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Adult Complexities of the Channelopathies

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www.heartsinrhythm.ca



CIHR IRSC

Canadian Institutes of Health Research
Instituts de recherche en santé du Canada



HEART
AND STROKE
FOUNDATION



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Conflict of Interest

- Consulting: Medtronic
- Research: Boston Scientific, Medtronic
- People of BC: Clinical Income
- Organizations: Canadian Cardiovascular Society, Heart Rhythm Society, Hearts in Rhythm Organization
- Families of Sudden Death Victims: Paul Brunes Chair in Heart Rhythm Disorders

I am an open access person – for slides, e mail akrahn@mail.ubc.ca
(I will repeat that at the end)

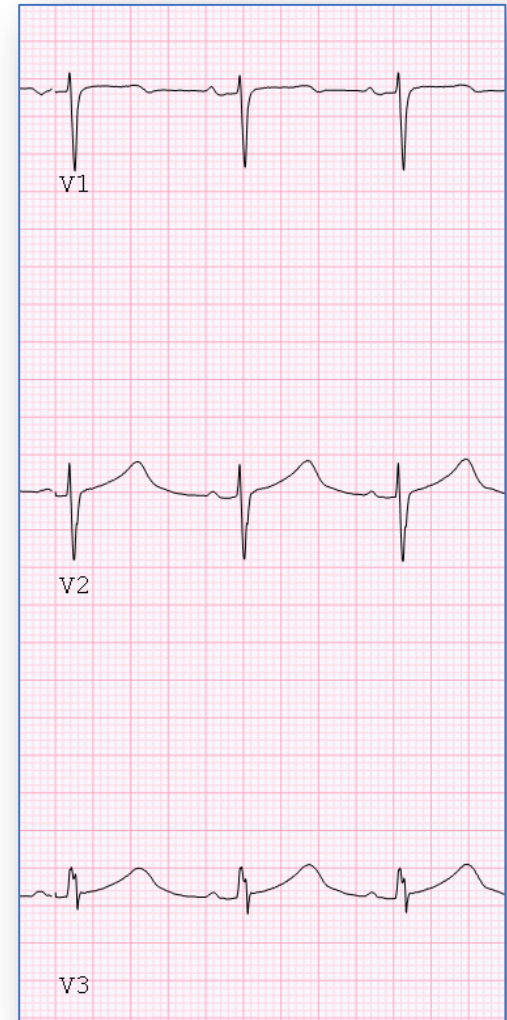


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The Bottom Line

- What are we talking about?
 - Long QT
 - Brugada
 - CPVT
 - Some uncommon odds and ends, IVF, Short QT, early repolarization



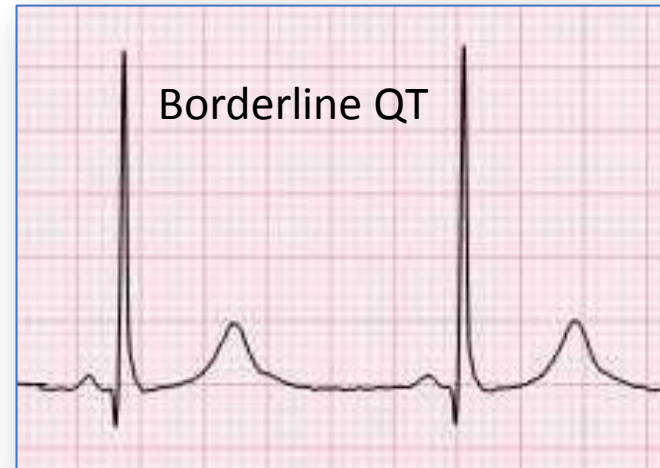
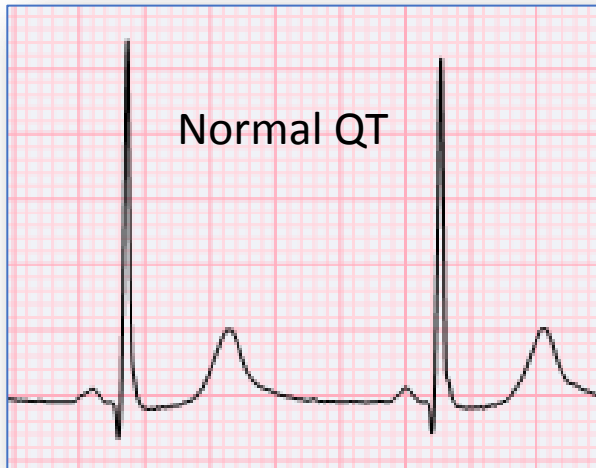


