

Learning Objectives to Disclose:

- To **CRITIQUE** the various diagnostic modalities used in the evaluation of LQTS and **UNDERSTAND** their limitations



MAYO CLINIC WINDLAND SMITH RICE SUDDEN DEATH GENOMICS LABORATORY

Conflicts of Interest to Disclose:

- Consultant – Boston Scientific, Gilead Sciences, Medtronic, St. Jude Medical, and Transgenomic/FAMILION
- Royalties – Transgenomic/FAMILION

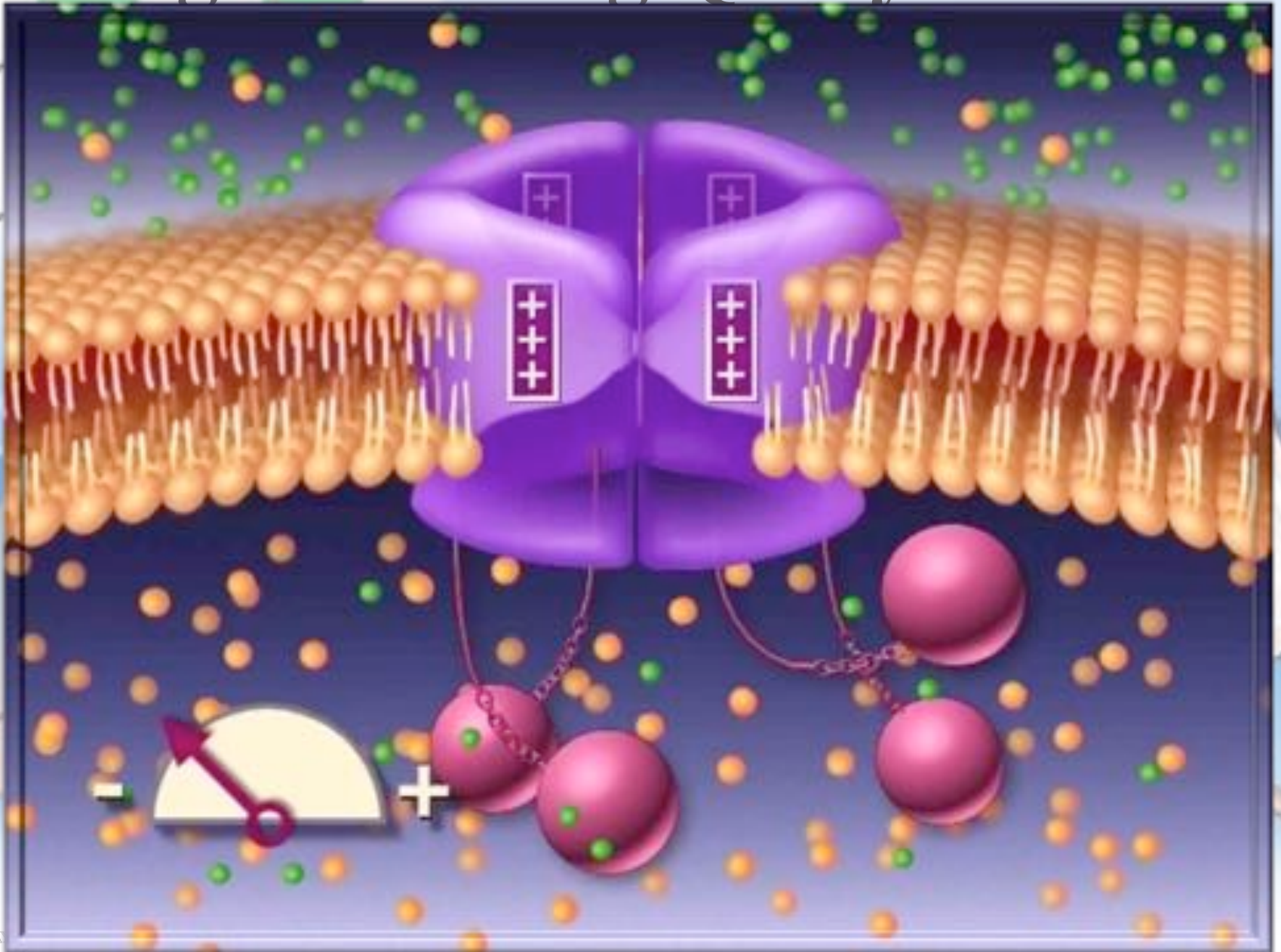
Congenital Long QT Syndrome

- ♥ 1957 – first clinical description – JLNS
- ♥ 1960s – Romano-Ward syndrome
- ♥ 1983 – “Schwartz/Moss score”
- ♥ 1991 – first LQTS chromosome locus
- ♥ March 10, 1995 – birth of cardiac channelopathies

Torsades de pointes



Congenital Long QT Syndrome



Congenital Long QT Syndrome

August 2011

**HRS/EHRA Consensus Statement on the
State of Genetic Testing for the
Channelopathies and Cardiomyopathies**

Ackerman, Priori, et al. *Heart Rhythm* 8:1308-1339, 2011

channelopathies

May 2013

**HRS/EHRA/APHRS Expert Consensus Statement
on the Diagnosis and Management of Patients
with Inherited Primary Arrhythmia Syndromes**

Priori, Wilde, et al. *Heart Rhythm* 10:1932-1963, 2013

Long QT Syndrome

Expert Consensus Recommendations on Diagnosis

1. LQTS is diagnosed:

- a) In the presence of an LQTS risk score ≥ 3.5 in the absence of a secondary cause for QT prolongation, *and/or*
- b) In the presence of an unequivocally pathogenic mutation in one of the LQTS genes, *or*
- c) In the presence of a QTc ≥ 500 ms in repeated 12-lead ECG and in the absence of a secondary cause for QT prolongation.

LQTS Diagnostic Criteria (1993-2011)

- aka "The Schwartz Score" -

Electrocardiographic Findings

	<u>Points</u>
A QTc	
≥ 480 ms	3
460-479 ms	2
450-459 ms (in males)	1
B QTc 4 th minute of recovery from stress test ≥ 480 ms	1
C Torsades de Pointes (TdP)	2
D T wave abnormalities	1
E No T wave abnormalities	1
F Low heart rate (bpm)	1/2

The Story is King!

