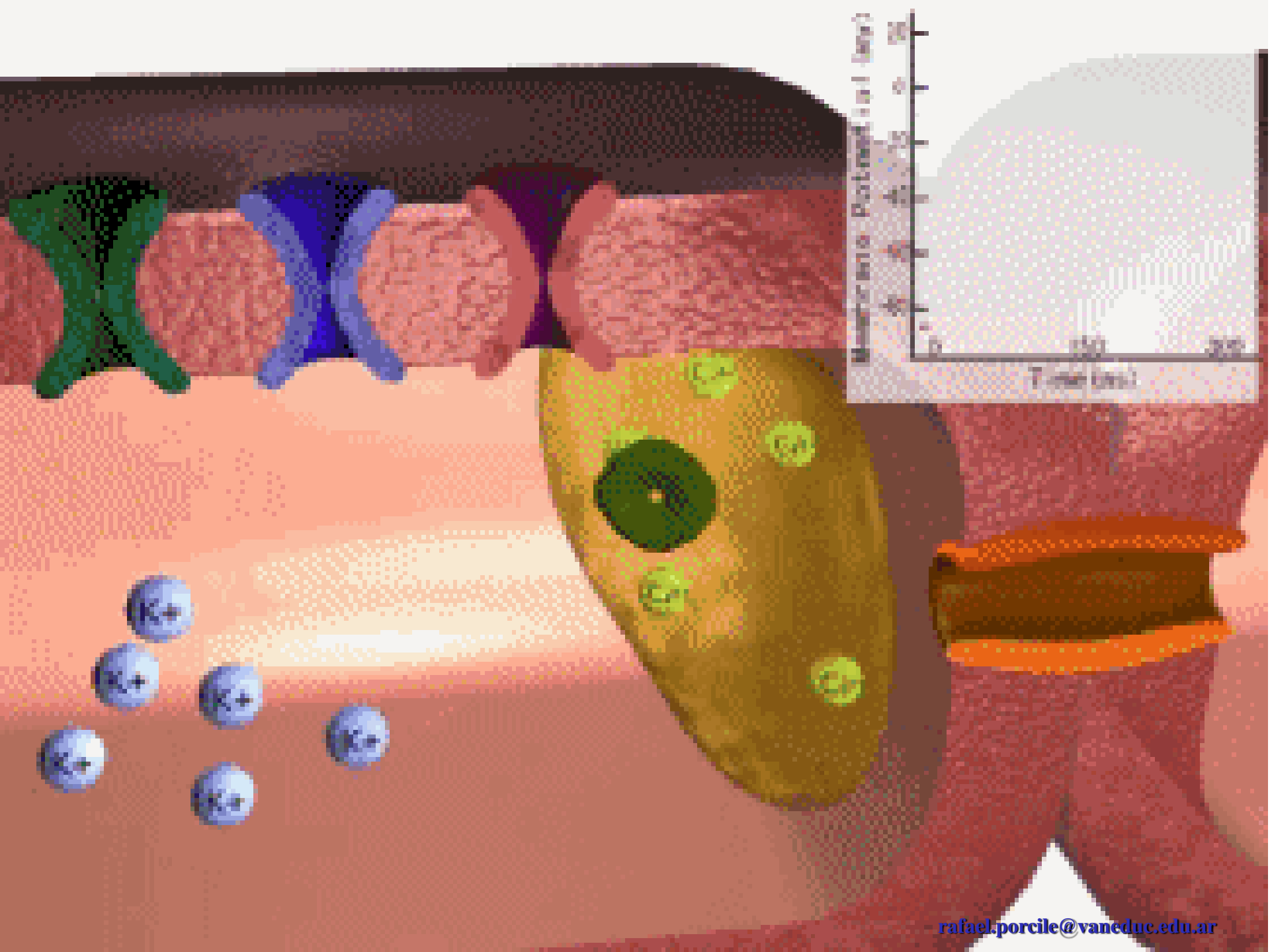
MODIFICADORES DEL PREPOTENCIAL

LAS FIBRAS MUSCULARES AURICULARES Y VENTRICULARES NO TIENEN PRE POTENCIALES O POTENCIALES MARCAPASOS NO SE DESPOLARIZAN A MENOS QUE ESTEN DAÑADAS (ARRITMIAS)

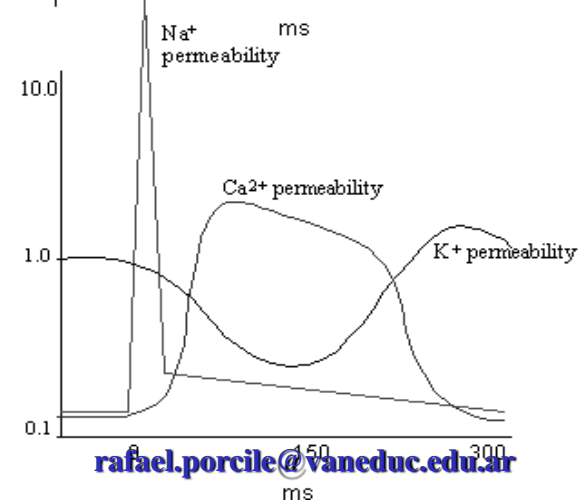
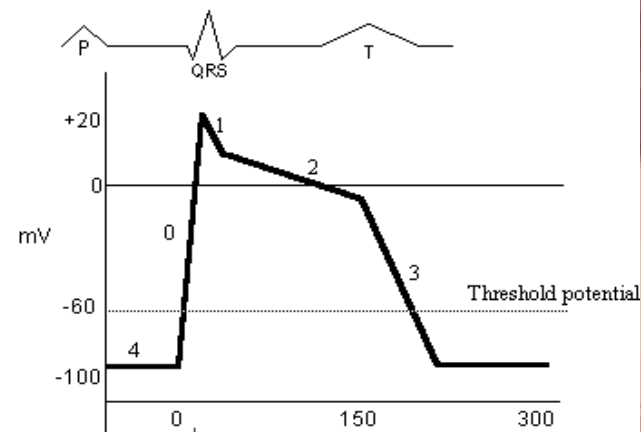
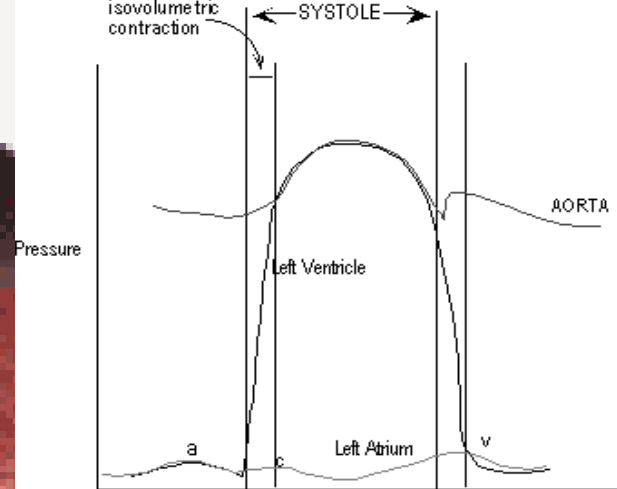
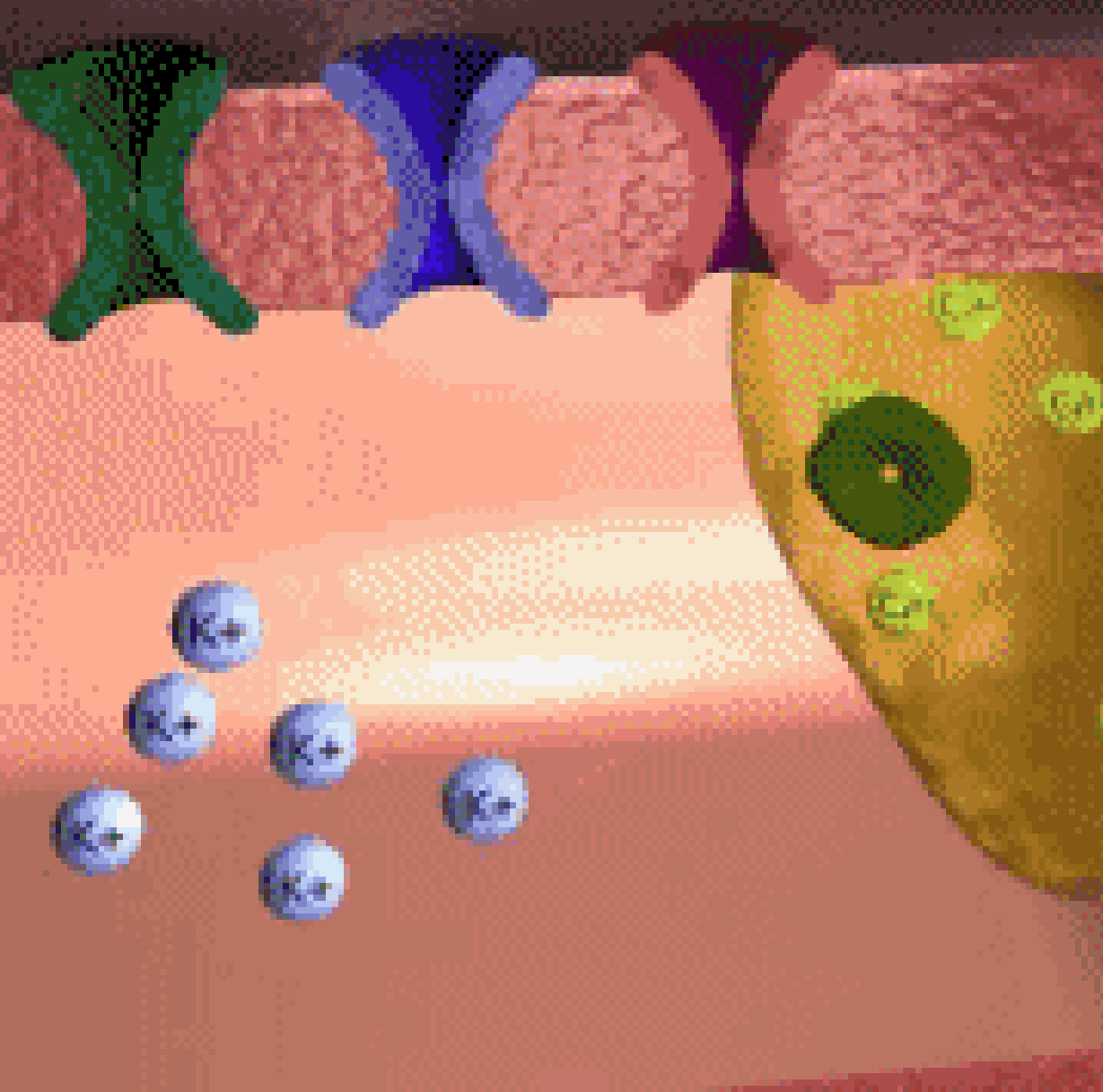
EL PARASIMPATICO HIPERPOLARIZAN LA MEMBRANA GENERANDO REDUCCION DE LA PENDIENTE DEL PREPOTENCIAL RECEPTOREN M2

LA ESTIMULACIÓN SIMPATICA AUMENTA LA PENDIENTE DEL PREPOTENCIAL AUMENTANDO LA FC POR ESTIMULACIÓN BETA 1 FACILITA LA APERTURA DE LOS CANALES L DE CA



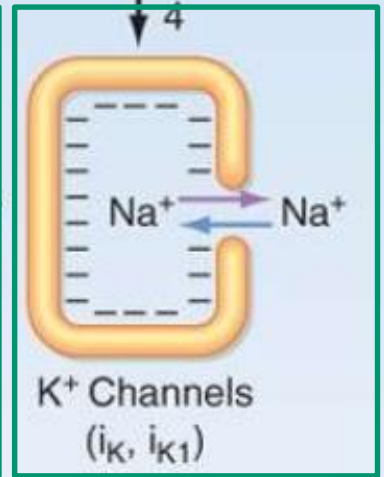
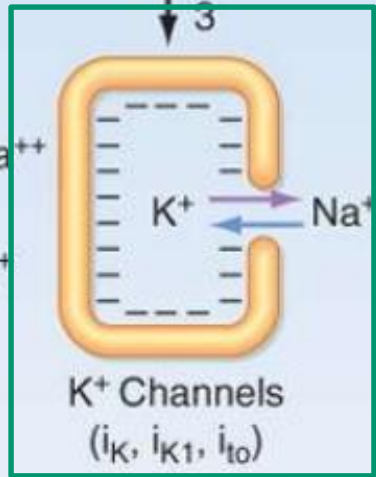
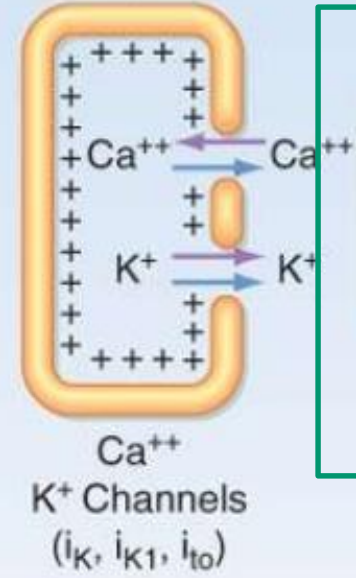
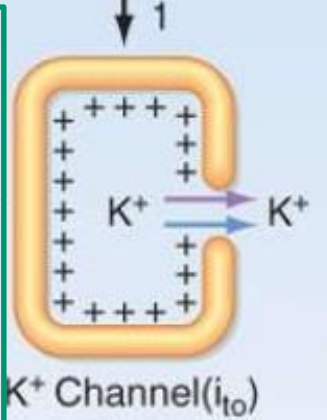
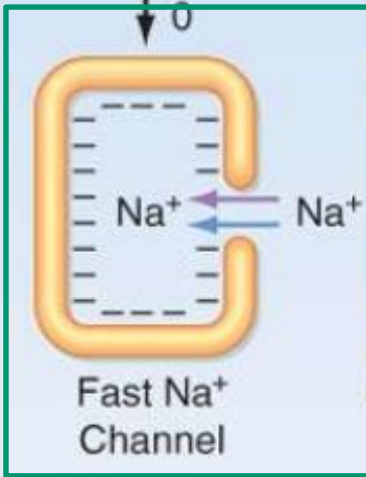
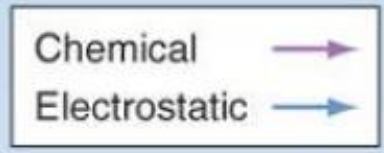
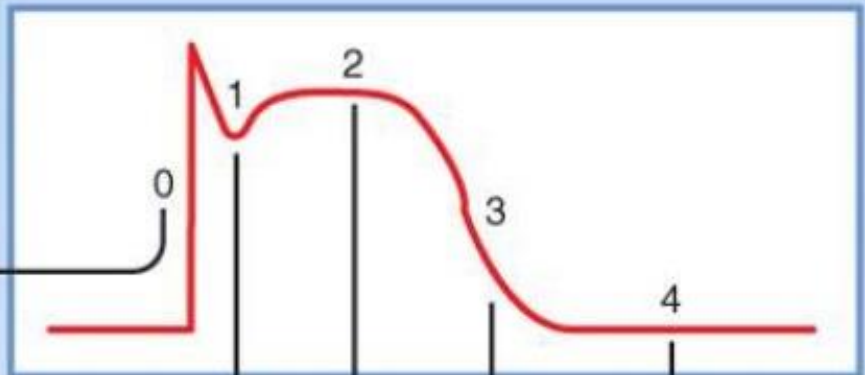


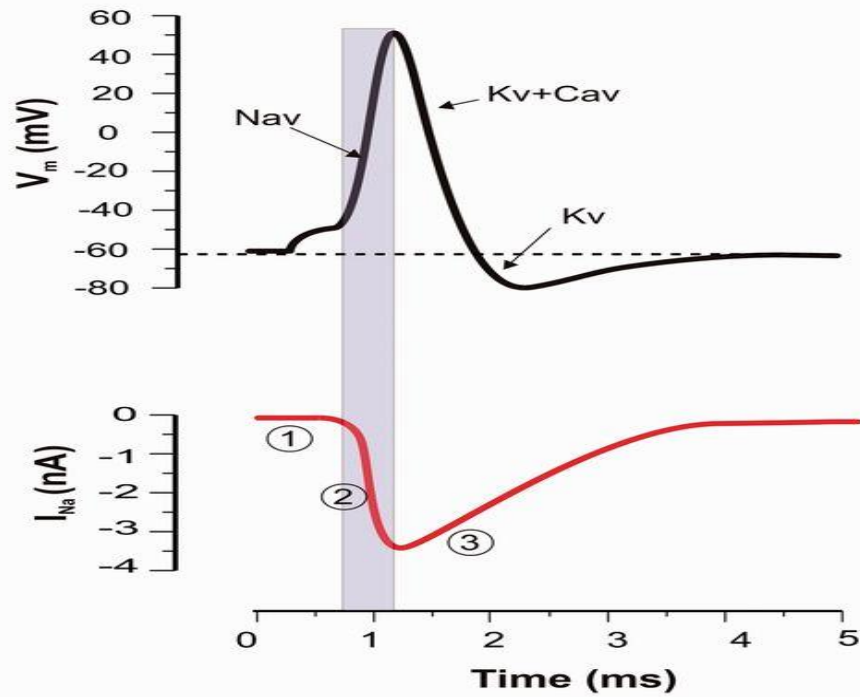
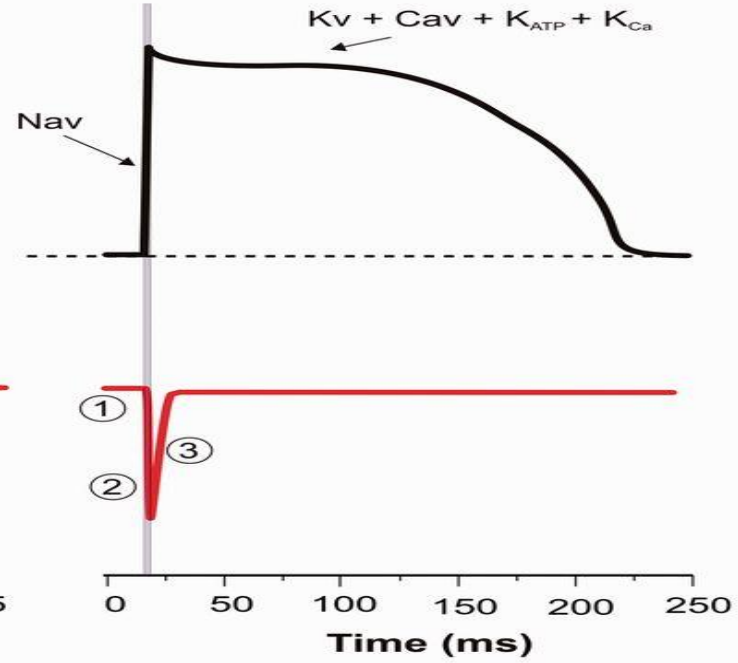
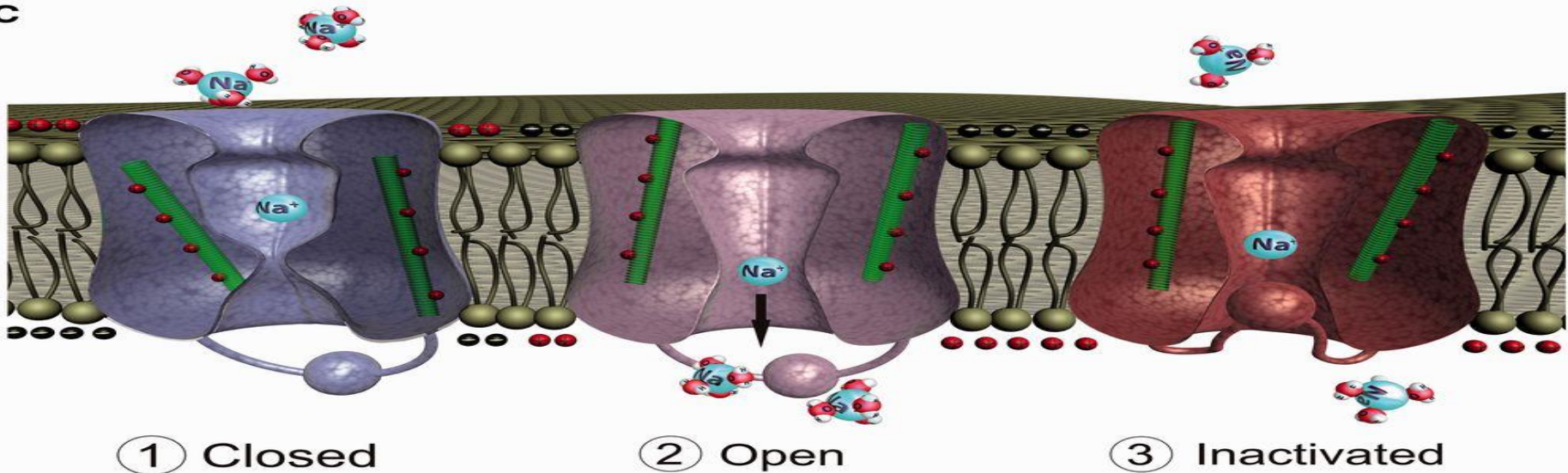
Correlación con el ciclo cardíaco

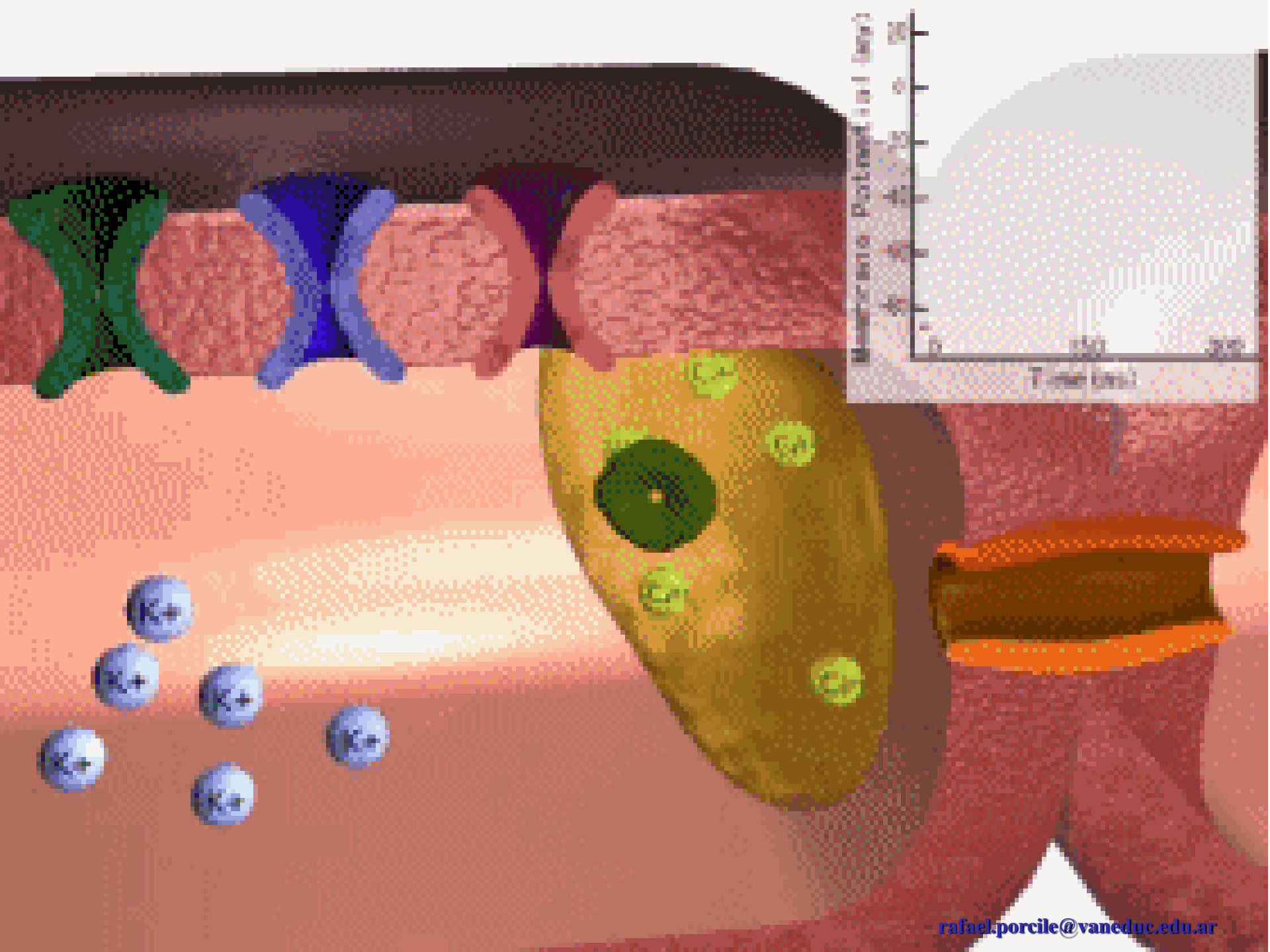


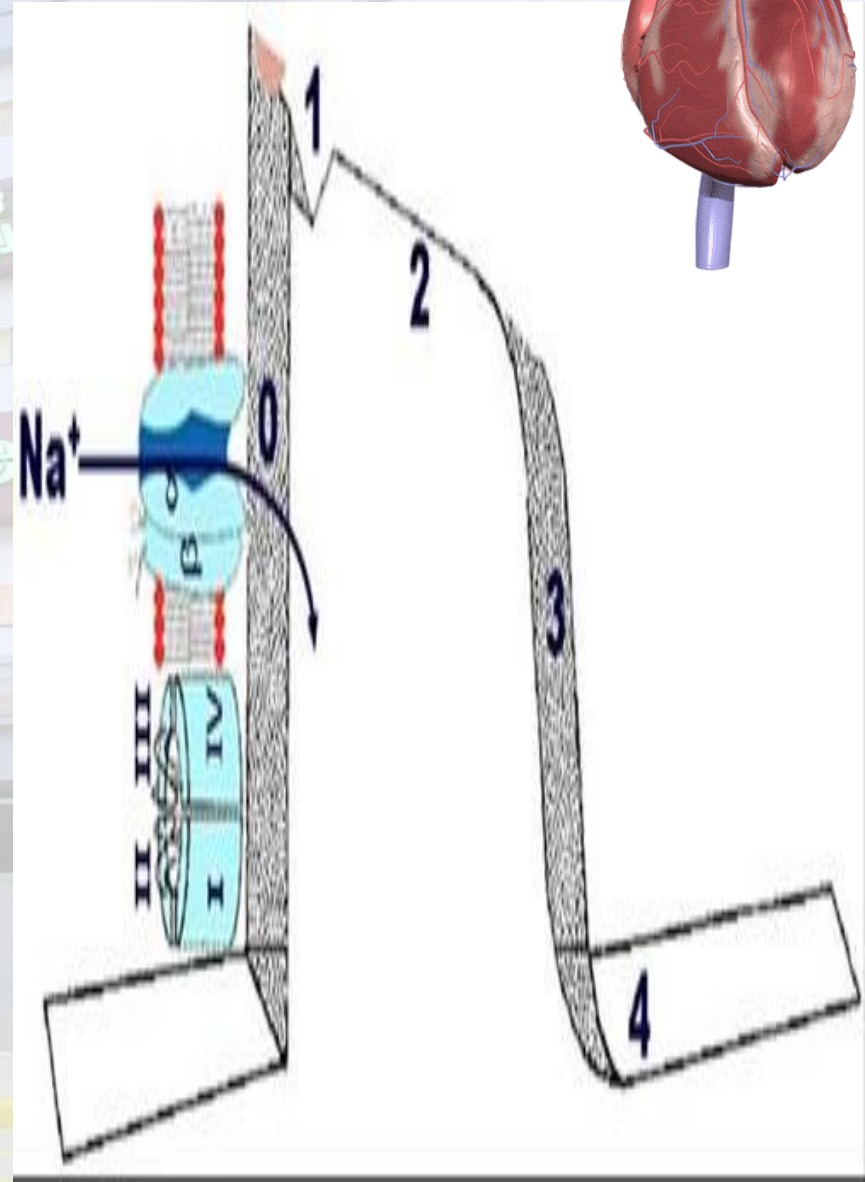
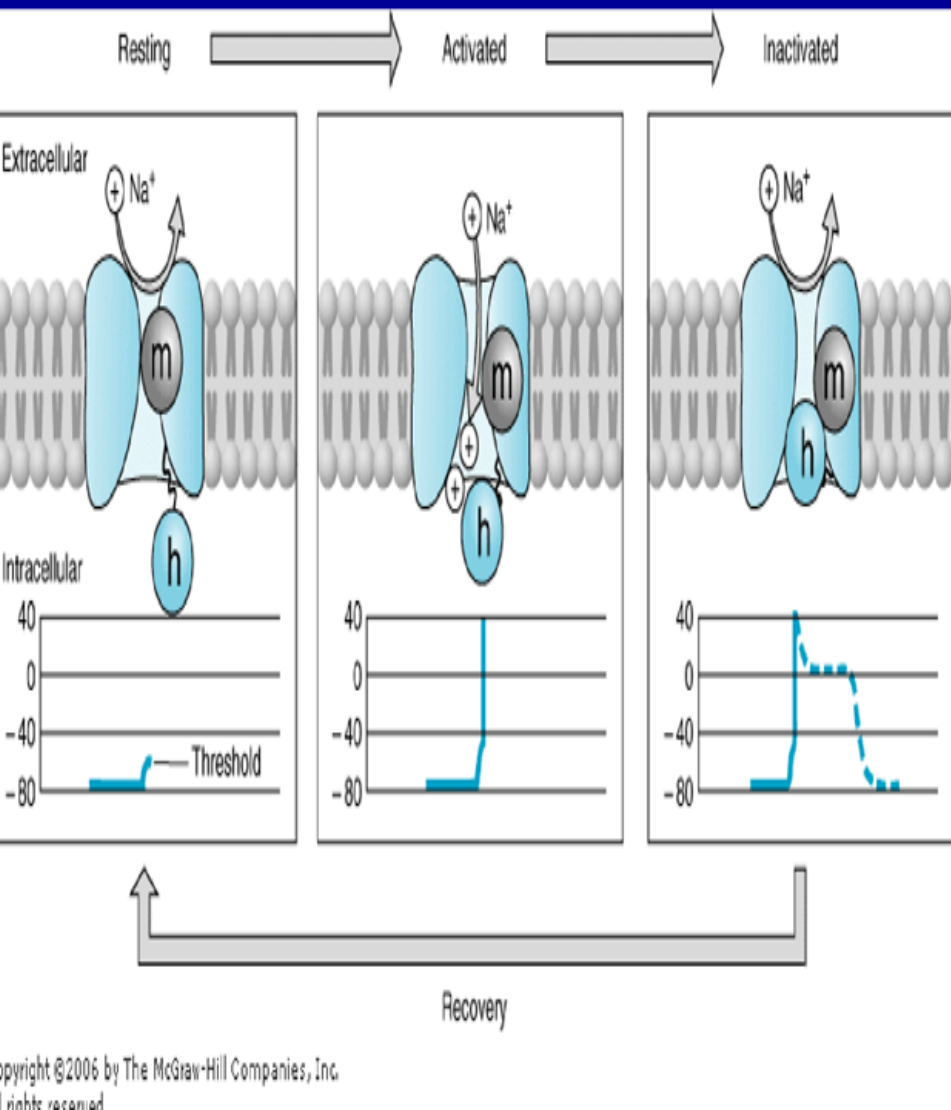
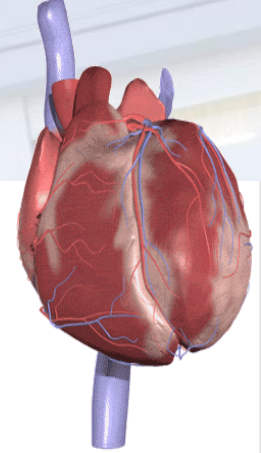
Los canales de Sodio

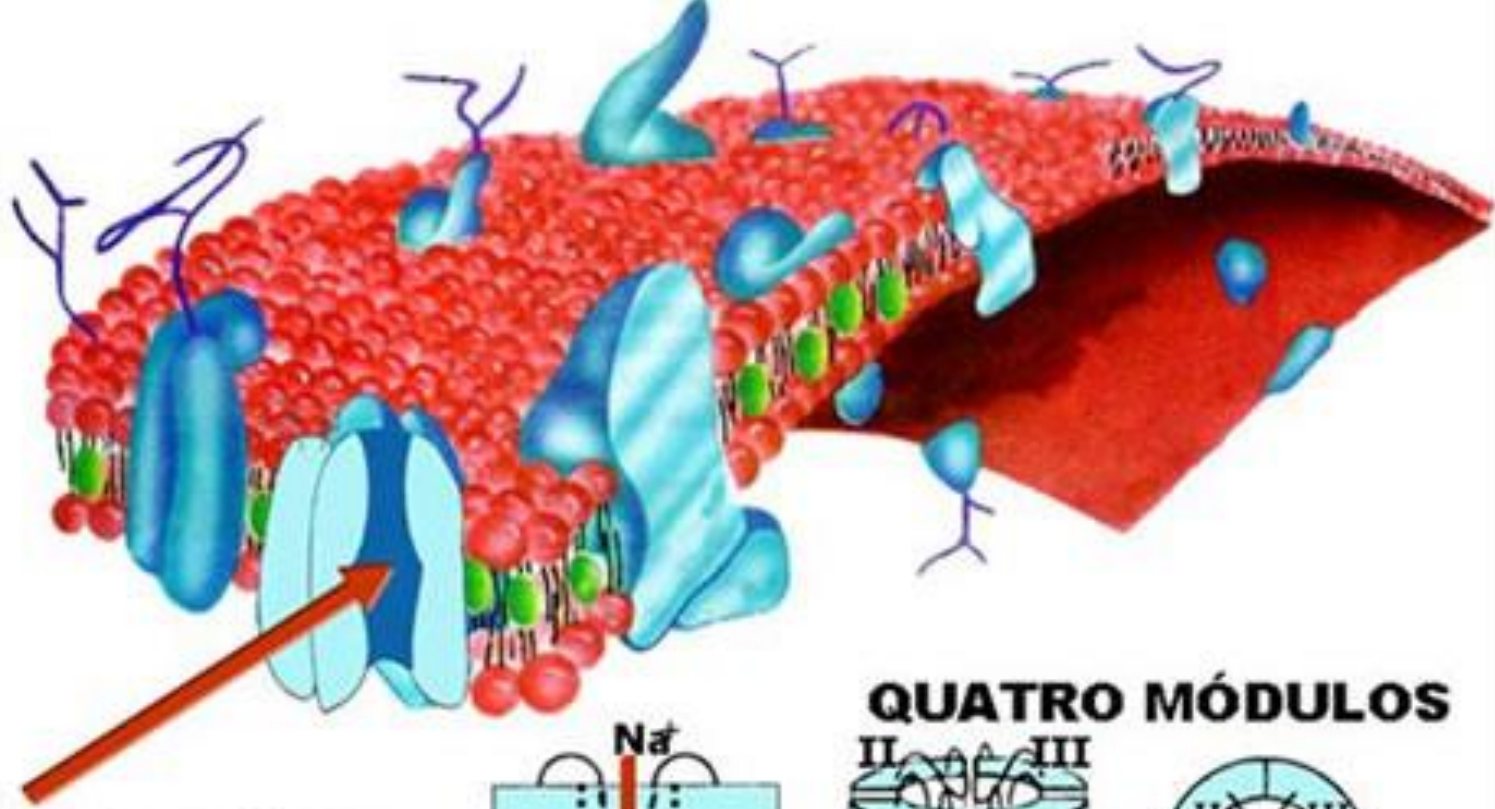




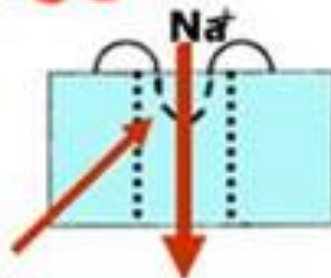
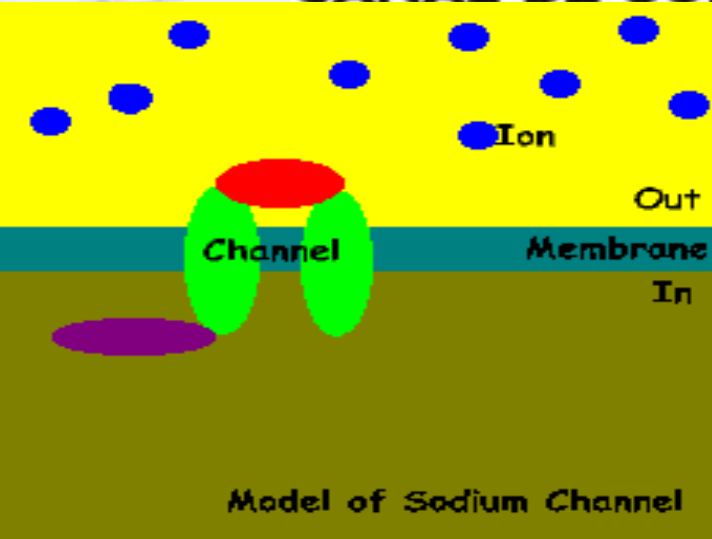
A**Neuronal action potential****B****Ventricular action potential****C**



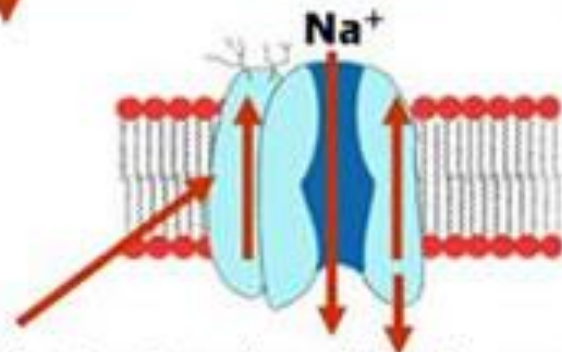
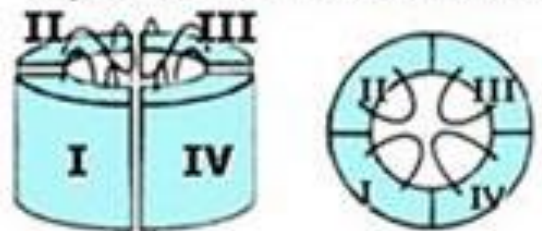


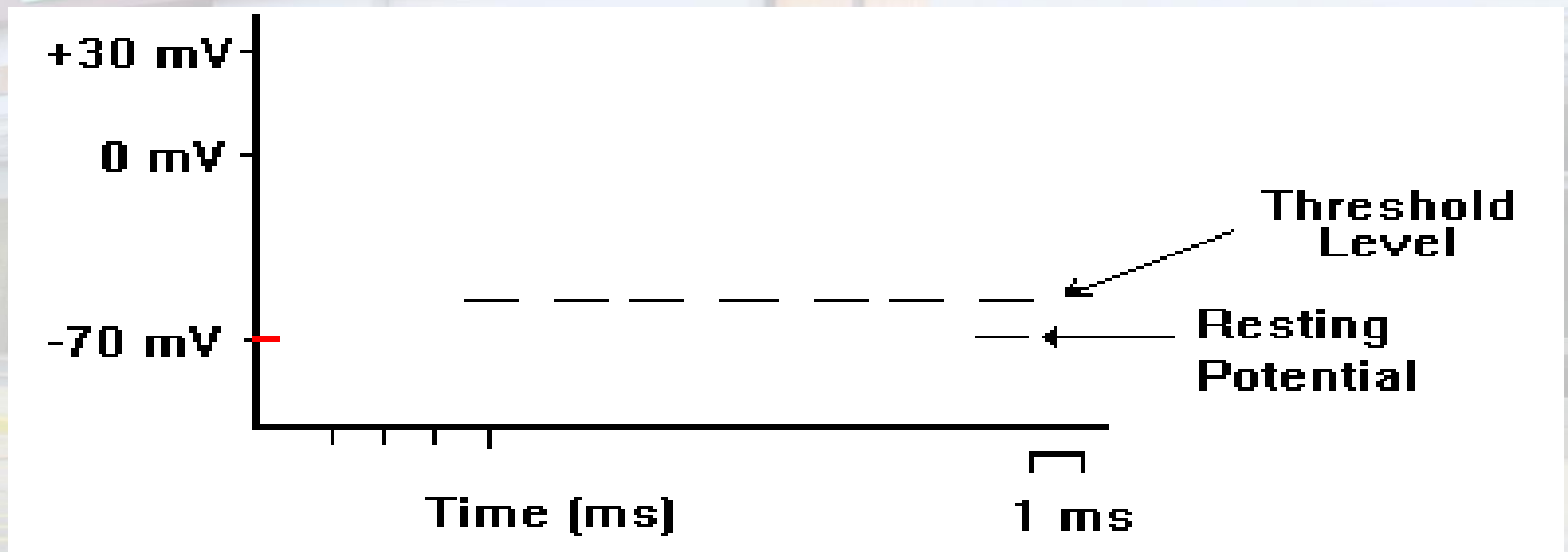
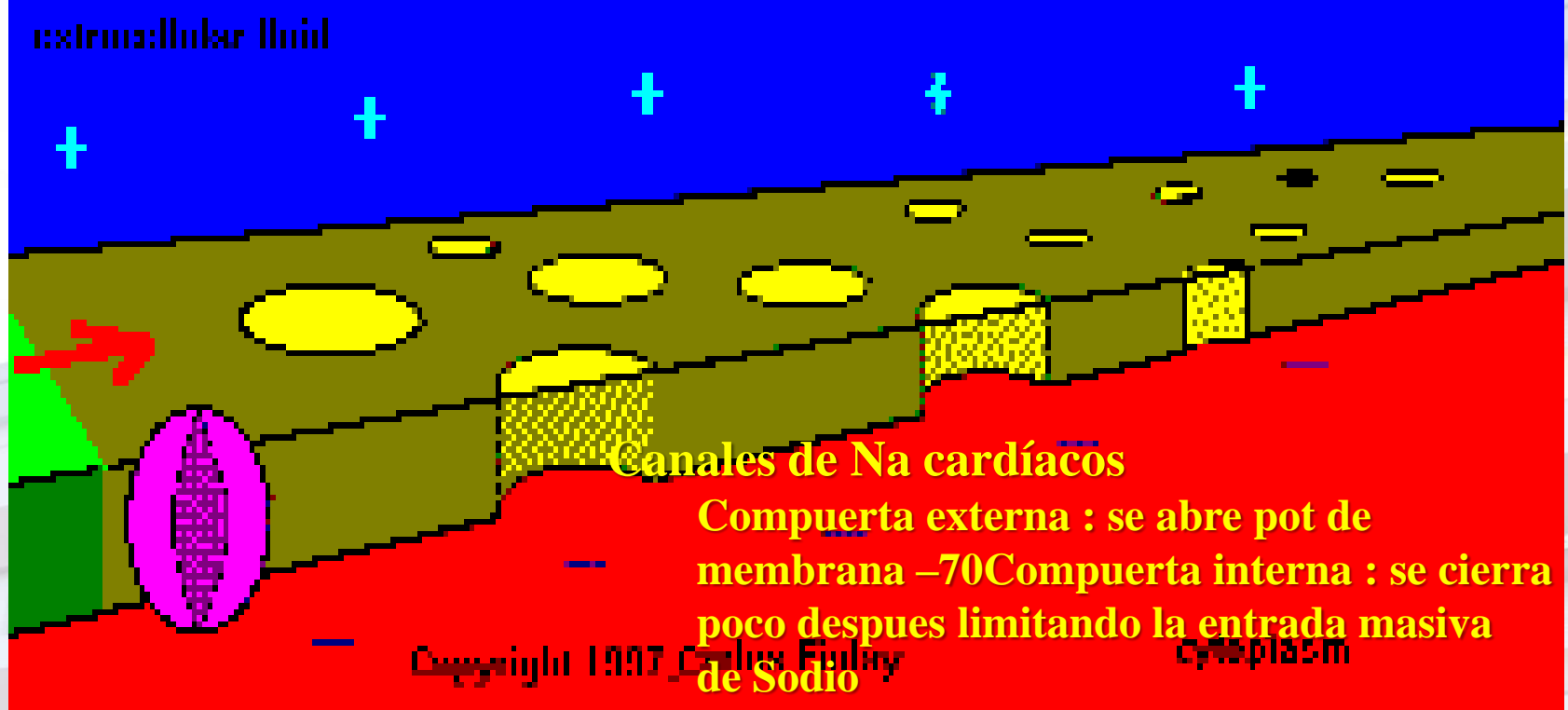


CANAL DE SÓDIO



QUATRO MÓDULOS





IONIC BASIS OF ACTION POTENTIAL OF AUTORRYTHMIC CELLS

Phase 1: Pacemaker Potential:

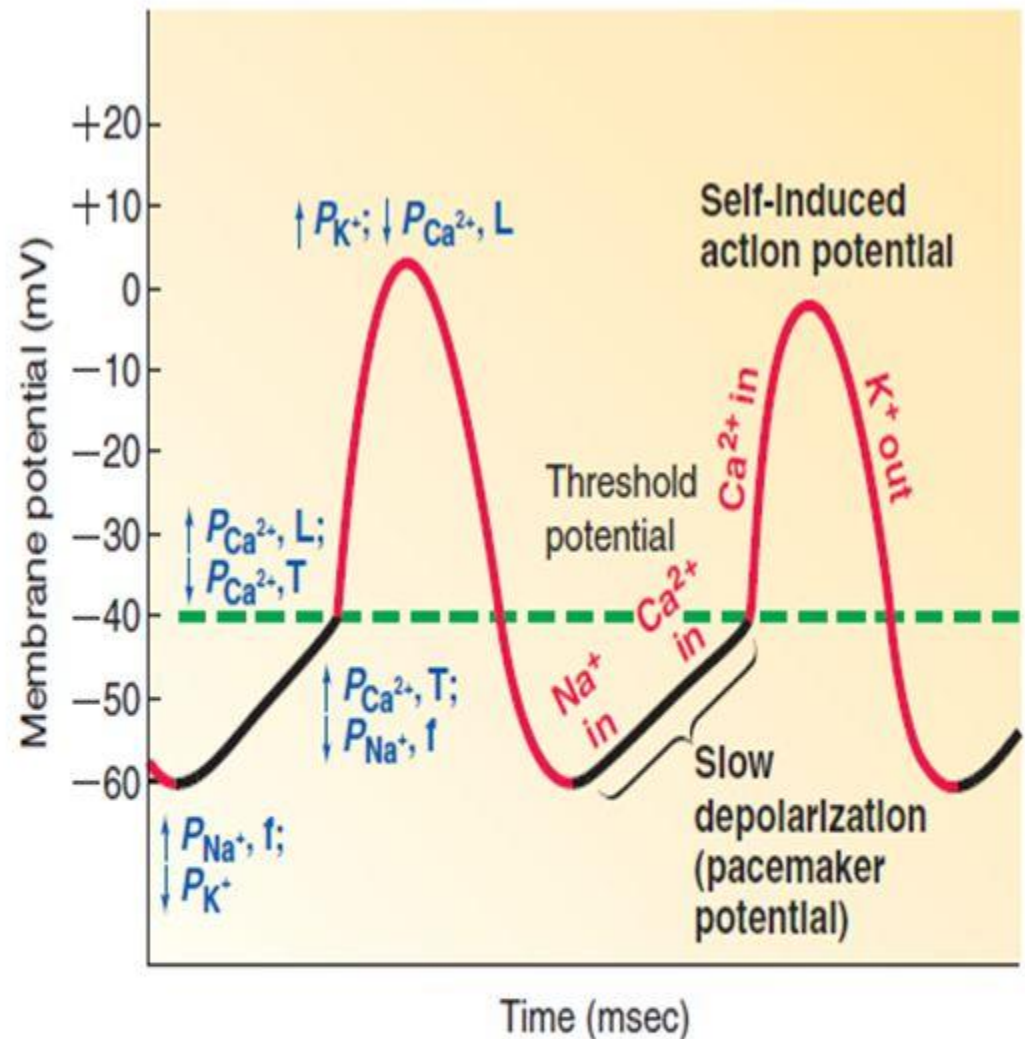
- Opening of voltage-gated Sodium channels called Funny channels (I_f or f channels).
- Closure of voltage-gated Potassium channels.
- Opening of Voltage-gated Transient-type Calcium (T-type Ca^{2+} channels) channels .