The Bottom Line

- Doesn't have to be complicated:
 1. You have a symptom, a family member or test that makes someone think you might have one of these conditions
 2. You go for heart tests, if they are suspicious, you have a genetic test, and you get a diagnosis
 3. You get lifestyle advice, maybe a beta blocker, maybe an ICD
 4. And its all good
- If we are lucky, this happens half the time

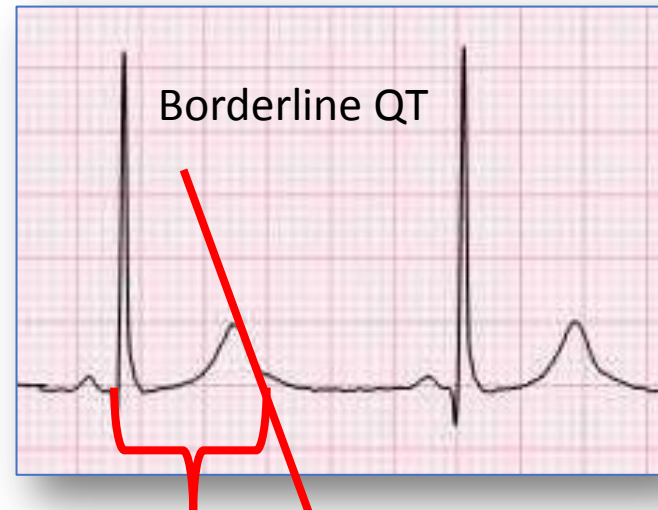
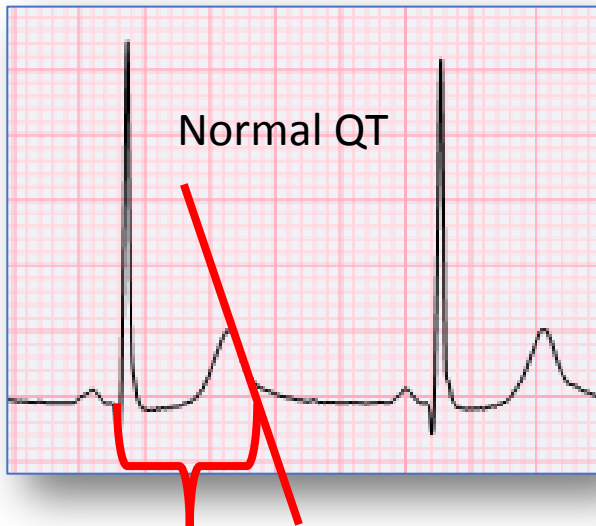
Lets look at an example - Annie

- 24 year old female, mother died of breast cancer 2 years ago
- Cousin in Halifax recently fainted and was diagnosed with Long QT
- Dad urges his daughter to get tested, she finds us online and requests a referral
- She is well, working after graduating from University



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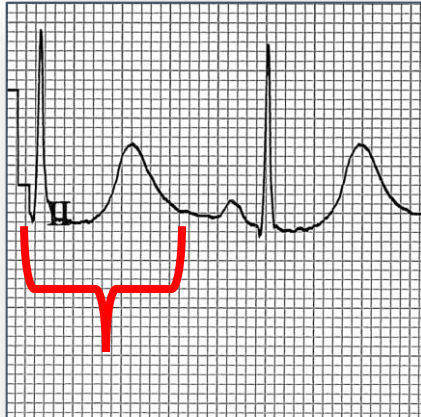