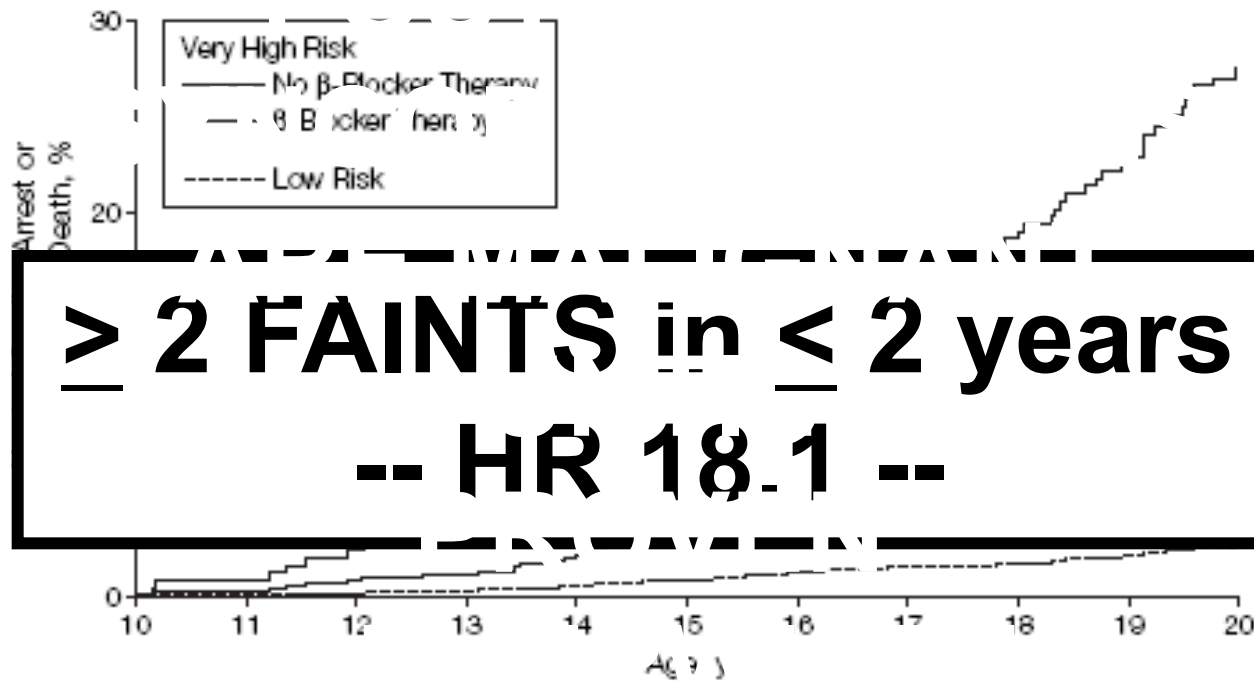
Clinical History

≤ 1 : Low Probability of LQTS	2
1.5 to 3: Intermediate Probability of LQTS	1
≥ 3.5 : High Probability of LQTS	1/2



“Don’t Blow Off a Blackout”

Figure 2. Cox Model-Based Time to First Aborted Cardiac Arrest or Sudden Cardiac Arrest Between Ages 10 and 20 Years for Females with Long-QT Syndrome



Hobbs et al. (LQTS Registry). Risk of aborted cardiac arrest or sudden cardiac death during adolescence in the Long QT Syndrome. *JAMA* 296:1249-1254, 2006

Glamour March 2000

Distinguish Be a Detective from the Sudden Death Warning Sign

~ 40% of the patients that came to Mayo Clinic with the diagnosis of LQTS left without it!

Taggart ... Ackerman. *Circulation* 115:2613-2620, 2007

WHEN?

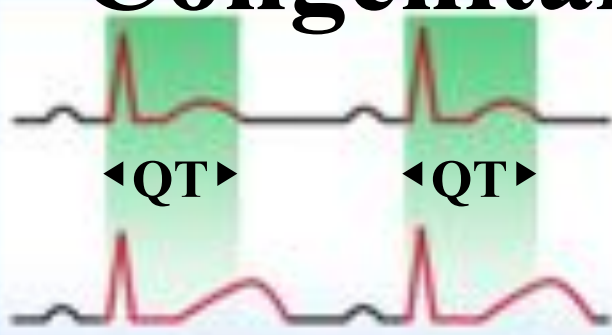
Vanilla Faint + Borderline QT \neq Possible LQTS

WHERE?

QT Inflation Secondary to U Wave Inclusion

WHY?

Congenital Long QT Syndrome



Normal QT interval

Prolonged QT

1. Syncope
2. Seizures
3. Sudden

How to Diagnose it in 2015?
- The 12-Lead ECG -

Torsades de pointes



LQTS Diagnostic Criteria (1993-2011)

- aka “The Schwartz Score” -

Electrocardiographic Findings

	<u>Points</u>
A QTc	
≥ 480 ms	3
460-479 ms	2
450-459 ms (in males)	1
B QTc 4th minute of recovery from stress test ≥ 480 ms	1
C Torsade de pointes	2
D T wave alternans	1
E Notched T wave in 3 leads	1
F Low heart rate for age ($< 2^{\text{nd}}$ percentile)	1/2