Phase 2: The Rising Phase or Depolarization:

- Opening of Long-lasting voltage-gated Calcium channels (L-type Ca^{2+} channels).
- Large influx of Calcium.

Phase 3: The Falling Phase or Repolarization:

- Opening of voltage-gated Potassium channels
- Closing of L-type Ca channels.
- Potassium Efflux.



KEY

- f = Funny channels
- T = Transient-type channels
- L = Long-lasting channels

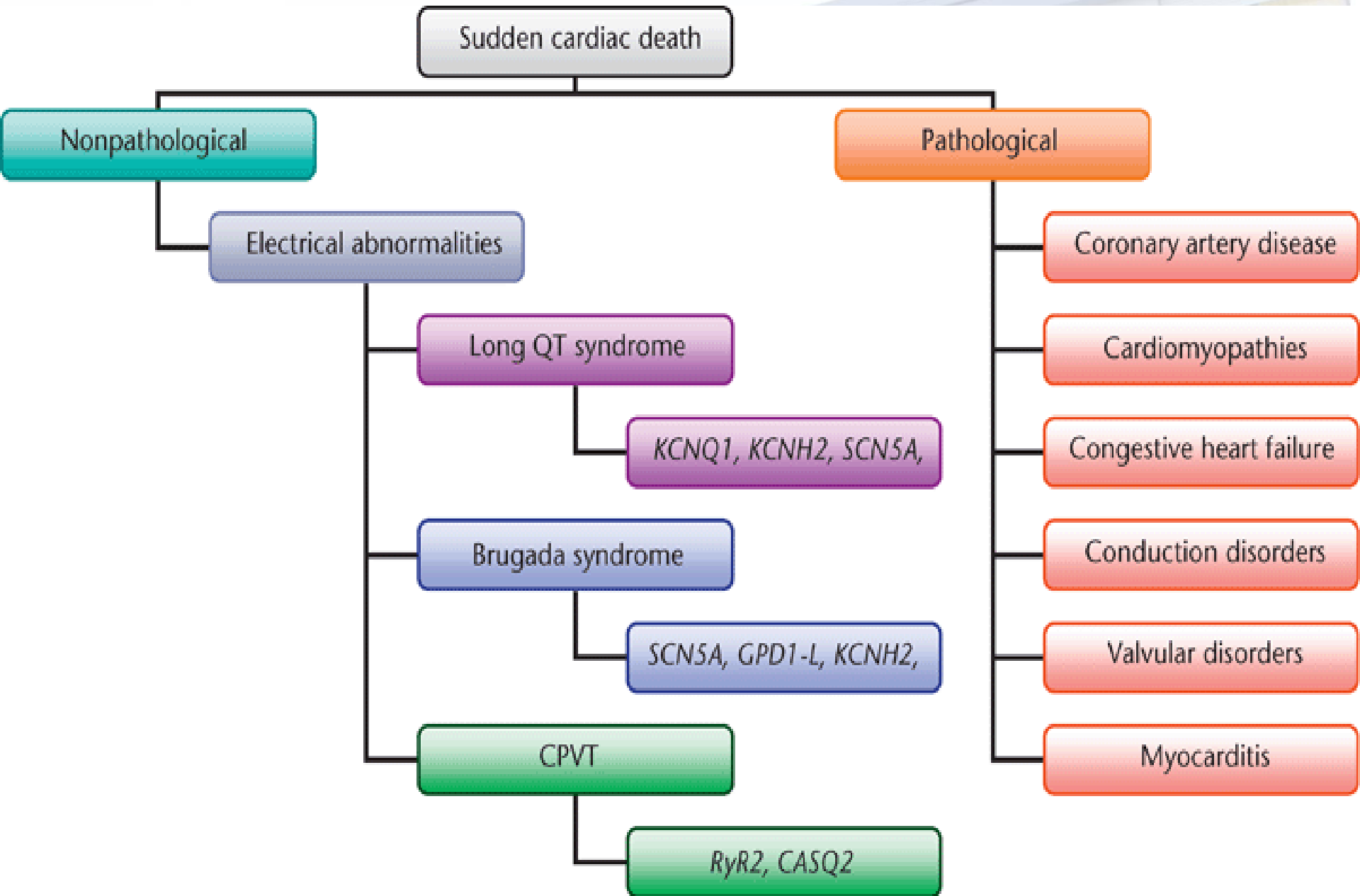
Trastornos en los canales de sodio

The background image shows the exterior of a multi-story building, identified as the Hospital Escuela Americana. The building has a light-colored facade with a prominent red horizontal band. On this band, the words "HOSPITAL ESCUELA AMERICANA" are written in large, green, illuminated letters. Above this band, there is another line of text in Spanish: "UNIVERSIDAD AMERICANA VENEZUELA". The building features several windows and a central entrance area with glass doors. The overall scene is brightly lit, suggesting daytime.

The image shows the exterior of a large, multi-story building, likely a school or hospital. The building has a light-colored facade with a prominent red horizontal band. On this band, the words "HOSPITAL ESCUELA" are written in large, green, illuminated letters. Above this band, there is another line of text in a different language, possibly Spanish or Portuguese, also in green. The building features several windows with white frames and a covered entrance area with a glass canopy. A yellow curb is visible in the foreground.

- **Congenitos**

- **Adquiridos**



The Primary Electrical Disease Syndromes

1. Congenital Long QT-syndrome, LQTS
2. Short QT syndrome, SQT
3. Brugada syndrome
4. Catecholaminergic polymorphic ventricular tachycardia, CPVT

What do they share in common?

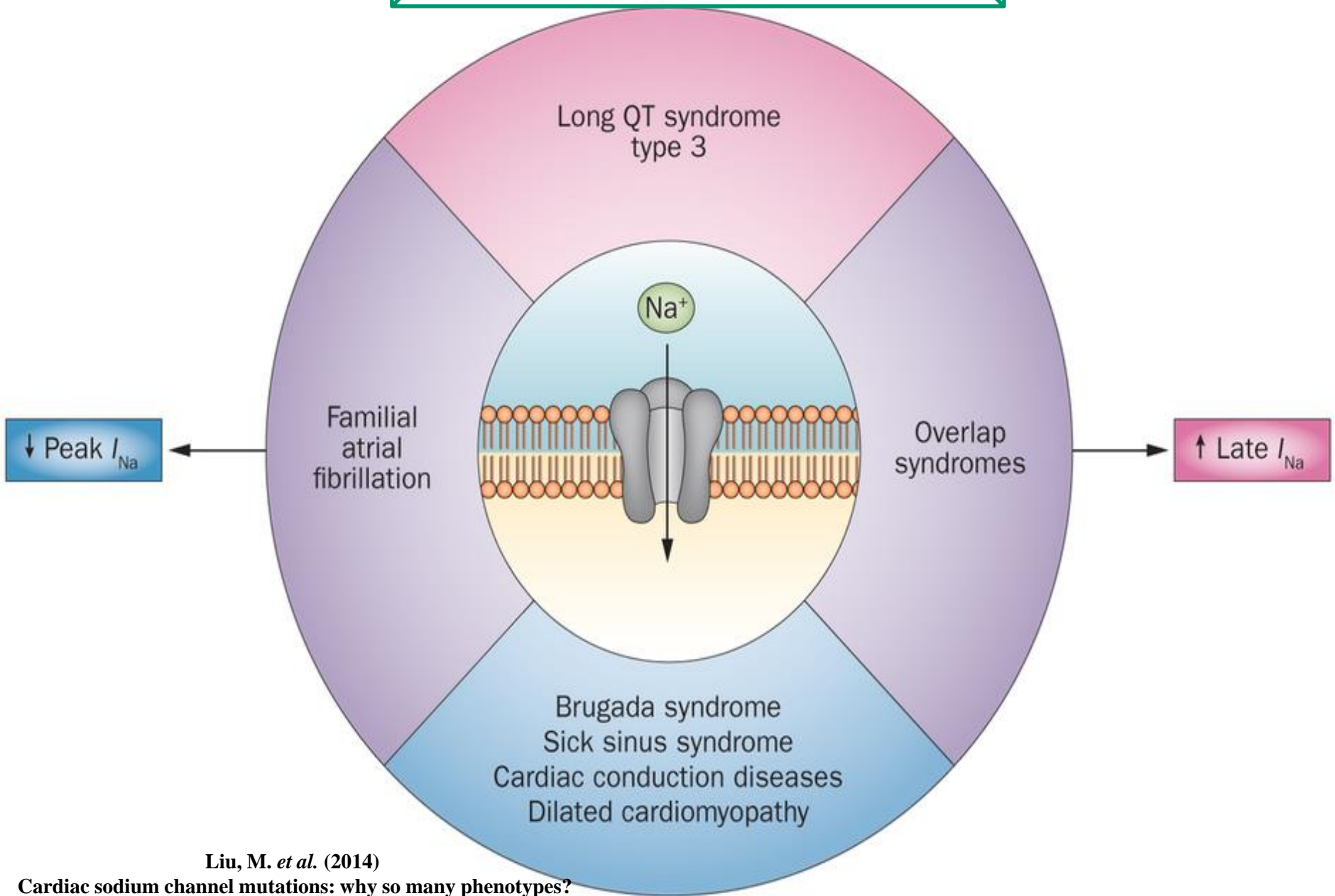
1. They cause polymorphic VT, syncope and sudden death
2. The ECG is the primary diagnostic tool.
3. They result from mutations in ion channels or their adaptor proteins



Canalopatías

- **Concepto:** son cardiopatías hereditarias que tienen la peculiaridad de suceder en corazones estructuralmente normales y causar **arritmias letales**: taquicardia ventricular, *torsade de pointes* y fibrilación ventricular.
- **Fisiopatología:** alteración en la actividad de un canal iónico con repercusión en el potencial de acción y en la estabilidad eléctrica del corazón.
- **Etiología:** habitualmente, son las **mutaciones** en los genes de los canales iónicos, las que originan cambios funcionales y dan origen a las *canalopatías*.

SCN5A gain-of-function mutations



Liu, M. *et al.* (2014)

Cardiac sodium channel mutations: why so many phenotypes?

Nat. Rev. Cardiol. doi:10.1038/nrcardio.2014.85

SCN5A loss-of-function mutations

rafael.porcile@vandeduc.edu.ar

SCN5A gain-of-function mutations can result in increased late I_{Na} , leading to long QT syndrome type 3. *SCN5A* loss-of-function mutations can lead to decreased peak I_{Na} , which is associated with Brugada syndrome, sick sinus syndrome, cardiac conduction diseases, and possibly dilated cardiomyopathy. Moreover, *SCN5A* mutations that cause both a gain in late I_{Na} and a loss of peak I_{Na} can be associated with a mixed phenotype or overlap syndromes (for example, Brugada syndrome and long QT syndrome type 3). Similarly, both gain-of-function and loss-of-function mutations have been associated with familial lone atrial fibrillation.

Liu, M. *et al.* (2014)

Cardiac sodium channel mutations: why so many phenotypes?

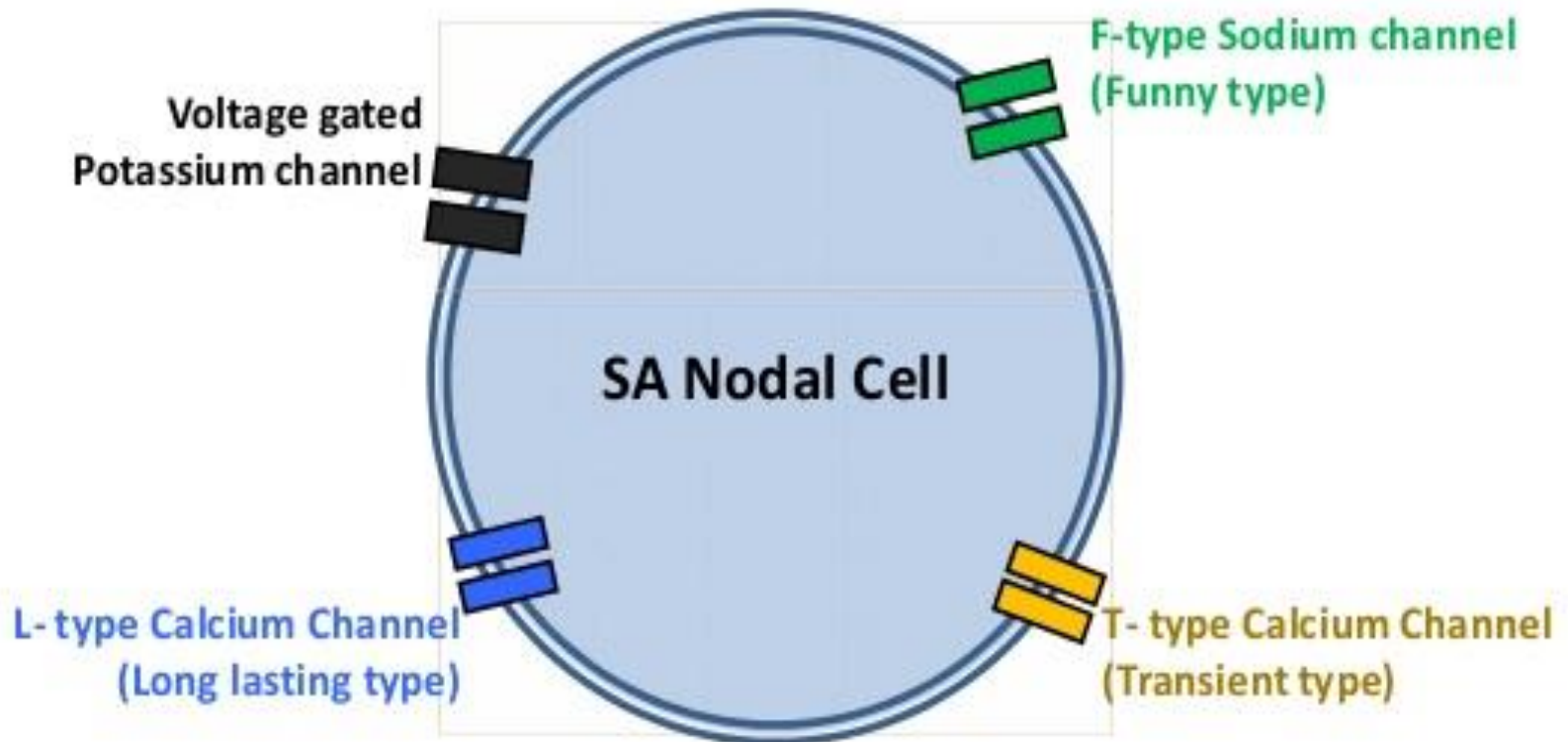
Nat. Rev. Cardiol. doi:10.1038/nrcardio.2014.85

rafael.porcile@vandeduc.edu.ar

Cont...SA NODE AP

Types of Channels

Enfermedad del
nodo sinusal y/o
FA familiar



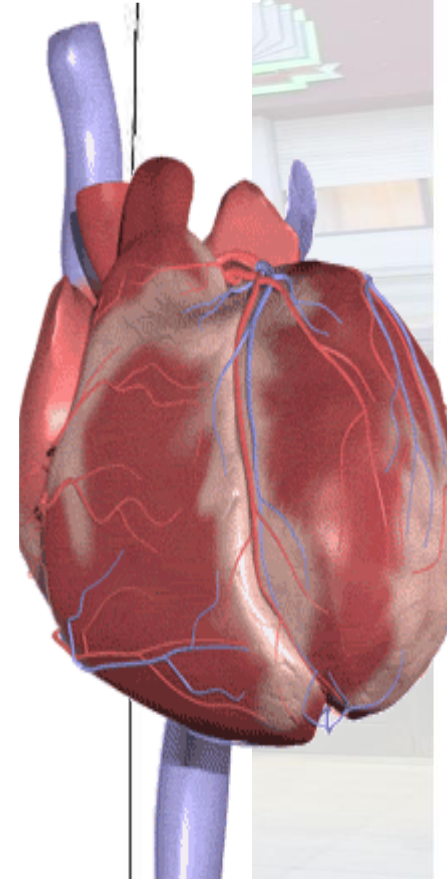
Canalopatías

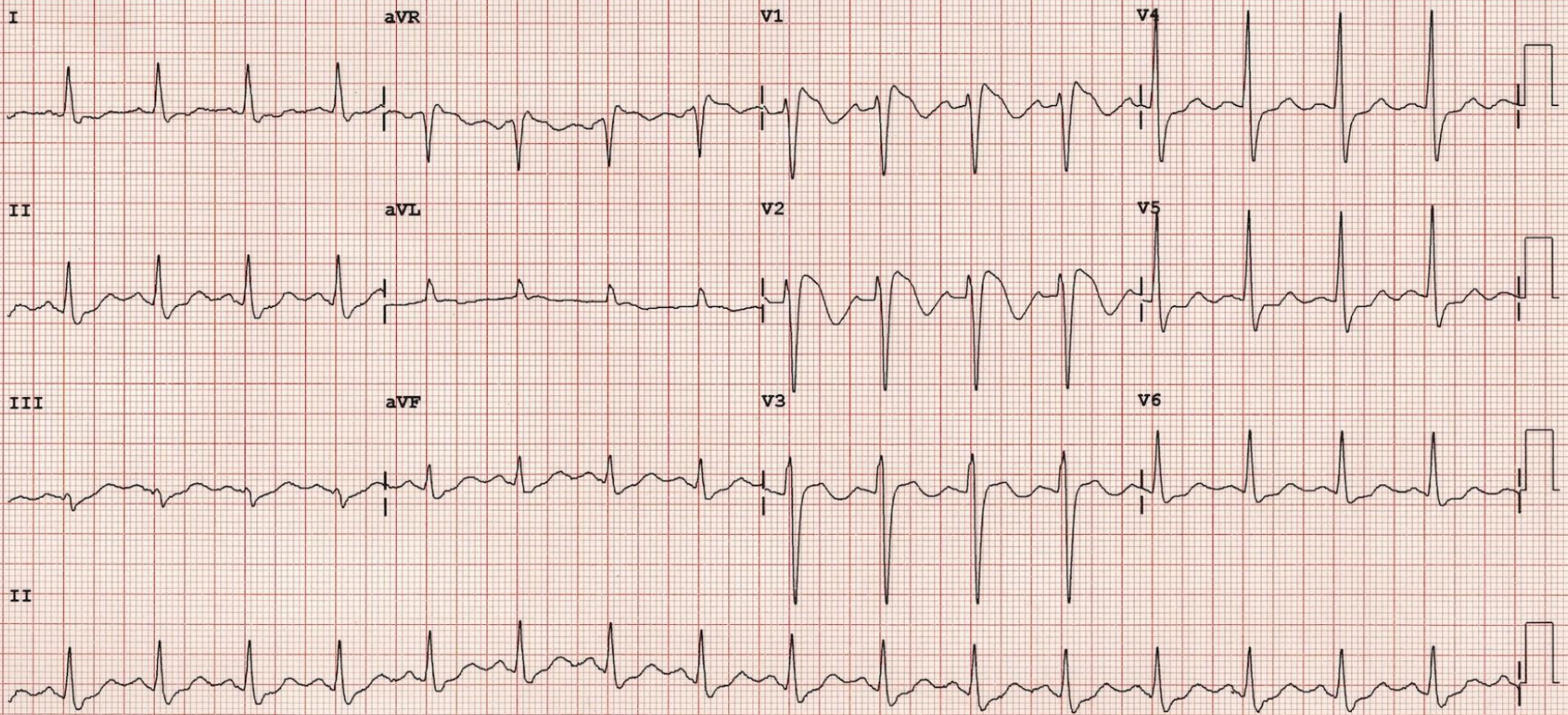
- Estrés físico/psíquico (QT largo)
- Reposo/sueño (síndrome de Brugada)

Dispersión heterogénea de la repolarización

Inestabilidad eléctrica

Fibrilación ventricular

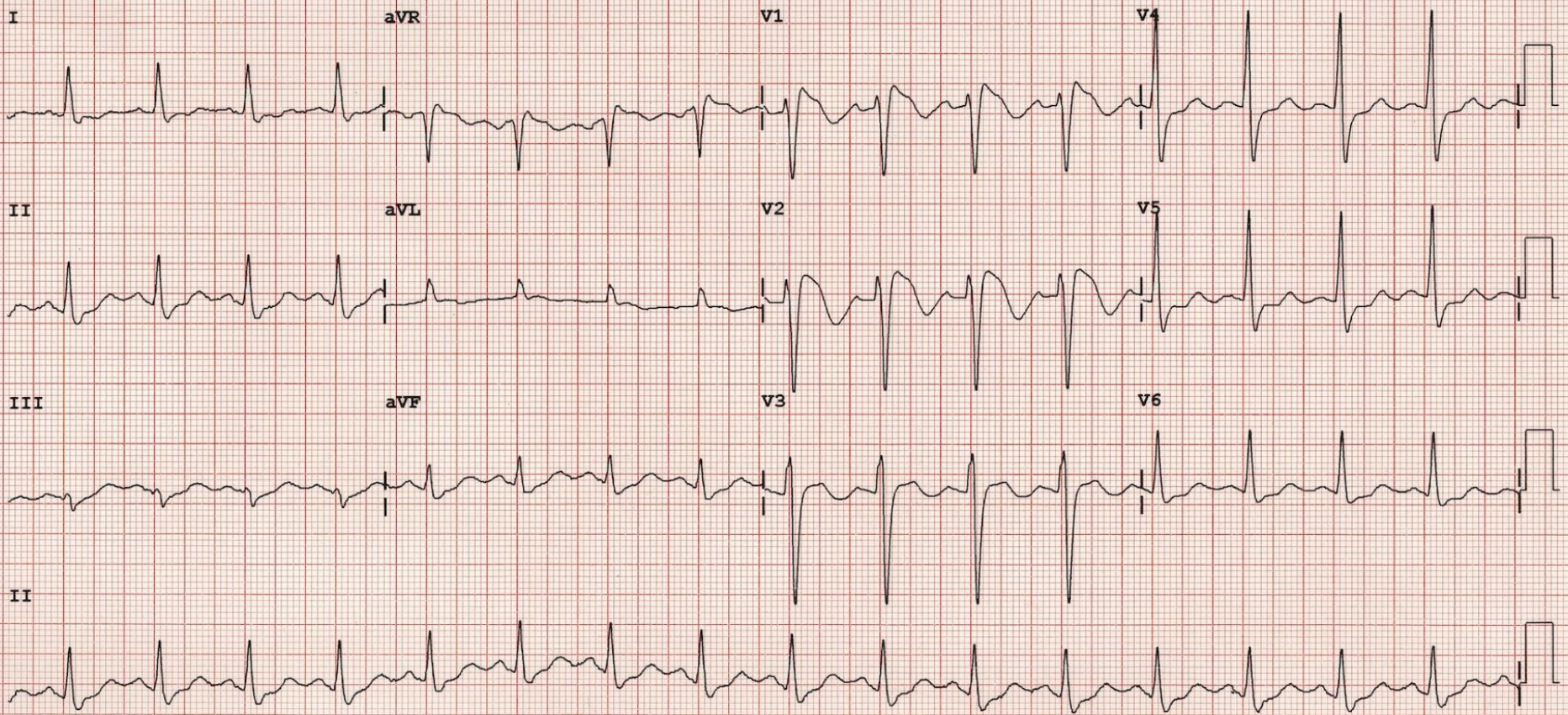




Dev: Speed: 25 mm/sec Limb: 10 μ /mV Chest: 10 mm/mV F 50~ 0.15-150 Hz PH08 P?

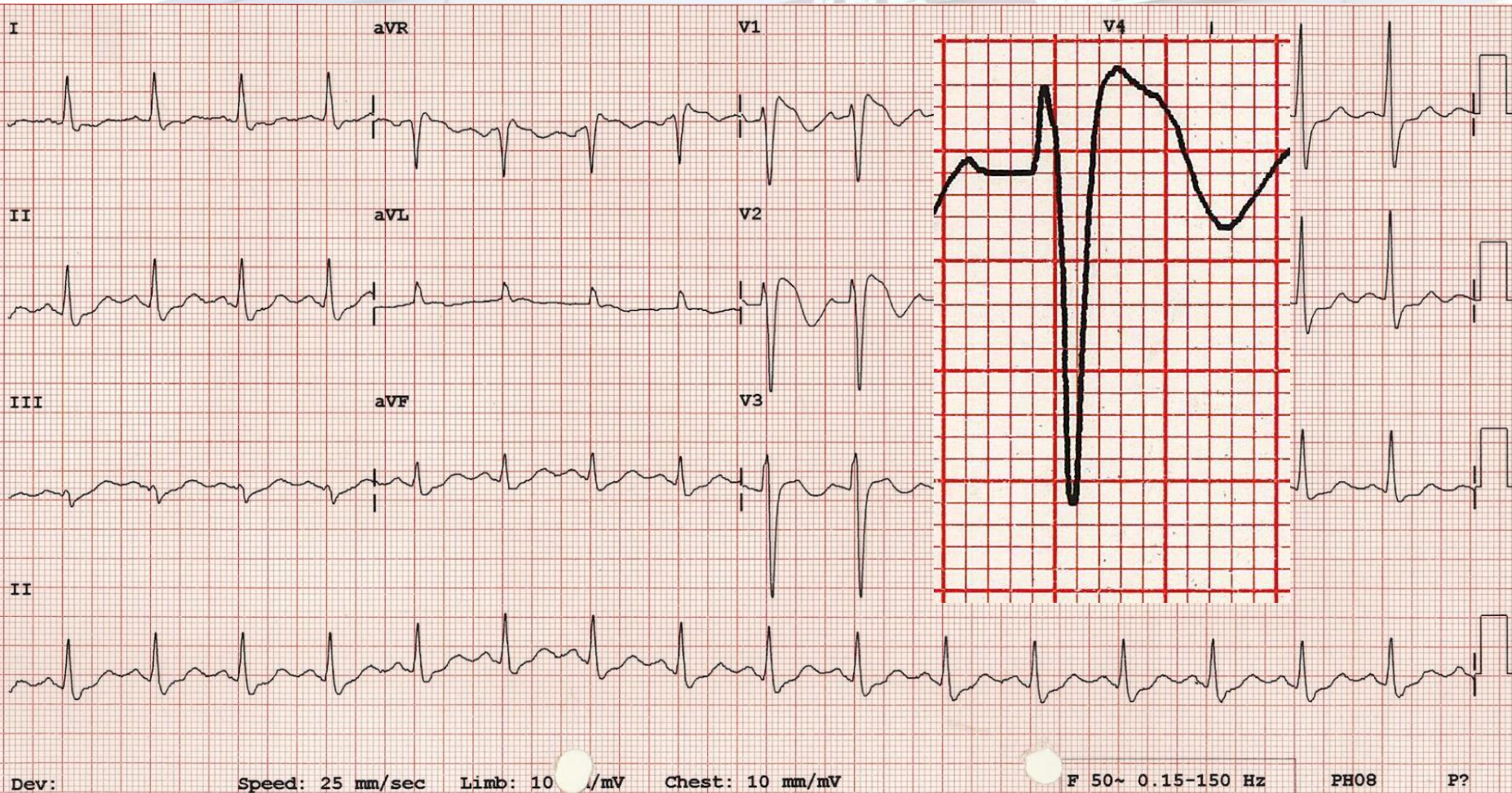
¿Que es?





Dev: Speed: 25 mm/sec Limb: 10 μ /mV Chest: 10 mm/mV F 50~ 0.15-150 Hz PH08 P?

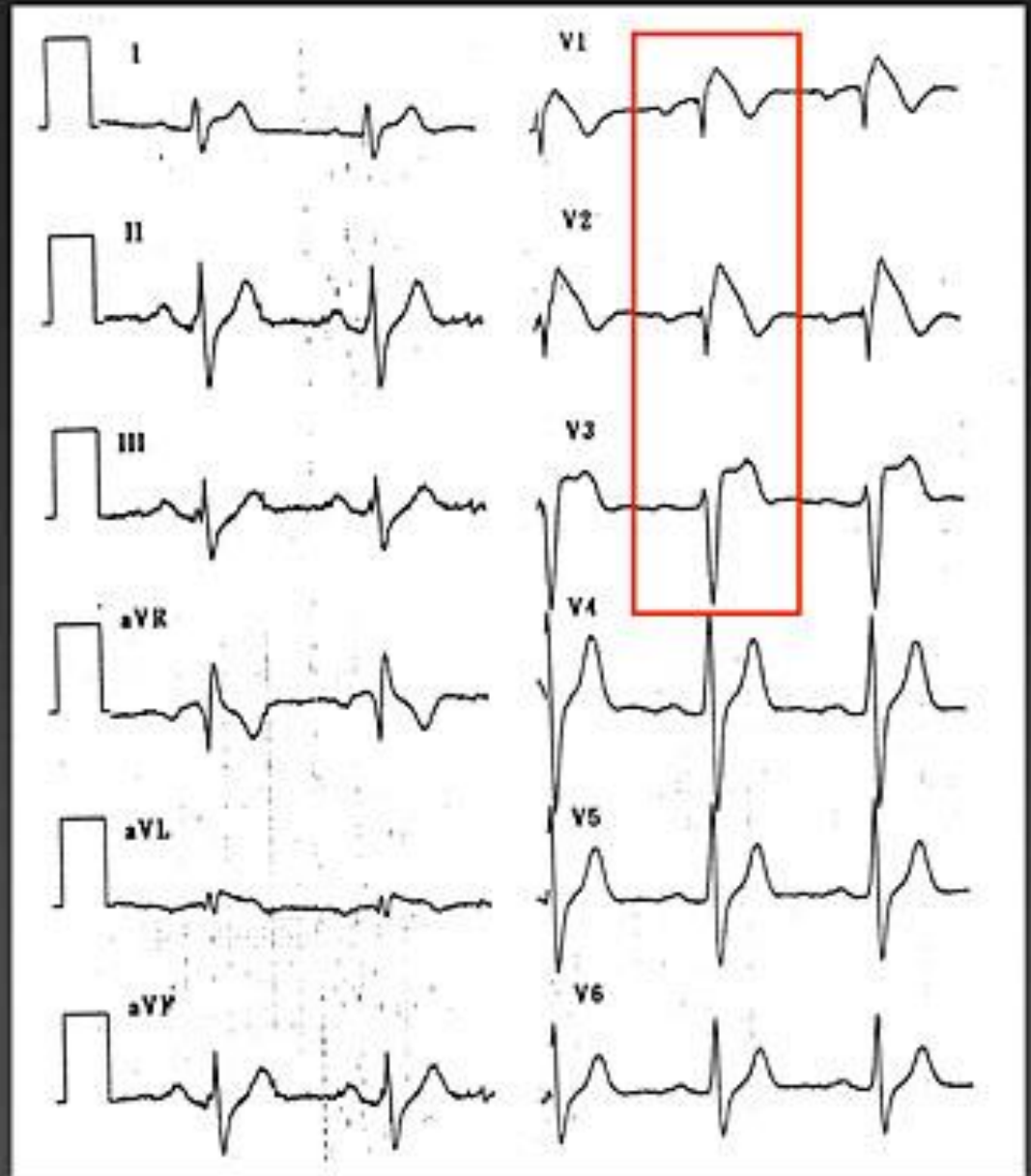
Síndrome de Brugada



Síndrome de Brugada

The ECG in Brugada syndrome

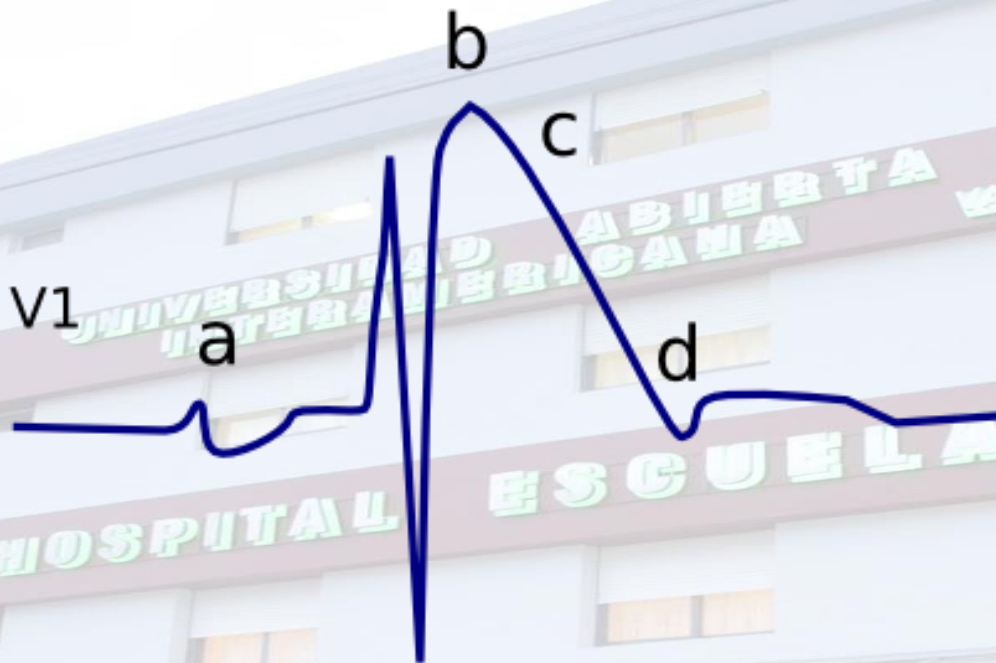
- Prolonged PR
- RBBB
- ST segment ↑



Síndrome de Brugada

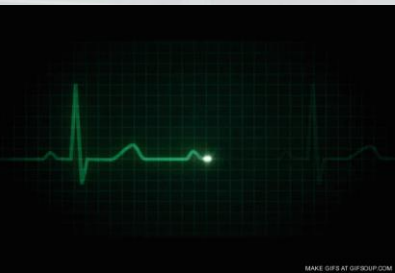
**El síndrome del bloqueo
de rama derecha,
elevación persistente del
segmento ST y muerte
súbita (MS)**

lead V1

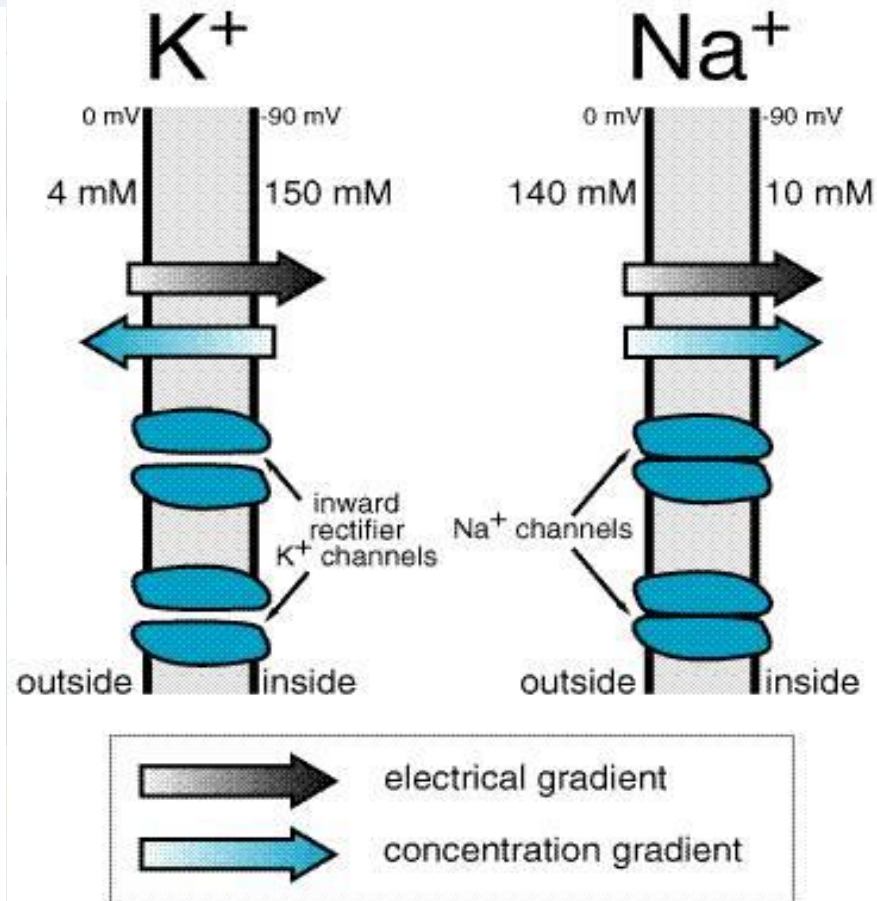
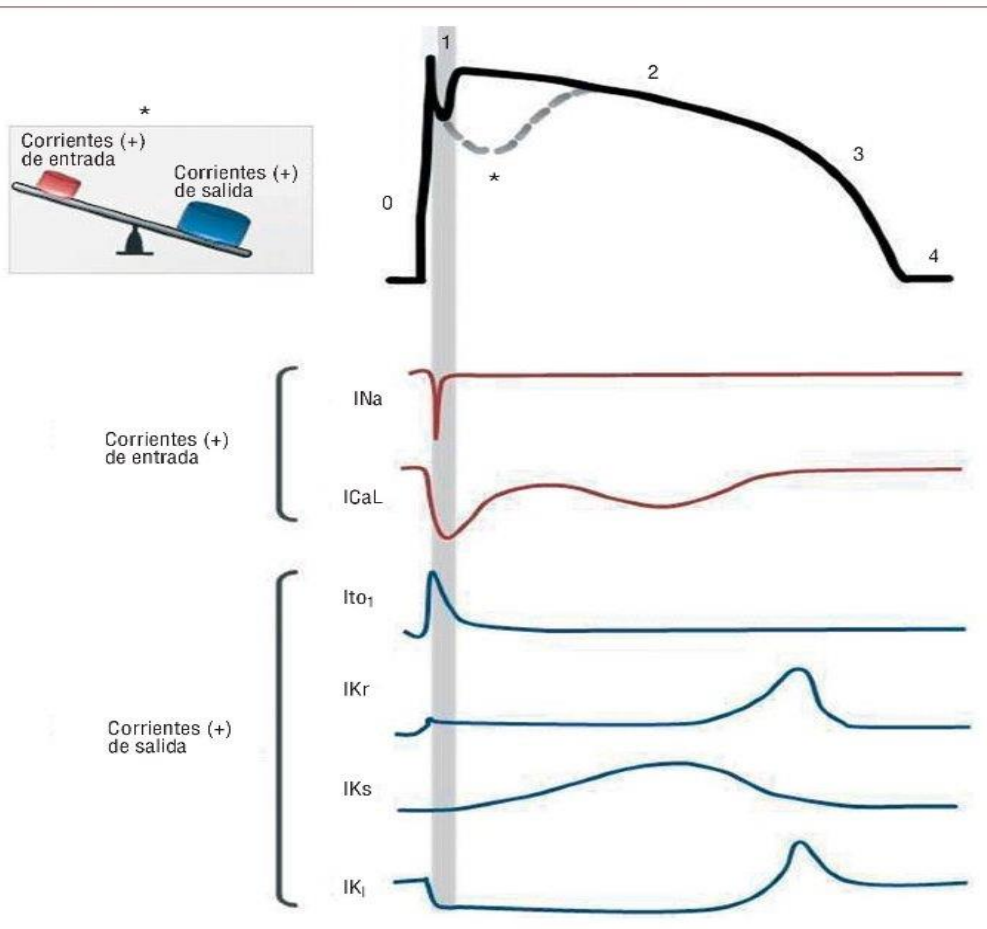