Next Steps (when it works out)

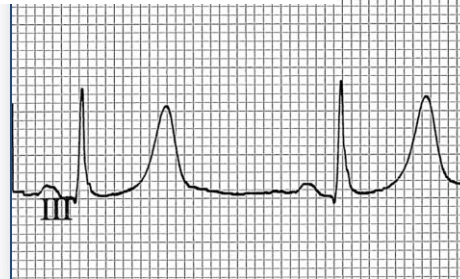
1. Comes to our clinic with her Dad and has a treadmill test
2. Meets the team and has a family tree compiled
3. Exercise test shows borderline QT that becomes abnormal
4. Told that she is likely to have Long QT, and that she would benefit from genetic testing
5. Given the SADS Long QT booklet, a list of medications to avoid
6. Consent for genetic testing and the national Long QT registry
7. Leaves a spit or blood sample
8. Takes the genetic counsellor's card and contacts her with questions
9. Genetic results from Dr. Gardiner's patient is used to test our patient that confirms Long QT, goes on a beta blocker



A Little More Complicated



SAME LONG QT MUTATION



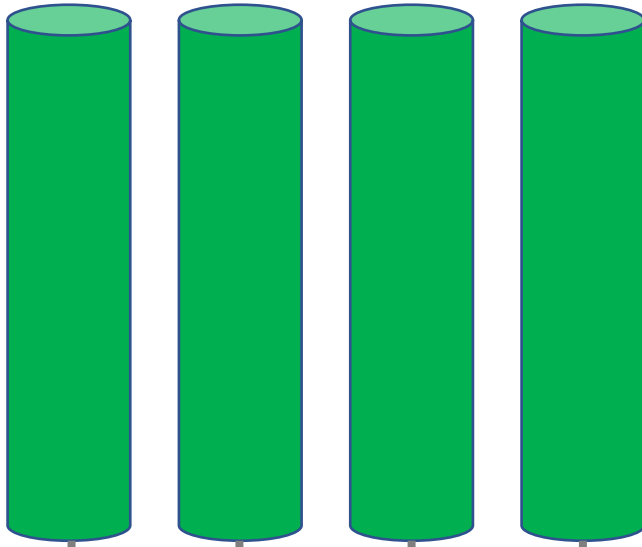
21 yo male
worrisome fainting

23 yo brother
asymptomatic

QT Gene

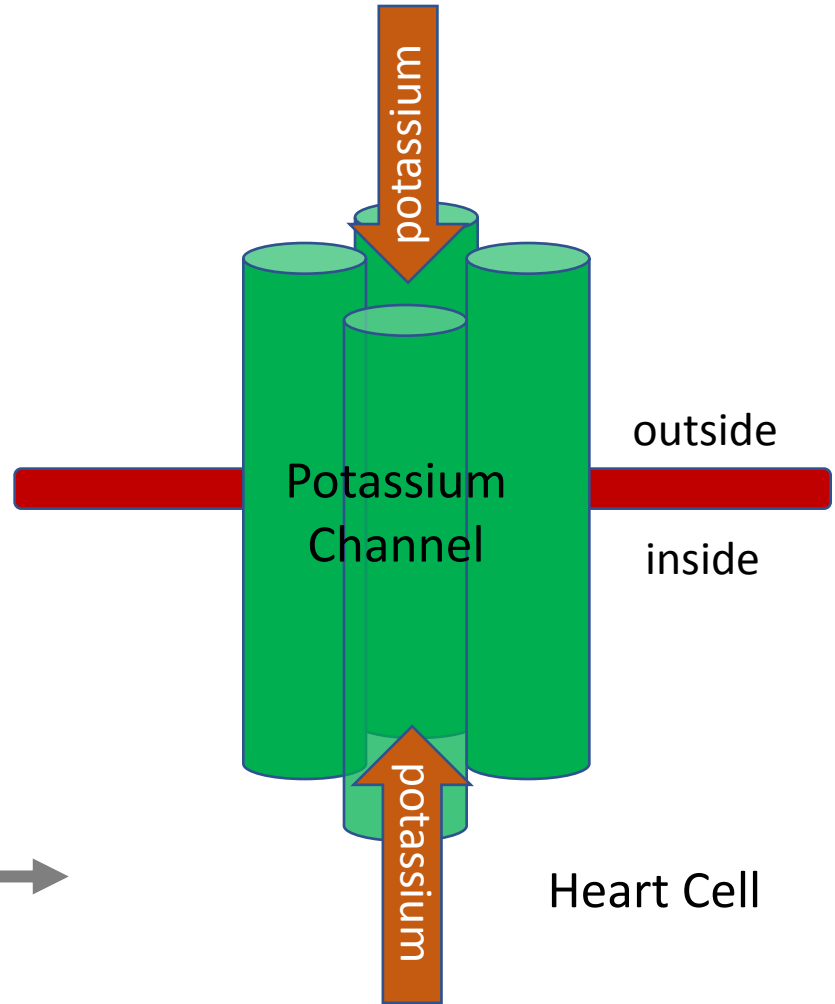