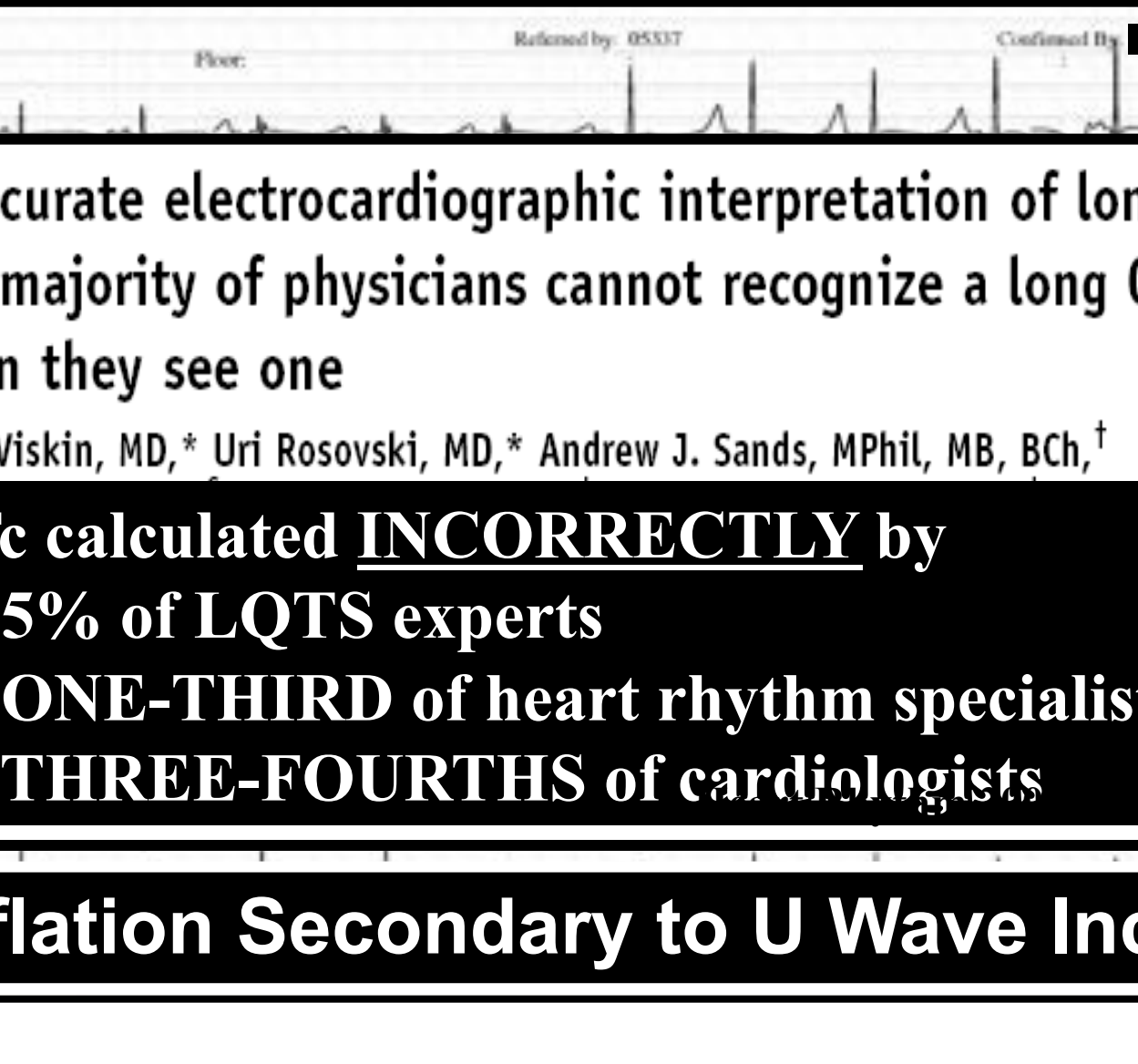
Clinical History

A Syncope	
With stress	2
Without stress	1
B Congenital deafness	1/2

Family History

A Family members with definite LQTS	1
B Unexplained sudden cardiac death < 30 years in near relative	1/2

The ECG and LQTS



Referred by: 05537 Confirmed By: [REDACTED]

I
II
III
II
VI

Inaccurate electrocardiographic interpretation of long QT:
The majority of physicians cannot recognize a long QT
when they see one

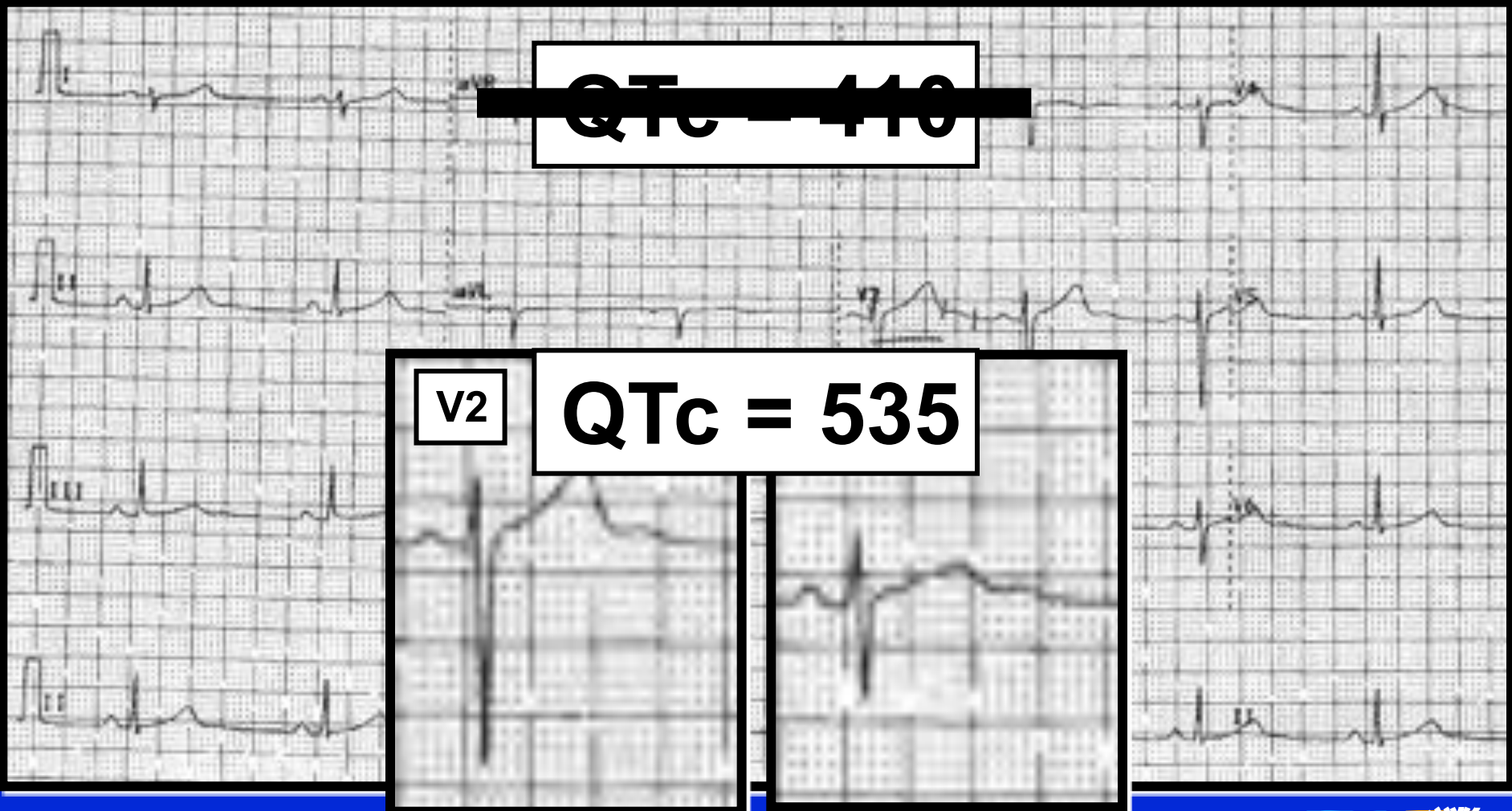
Sami Viskin, MD,* Uri Rosovski, MD,* Andrew J. Sands, MPhil, MB, BCh,[†]

QTc calculated INCORRECTLY by

- < 5% of LQTS experts
- > ONE-THIRD of heart rhythm specialists
- > THREE-FOURTHS of cardiologists

QT Inflation Secondary to U Wave Inclusion

“QTc Inflation Due to U Wave Inclusion”



The QT Interval

02-AUG-2008 21:02:17

MAYO CLINIC-S-ED ROUTINE RECORD

25-NOV-1991 (16 yr)