- ECG characteristics in Brugada Syndrome
- a. Broad P wave with some PQ prolongation
 - b. J point elevation
 - c. Coved type ST segment elevation
 - d. Inverted T wave

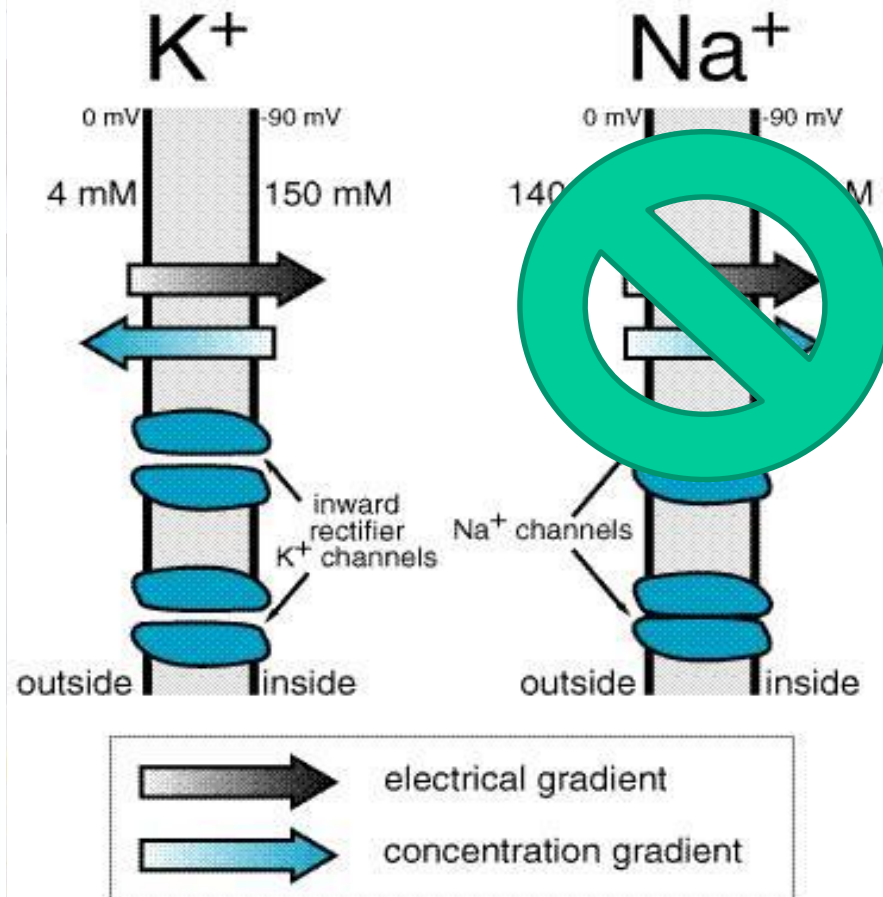
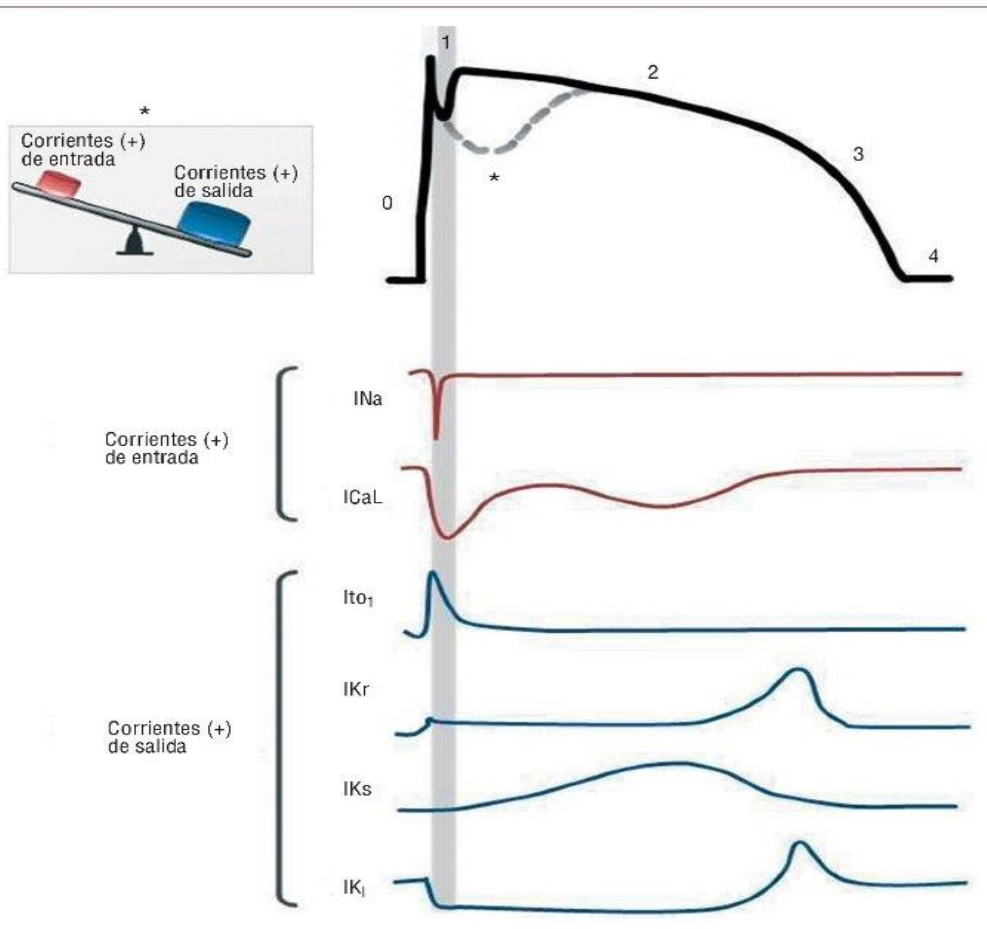
Las Canalopatías son enfermedades determinadas genéticamente, que afectan genes que codifican proteínas de los canales iónicos cardíacos.



Bugada: predominio en las corrientes de salida déficit en la entrada



Bugada: predominio en las corrientes de salida déficit en la entrada



Alrededor del 20 % de los casos de síndrome de Brugada están asociados con la mutación en el gen que codifica los canales de sodio en las membranas de los miocitos

Densidad de Canales es mayor en epicardio que en endocardio

Este fenómeno ocurre de forma heterogénea en la pared ventricular y da lugar a un gradiente transmural de voltaje,

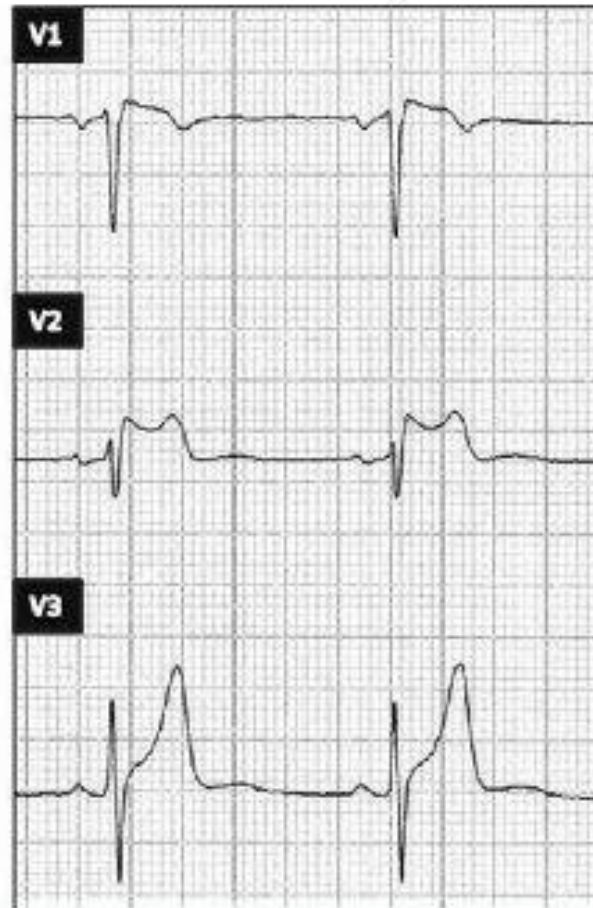
Produce la elevación característica del segmento ST en el electrocardiograma

Aunque el paciente puede tener varios patrones secuenciales solo el tipo I es diagnostico

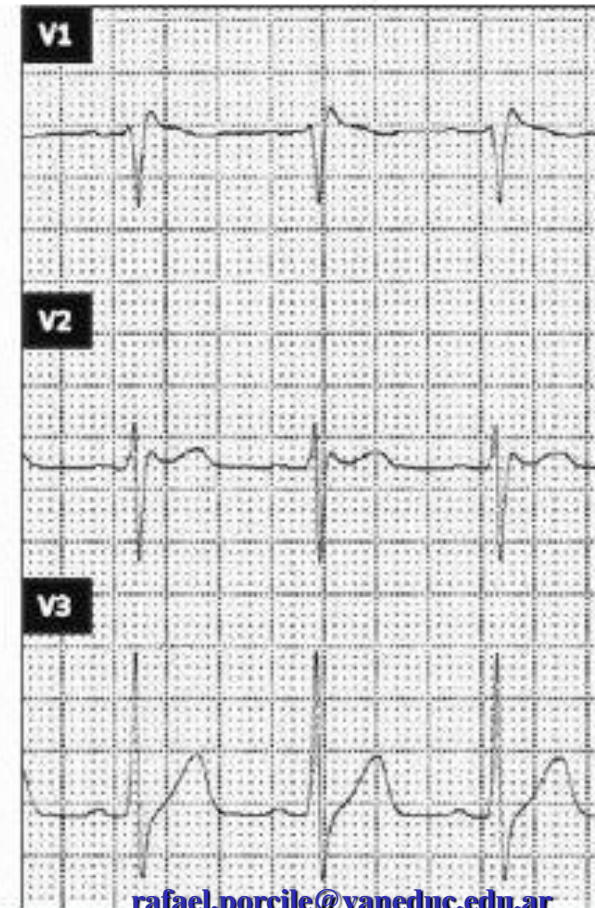
ECG tipo I



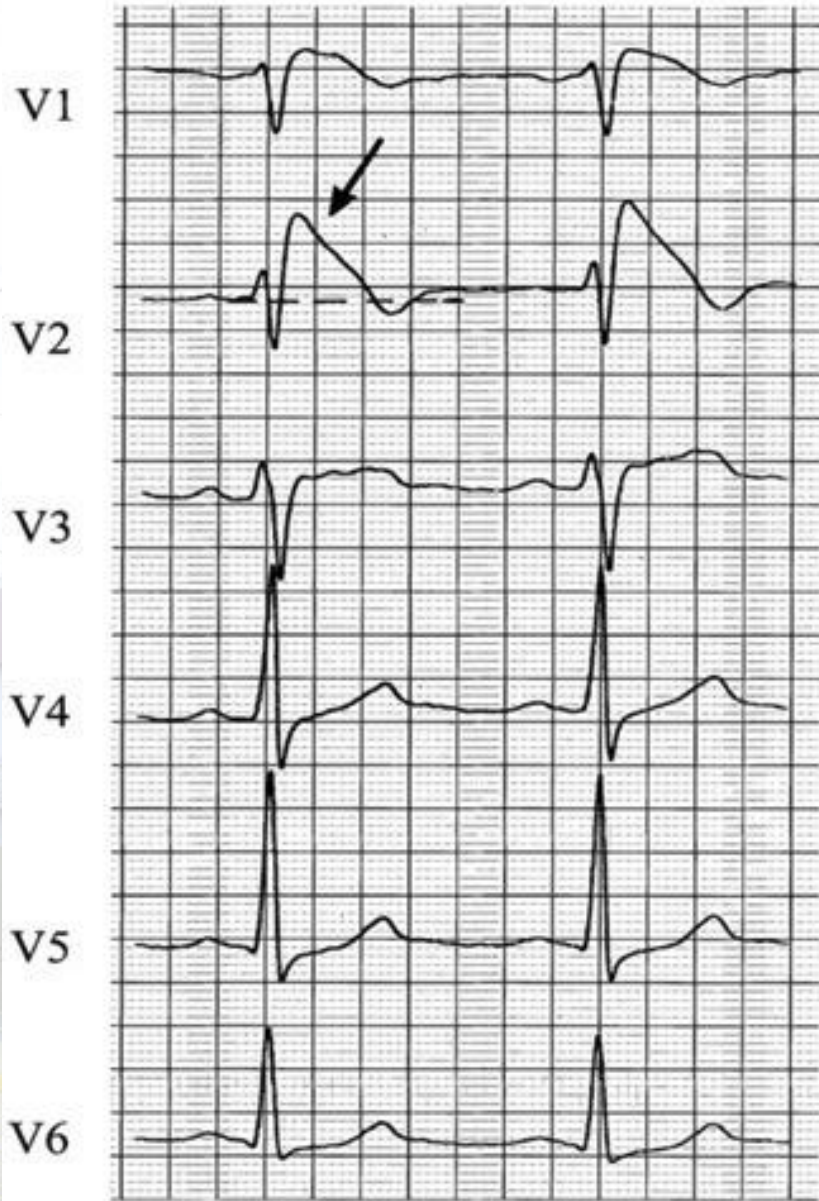
ECG tipo II



ECG tipo III



type 1



type 2

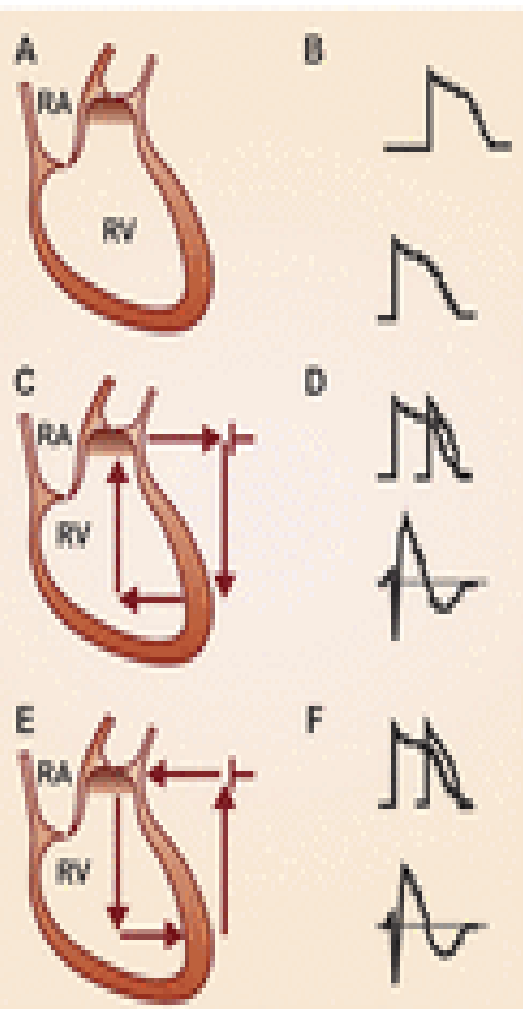


type 3

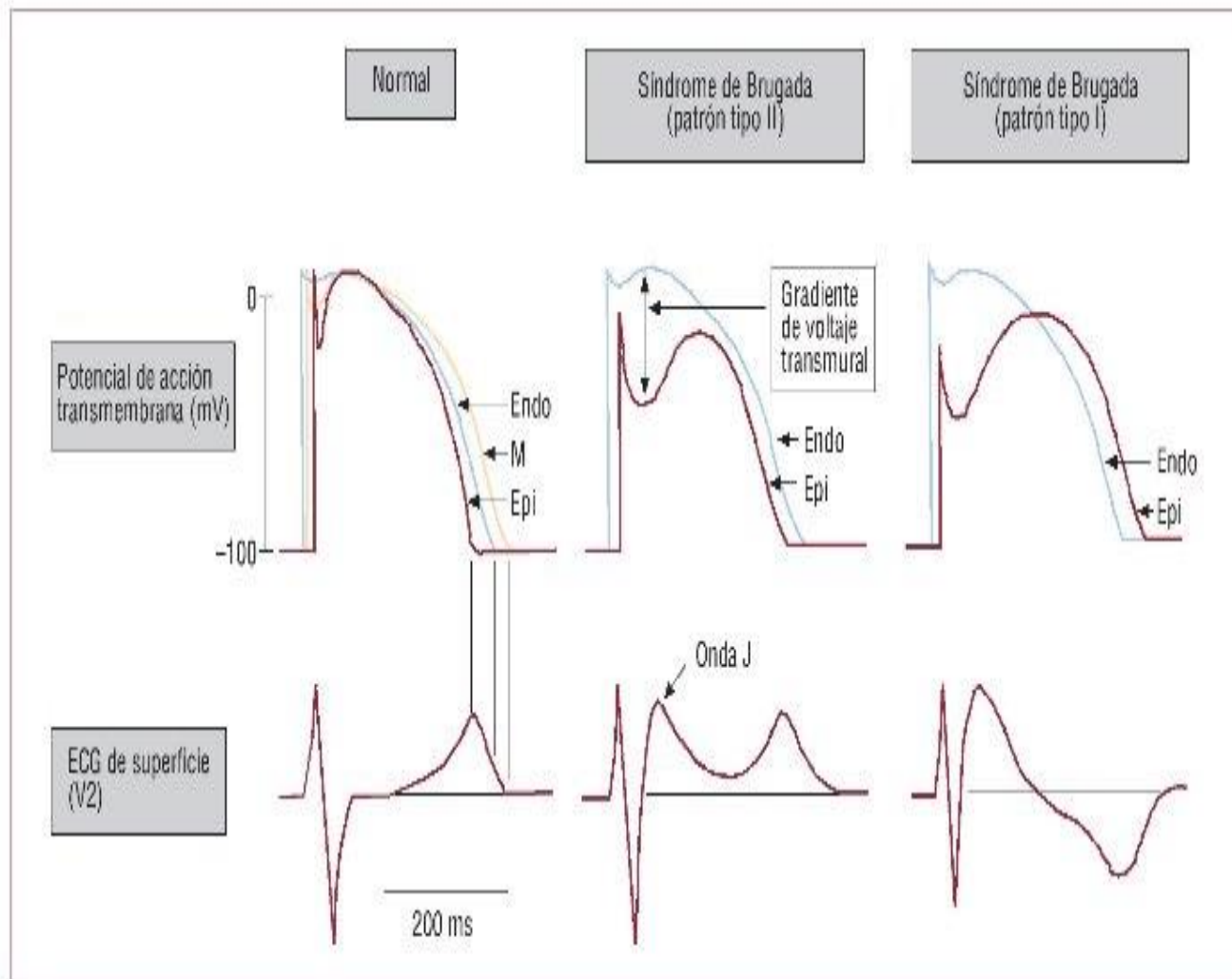


1 mV

Slow conduction



Repolarization abnormality



Development abnormality

Diagnostico diferencial

TABLA 1. Condiciones que pueden cursar con ECG similar al del síndrome de Brugada

Diagnóstico diferencial

¿Predisposición genética?

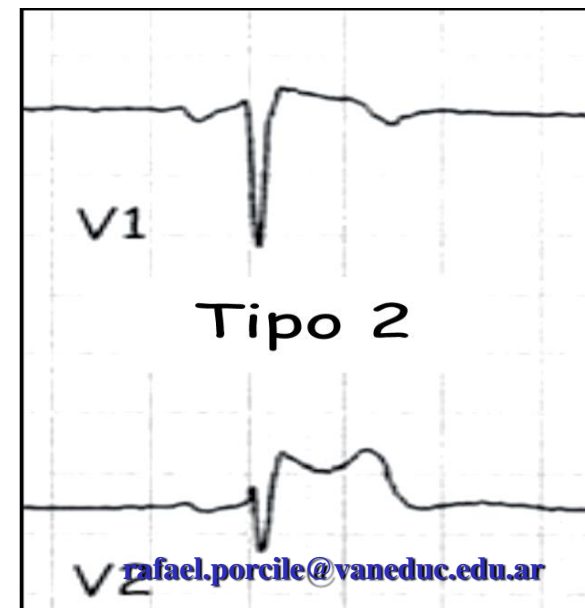
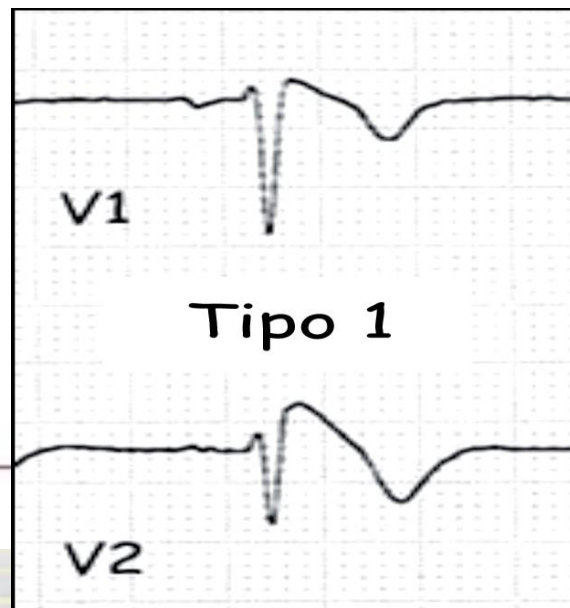
Bloqueo de rama derecha atípico
 Infarto agudo de miocardio, especialmente de ventrículo derecho (VD)
 Pericarditis/miopericarditis aguda, derrame pericárdico
 Tromboembolia pulmonar
 Aneurisma disecante de aorta

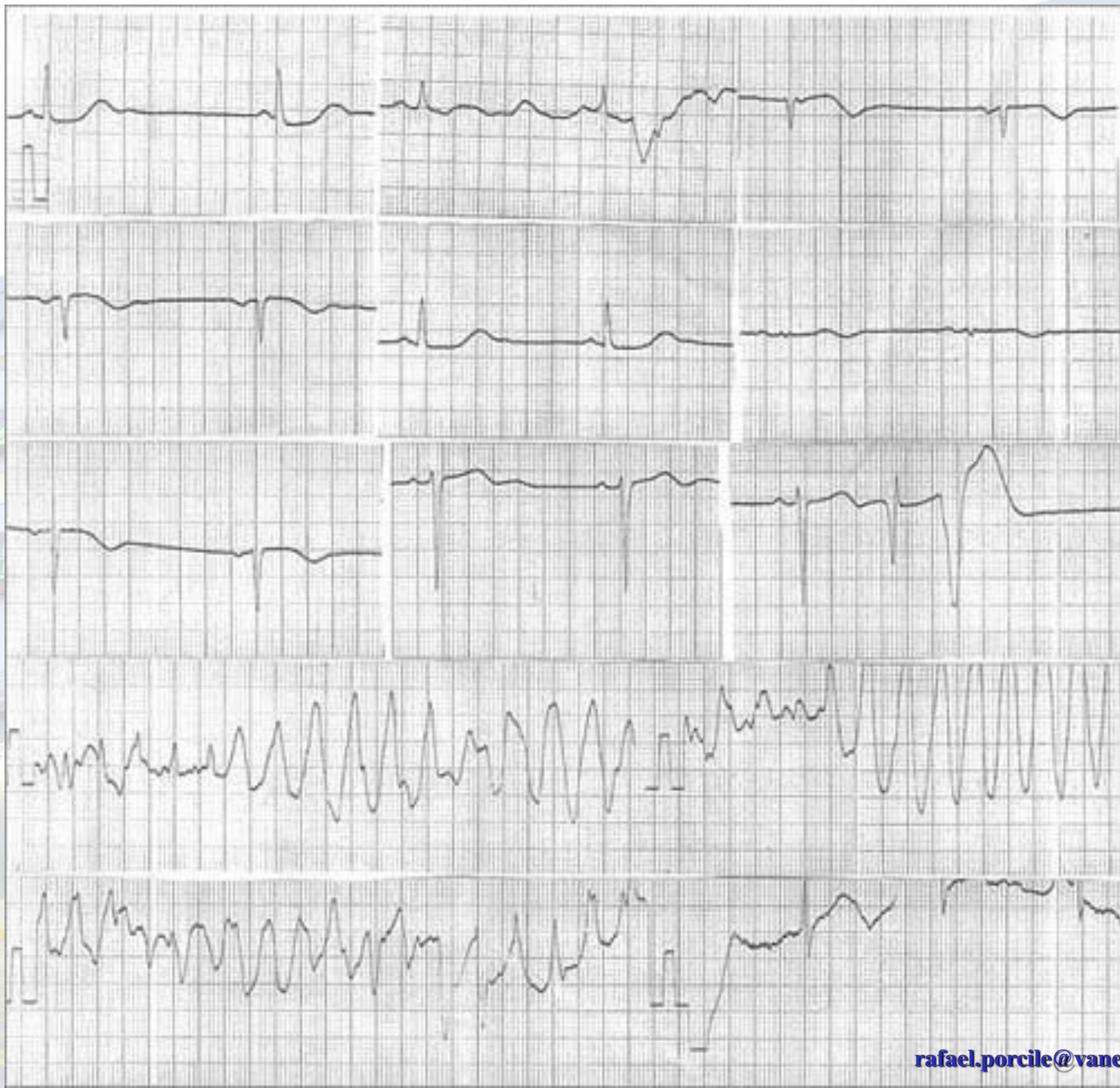
Hiperpotasemia
 Hipercalcemia
 Intoxicación por cocaína, alcohol
 Tratamiento con:
 I. Fármacos antiarrítmicos: bloqueadores del canal de Na (clase IC, clase IA), bloqueadores del calcio, bloqueadores beta
 II. Fármacos antianginosos: bloqueadores del calcio, nitratos
 III. Fármacos psicotrópicos: Antidepresivos tricíclicos/tetracíclicos, fenotiacinas, inhibidores selectivos de la recaptación de serotonina, litio

Trastornos de los sistemas nerviosos central y autonómico
 Distrofia muscular de Duchenne

Ataxia de Friedreich
 Hipertrofia ventricular izquierda
 Displasia arritmogénica de VD
 Compresión mecánica del tracto de salida de VD
 Tumor mediastínico
Pectus excavatum
 Tras cardioversión eléctrica
 Repolarización precoz, especialmente en atletas
 Hipotermia

Reproducido con autorización de Benito et al².





17-42% de ellos presentan síncope o MS como consecuencia de una arritmia ventricular en algún momento de su vida. Esta cifra probablemente sobrestima la incidencia real de eventos, dado que no se diagnostica a una gran parte de los pacientes asintomáticos.



Risk Factors of Brugada Syndrome

Risk factors for Brugada syndrome include:

Being male: Adult men are diagnosed more frequently than women.

Race: Brugada Syndrome occurs more frequently in Asians than in any other races.

Fever: Having a fever does not bring on Brugada Syndrome itself, but it can increase the risk of fainting or other complications of Brugada Syndrome.



PATRON ECG BRUGADA

- MUERTE CARDIACA SUBITA REANIMADA
- SINCOPE
- FAMILIARES CON CUADRO SINCOPALES O MSC
- RAZA SUDESTE ASIATICO

SI

DUDA

NO

D.A.I

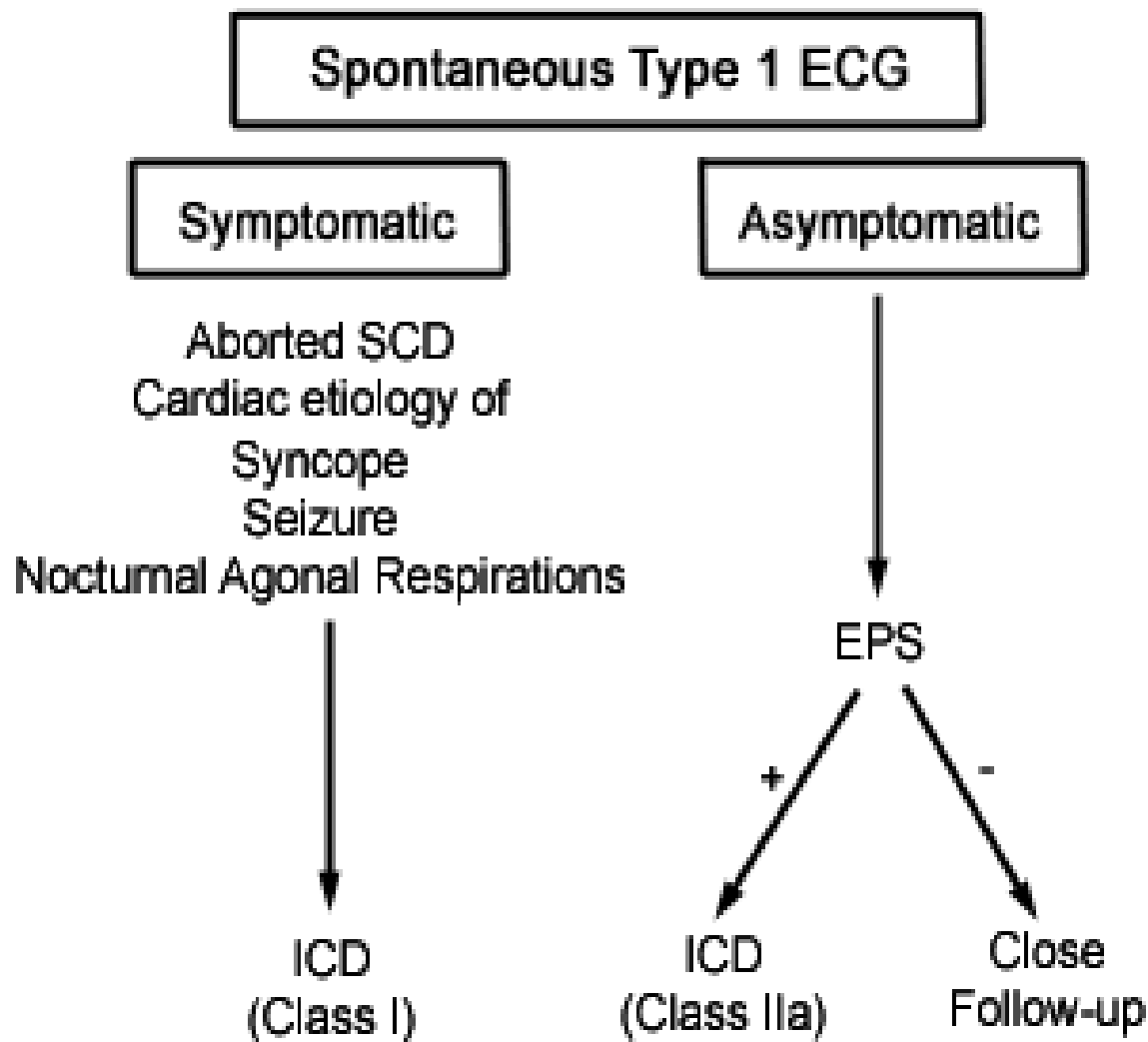
+

- ELECTROFISIOLOGICO
- TEST FARMACOLOGICO
- ESTUDIO FAMILIAR

-

SEGUIMIENTO CLÍNICO

Indications for ICD Implantation in Brugada Syndrome



Bloqueantes de canales de Sodio utilizados para desenmascarar electrocardiograma de síndrome de Brugada¹⁰

Compuesto	Dosis	Vía
Ajmalina	1 mg/kg en 5 min	Intravenosa
Flecainida	2 mg/kg en 10 min	Intravenosa
	400 mg	Oral
Procainamida	10 mg/kg en 10 min	Intravenosa
Pilsicainida	1 mg/kg en 10 min	Intravenosa

Tratamiento farmacológico en síndrome de Brugada

Fármacos que inhiben la corriente Ito o incrementan las corrientes de Na⁺ y Ca⁺²

El isoproterenol (que incrementa la corriente I_{CaL}) ha probado ser útil para el tratamiento de las tormentas eléctricas

La quinidina, un antiarrítmico clase IA que posee efecto bloqueante de las corrientes Ito e I_{Kr} ha

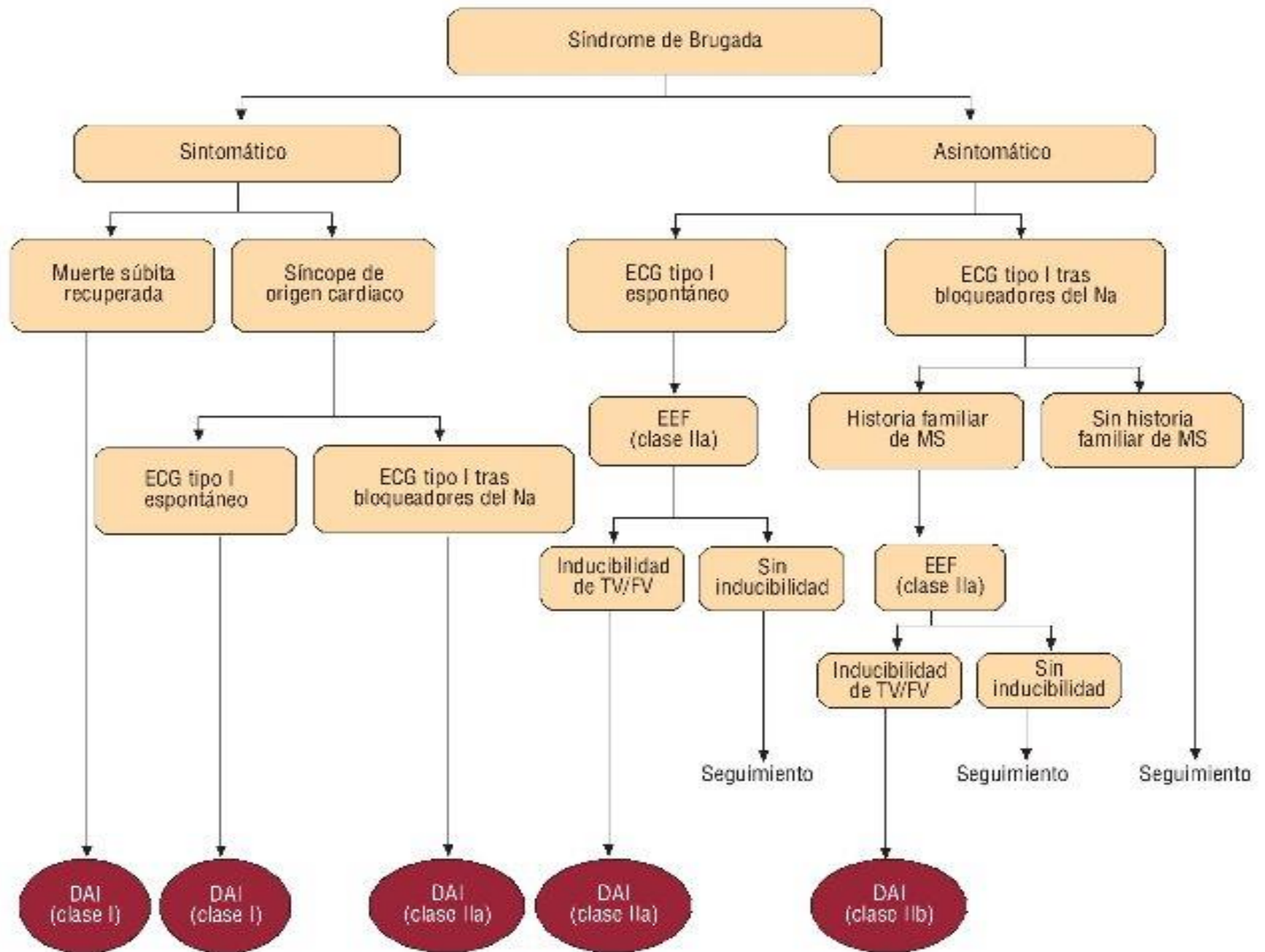
La disopiramida ha demostrado también su utilidad en caso de tormenta eléctrica en algunos pacientes reportes.



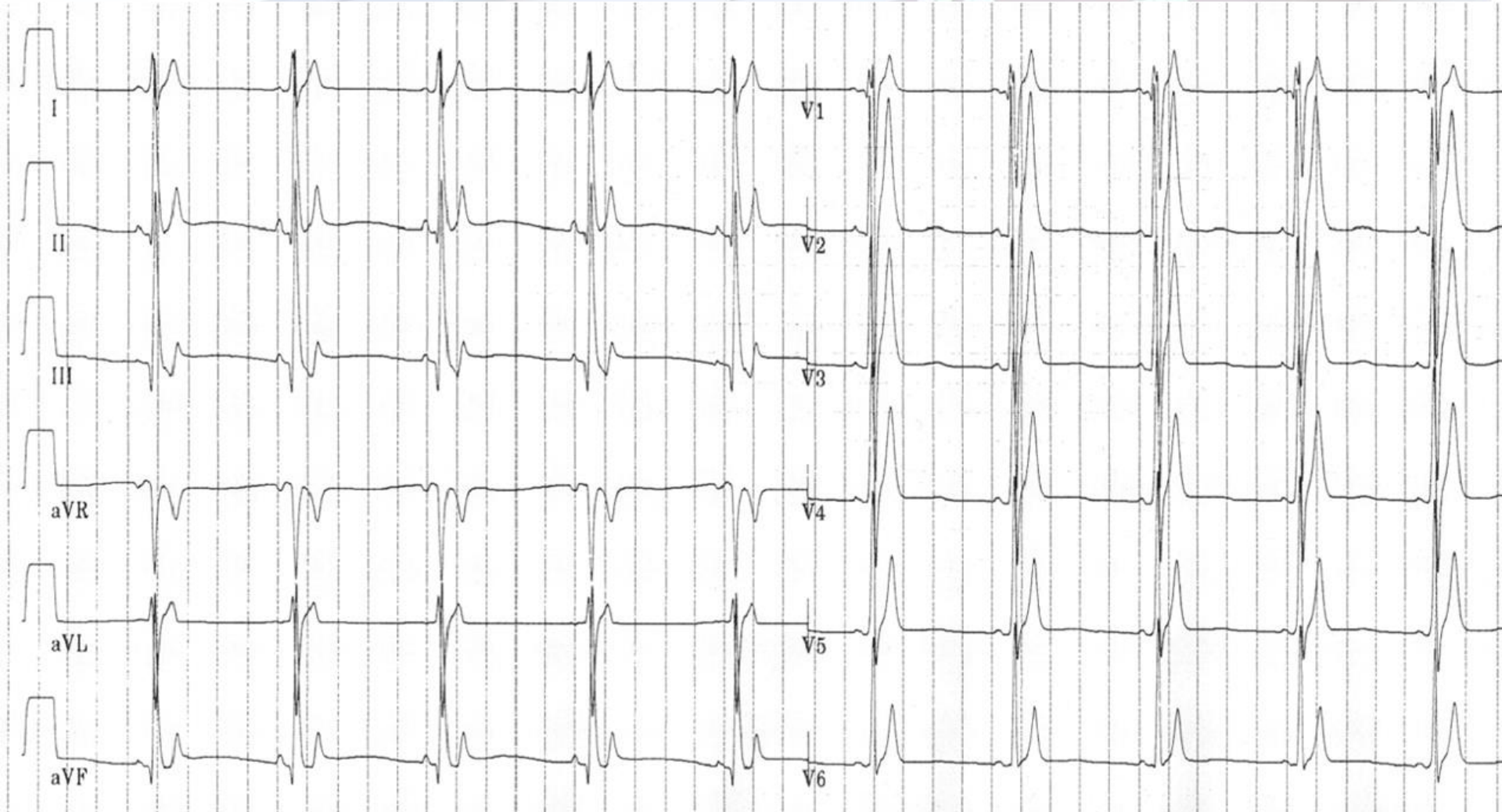
Las estrategias apuntan a la
prevención primaria o
secundaria

Para ello los recursos
farmacológicos son escasos

El DAI debe ser
considerado

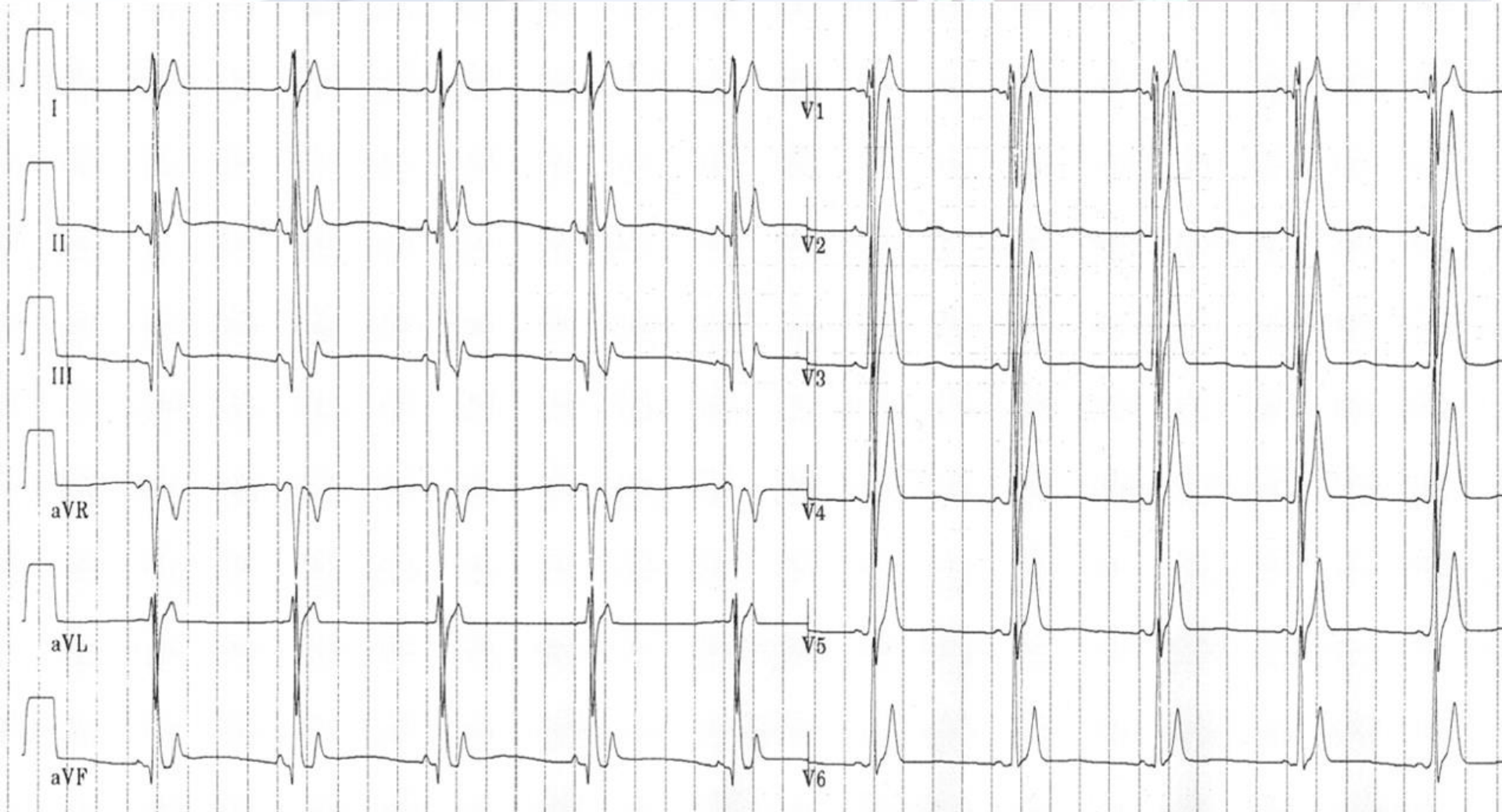






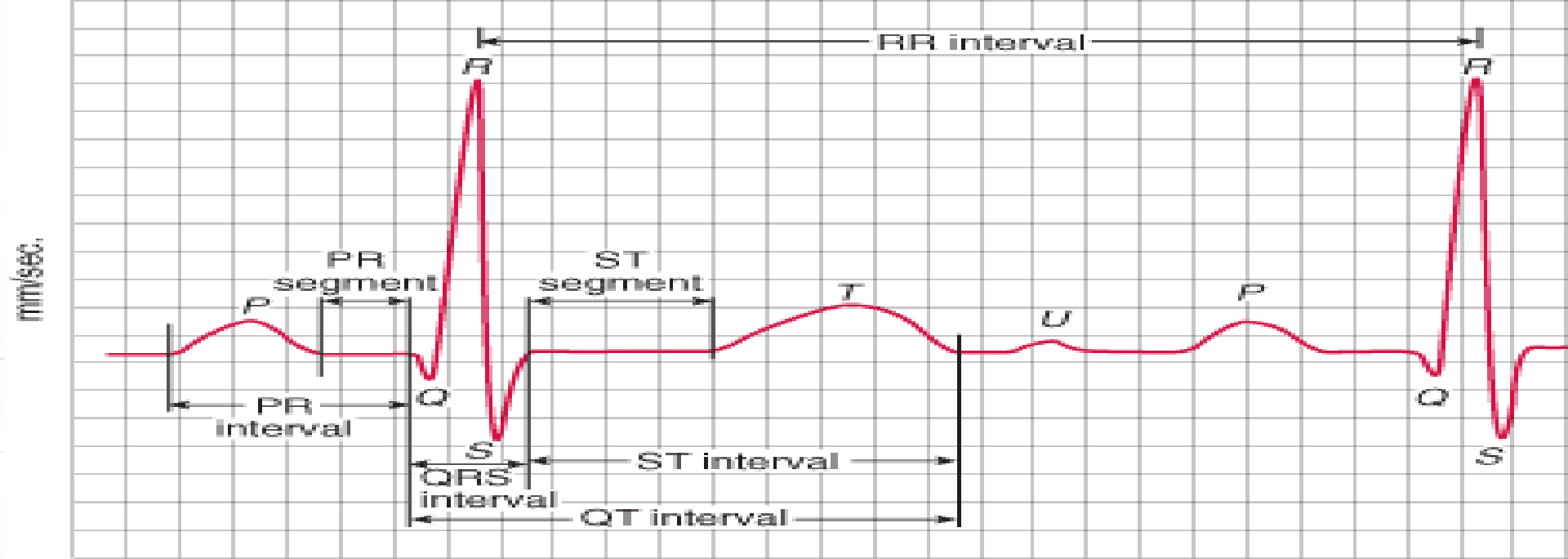
¿Que es esto?