translator



assembler

Our QT Channels



Crude Schematic

mutant

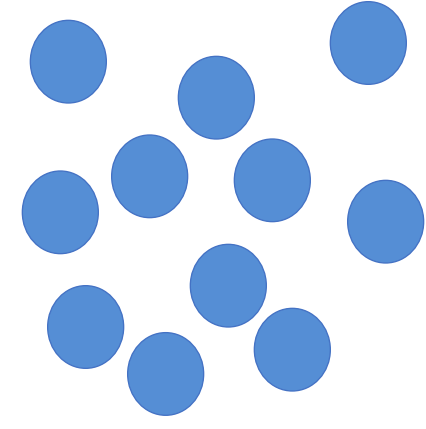


+

GG translator allele



=



2 strands:

normal

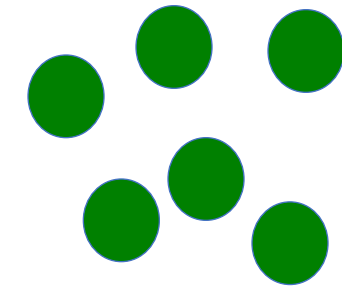


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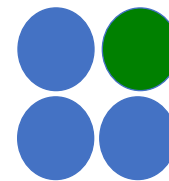
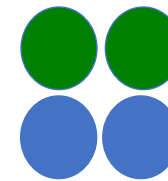
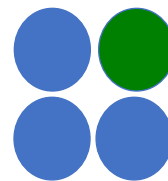
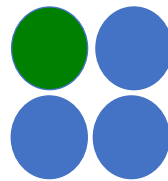
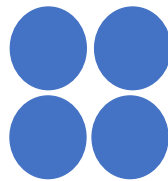
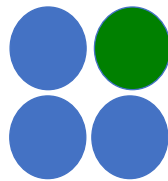
AA translator allele



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Assembly into
tetramers



Lots of mutant subunits – poor channel function – longer QT

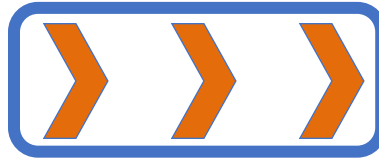
Crude Schematic

mutant

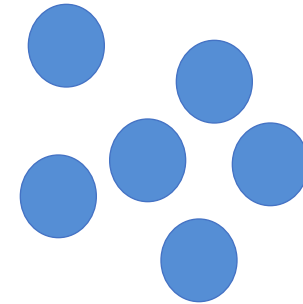


+

AA translator allele



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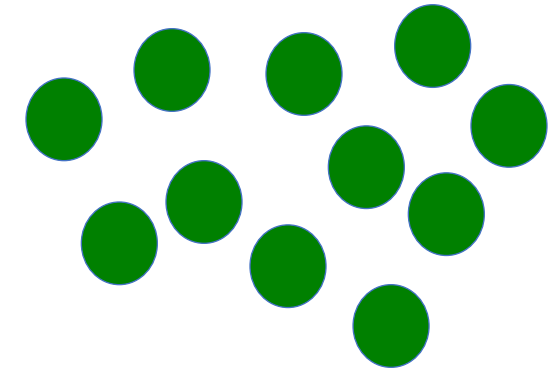