Vent. rate

73 BPM

Female

PR interval

128 ms

0cm

Room

Loc:3

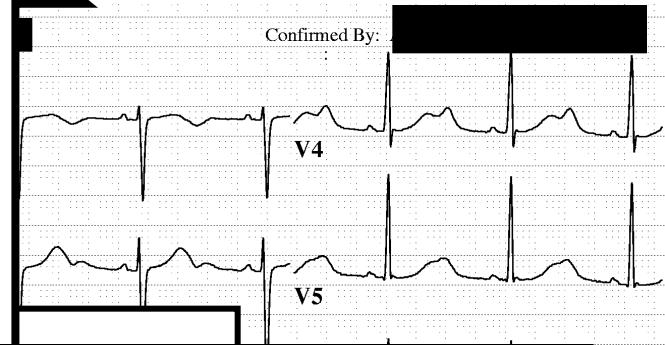
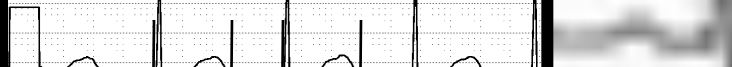
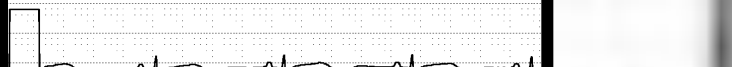
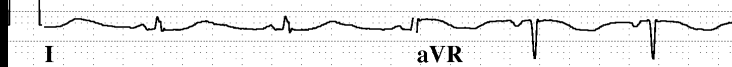
Prolonged QT Interval

560 ms

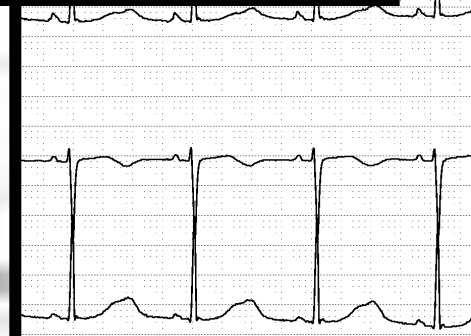
Section

Refer

Confirmed By:



This is the ECG, not



25mm/s 10mm/mV 100Hz 005E 12SL 237 CID: 1

16:15 09-DEC-2008 ORDER: 208107459 ACCOUNT: 432377

Page 1 of

“... the Rest of her Story”