Síndrome de QT largo





mm/mV 1 square = 0.04 sec/0.1mV

- **Bazett's formula:** $QT_C = QT / \sqrt{RR}$
- **Fredericia's formula:** $QT_C = QT / RR^{1/3}$
- **Framingham formula:** $QT_C = QT + 0.154 (1 - RR)$
- **Hodges formula:** $QT_C = QT + 1.75 (\text{heart rate} - 60)$

The Primary Electrical Disease Syndromes

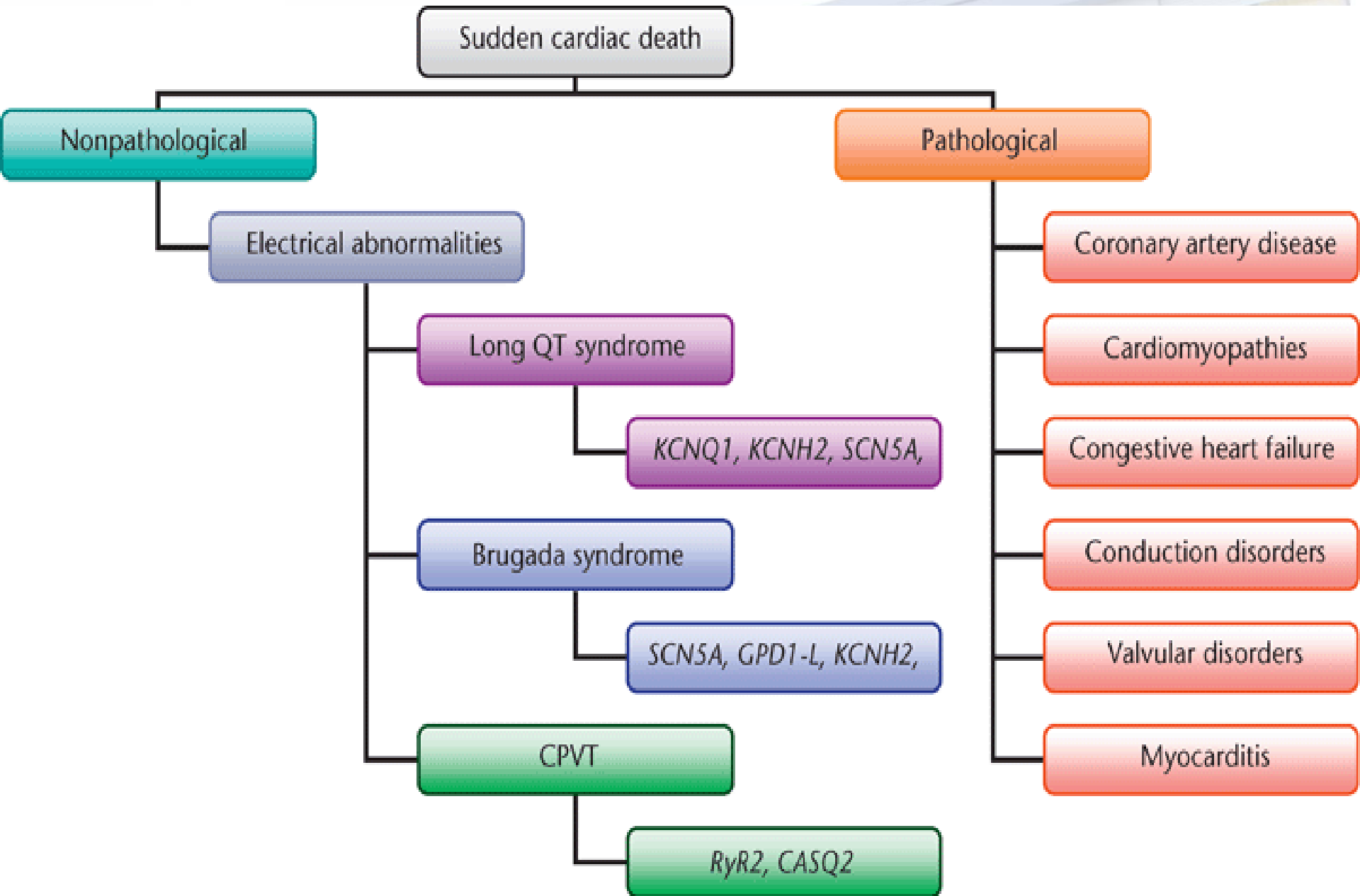
1. Congenital Long QT-syndrome, LQTS
2. Short QT syndrome, SQT
3. Brugada syndrome
4. Catecholaminergic polymorphic ventricular tachycardia, CPVT

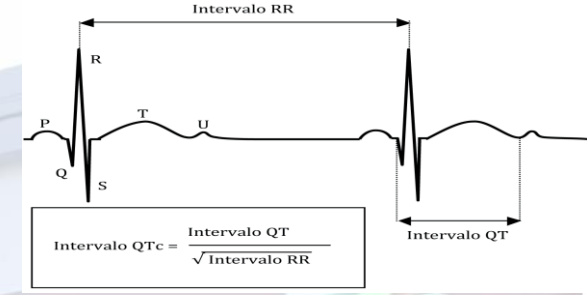
What do they share in common?

1. They cause polymorphic VT, syncope and sudden death
2. The ECG is the primary diagnostic tool.
3. They result from mutations in ion channels or their adaptor proteins

GENETIC BASIS OF LONG QT SYNDROME

DESIGNATION	GENE	GENE PRODUCT	ION CHANNEL	CHROMOSOME LOCUS
LQT1	KvLQT1	I_{ks} α -subunit	I_{ks}	11p15.5
LQT2	HERG	I_{kr} α -subunit	I_{kr}	7q35-36
LQT3	SCN5A	Na ⁺ channel unit	I_{Na}	3q21-24
LQT4	ANKB	Ankyrin-B	-	4q25-27
LQT5	Mink	I_{ks} β -subunit	I_{ks}	21q22.1-2
LQT6	MiRP1	I_{kr} β -subunit	I_{kr}	21q22.1
LQT7	KCNJ2	I_{KI}	I_{KI}	17q23





QT Largo

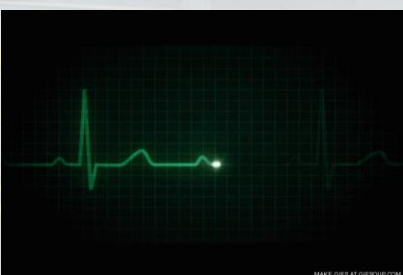
Estas mutaciones causan un aumento en la duración de la repolarización del potencial de acción cardíaco que se manifiesta con un aumento de la duración del intervalo QT y predisposición a arritmias ventriculares malignas (Torsión de Puntas) y muerte súbita.

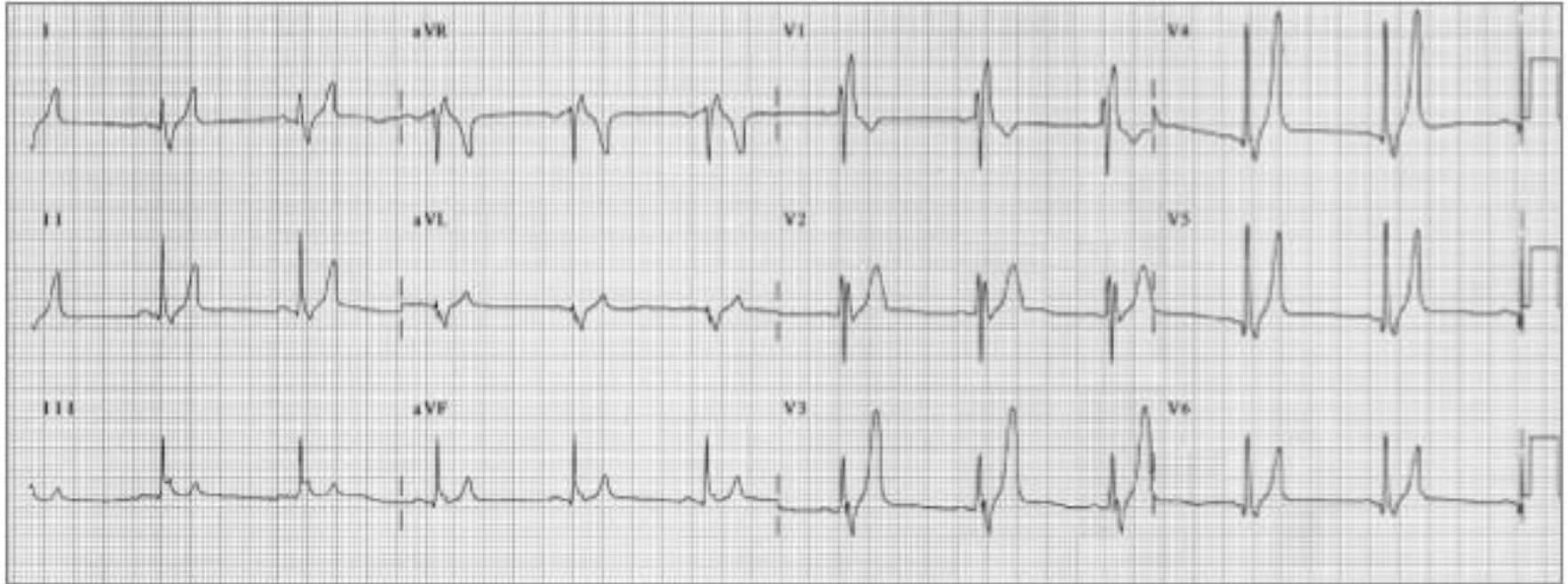
TABLA 1
PUNTUACIÓN DE SCHWARTZ
PARA EL DIAGNOSTICO DE
SQTL

a- QTc calculado según fórmula de Bazett.
b- FC en reposo por debajo del segundo percentil para la edad.
c- El mismo familiar no debe considerarse en ambos.

ELECTROCARDIOGRAMA	
QTc ms (a) ≥ 480	3
QTc ms 460 - 470	2
QTc ms 450 (varones)	1
Torsion de puntas	2
Alternancia onda T	1
Muecas onda T en 3 derivaciones	1
Bradycardia (b)	0,5
HISTORIA CLINICA	
Sincope con Stress	2
Sincope sin stress	1
Sordera congénita	0,5
HISTORIA FAMILIAR (c)	
Familiares con SQTL confirmado	1
MS inexplicada en familiares de primera linea menores a 30 años	0,5

Schwartz P et al. Circulation 1993; 88 (2): 782-4



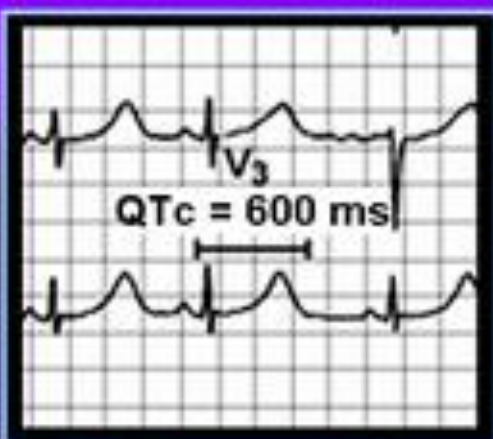


Pérez Riera y cols., publican el primer caso en América Latina de Síndrome de QT Corto Congénito

1. Pérez Riera AR, Ferreira C, Dubner SJ, Schapachnik E, Soares JD, Francis J. Brief review of the recently described short QT syndrome and other cardiac channelopathies. *Ann Noninvasive Electrocardiol.* 2005 Jul;10:371-377.

Long QT Syndrome

Clinical



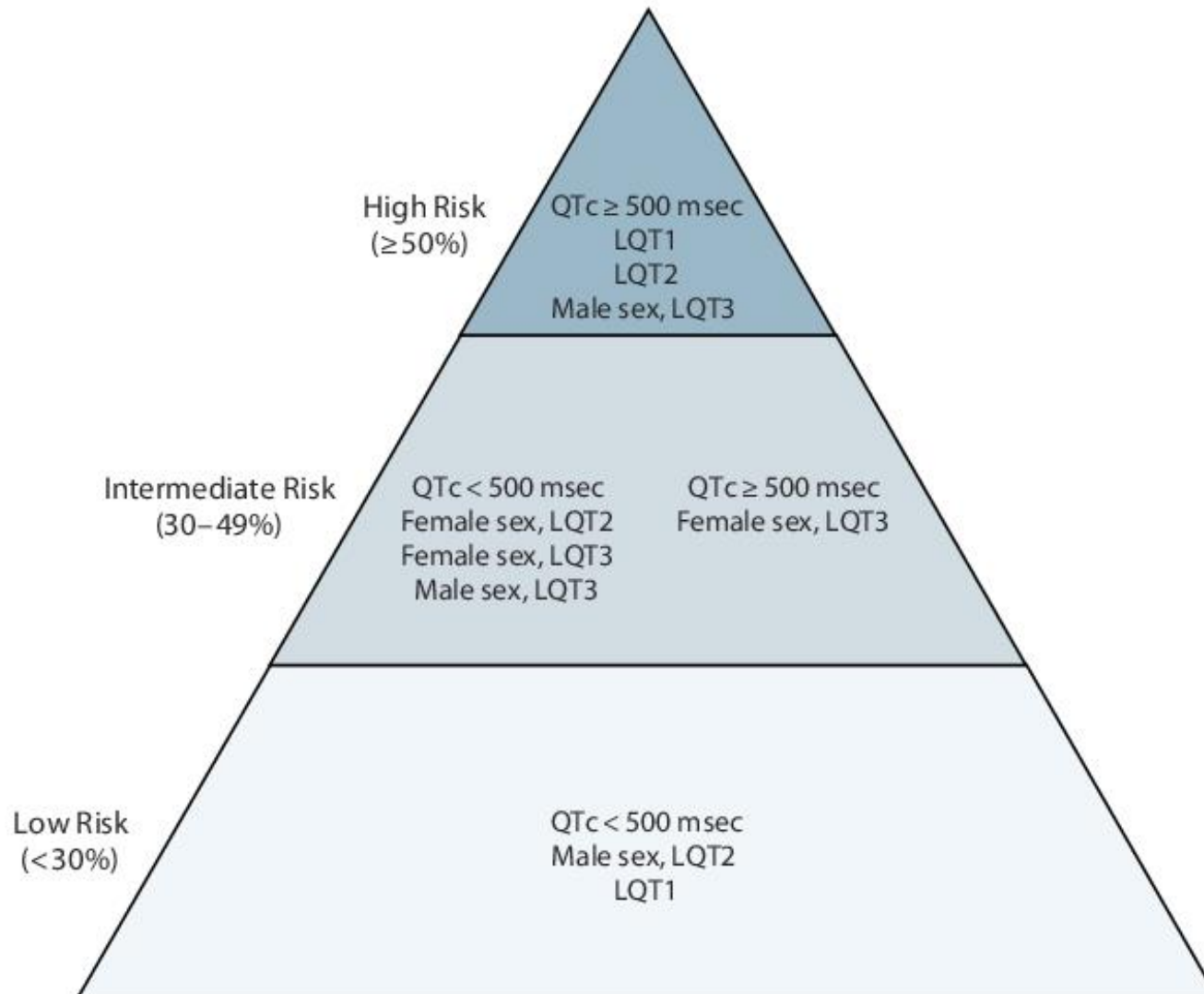
1. Syncope
2. Seizures
3. Sudden death



Torsade de pointes



Proposed Scheme for Risk Stratification Among Patients With LQTS According to Genotype and Gender



**TABLA 1
PUNTUACIÓN DE SCHWARTZ
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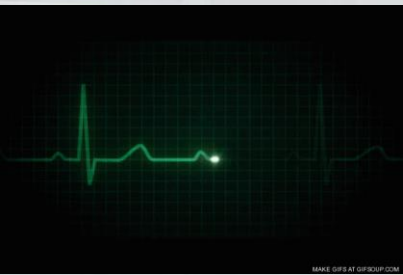


TRATAMIENTO DEL QT Largo

El tratamiento está orientado a evitar los gatillos, así como las drogas que prolonguen el intervalo QT.

Indicar betabloqueantes (indicación clase I) y deben titularse con prueba ergométrica (la FC máxima alcanzada debe ser menor al 85% de la FC máxima teórica).

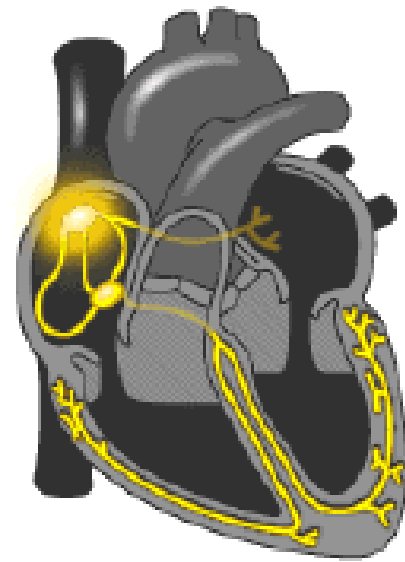
En pacientes que hayan presentado muerte súbita recuperada está indicado el implante de un **cardiodesfibrilador** automático, así como en pacientes que persistan con síncope pese al tratamiento con betabloqueantes. En estos pacientes también debería evaluarse la realización de una simpatectomía izquierda

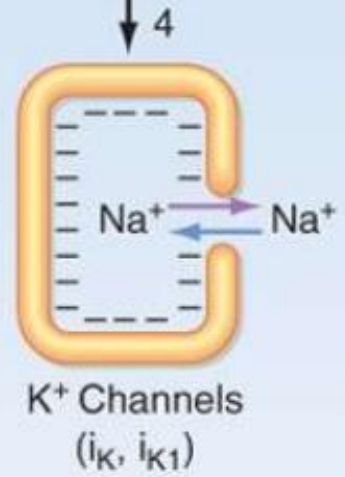
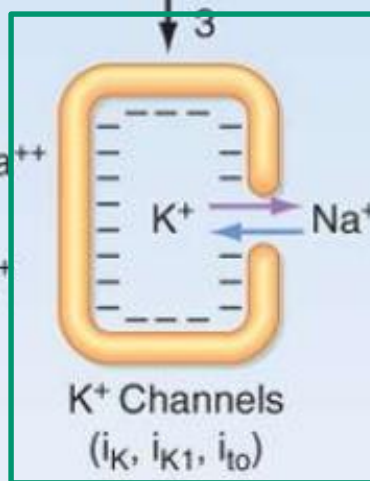
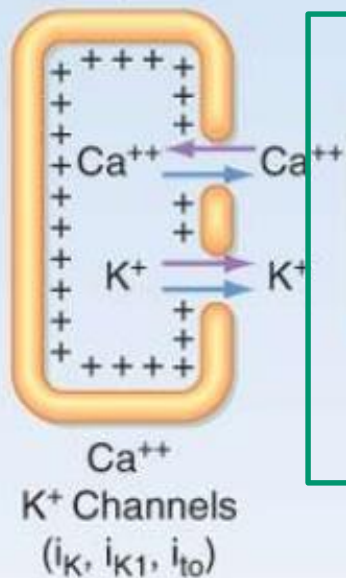
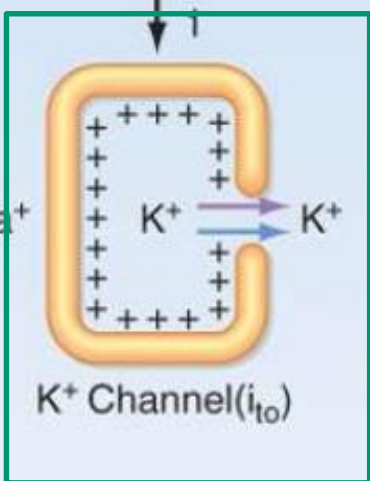
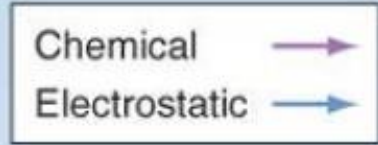
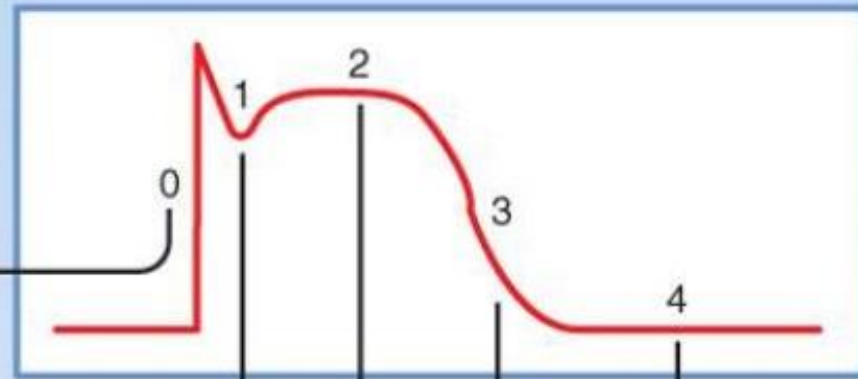


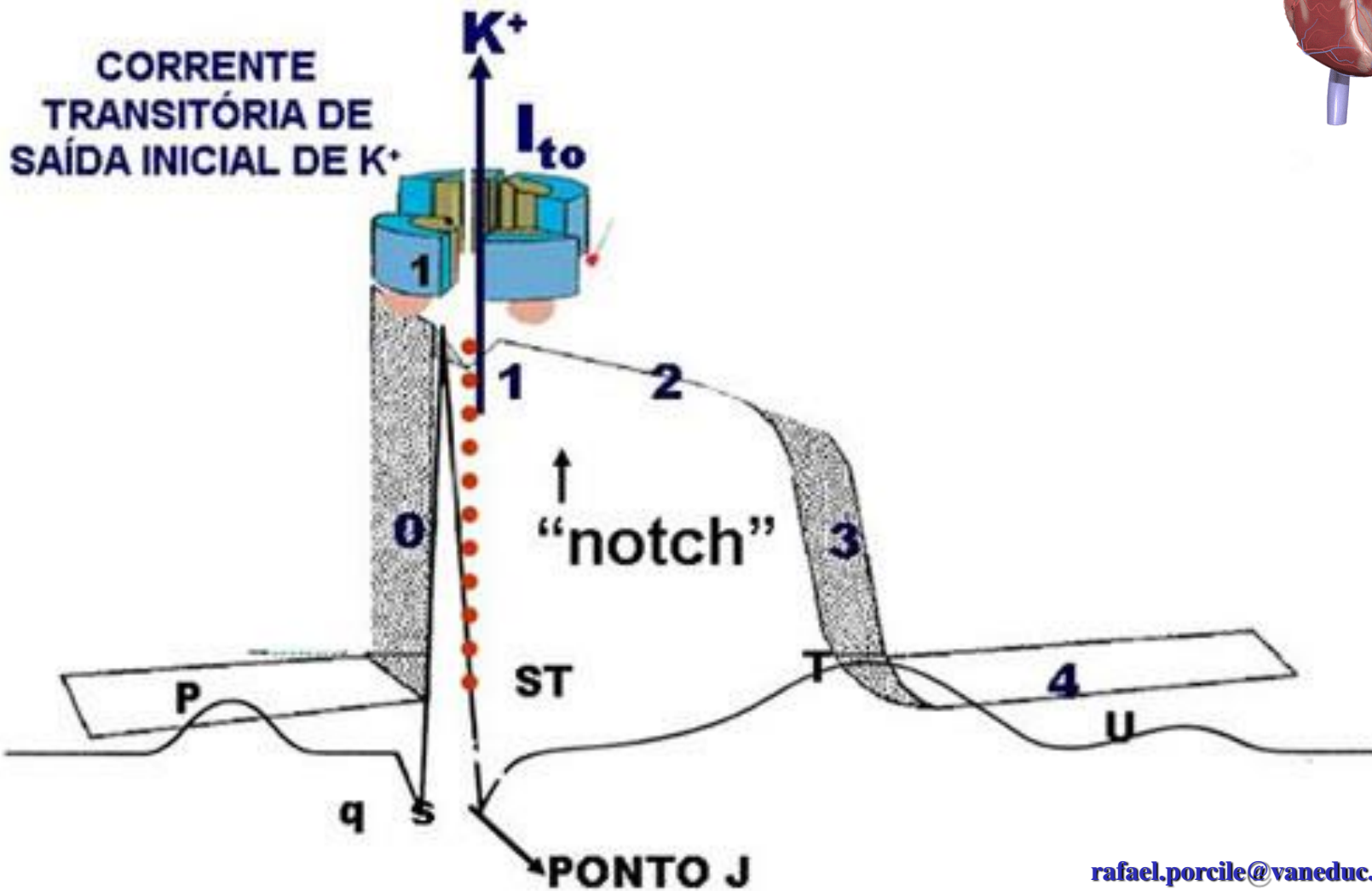
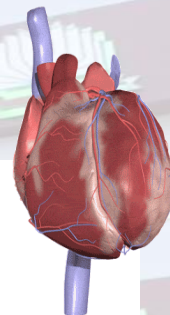
Los

canales

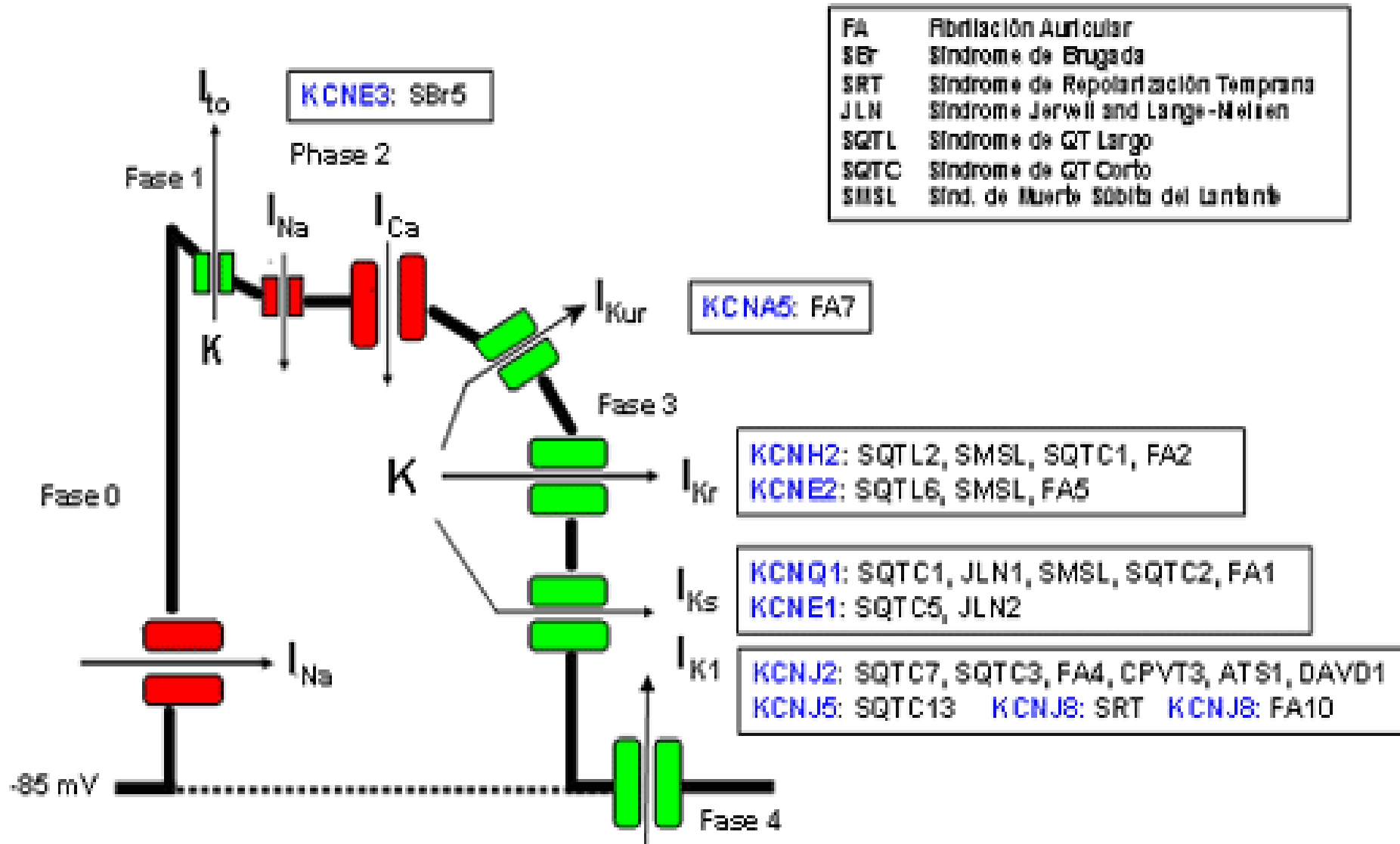
de potasio



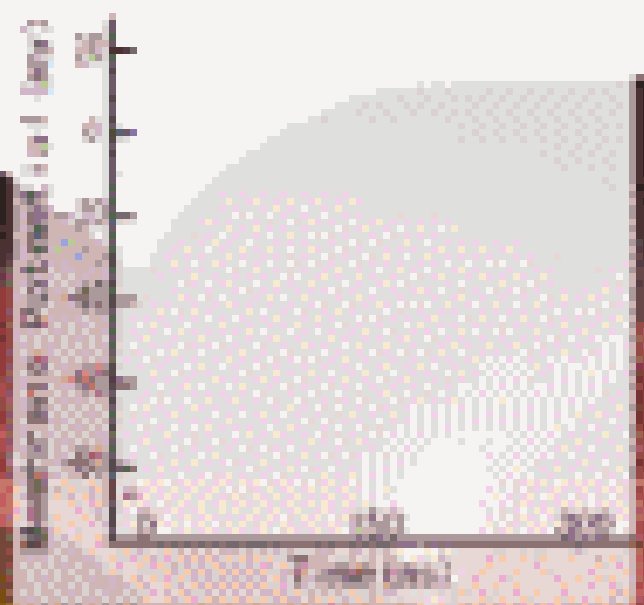
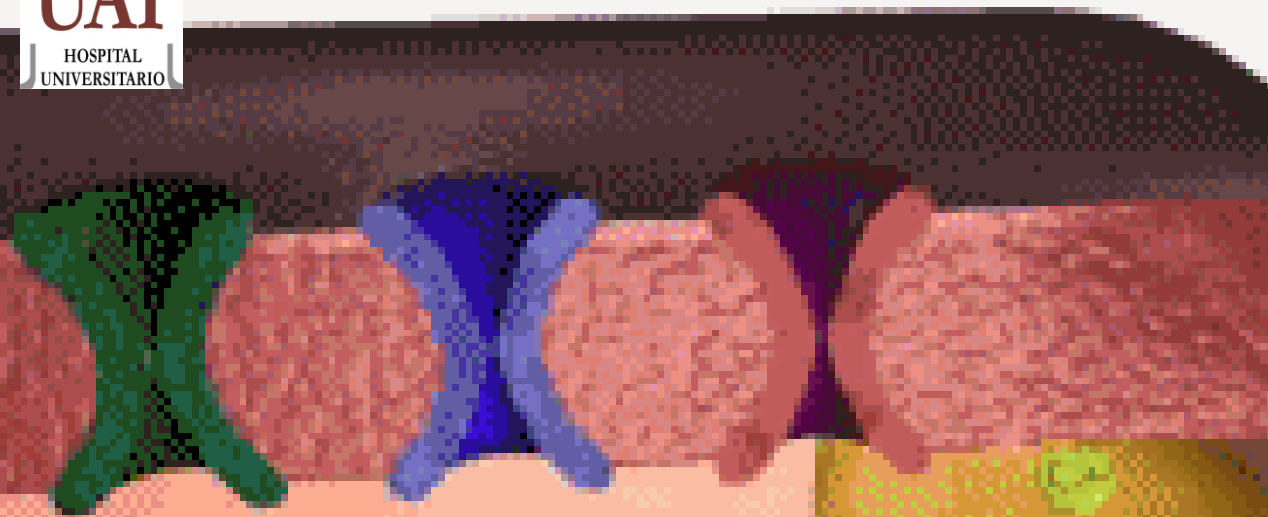




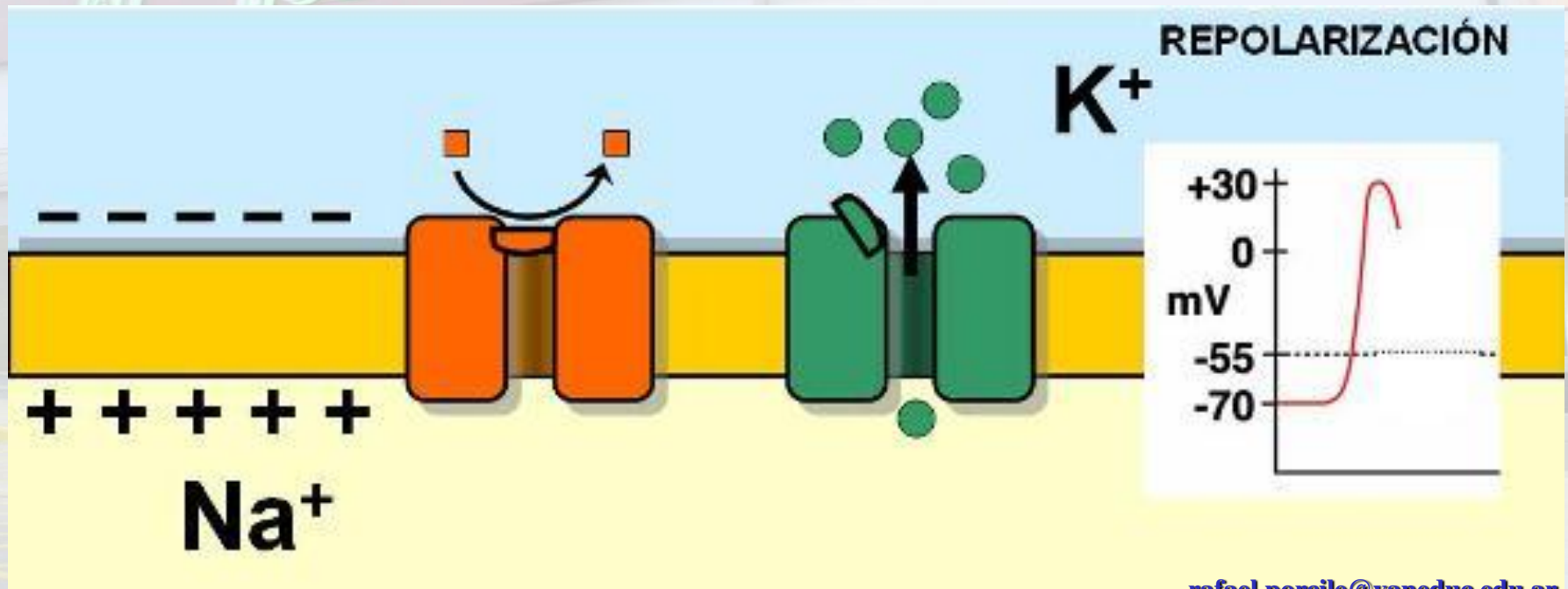
Canalopatías a asociadas a mutaciones en los canales de K⁺ cardiacos



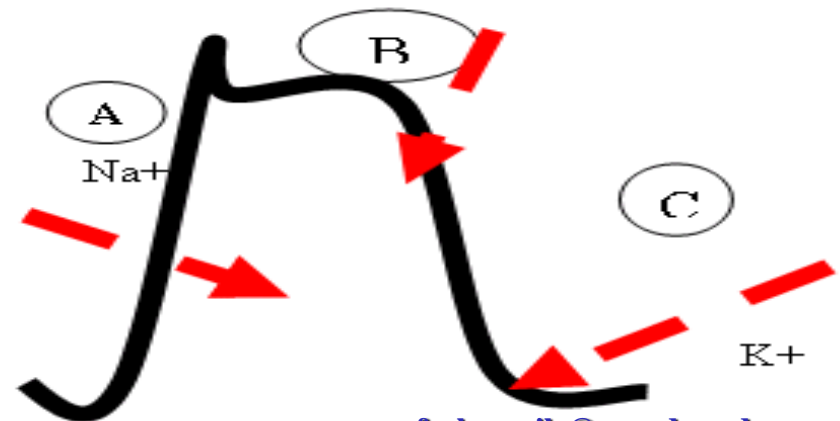
FA	Fibrilación Auricular
SBr	Síndrome de Brugada
SRT	Síndrome de Repolarización Temprana
JLN	Síndrome Jerwell and Lange-Nelken
SQTL	Síndrome de QT Largo
SQTC	Síndrome de QT Corto
SMSL	Sínd. de Muerte Súbita del Lantán



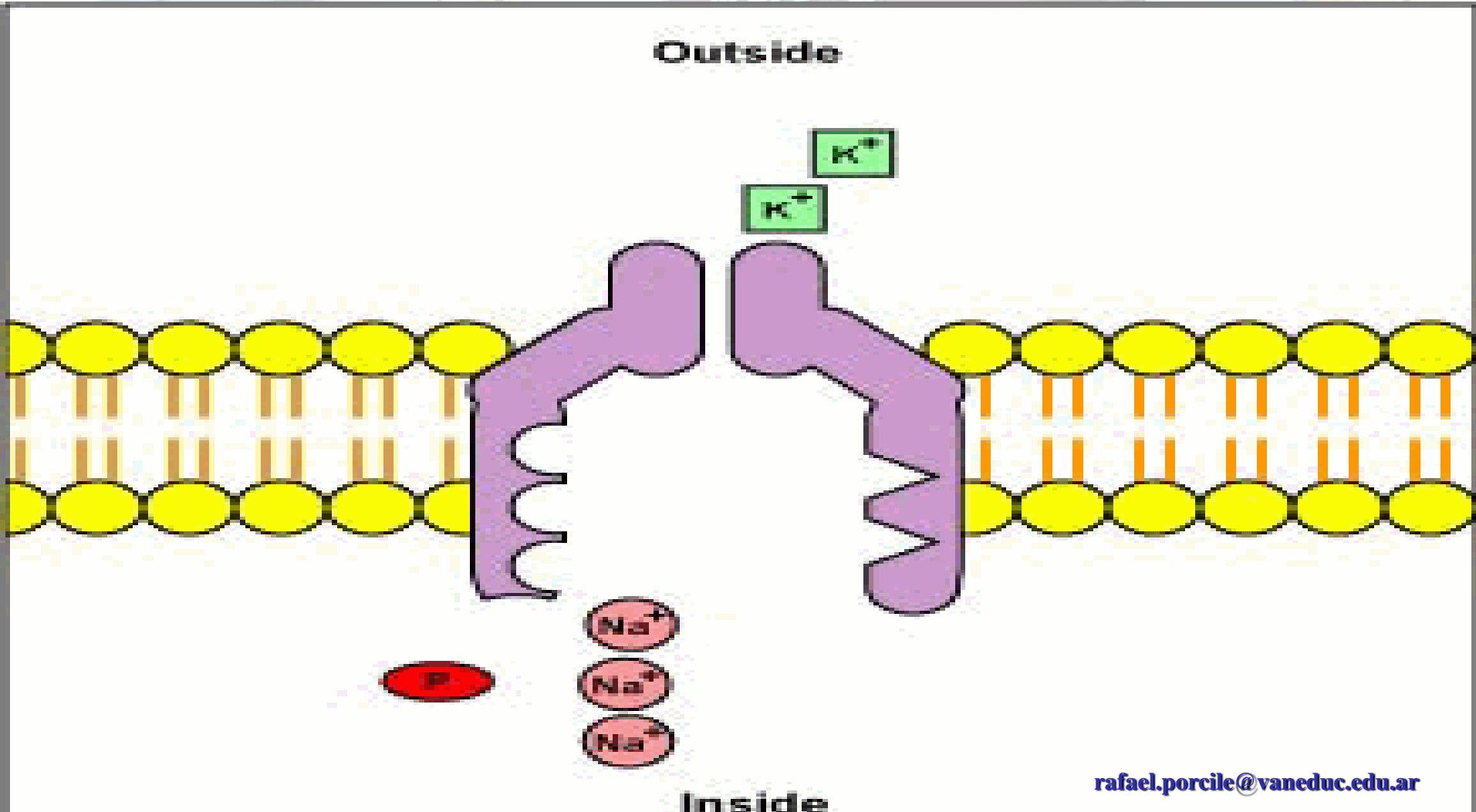
El K es el protagonista de la repolarización



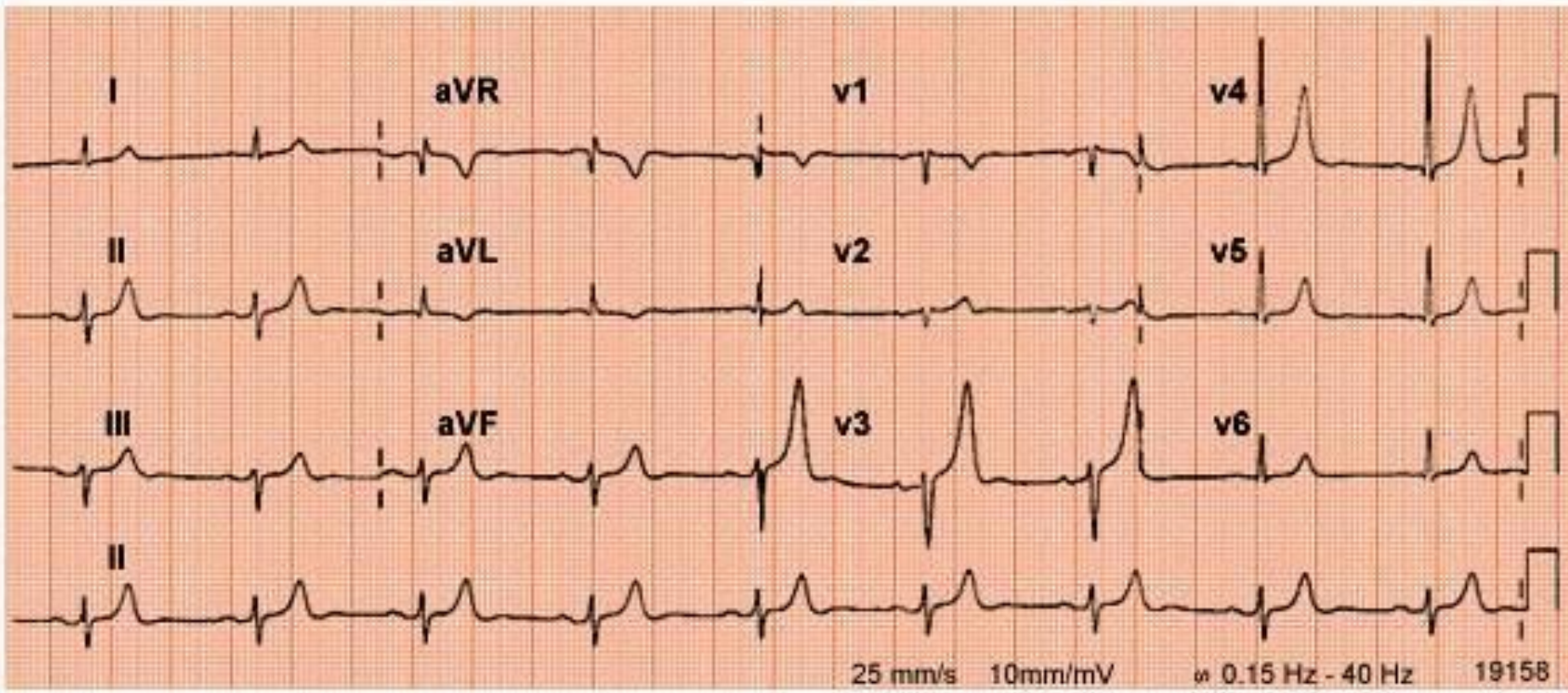
- Cuando se abre el canal de potasio el potencial de la membrana se hace más negativo (hiperpolarización).
- El potasio está más concentrado en el interior de la célula, por ese motivo cuando se abren canales de potasio este ion tiende a salir por gradiente de concentración. Esto extrae cargas eléctricas positivas del interior de la célula, y deja el potencial de ésta negativo (repolarización)



BOMBA SODIO POTASIO

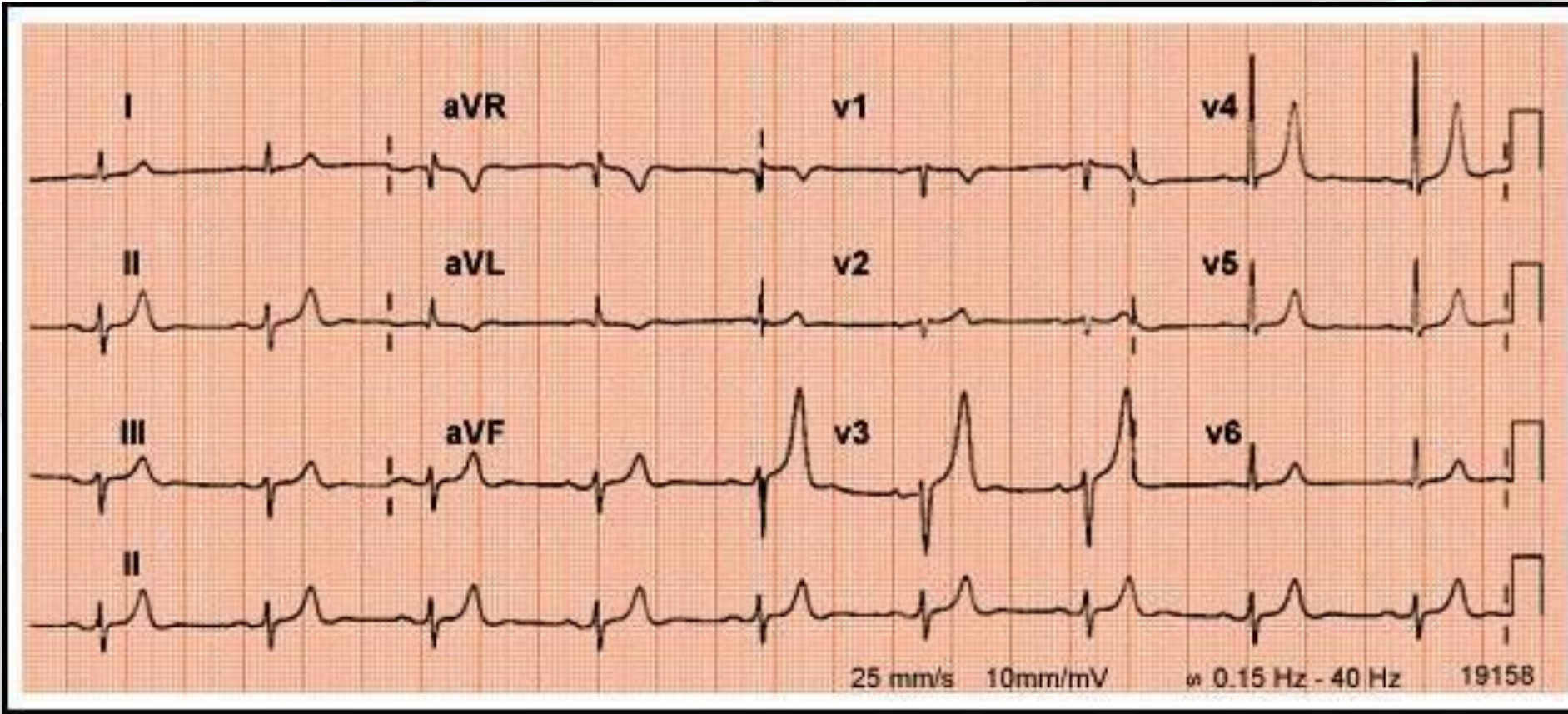




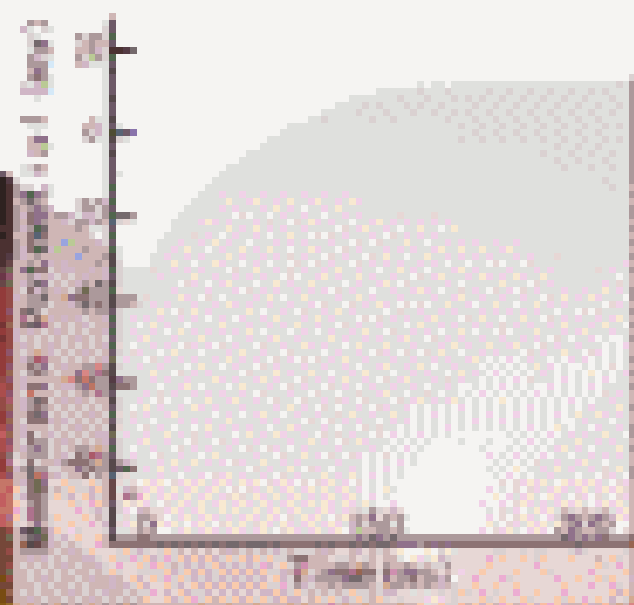


¿Que es esto?





QUE PASA EN LA HIPOPOTASEMIA

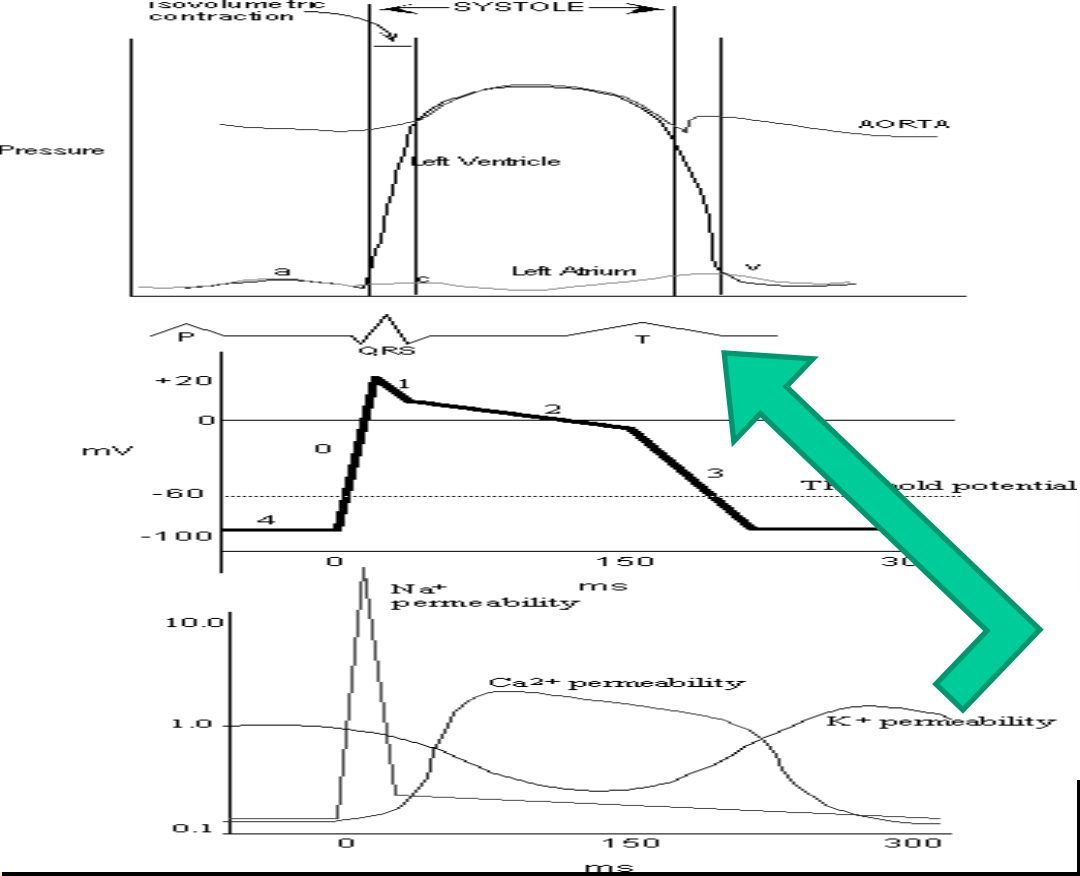


LOS CANALES **NO** ESTAN OBSTRUIDOS



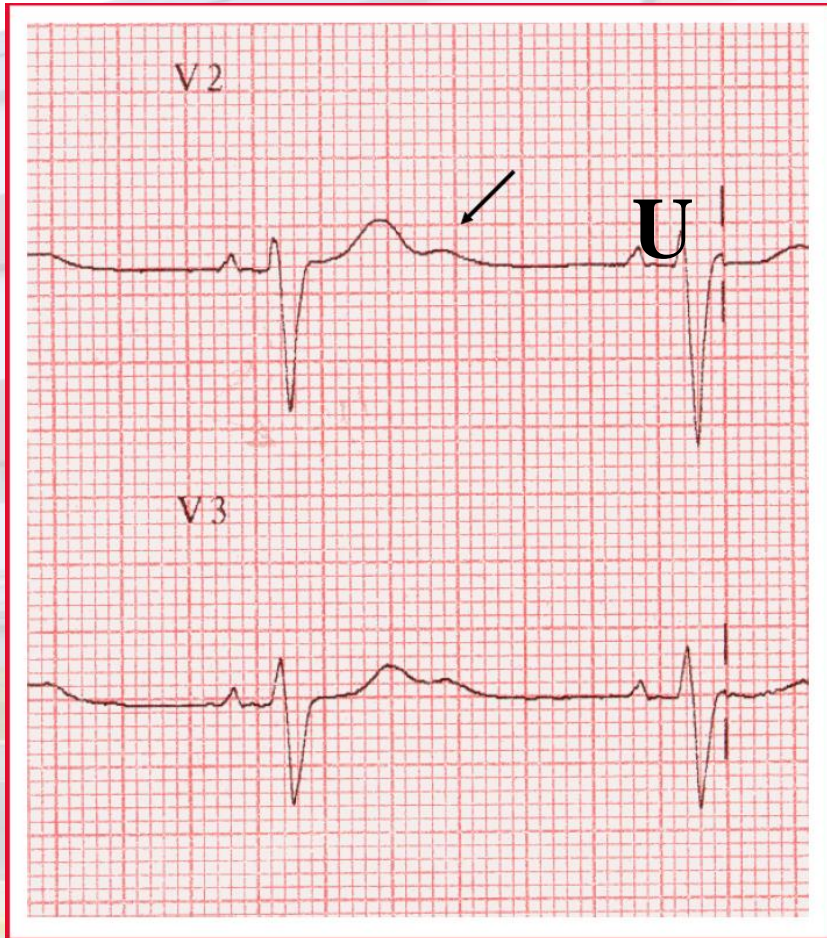
En la hipokalemia todo es lento hasta llegar al paro en diastole



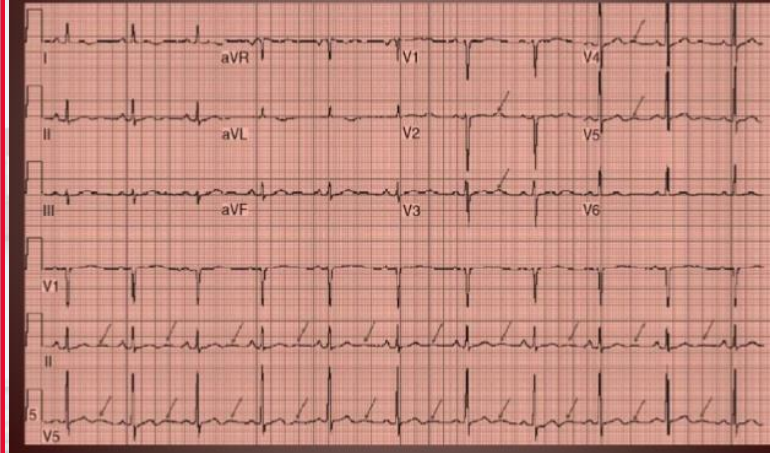


**Menos K extracelular AL
AUMENTAR EL GRADIENTE
DE K SE
Se libera y facilita SU SALIDA
T APLANADAS
CON ONDA U**

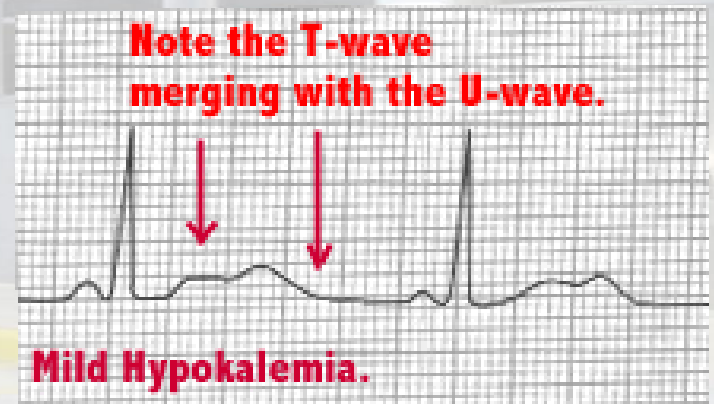
Hipopotasemia



HIPOKALEMIA

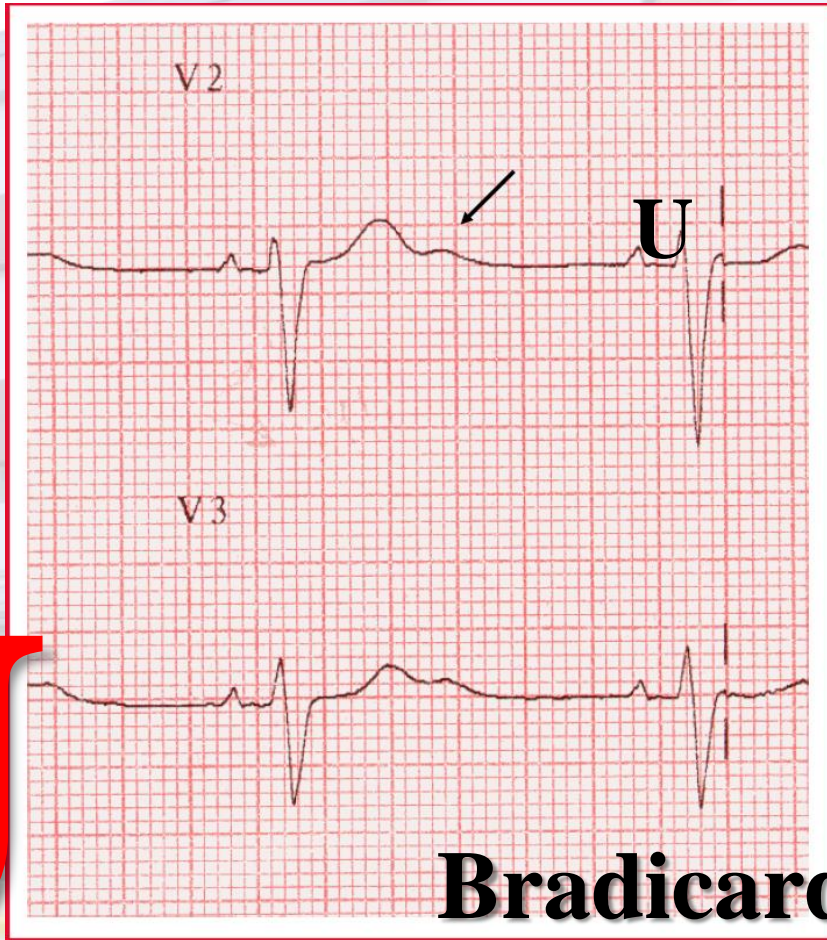
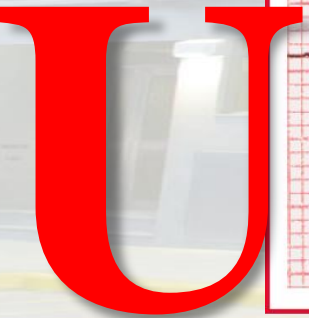
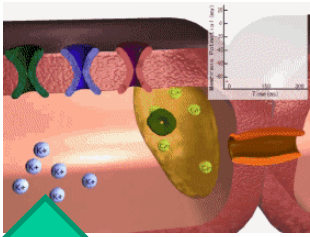


Note the T-wave merging with the U-wave.

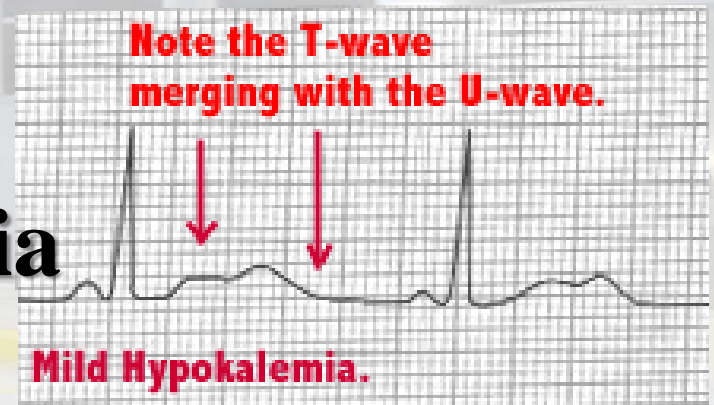
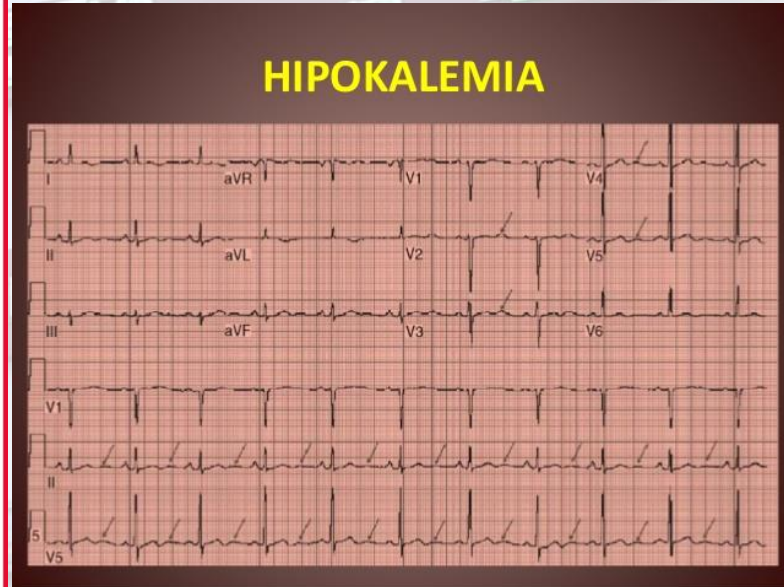


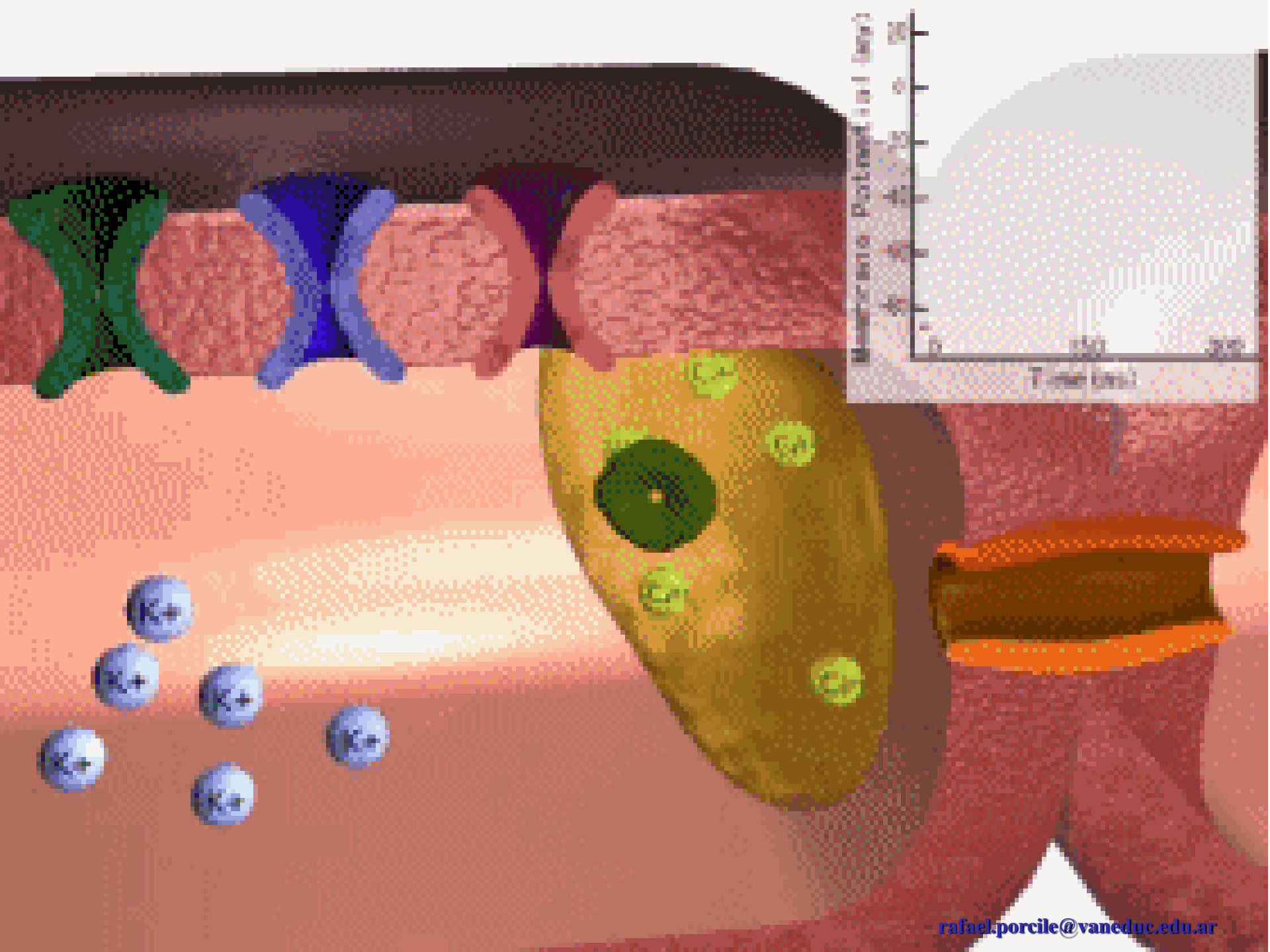
Mild Hypokalemia.

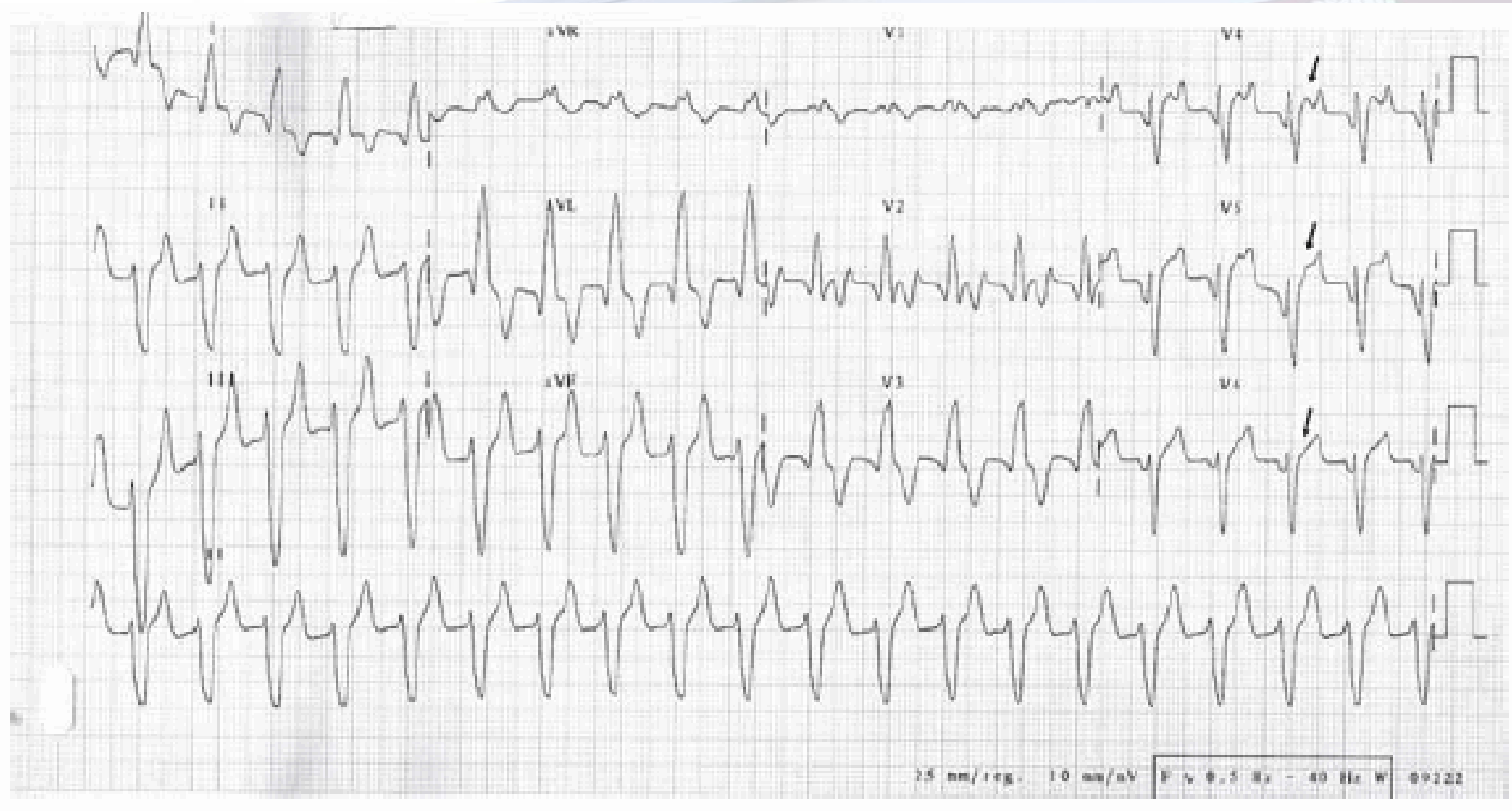
Hipopotasemia



Bradycardia

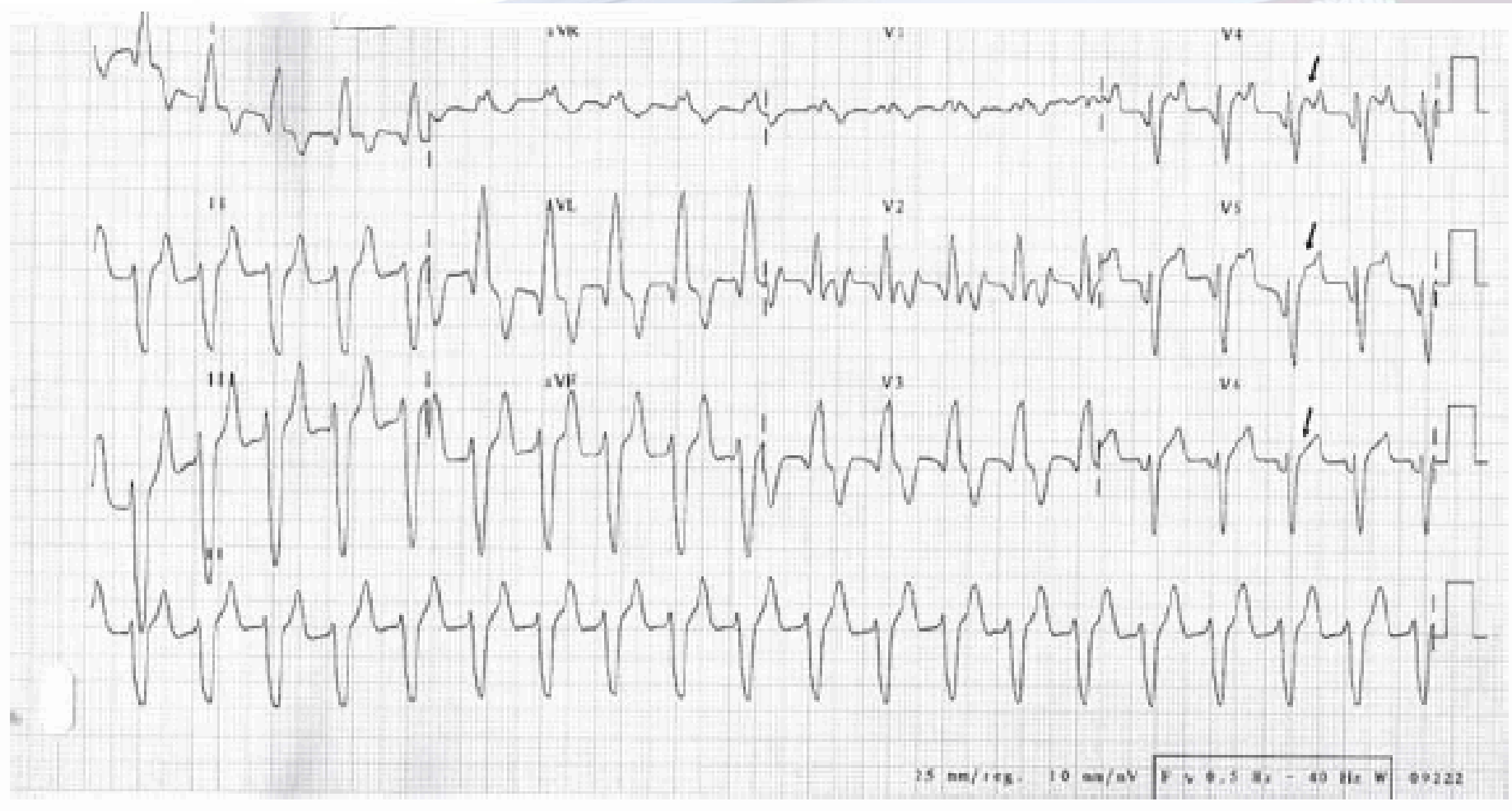




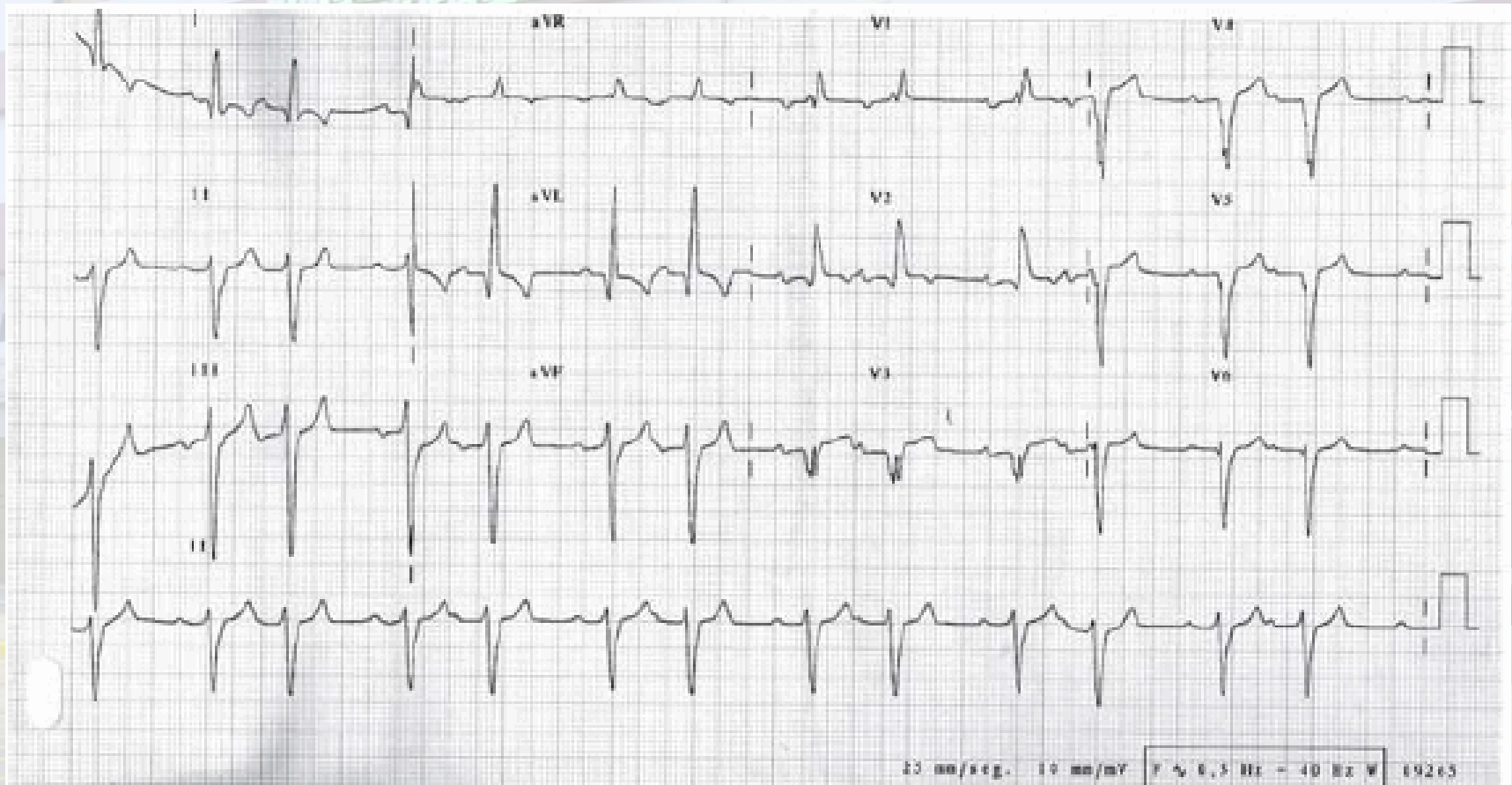


¿Que es esto?