Photo used with permission

MAY/JUNE 2010
COMPLIMENTARY



RW

Purses to purchase

Locally-grown food

What public defenders fight for

Saved: Stephanie Cors resuscitates her daughter

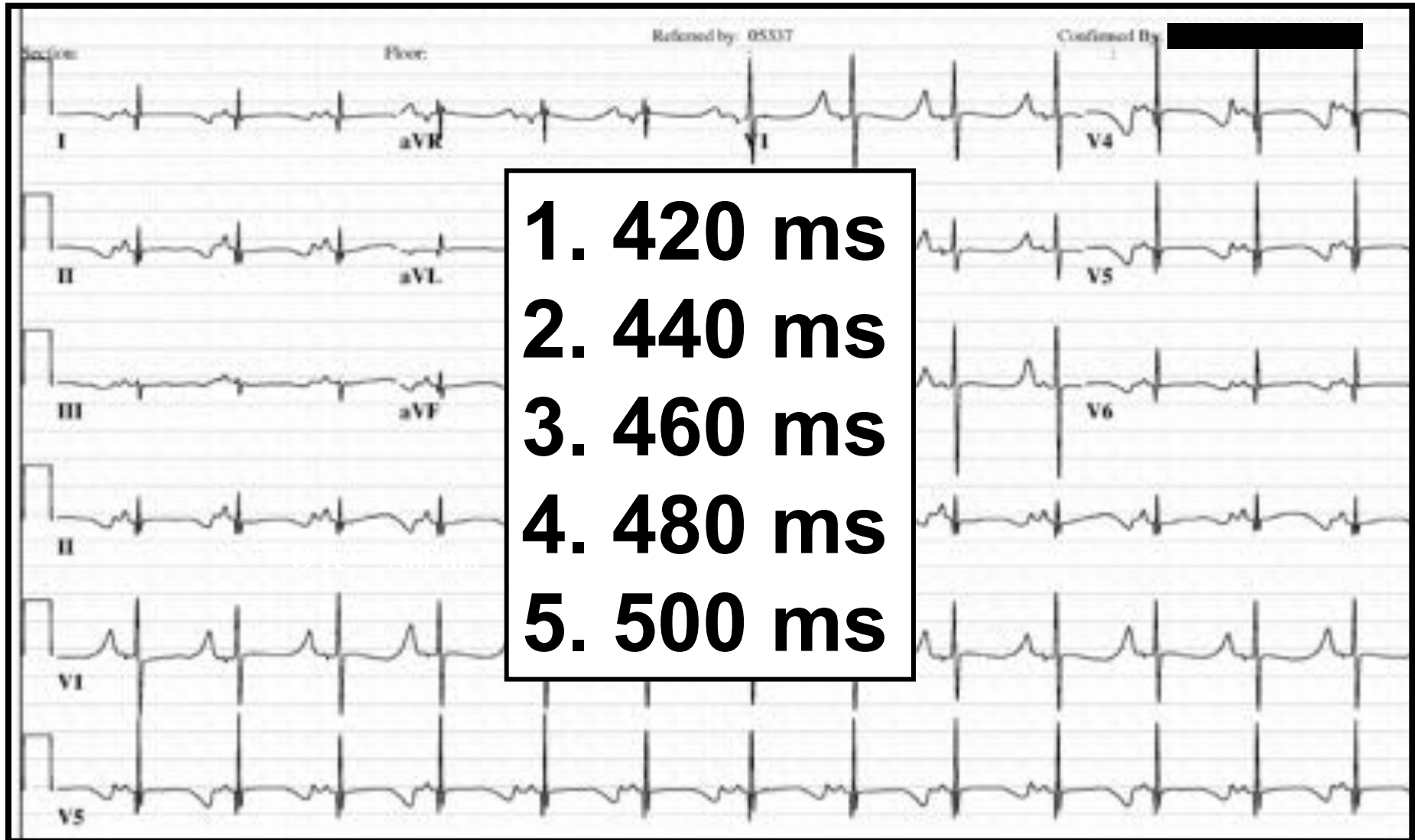
Labor of love: midwives and doulas

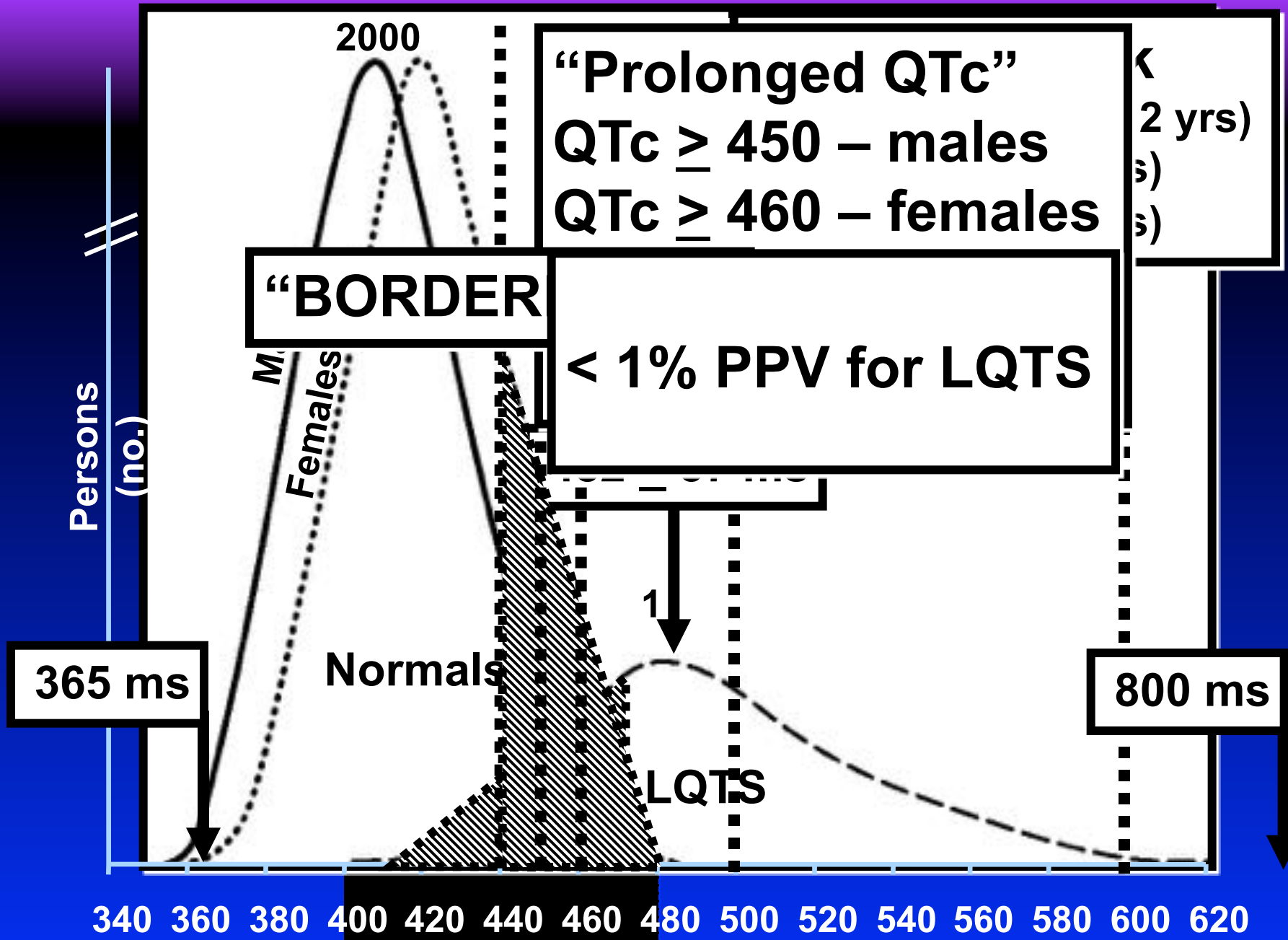
Stephanie Cors

10 years
Since 2000