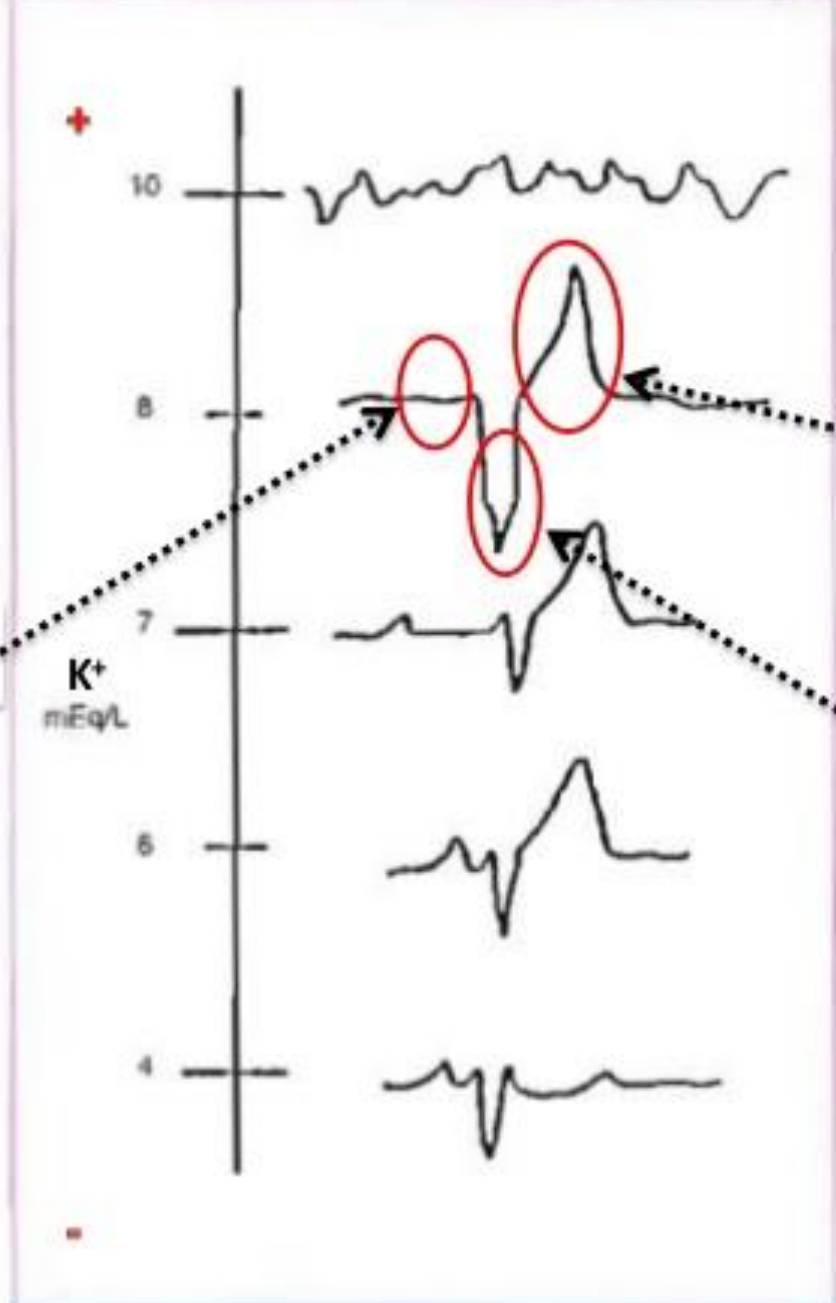




Corregida la Hiperkalemia



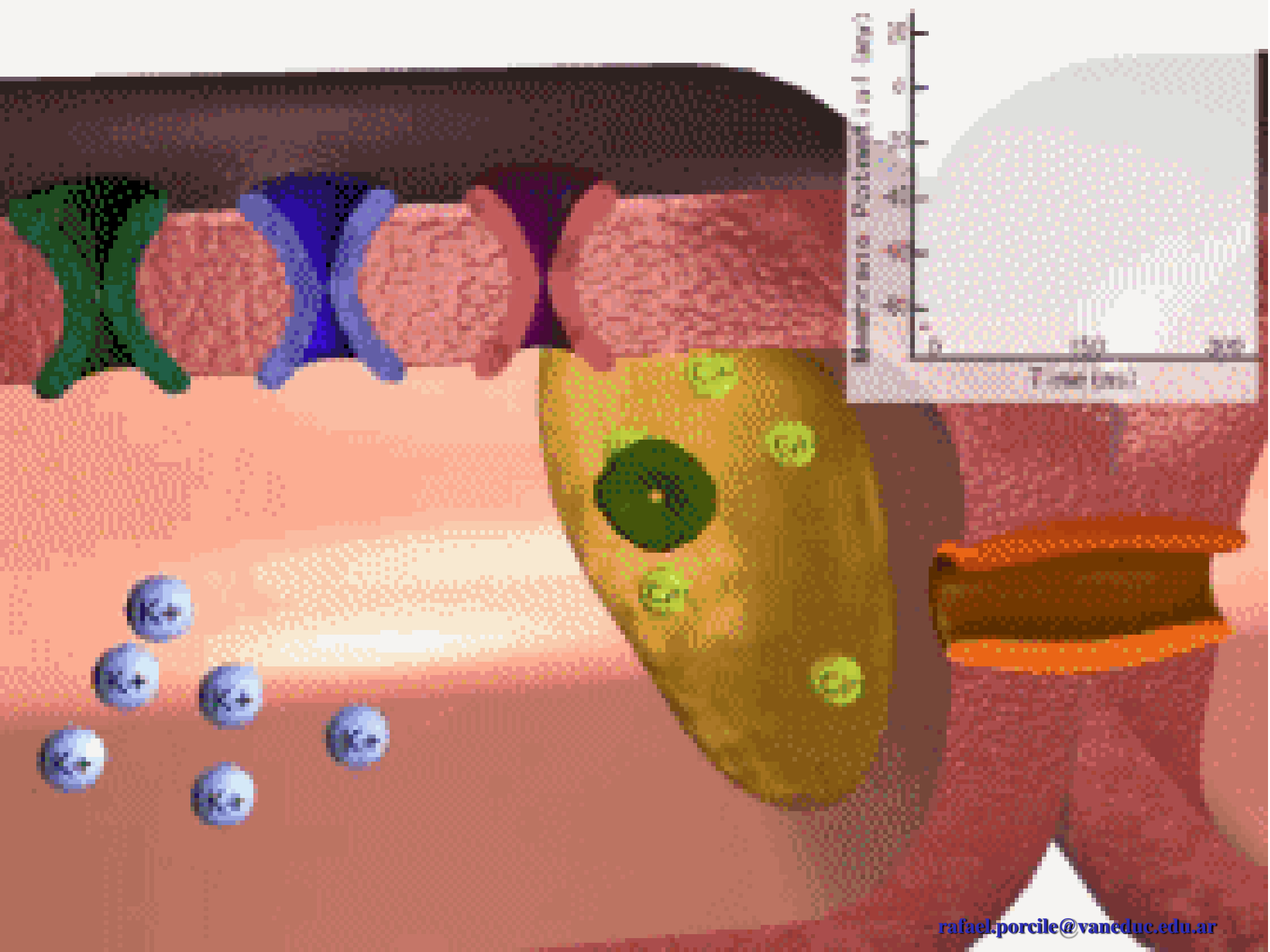
Pérdida onda P



T: Picudas

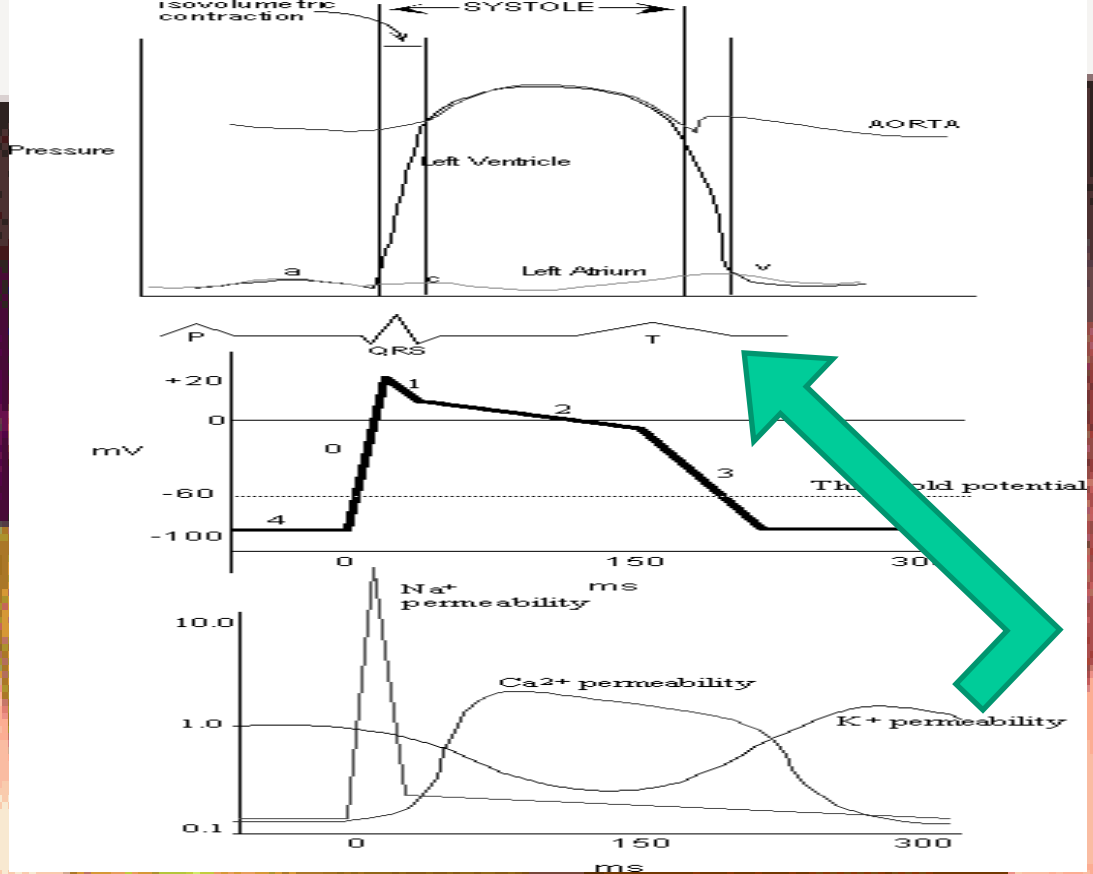
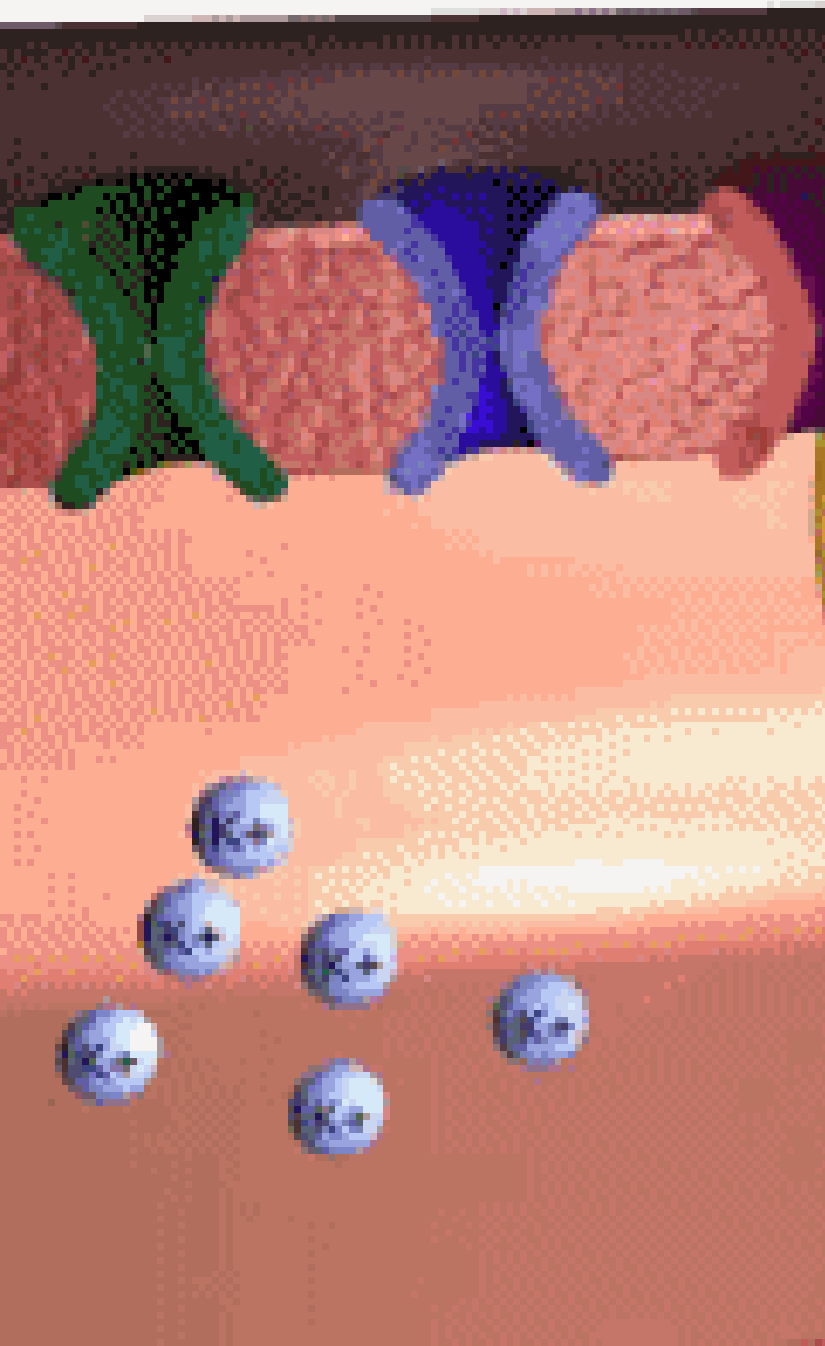
QRS ancho

Figura 48-6-4. Cambios electrocardiográficos en la hiperpotasemia.





QUE PASA EN LA HIPERKALEMIA



**AL REDUCIRSE EL GRADIENTE
DE EL K SE
SE DIFICULTA SU SALIDA**

**SE PROLONGAN Y POTENCIAS
PR LARGO
T PICUDAS**

Obstaculización a la salida del K por alta concentración extracelular

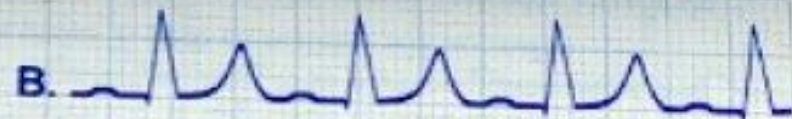


Se tiende a la hiperpolarización
porque al k le cuesta salir

bossgifz.tumblr



- ± 6.5 mEq/l \rightarrow ondas T picudas
- > 7 mEq/l $\rightarrow \uparrow$ PR, se pierde la onda P y \uparrow QRS.
- > 8 mEq/l \rightarrow arritmias ventriculares (taquicardia o fibrilación ventricular) \rightarrow paro cardíaco.



Concentración de potasio

A. normal (3,5-5,0 mEq/l)

B. próxima a 7,0 mEq/l

C. 8,0-9,0 mEq/l

D. $>10,0$ mEq/l





Trastornos

Farmacológicos

De los canales

DE POTASIO

QT largo adquirido

Hypomagnesemia

Hypocalcemia

Hypokalemia.

In addition to certain drugs

cardiac ischemia

cocaine abuse

HIV

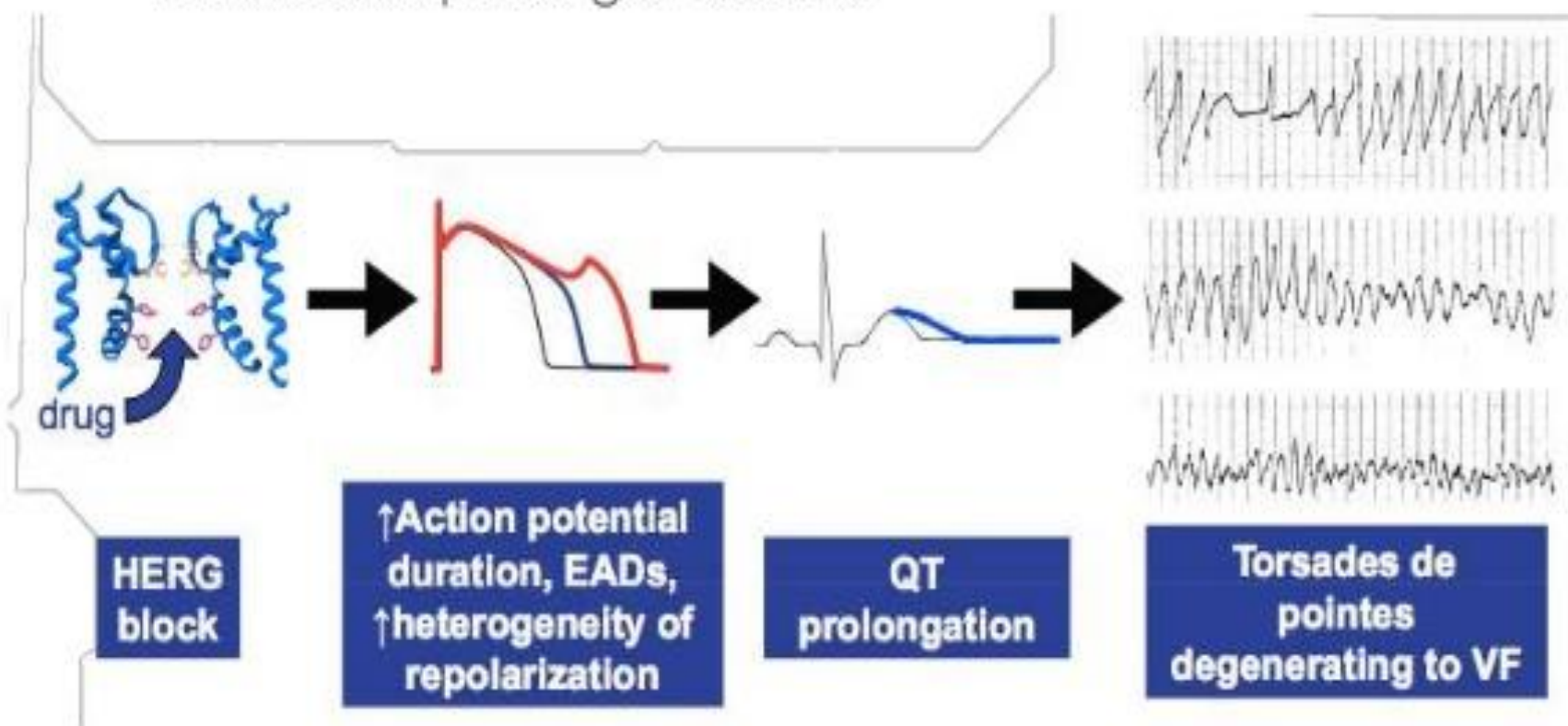
Subarachnoid hemorrhage

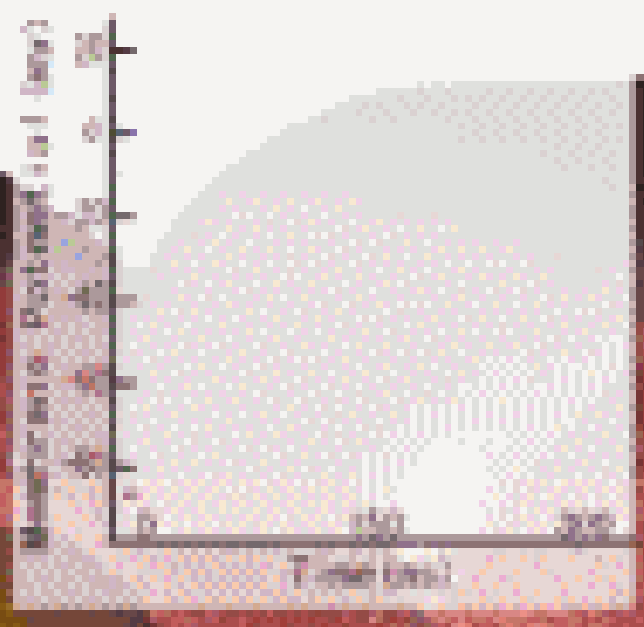
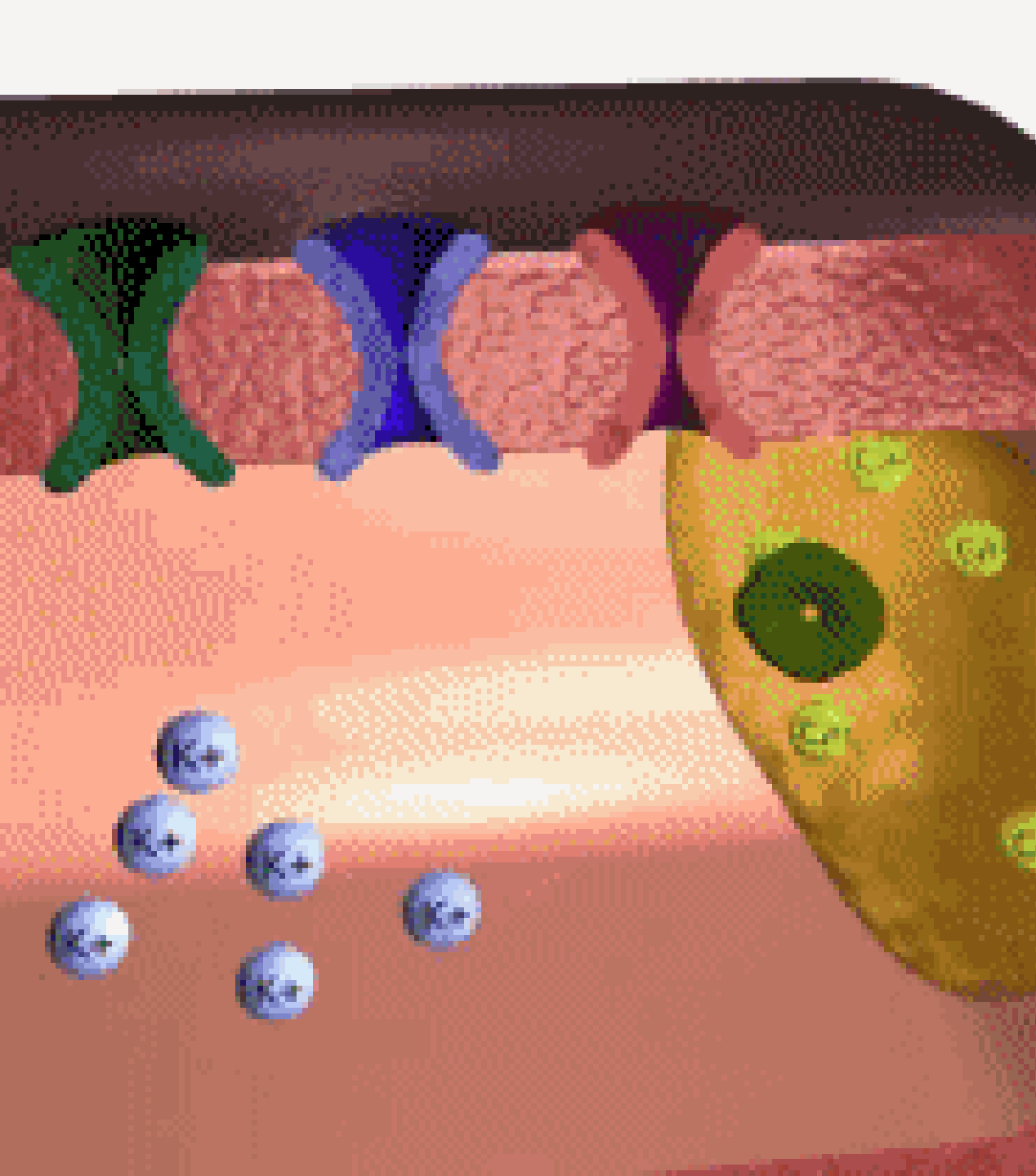
Drug Interactions That May Delay Repolarization

Isozyme	Drug Shown to Prolong QT	Inhibitor
CYP3A4	Amiodarone Erythromycin Quinidine Haloperidol Pimozide Tacrolimus Cisapride Dofetilide Disopyramide Tamoxifen Mesoridazine	Cimetidine Erythromycin Indinavir Ketoconazole Ritonavir Diltiazem Clarithromycin Itraconazole
CYP1A2	Imipramine	Cimetidine Fluvoxamine Ciprofloxacin
CYP2D6	Thioridazine Imipramine Amitriptyline Flecainide Doxepin Tamoxifen	Amiodarone Diphenhydramine Chlorpheniramine Quinidine Fluoxetine

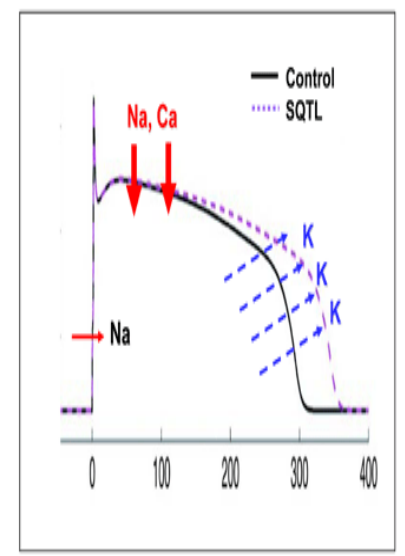
Síndrome de QT largo adquirido

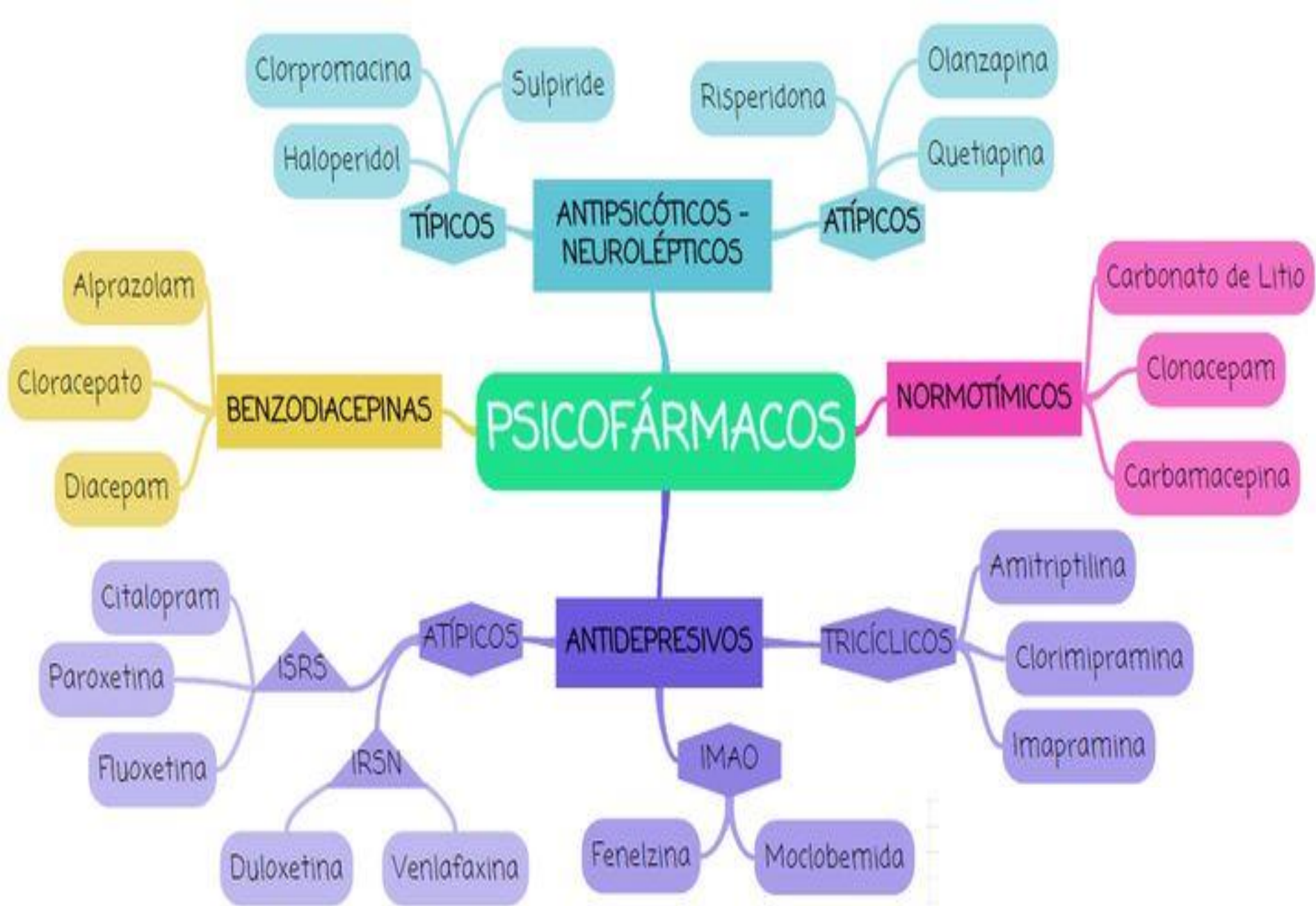
- El mecanismo principal implicado es el bloqueo de IKr
- La corriente IKr esta mediada por el canal de potasio codificado por el gen KCNH2

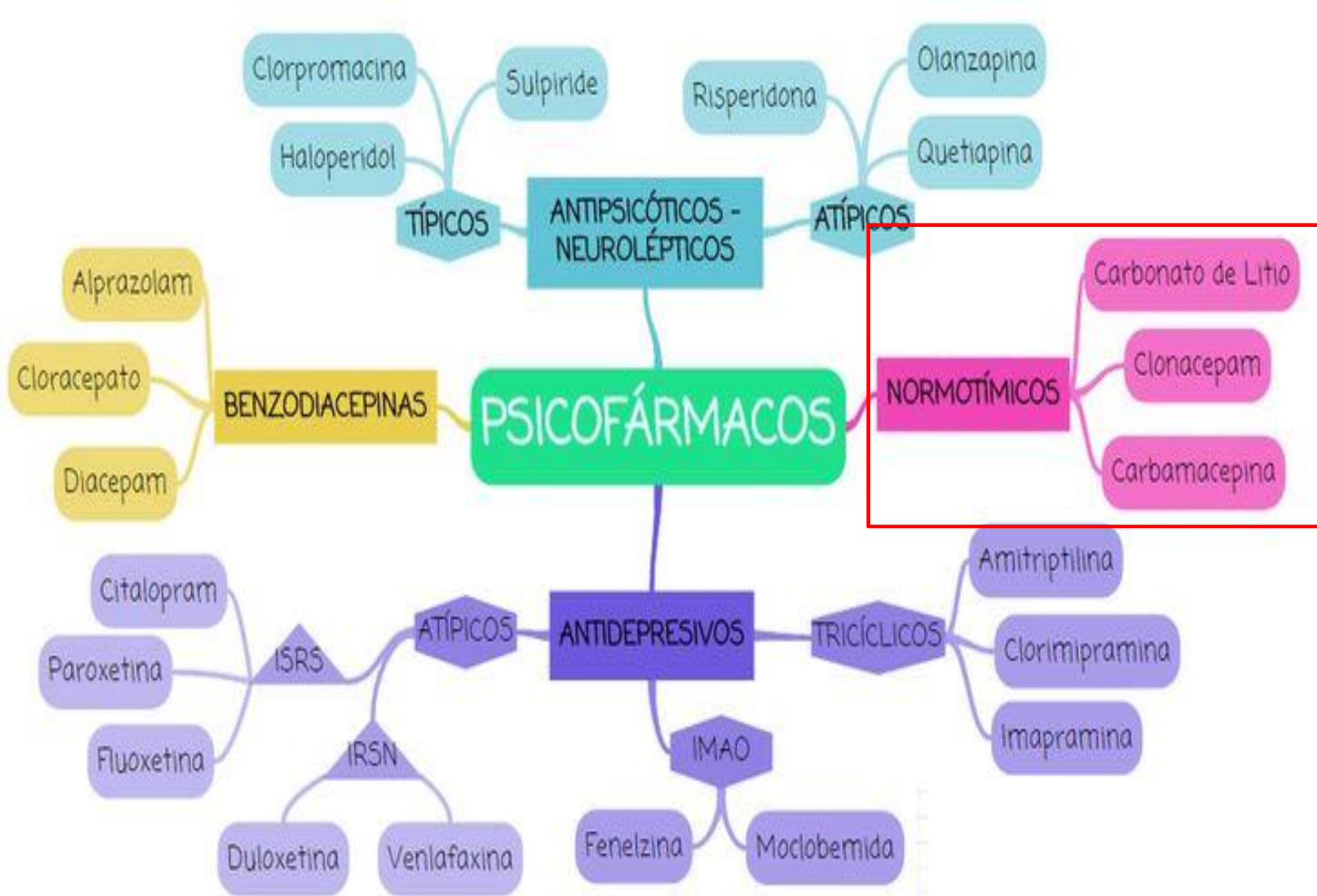




Síndrome de QT largo

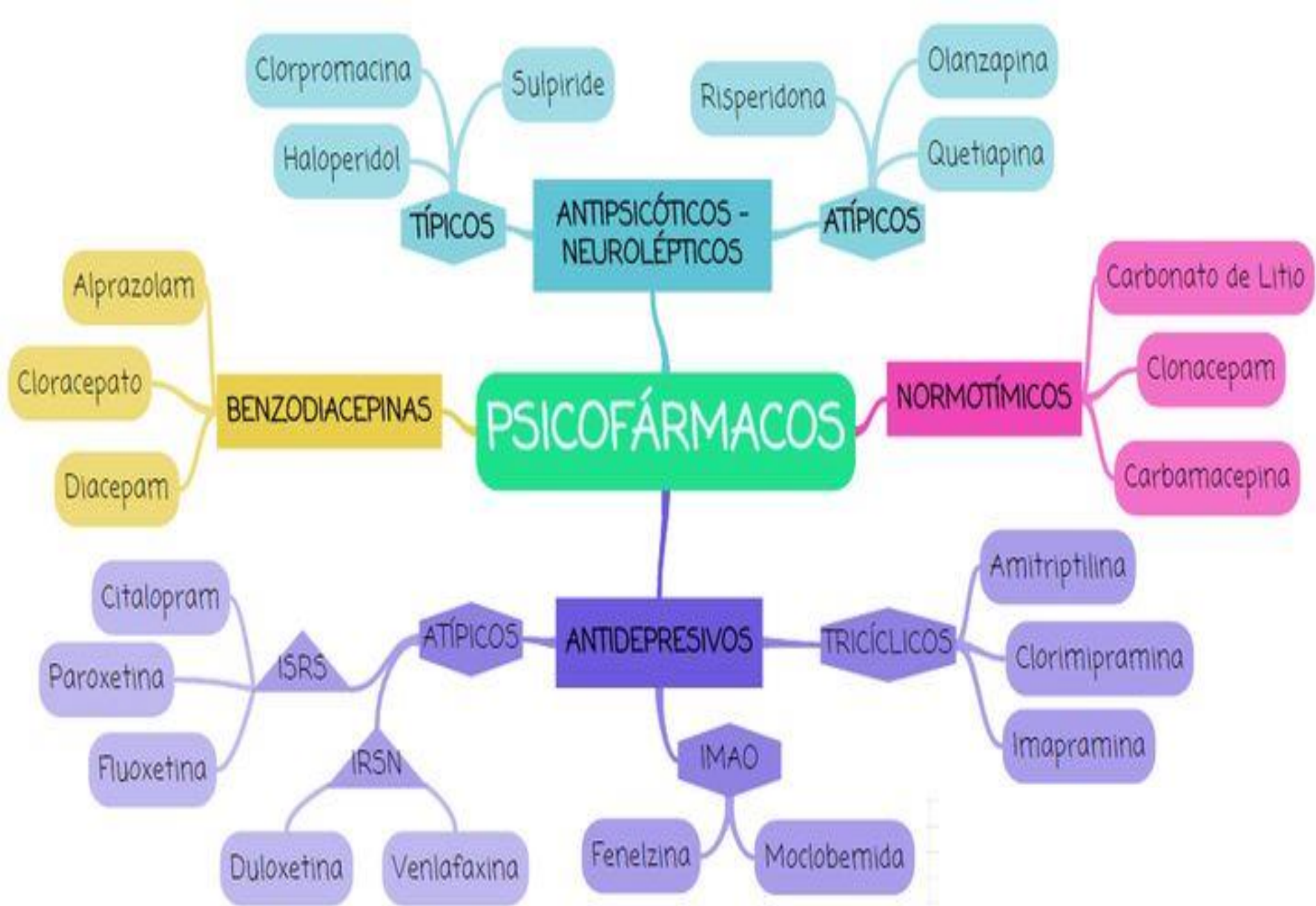


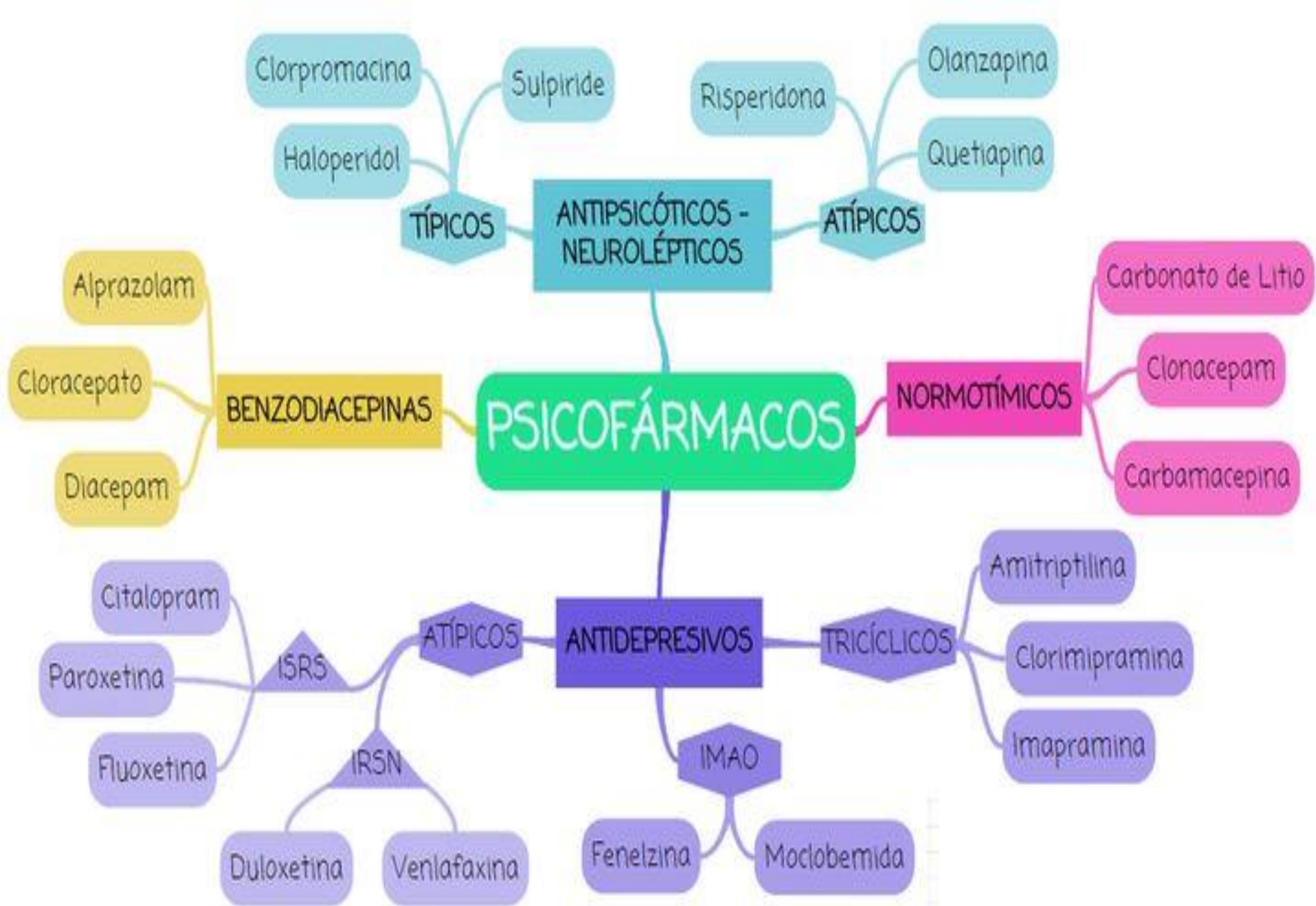


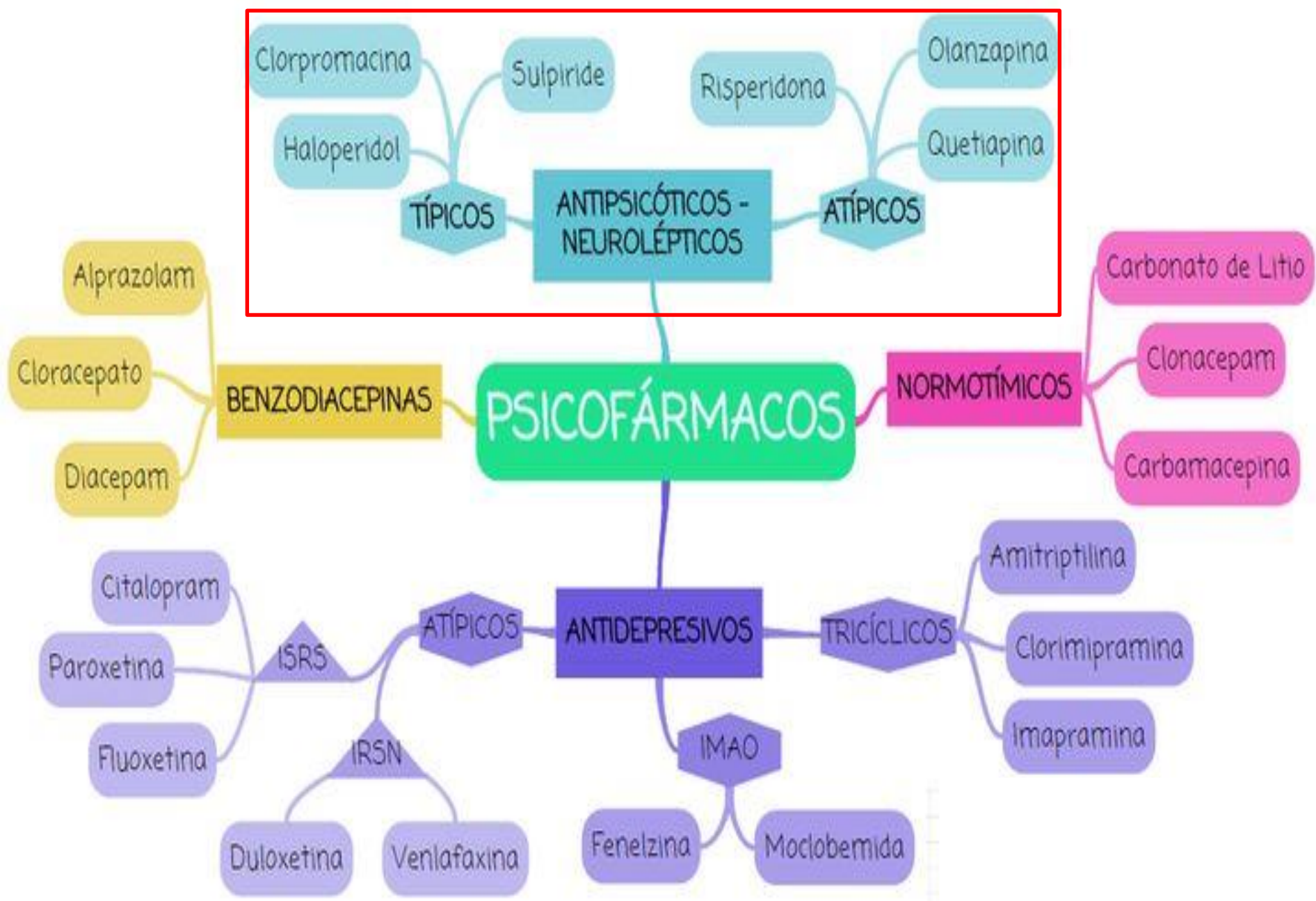


Na Channel blockers

- Blocks voltage gated Na channel by selectively binding to the channel in the inactive state and slowing its rate of recovery
 - Phenytoin (Dilantin)
 - Fosphenytoin (Cerebyx)
 - Carbamazepine (Tegretol)
 - Oxcarbamazine (Trileptal)
 - Valproic acid (Valproate, Depakene, Depakote)
 - Lamotrigine (Lamictal)
 - Topiramate (Topamax)
 - Zonisamide (Zonegran)



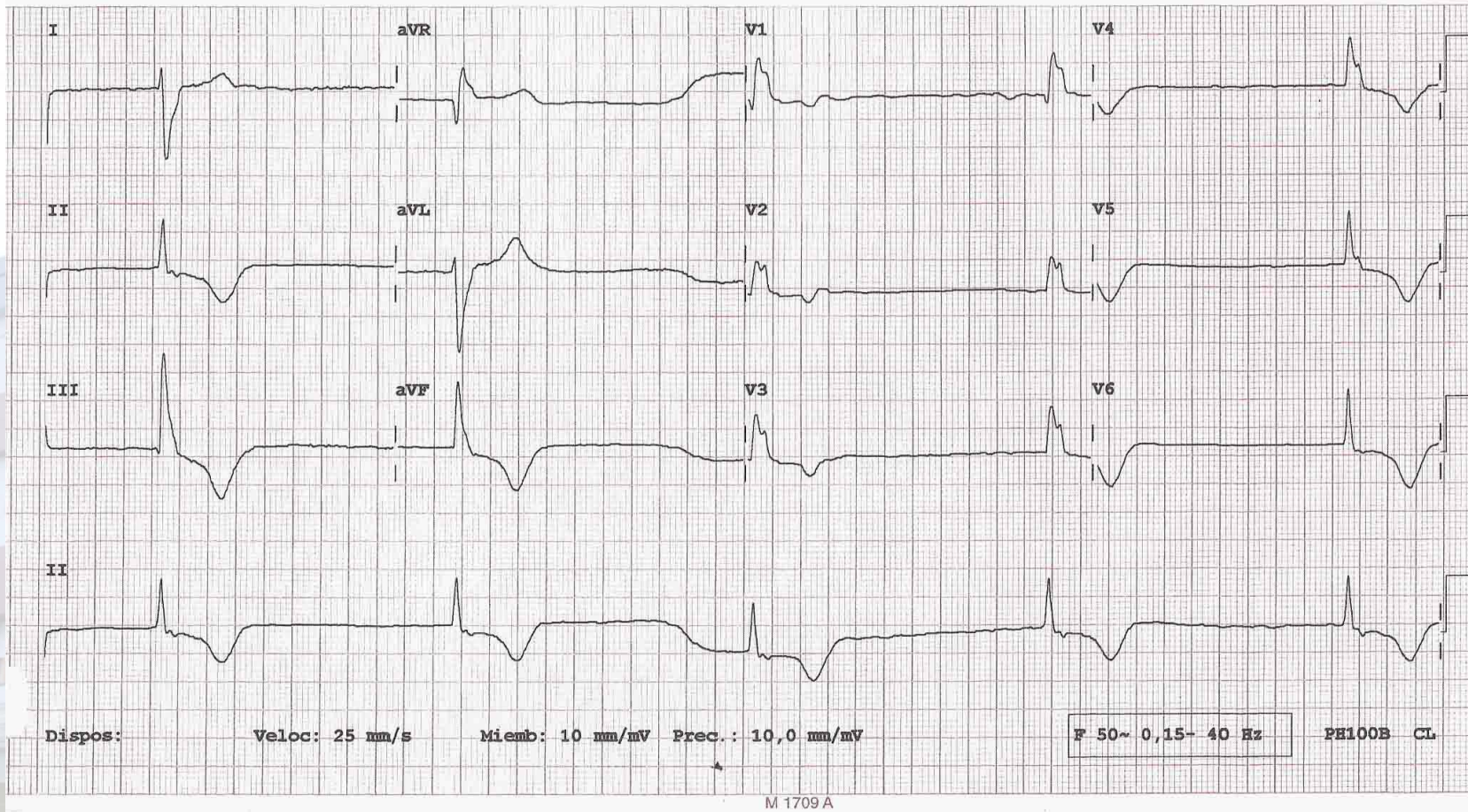




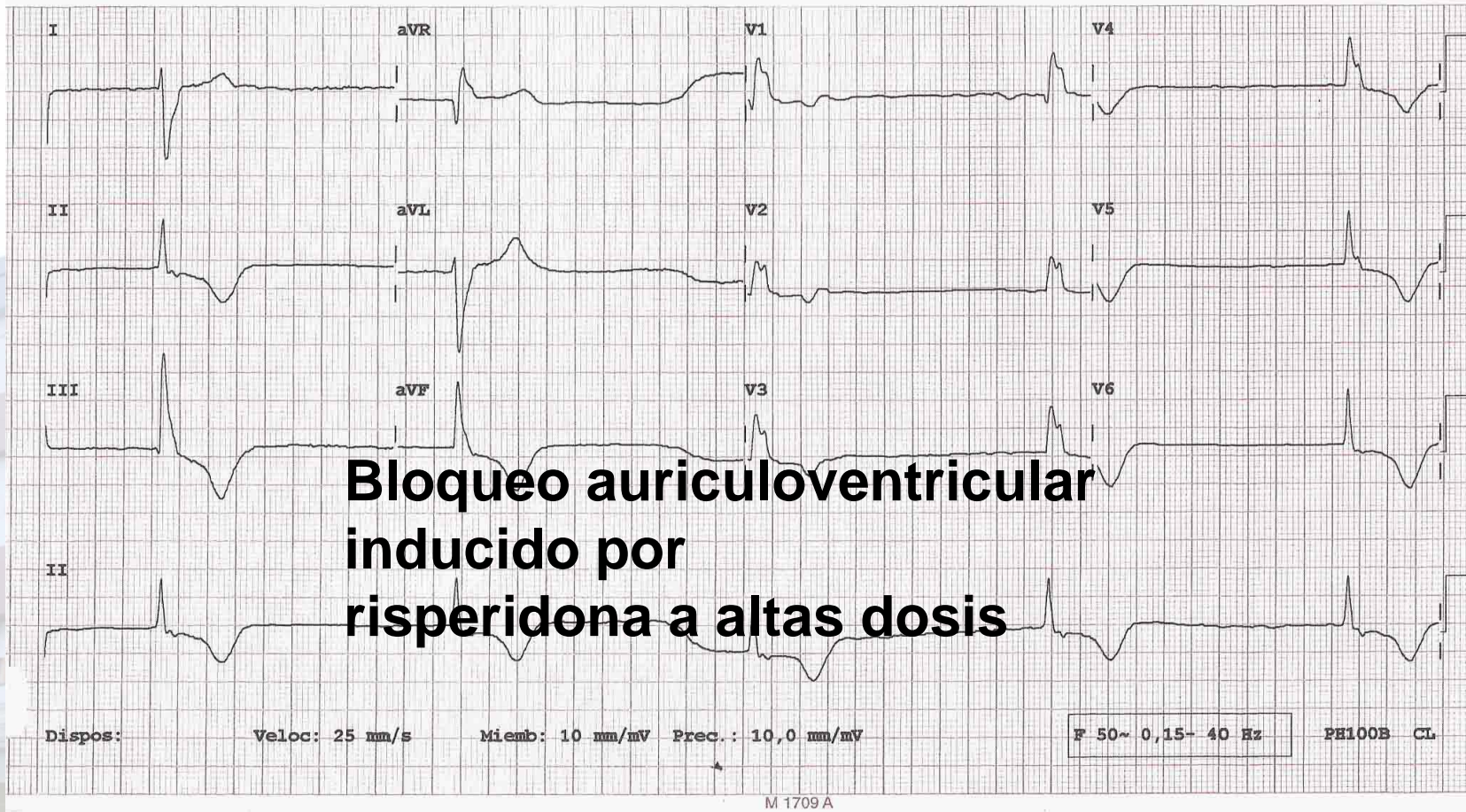
QRS 119
T -77
12 derivaciones; colocación estándar

- ECG ANOMALO -

Unconfirmed Diagnosis



Varón de 84 años acude remitido por su MAP por hallazgo casual de bradicardia en un control rutinario. No refiere síncope ni mareos. No dolor torácico ni disnea.