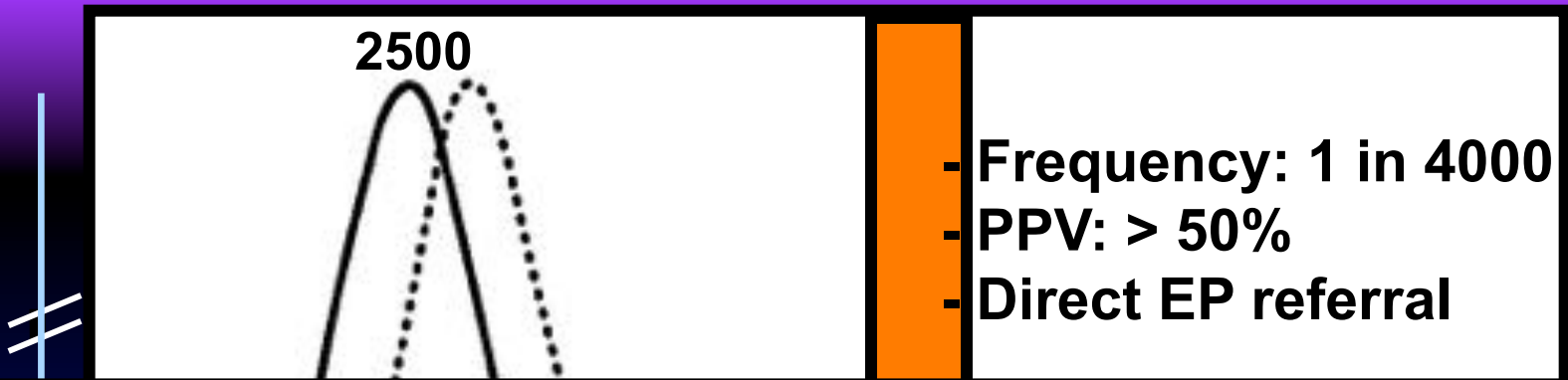
RWmagazine.com

I Think a QTc > ___ is Too Long

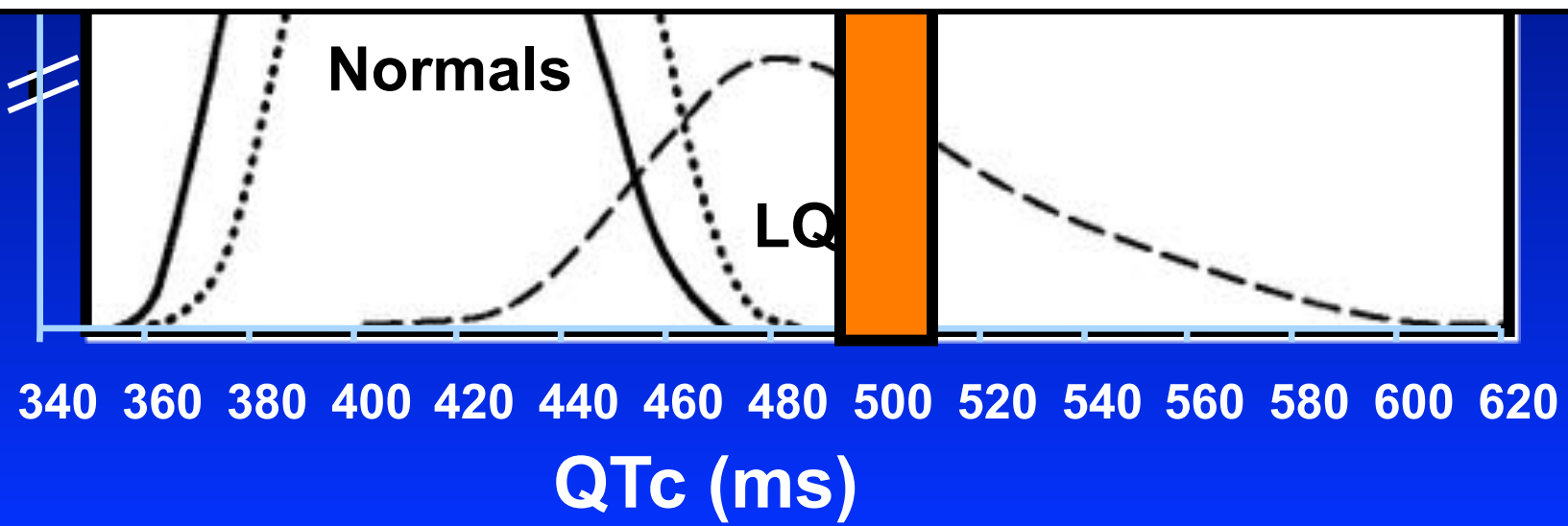




From the LQTS Registry. *JAMA* 2008, *Circulation* 2008, *Circulation* 2008



**Do NOT disrespect
the 500 ms line!**



Long QT Syndrome

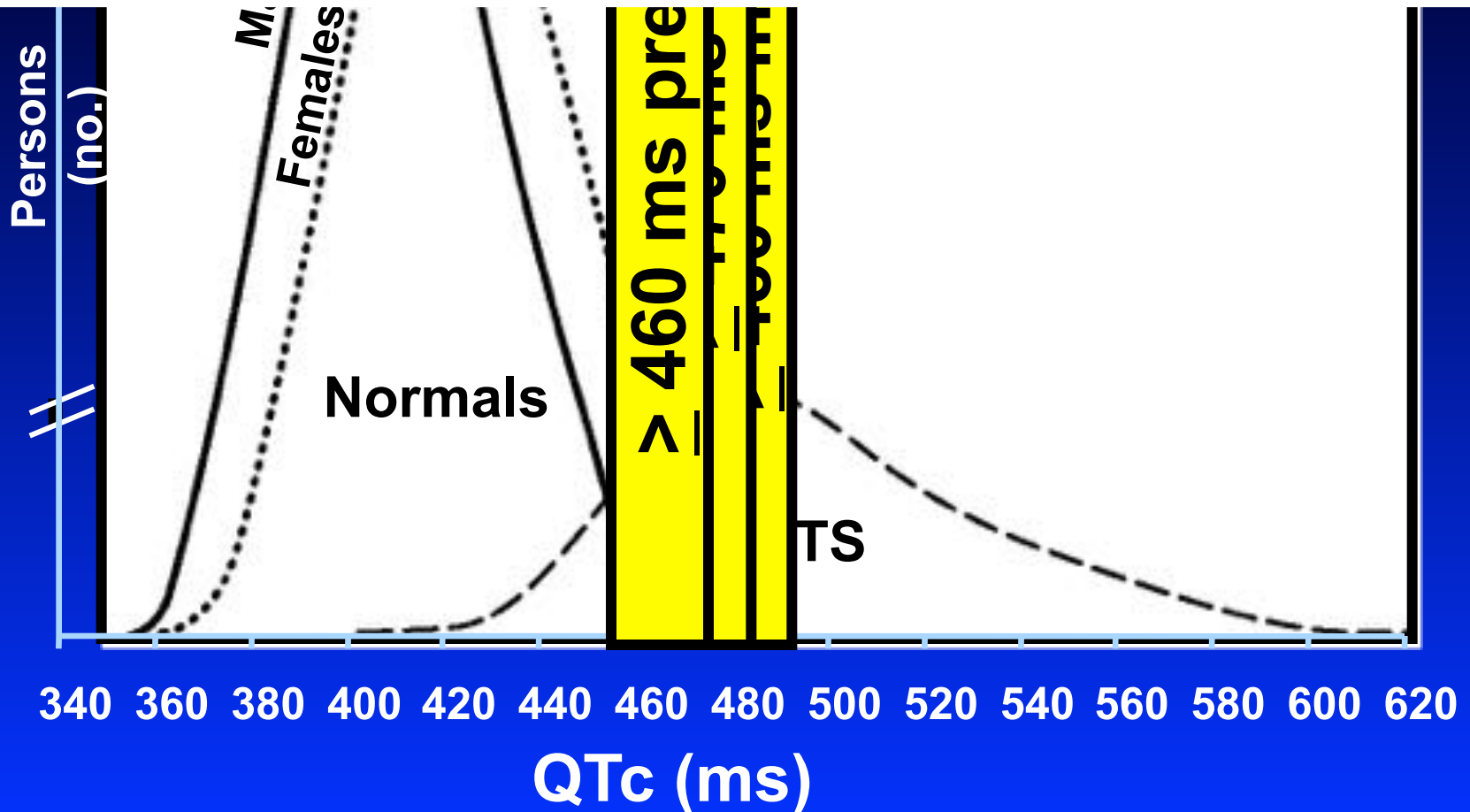
Expert Consensus Recommendations on Diagnosis

1. LQTS is diagnosed:

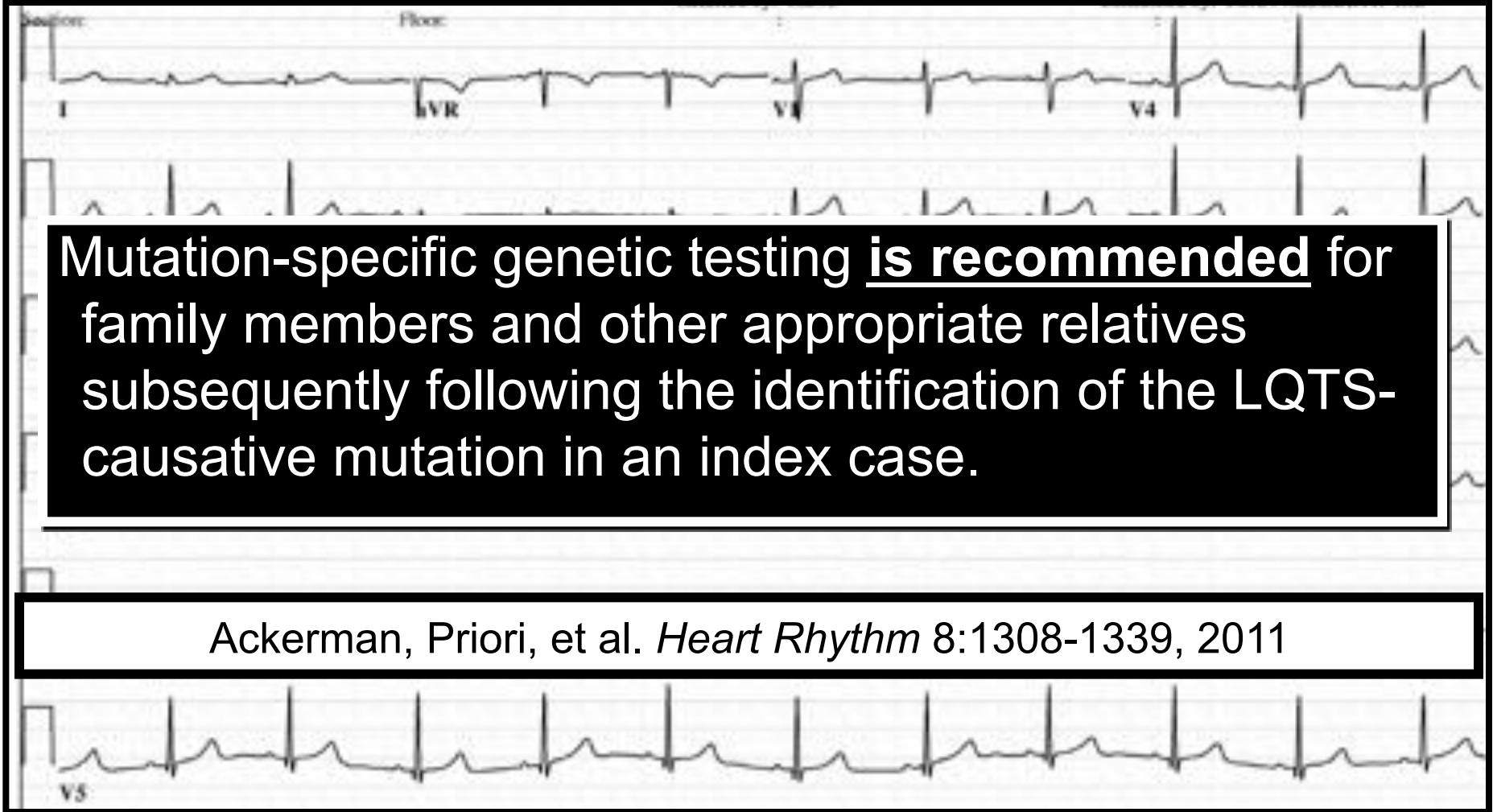
- a) In the presence of an LQTS risk score ≥ 3.5 in the absence of a secondary cause for QT prolongation, *and/or*
- b) In the presence of an unequivocally pathogenic mutation in one of the LQTS genes, *or*
- c) In the presence of a QTc ≥ 500 ms in repeated 12-lead ECG and in the absence of a secondary cause for QT prolongation.

2500

Remember, an intermediate probability
“Schwartz score” for LQTS
is **ONLY** a 10% chance!



The ECG and LQTS

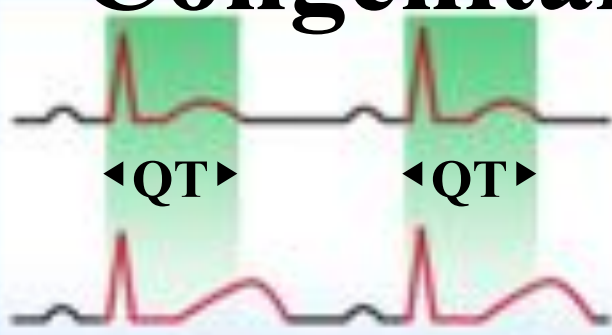


Mutation-specific genetic testing is recommended for family members and other appropriate relatives subsequently following the identification of the LQTS-causative mutation in an index case.

Ackerman, Priori, et al. *Heart Rhythm* 8:1308-1339, 2011


QTc = 415

Congenital Long QT Syndrome



Normal QT interval

Prolonged QT

- 
1. Syncope
 2. Seizures
 3. Sudden

**How to Diagnose it in 2015?
- Genetic Testing -**

Torsades de pointes

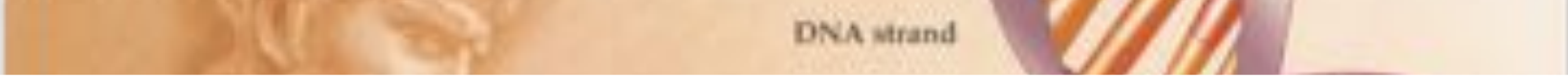


Congenital LQTS: How Should We Diagnose it in 2015?

Disease	Diagnostic	Prognostic	Therapeutic
LQTS	++++	++++	++
CPVT	+++	+	-
BrS	+	+	-
CCD	+	+	+
SQTS	+/-	-	-
AF	-	-	-
HCM	+++	++	+
ARVC	+	+/-	-
DCM	+/-	-	-
LVNC	+	-	-
RCM	+	+	+

Ackerman, Priori, et al. *Heart Rhythm* 8:1308-1339, 2011

Long QT Syndrome Genetic Testing



1. Comprehensive or LQT1-3 (KCNQ1, KCNH2, and SCN5A) targeted LQTS genetic testing is recommended for any patient in whom a cardiologist has established a strong clinical index of suspicion for LQTS based on examination of the patient's clinical history, family history, and expressed electrocardiographic (resting 12-lead ECGs and/or provocative stress testing with exercise or catecholamine infusion) phenotype.

Long QT Syndrome

Expert Consensus Recommendations on Diagnosis

1. LQTS is diagnosed:

- a) In the presence of an LQTS risk score ≥ 3.5 in the absence of a secondary cause for QT prolongation, *and/or*
- b) In the presence of an unequivocally pathogenic mutation in one of the LQTS genes, *or*
- c) In the presence of a QTc ≥ 500 ms in repeated 12-lead ECG and in the absence of a secondary cause for QT prolongation.

Genetic Testing's Achilles' Heel

- “Maybe” Test Result ?

“Possible Deleterious”

“Variant of Uncertain Significance (VUS)”

“Genetic Purgatory is a
Real Place and its
Scary!”