Varón de 84 años acude remitido por su MAP por hallazgo casual de bradicardia en un control rutinario. No refiere síncope ni mareos. No dolor torácico ni disnea.

QTc prolongation with common antipsychotic drugs: 183 patients with normal ECGs at baseline were randomized to one of six antipsychotic drugs at maximum daily doses of: ziprasidone 160 mg, risperidone 16 mg, olanzapine 20 mg, quetiapine 750 mg, thioridazine...

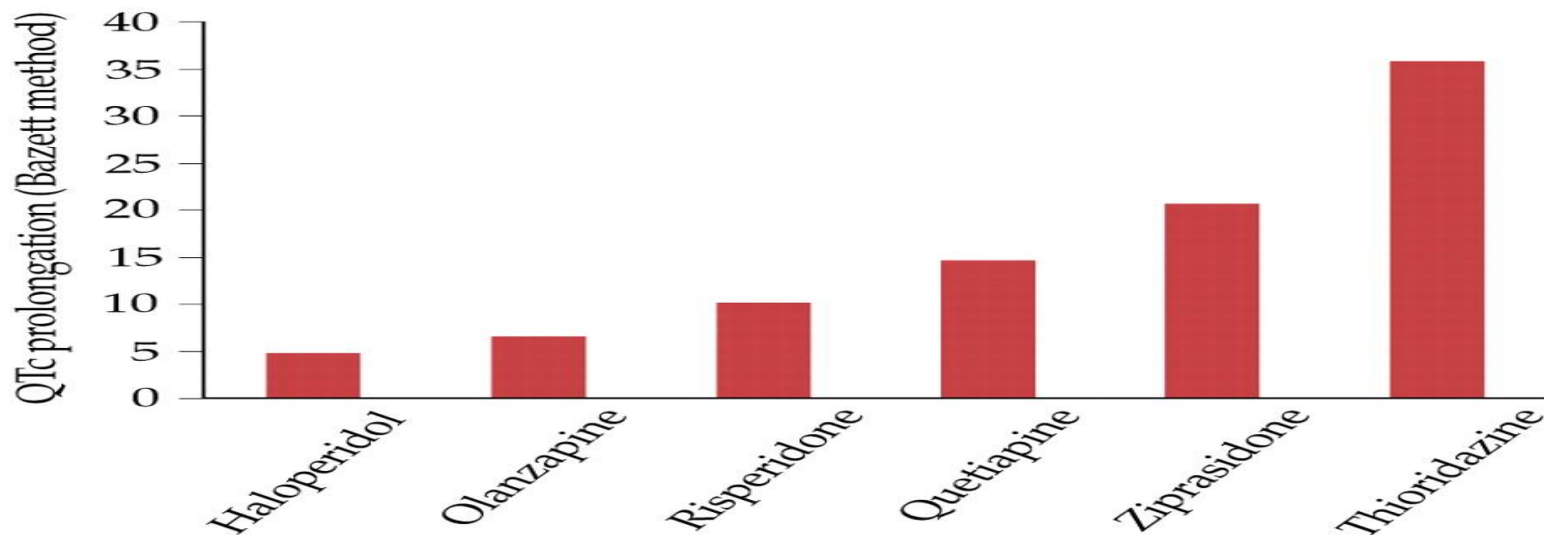


Fig 1 QTc prolongation with common antipsychotic drugs: 183 patients with normal ECGs at baseline were randomized to one of six antipsychotic drugs at maximum daily doses of: ziprasidone 160 mg, risperidone 16 mg, olanzapine 20 mg, quetiapine 750 mg, thioridazine 300 mg and haloperidol 15 mg (Data from PsychoPharmacological Drugs Advisory Committee, 2000).

Nasser Abdelmawla, and Alex J. Mitchell APT 2006;12:35-44

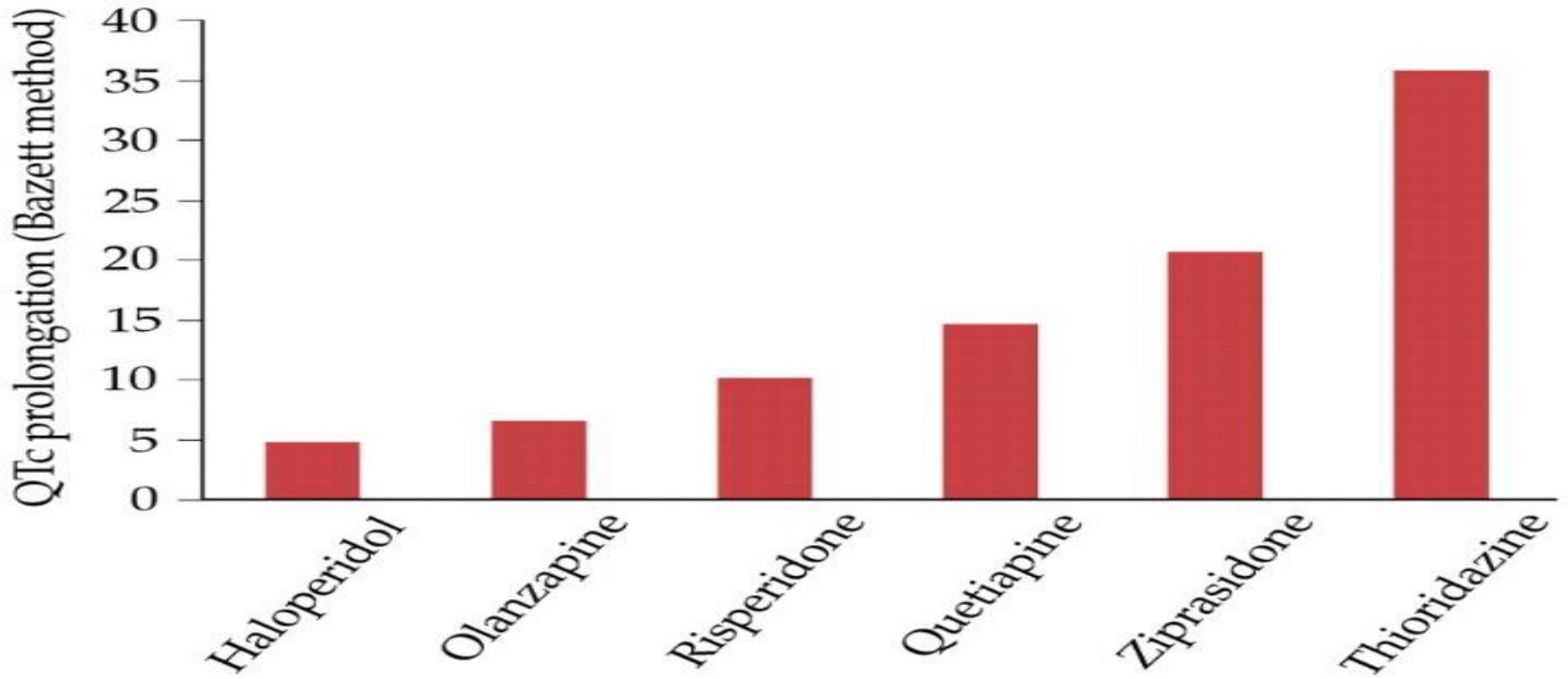
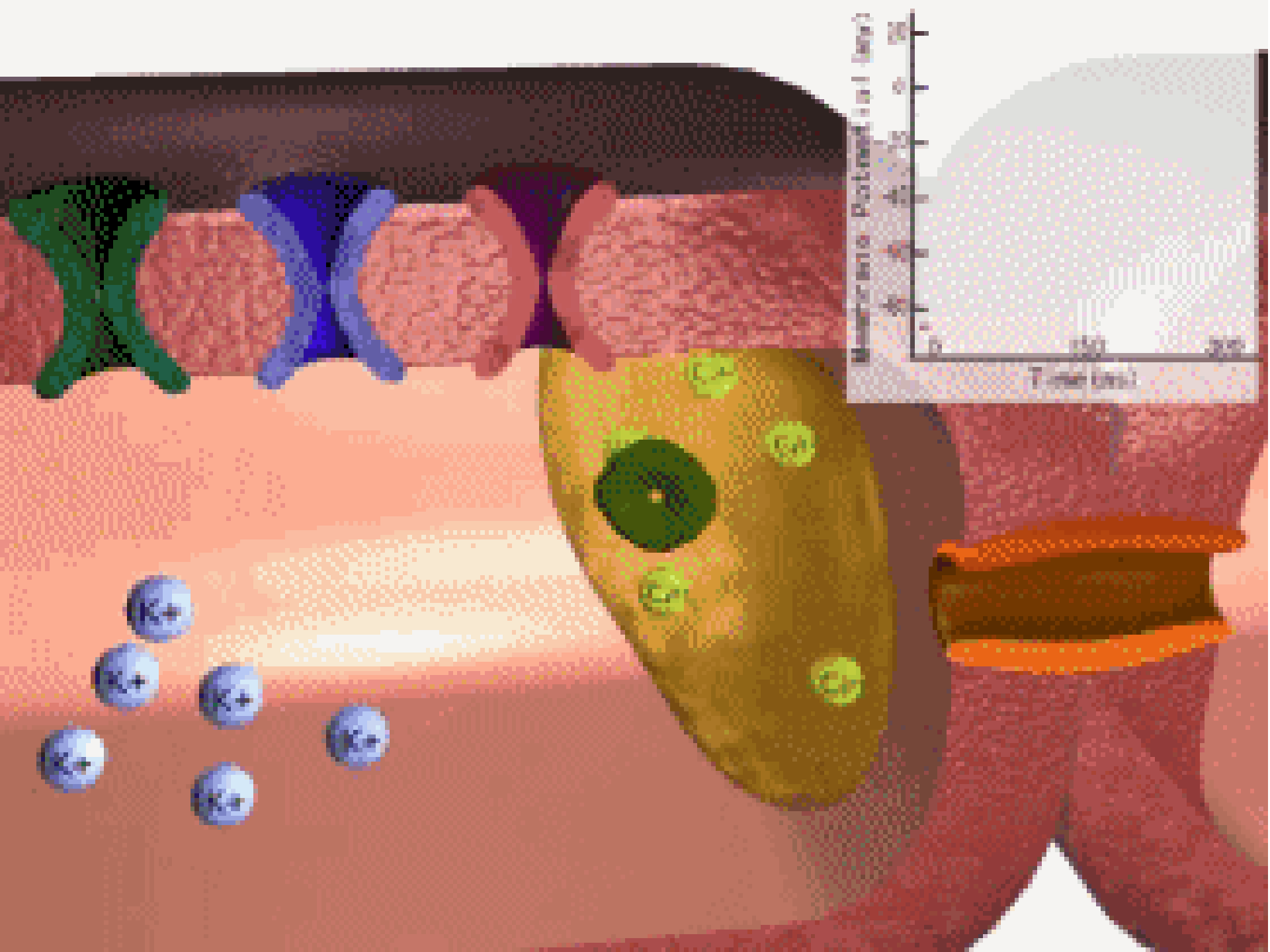
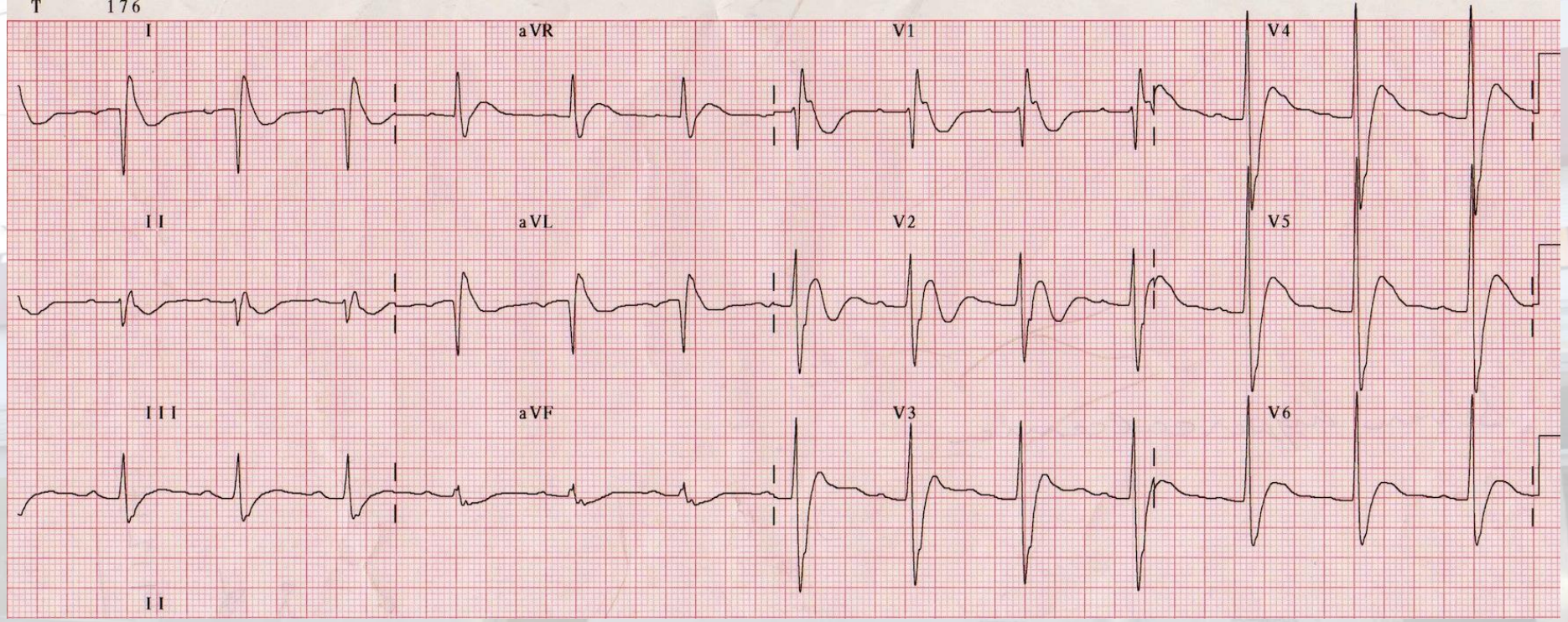


TABLA III
EFFECTOS SECUNDARIOS DE LOS ANTIPSIKÓTICOS

		Clásicos Inesivos	Clásicos Sedante	Clozapina	Risperidona ^a	Olanzapina ^a	Quetiapina ^a	Ziprasidona ^a	Sulpirid ^a	Zolopina ^a
SNC	<i>Parkinsonismo</i>	+++	+	0	0 a ++	0	0	0 a +	a ++	0 a ++ ?
	<i>Acatisia</i>	+++	+	0	0 a ++	0	0	0 a +	a ++	0
	<i>Disinestesia tardia</i>	+++	+++	0	?	?	?	?	?	?
	<i>Convulsiones</i>	0	+	+++	0	0	0	0	0 a +	+
	<i>Sedación</i>	+	+++	+++	+	+	+	+	0 a +	+
Cardio- vasculares	<i>Hipotensión ortostática</i>	+	+++	0 a +++	+	+	+ a ++	+	0	+
	<i>Cambios ECG. Alargamiento QTc</i>	0 ^b	+	0	0 a +	0	0 a +	+	0	+



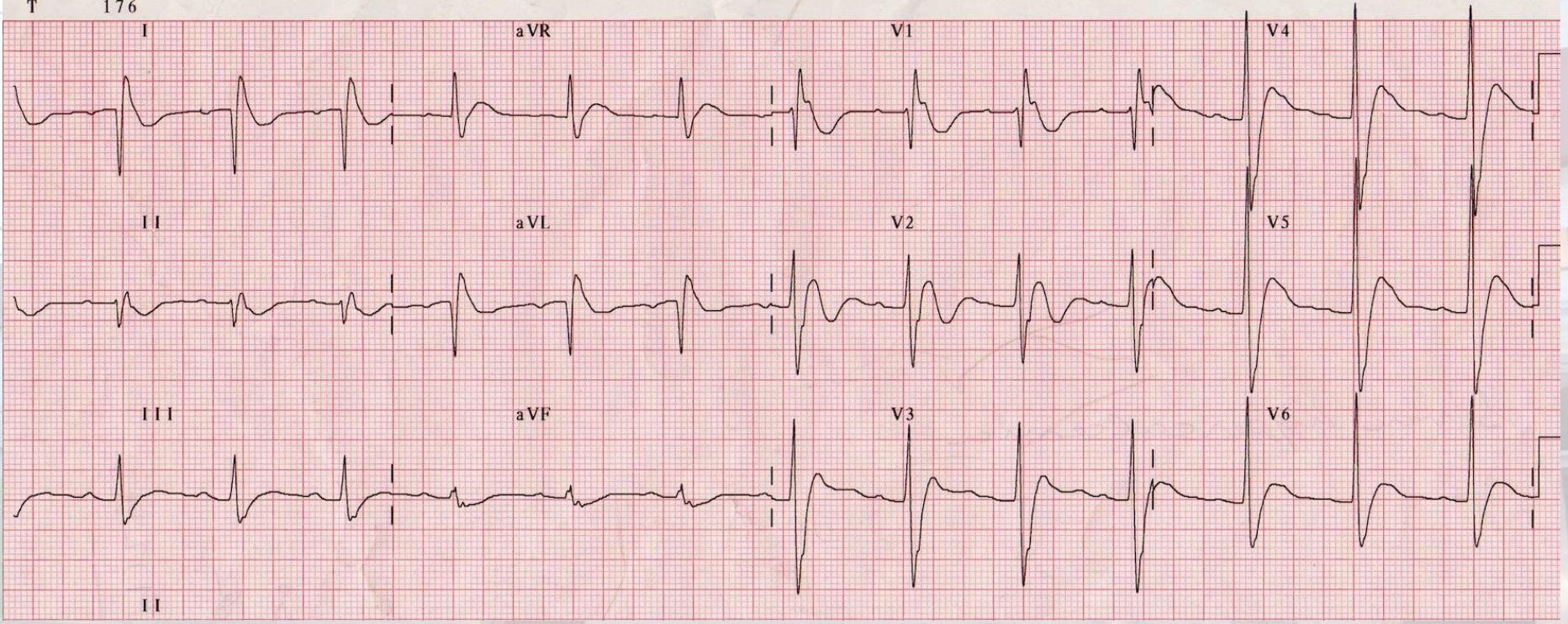
T 176



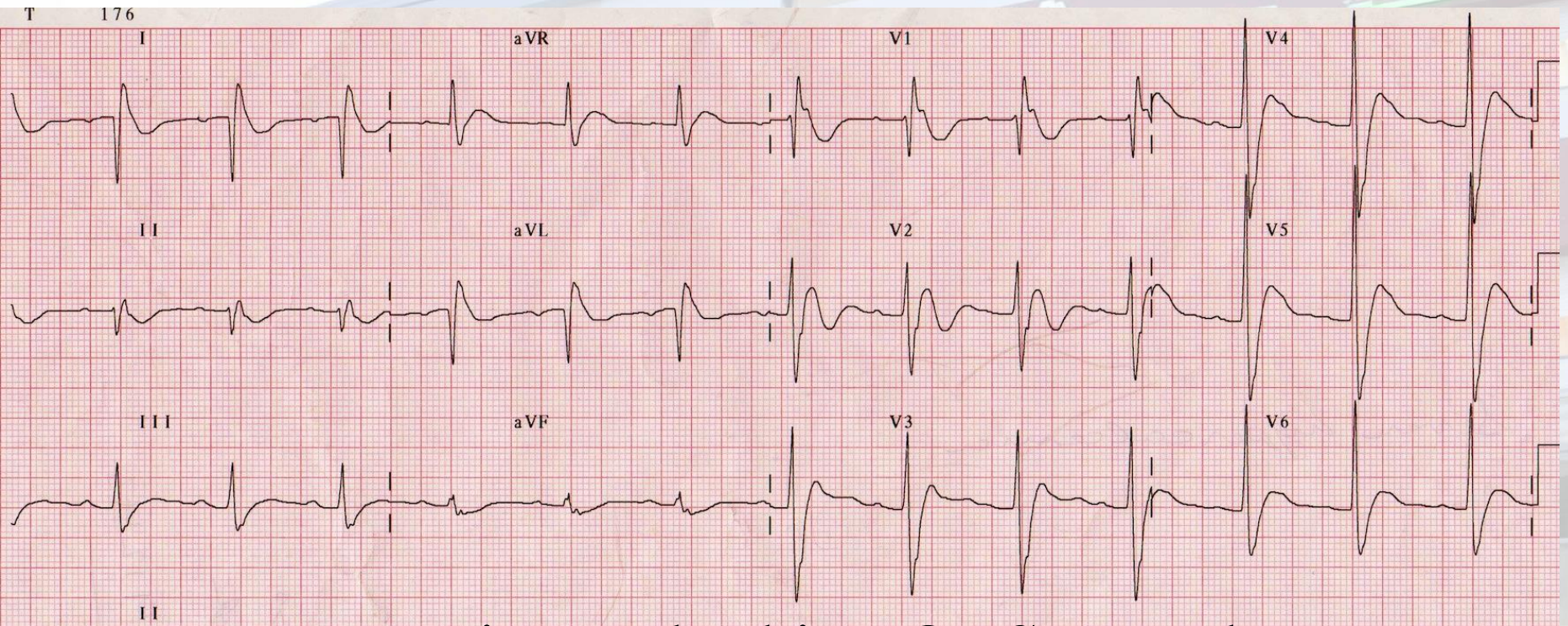
¿Que es esto?



T 176



Hipercalcemia

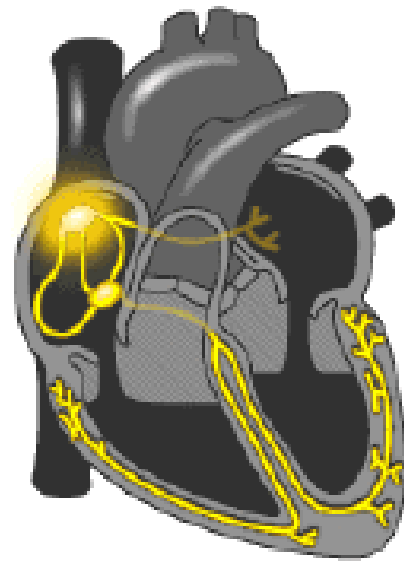


- Bizarre-looking QRS complexes
- Very short QT interval
- J waves = notching of the terminal QRS, best seen in lead V1

Los

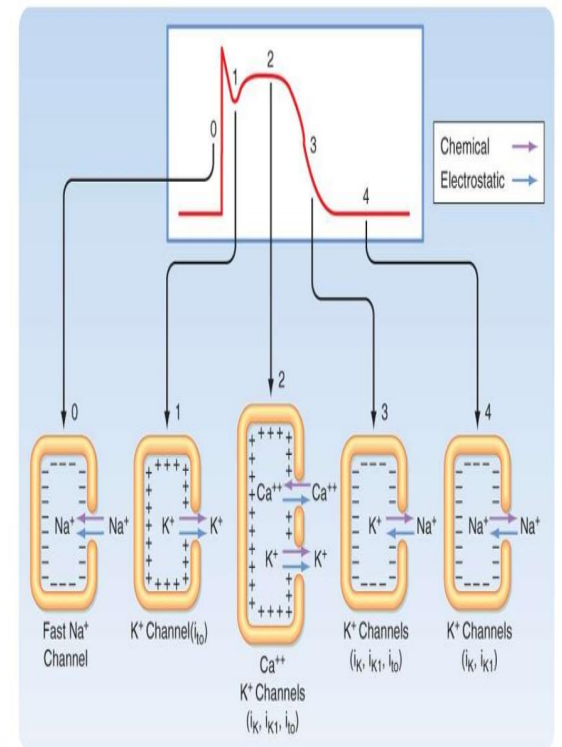
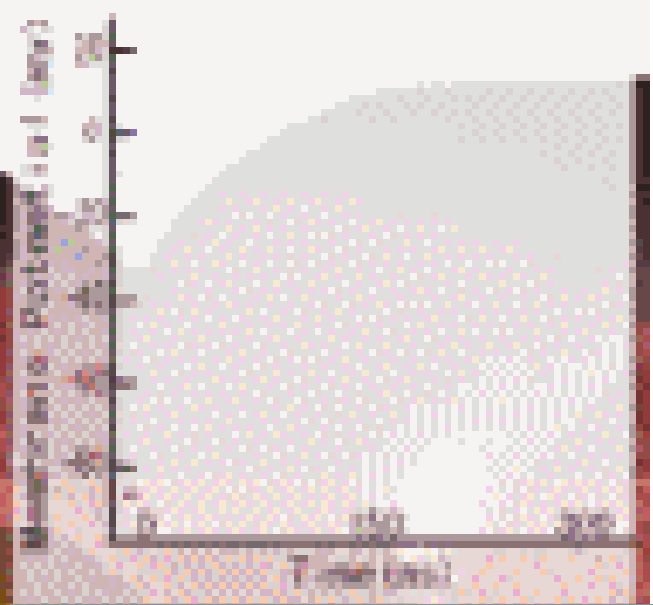
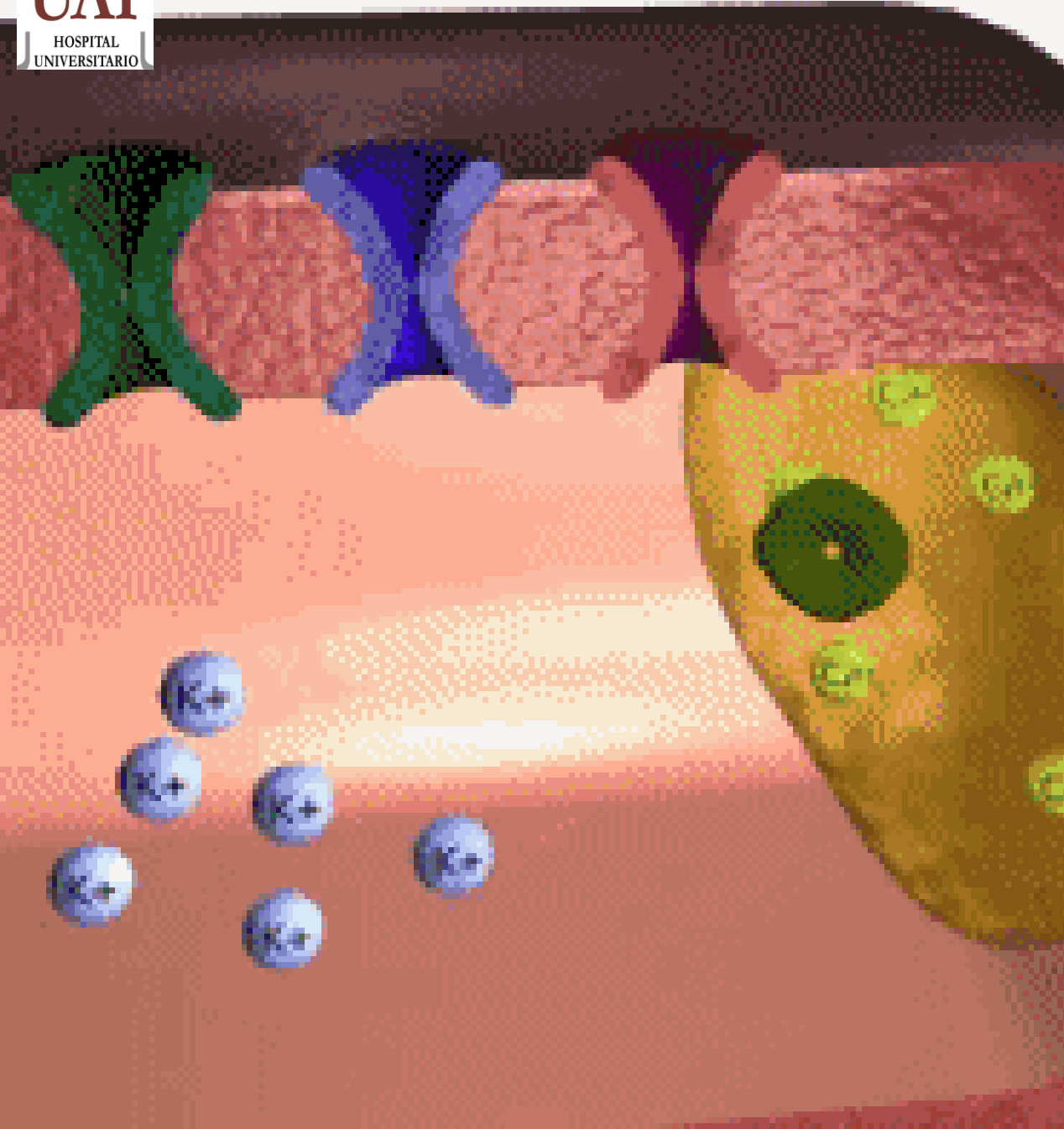
canales

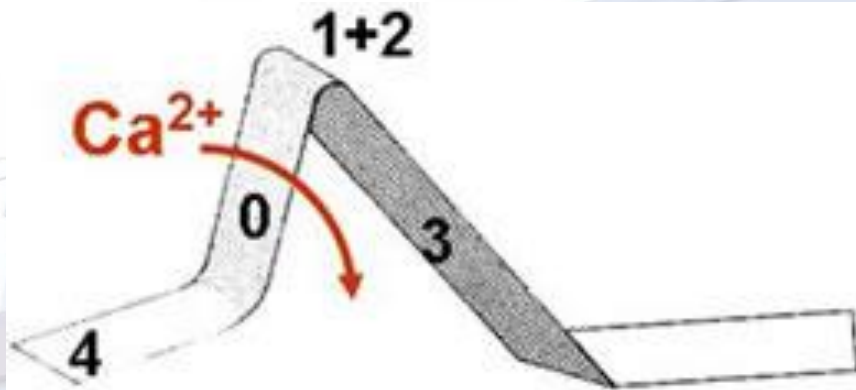
de Calcio



MODIFICADORES DEL PREPOTENCIAL

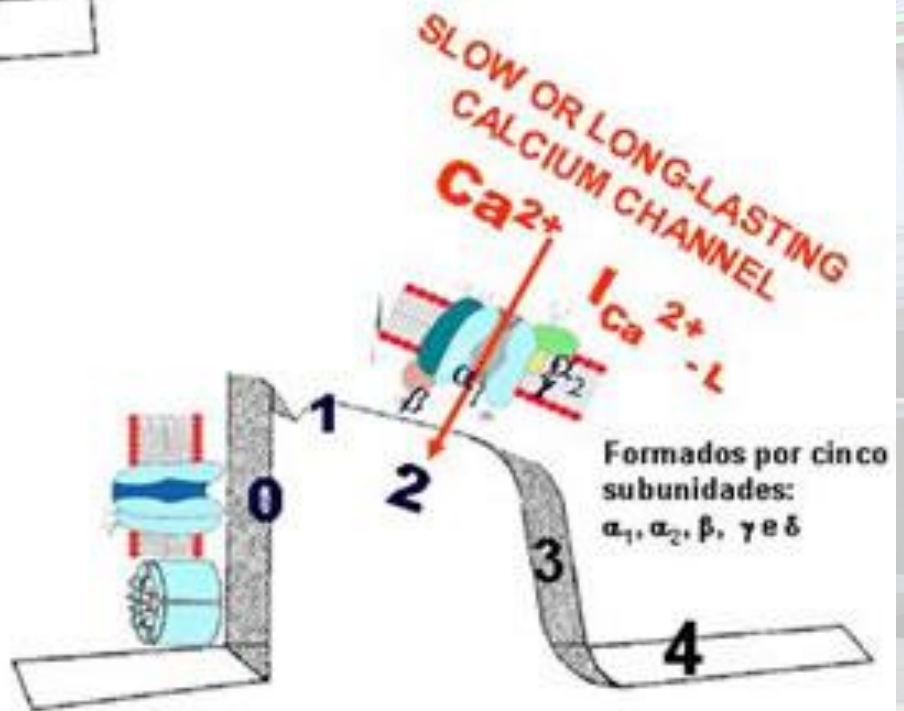
- Canales de Ca del corazon
 - Canales T : transitorios
 - Se ingresa calcio cuando origen a la apertura de los
 - Canales L Lentos
 - Que generan la apertura de los canales de Sodio y la F0



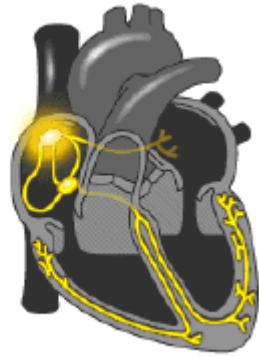
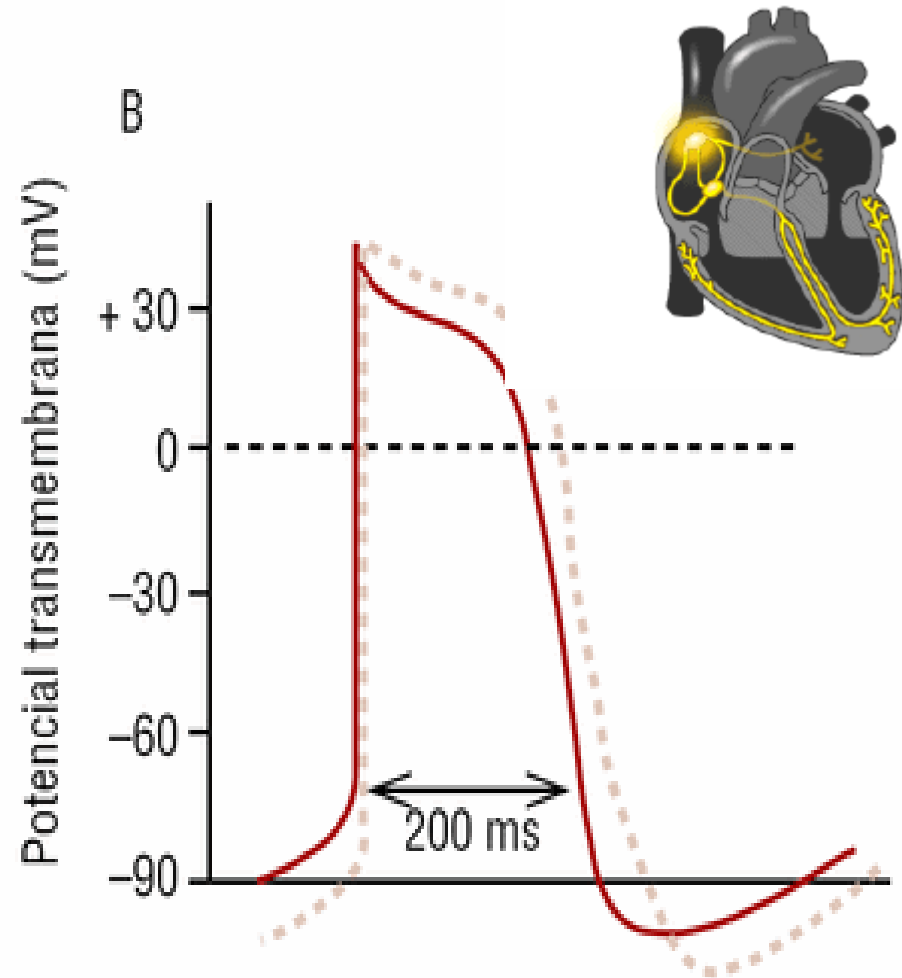
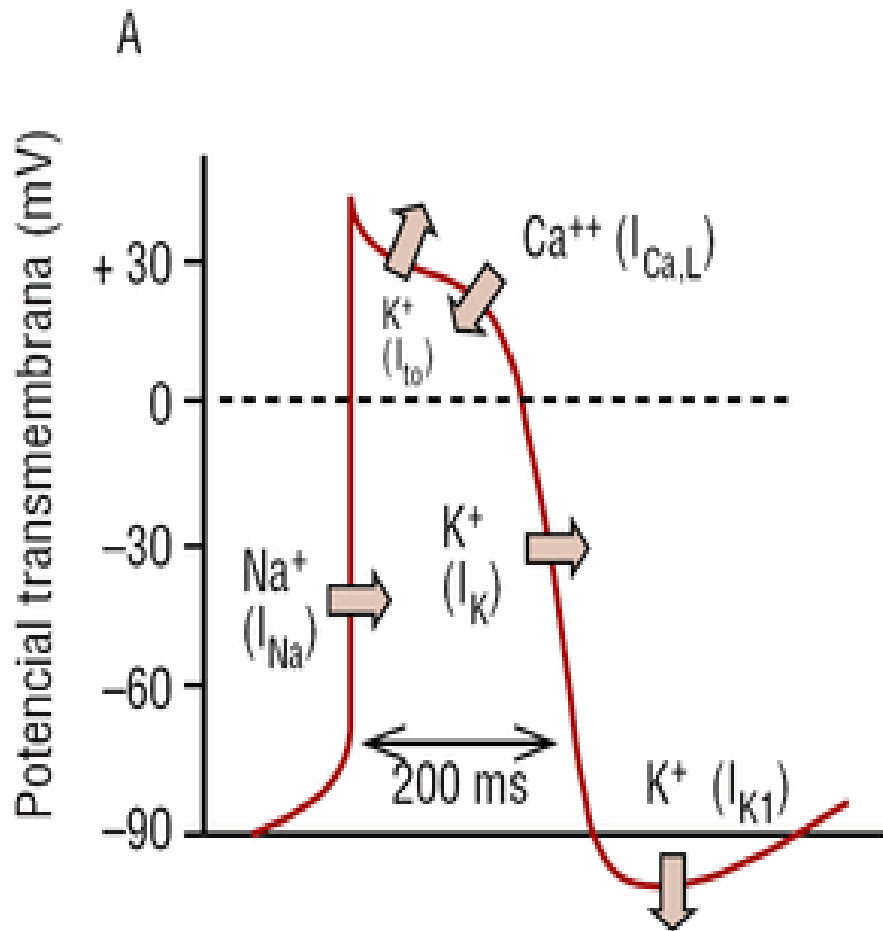


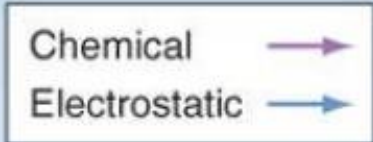
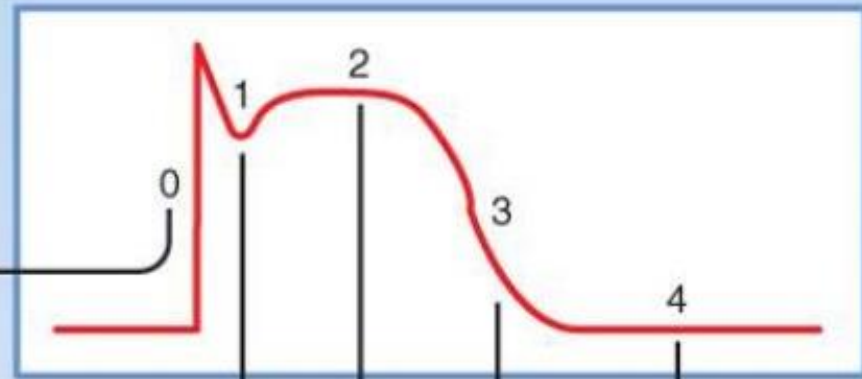
FIBRA RÁPIDA

FIBRA LENTA

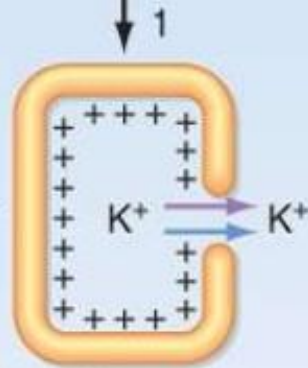


FIBRAS AUTOMATICAS

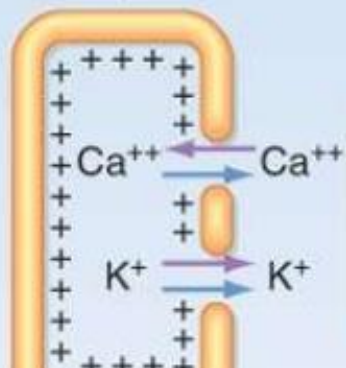




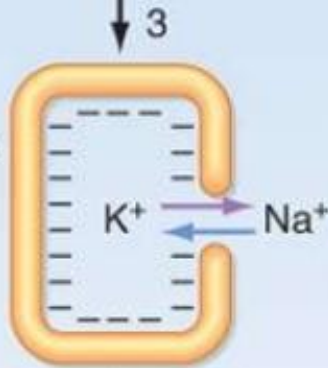
Fast Na⁺ Channel



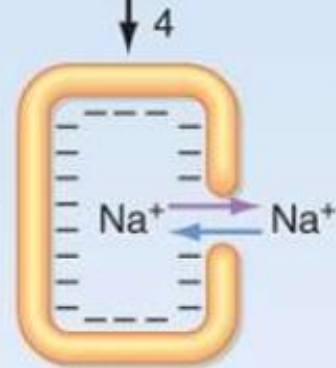
K⁺ Channel (i_{to})