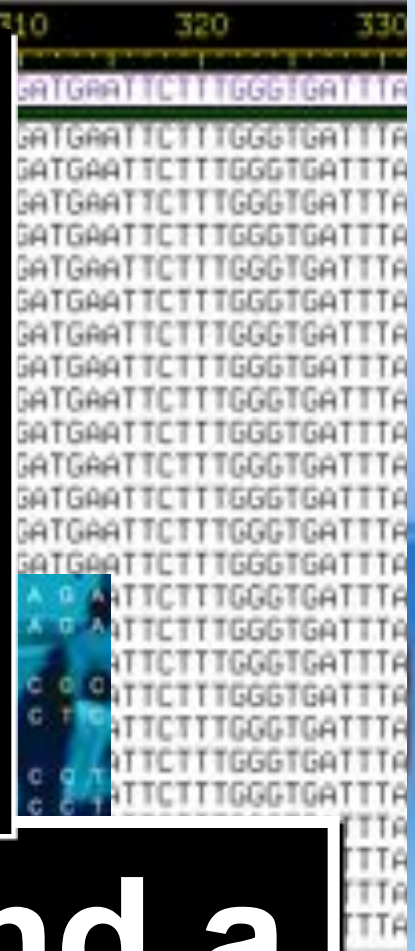


Congenital Long QT Syndrome: How Do We Diagnose it in 2015?

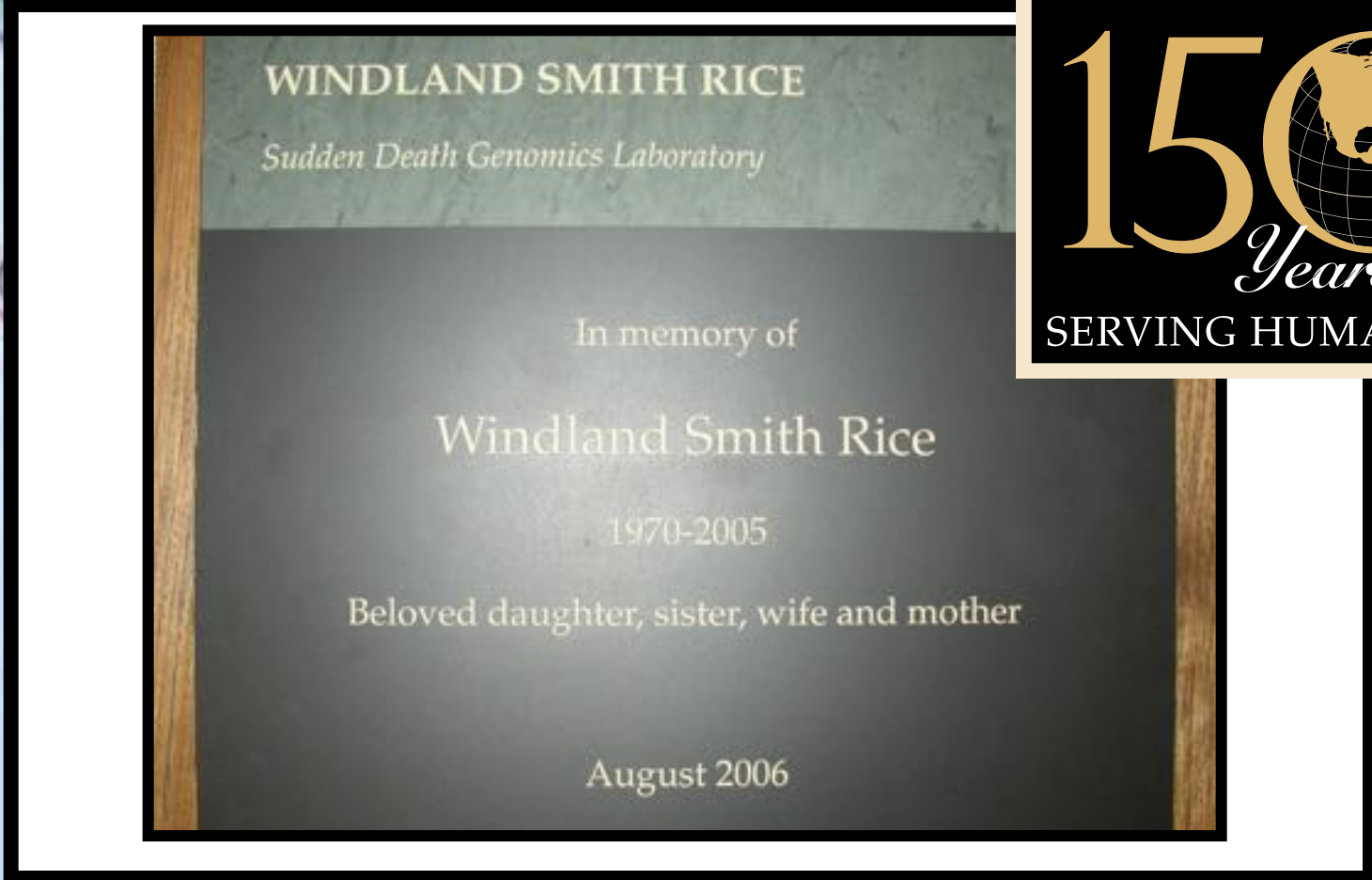
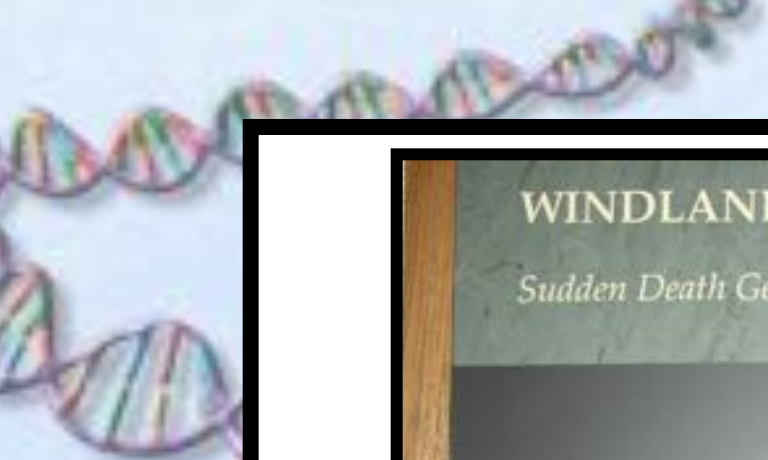
Take Home Points

1. Remember to “be a detective”, the story is KING/QUEEN! A wimpy story and a “borderline” QTc does NOT equal LQTS!
2. Remember to “avoid the tails”. Do NOT commit the sin of QT inflation due to U wave inclusion!
3. Take careful stock of the patient with a QTc \geq 500 ms!
4. Genetic tests are PROBABILISTIC tests! “X” does NOT always mark the spot. Genetic purgatory really exists!

Congenital Long QT Syndrome



**Be a Wise User and a
Wiser Interpreter!**



**Dr. Scholl Foundation, CJ Foundation for SIDS
Hannah Wernke Memorial Foundation**

**“To heal the sick and advance the science”
Sheikh Zayed Saif Mohammed Al Nahyan Fund
National Institutes of Health
Dr. Charles W. Mayo**