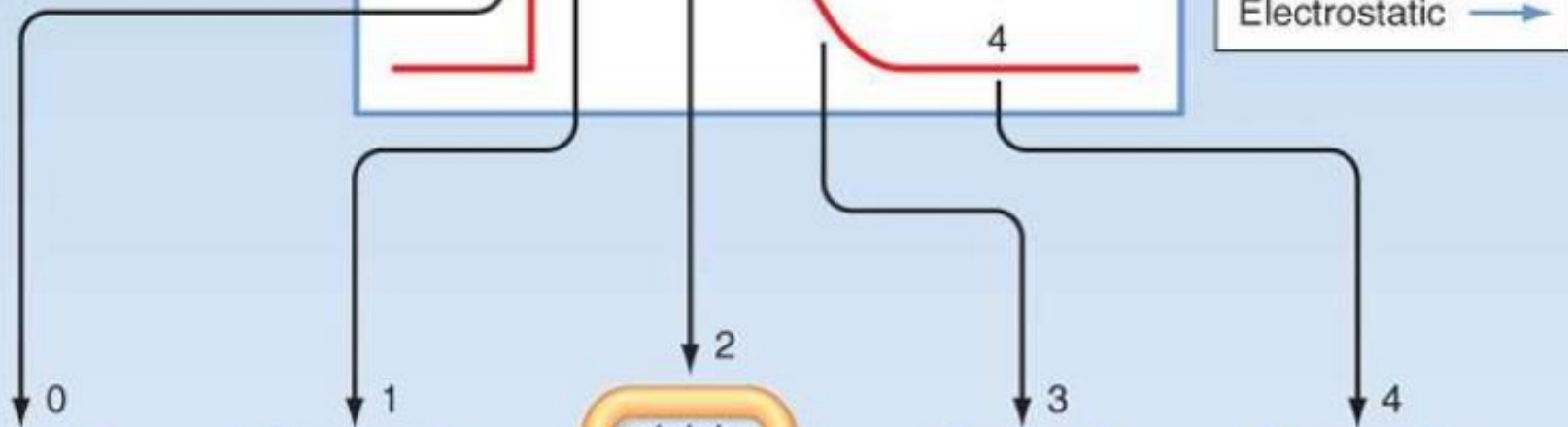
Ca⁺⁺
K⁺ Channels
(i_K, i_{K1}, i_{to})

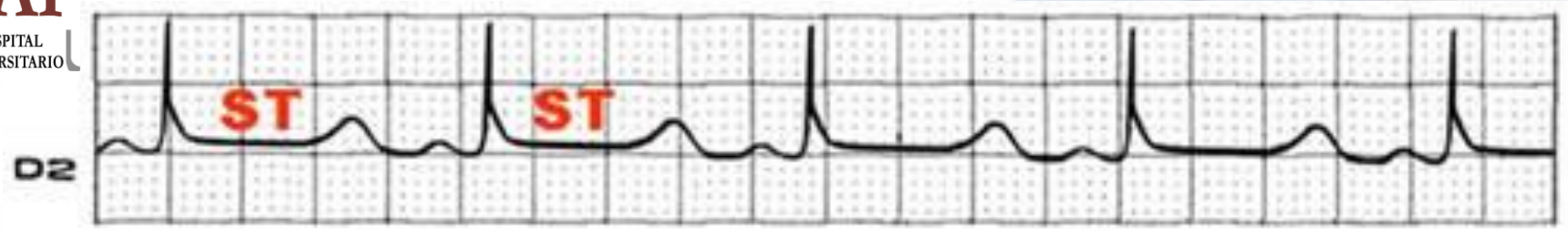


K⁺ Channels
(i_K, i_{K1}, i_{to})

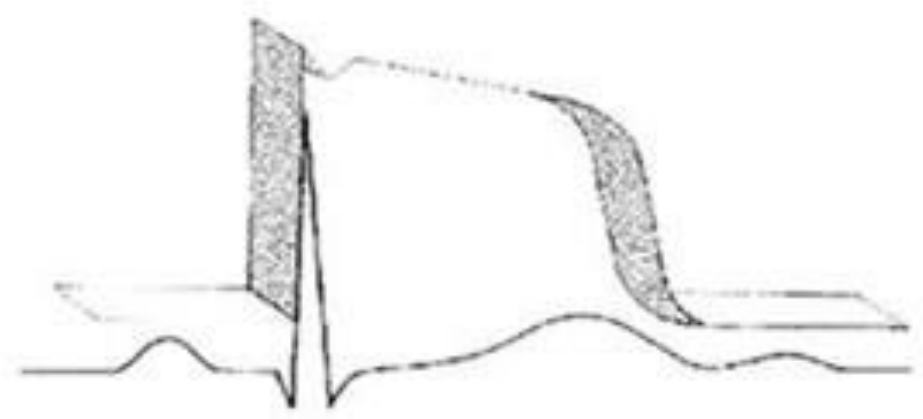


K⁺ Channels
(i_K, i_{K1})





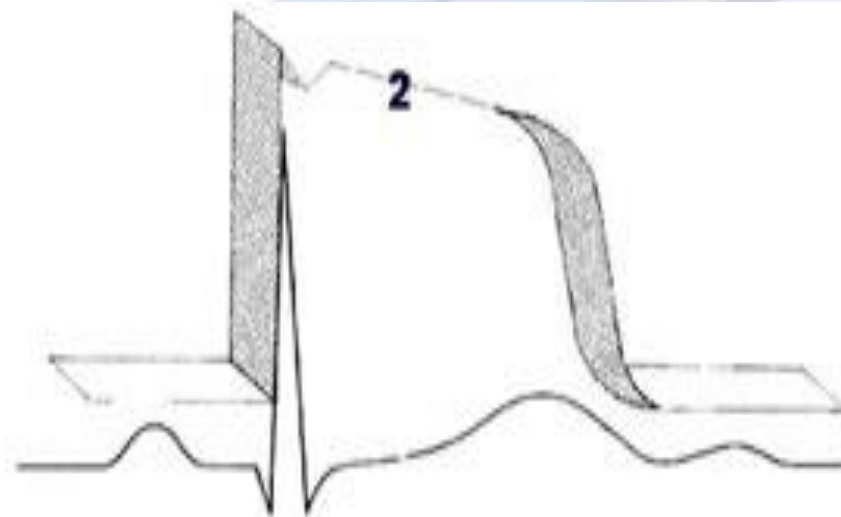
NORMAL



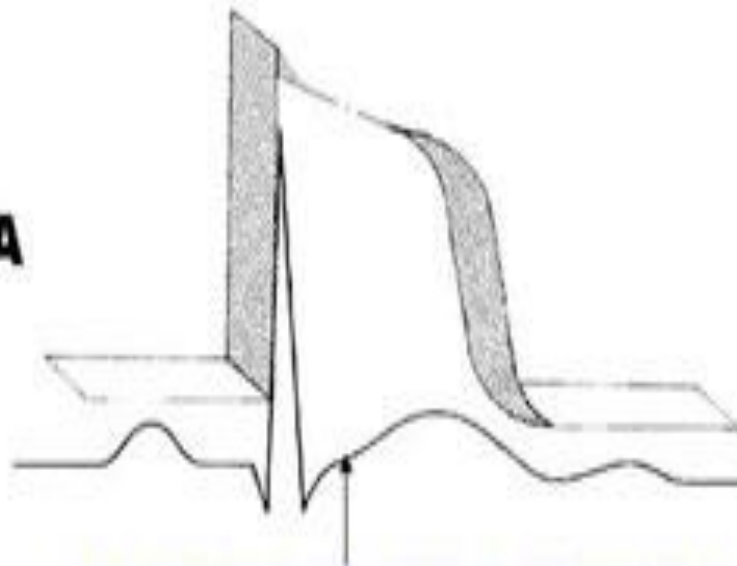
HIPOCALCEMIA



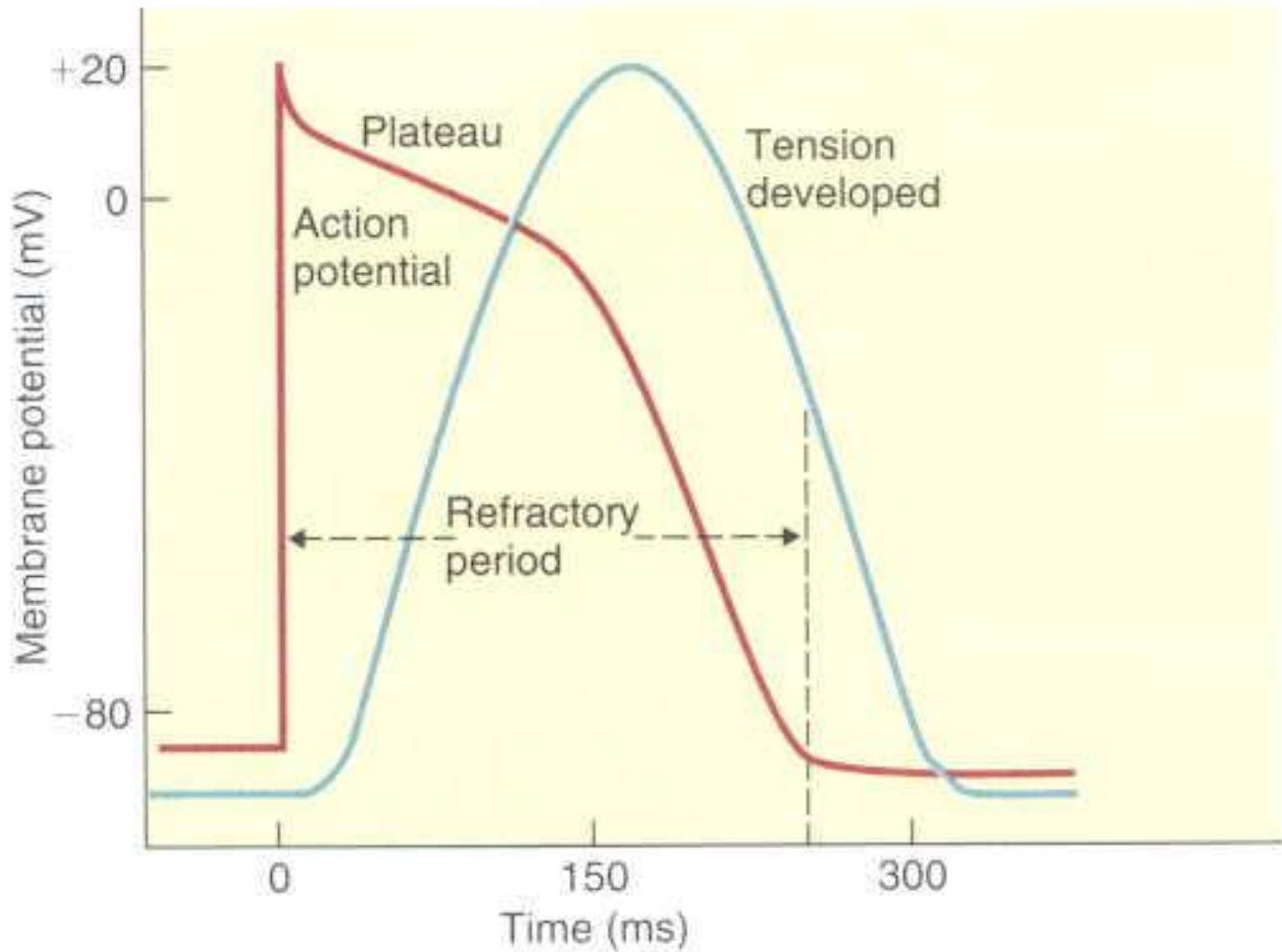
NORMAL

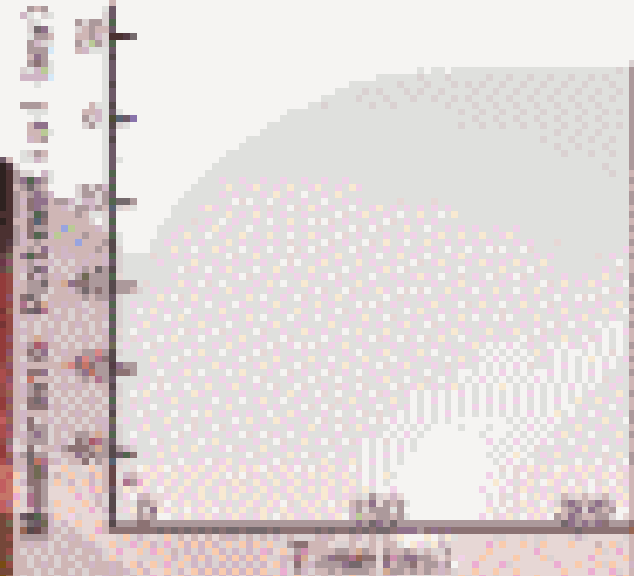
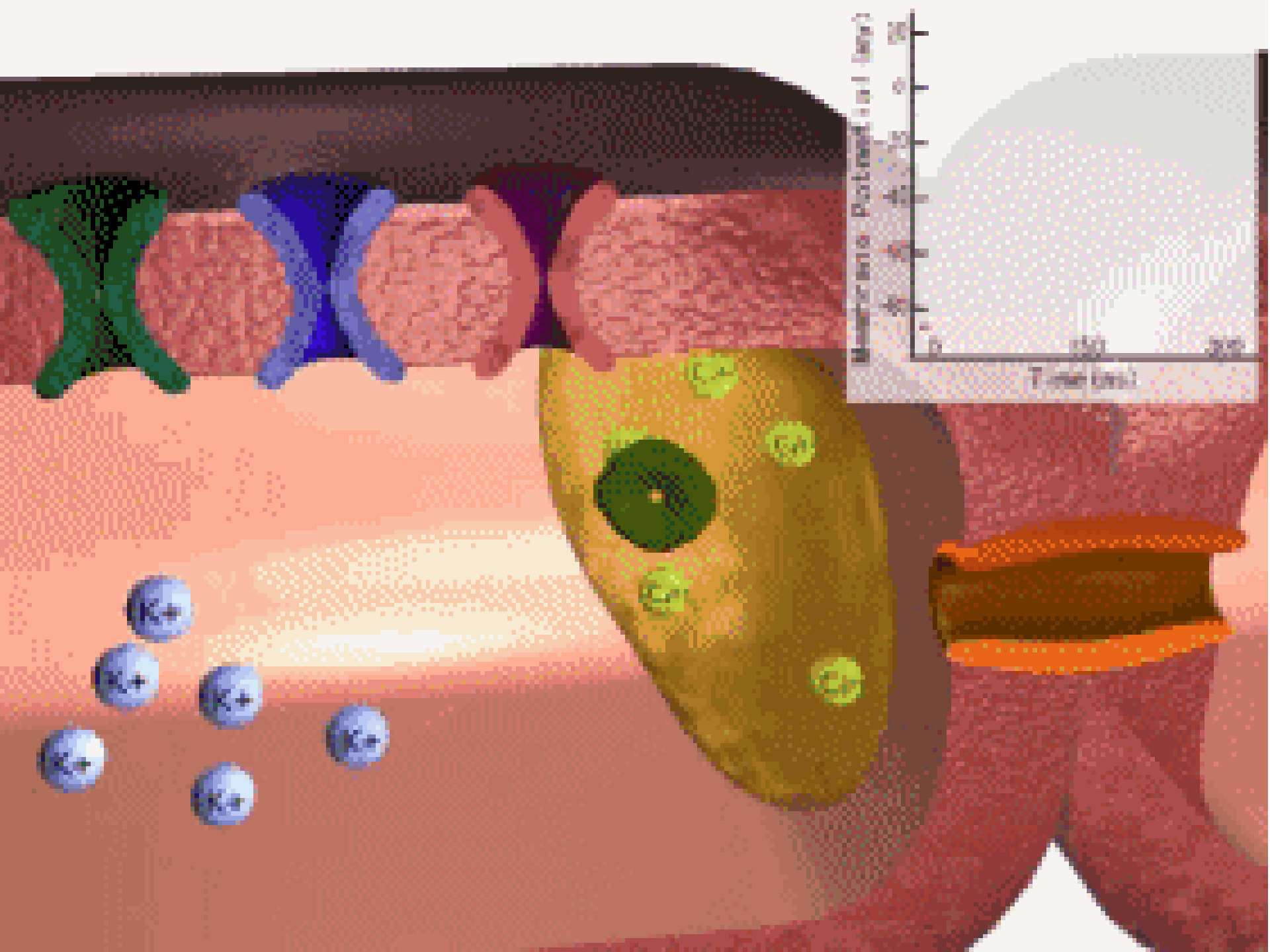


HIPERCALCEMIA

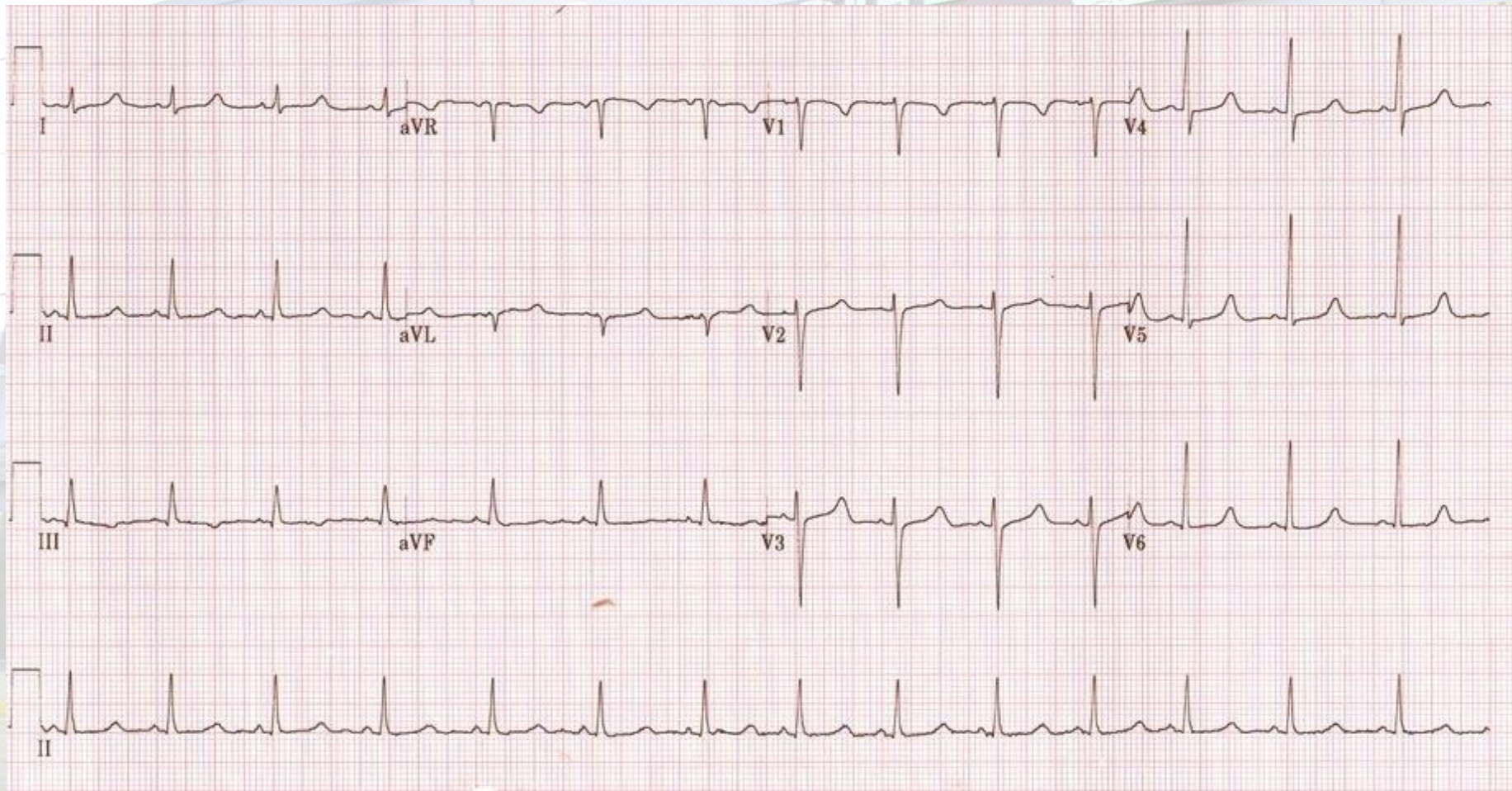


SEGMENTO ST QUASE AUSENTE

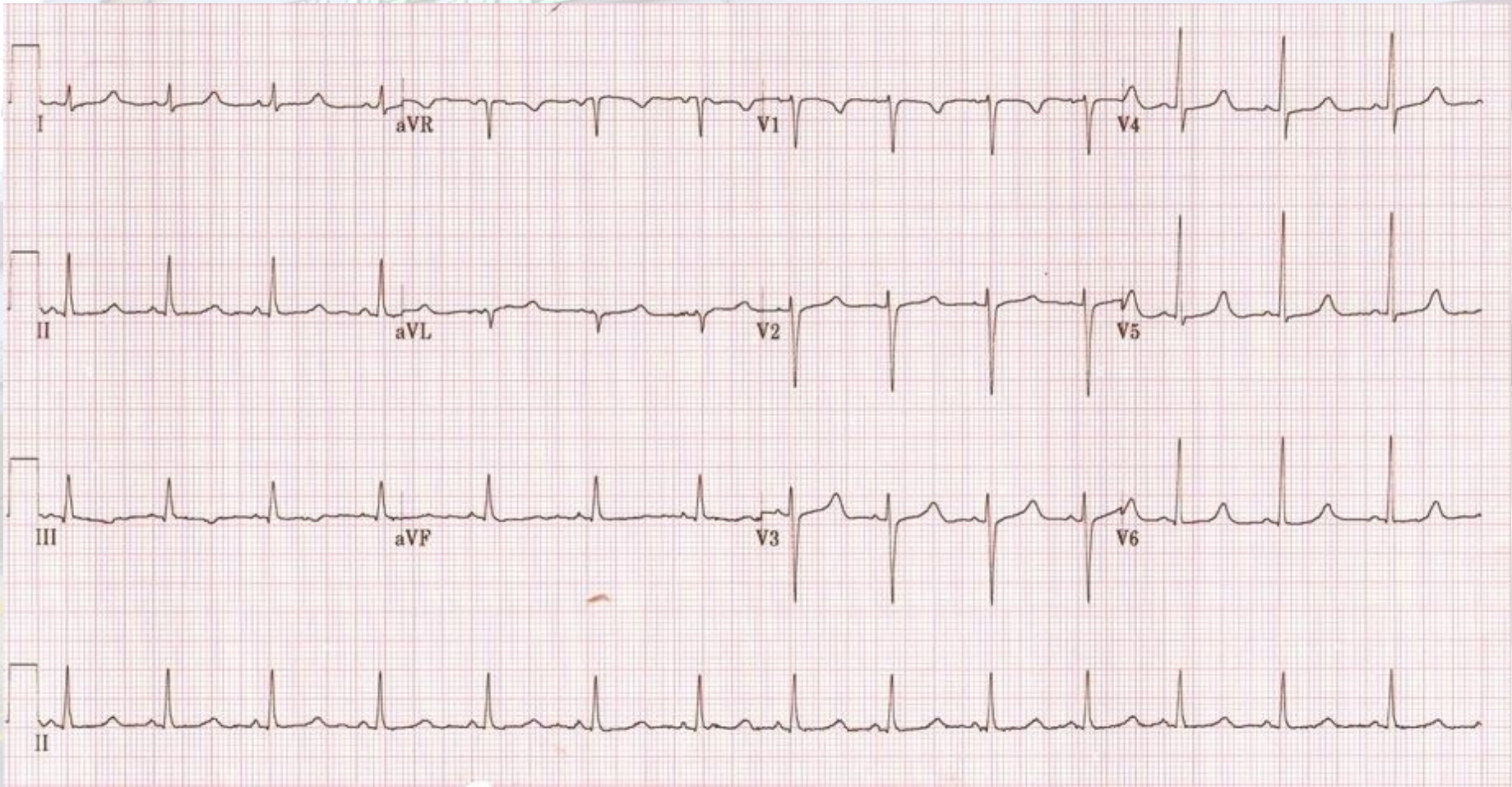




Y esto...?



QTc 500ms in a patient with hypoparathyroidism (post thyroidectomy) and serum corrected calcium of 1.40 mmol/L



Electrocardiograma en la hipercalcemia e hipocalcemia

A. Normal

Intervalo QT normal: 0,36 seg
(dentro del rango QT_C de 0,32-0,39 seg para una frecuencia cardíaca de 80)



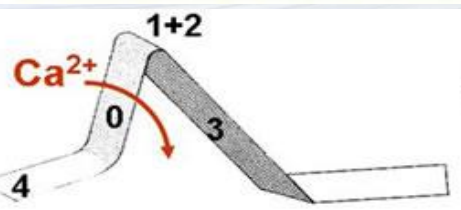
B. Hipercalcemia

Intervalo QT anómalo: 0,30 seg
(inferior al rango QT_C de 0,32-0,39 seg para una frecuencia cardíaca de 80)

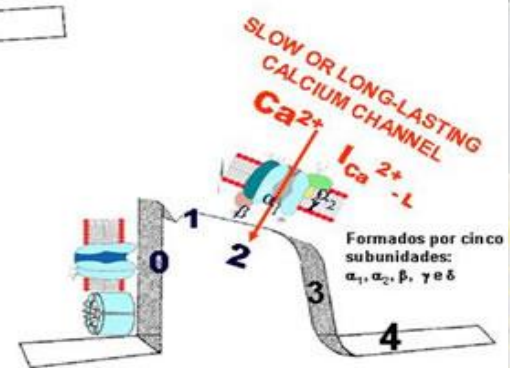


C. Hipocalcemia

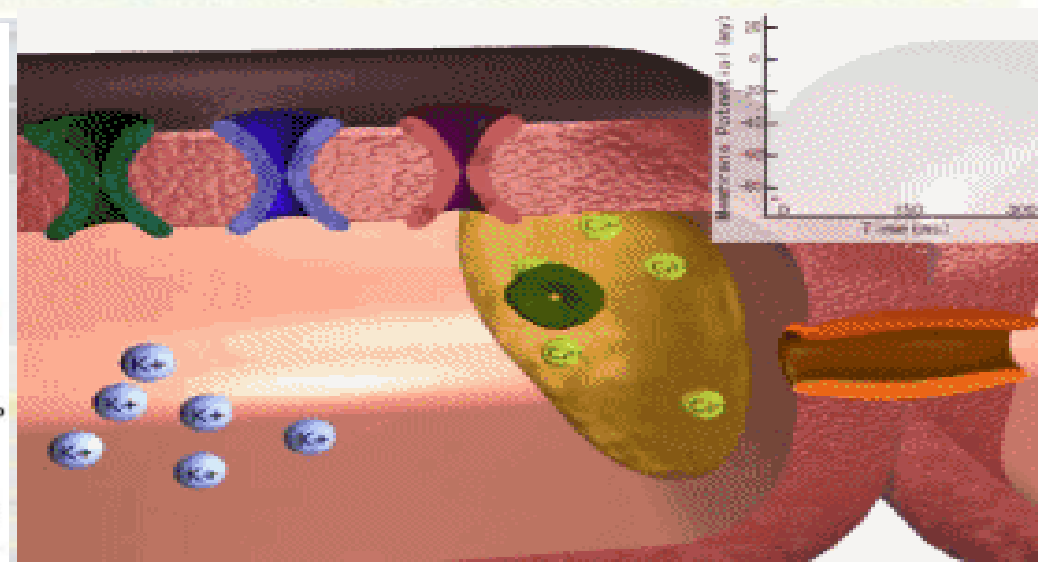
Intervalo QT anómalo: 0,44 seg
(superior al rango QT_C de 0,32-0,39 seg para una frecuencia cardíaca de 80)

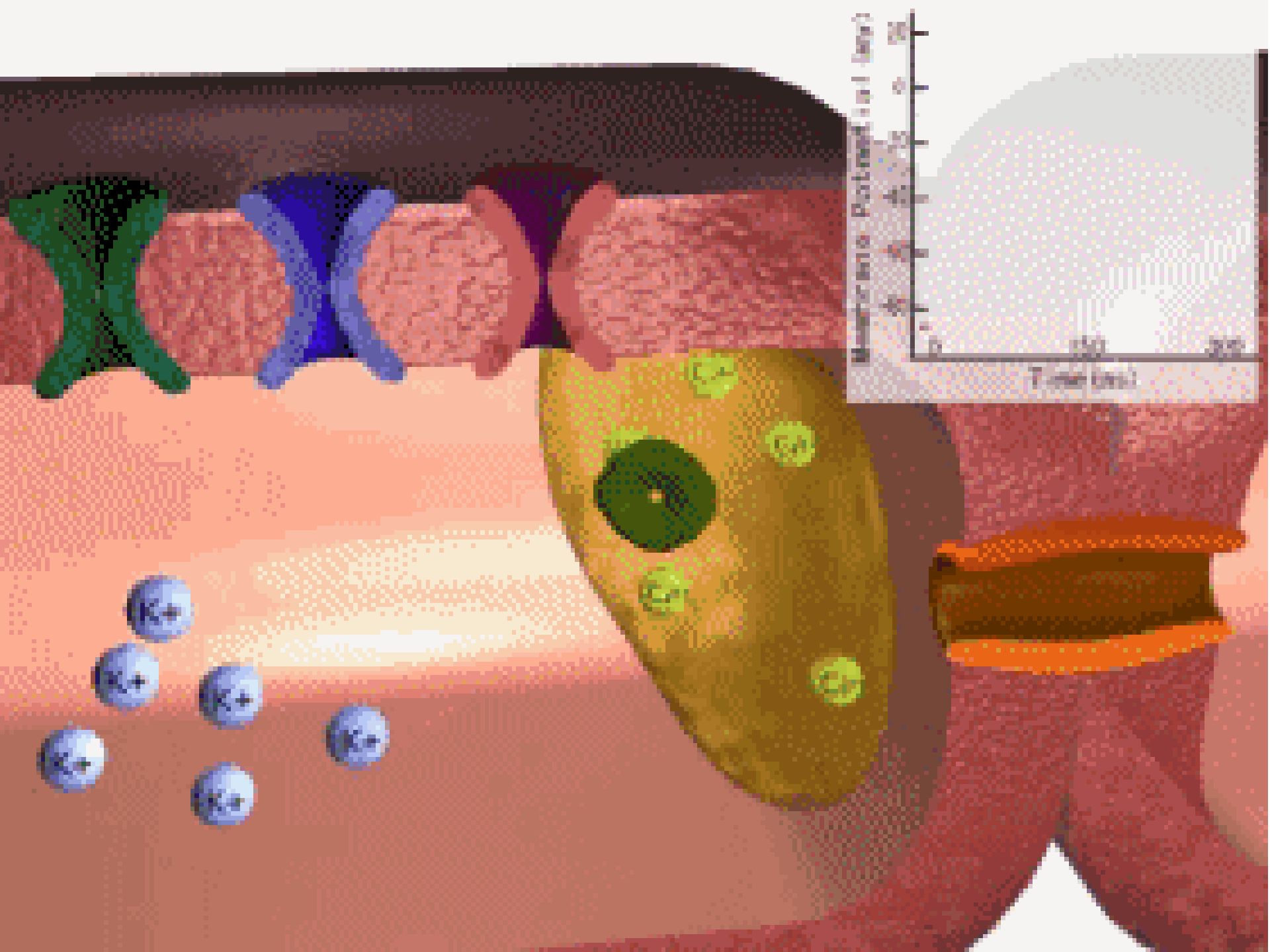


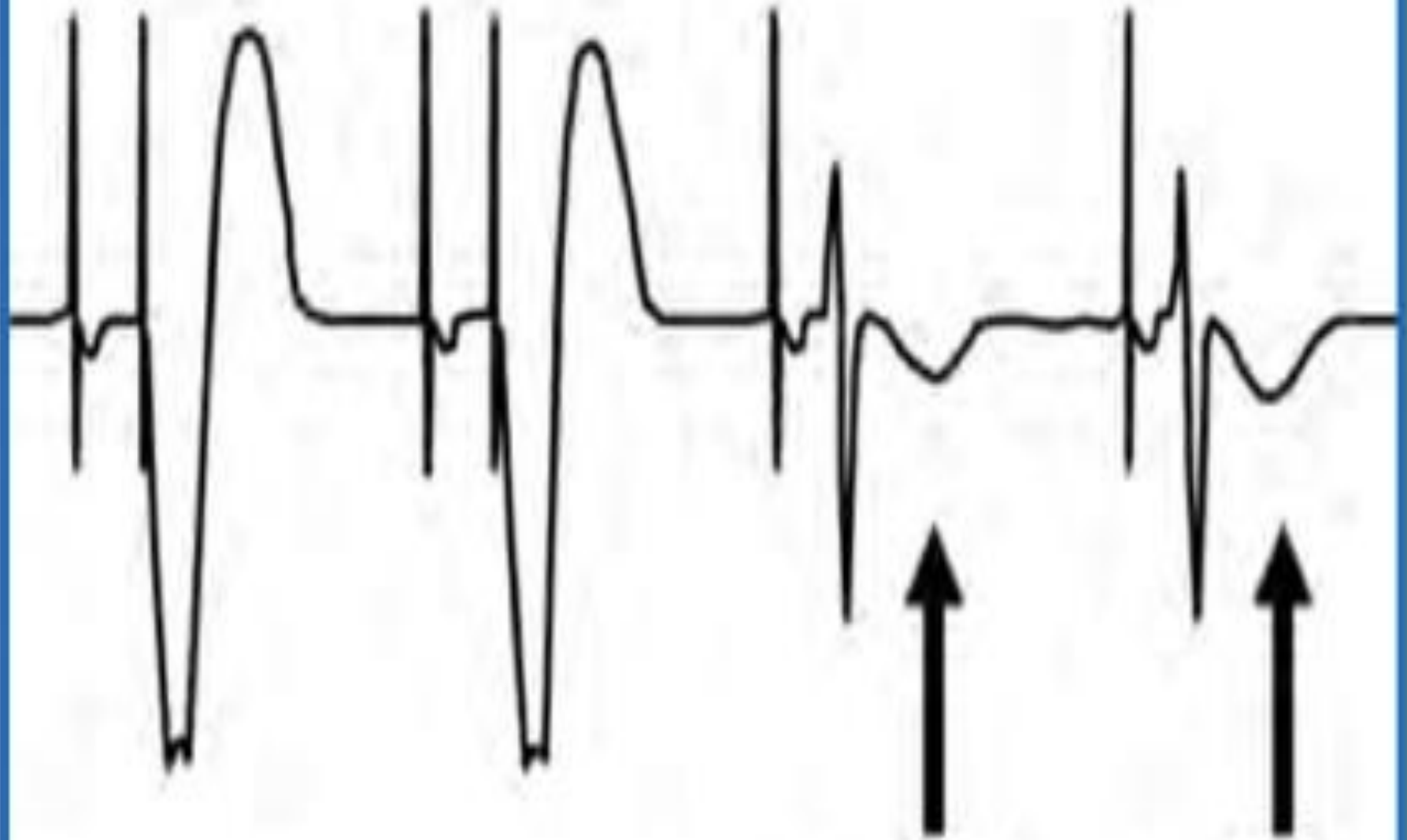
FIBRA LENTA



FIBRA RÁPIDA

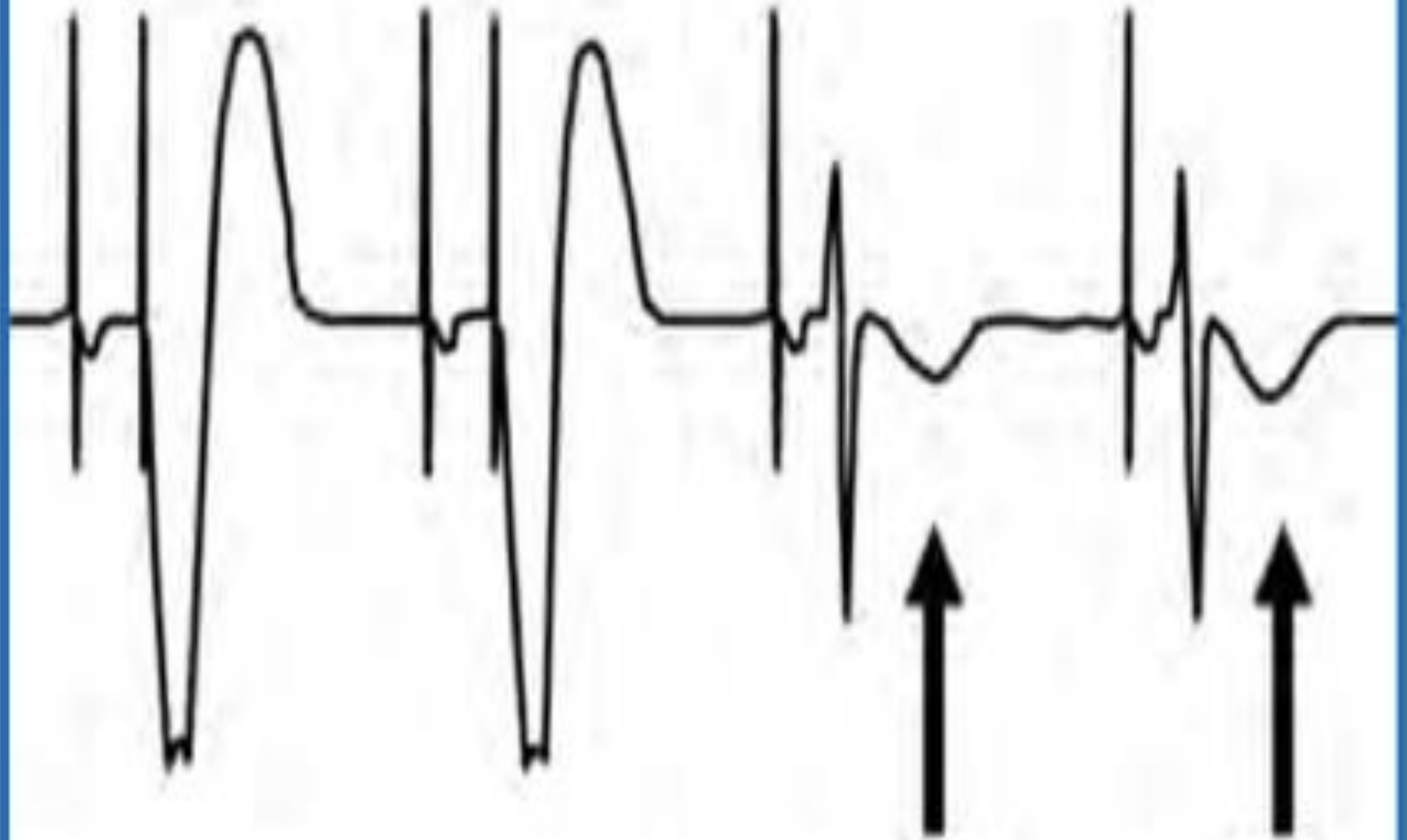






¿Que es?





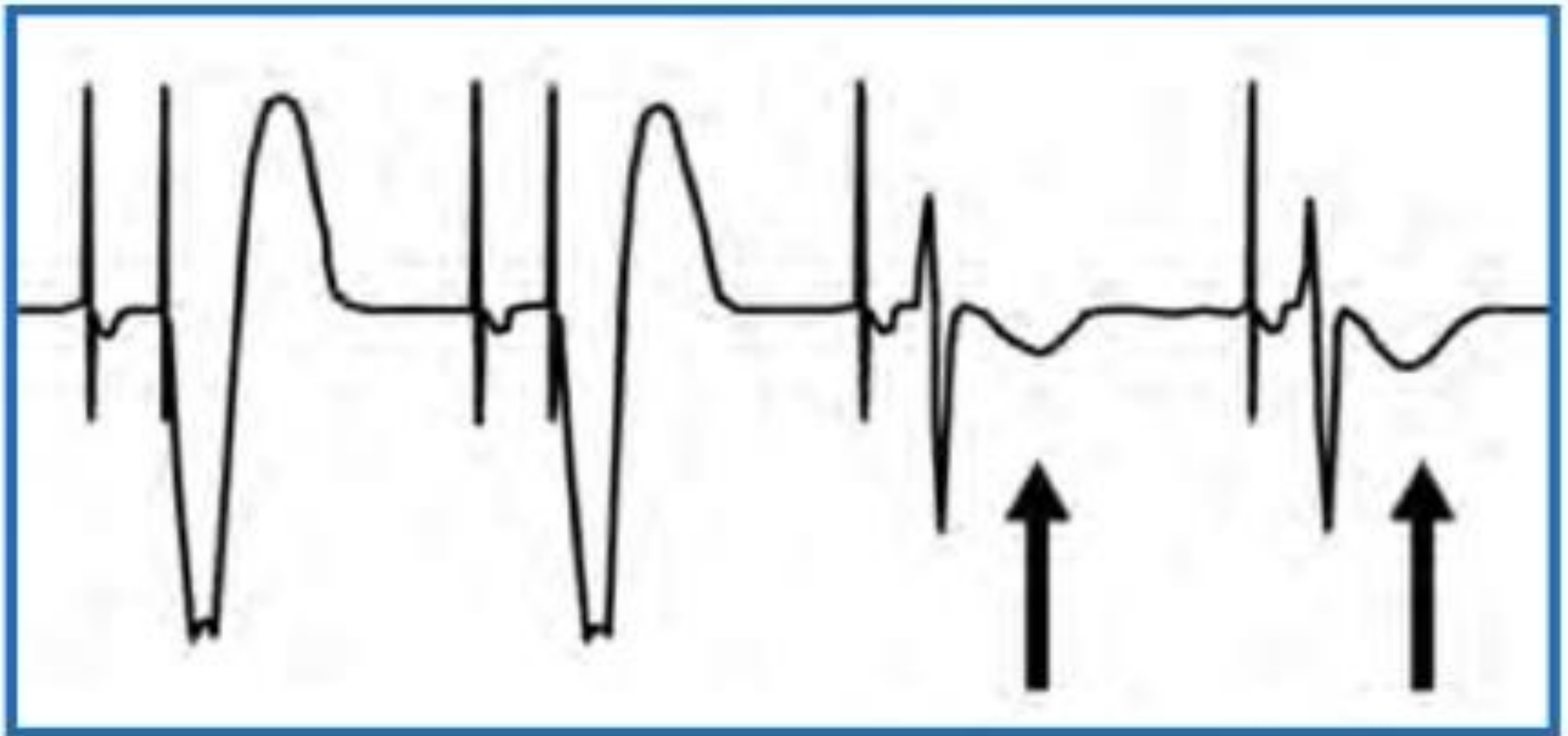


Fig. 2. Los 2 primeros latidos son estimulados, tanto en atrios como en ventrículos; los siguientes, solo en el atrio. Obsérvese que a pesar que la despolarización ventricular es intrínseca (es decir, ritmo propio sinusal), la morfología de la onda T es anormal (flechas) producto de la despolarización ectópica de los complejos precedentes.



**RETRASO
ADAPTATIVO DE LOS
CANALES IONICOS**

MEMORIA
ELECTROTONICA



RECONOCIMIENTO A NUESTROS MAYORES



Dr Marcel Elizari



Ex presidente de la Sociedad Argentina de Cardiología
Miembro de la Academia nacional de Medicina