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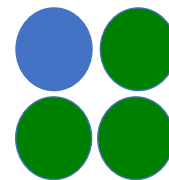
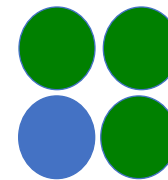
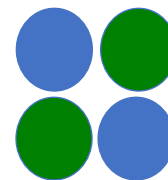
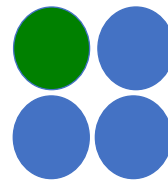
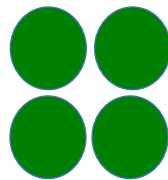
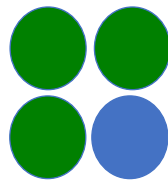
GG translator allele



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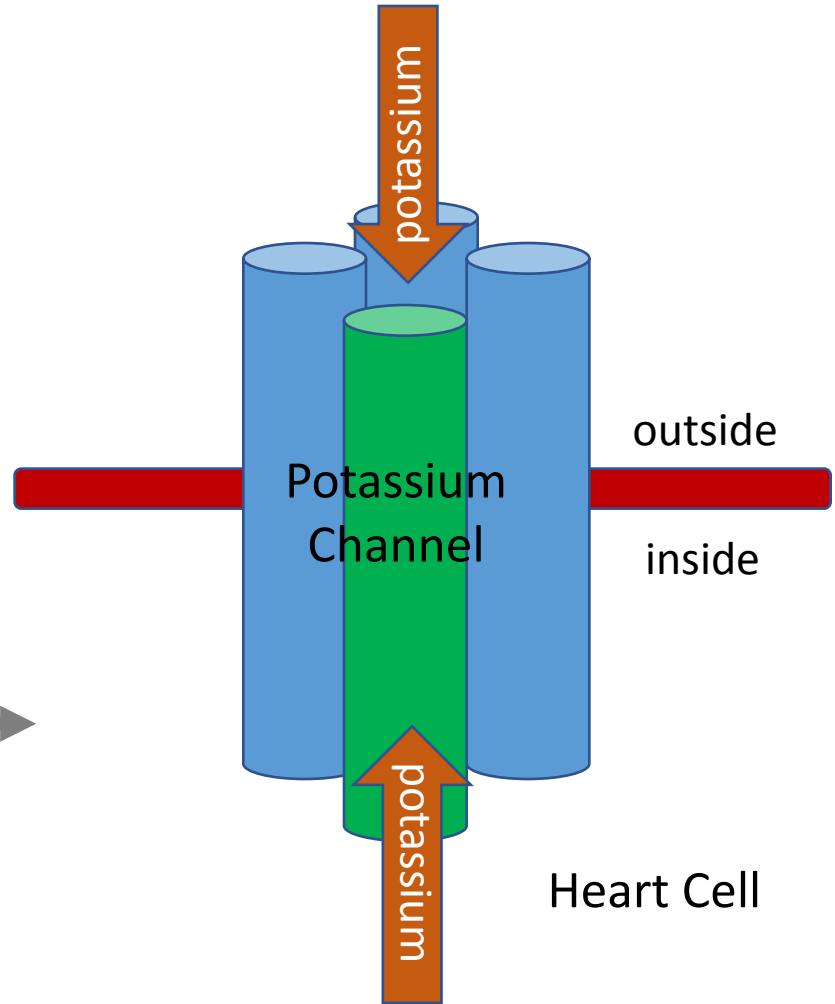
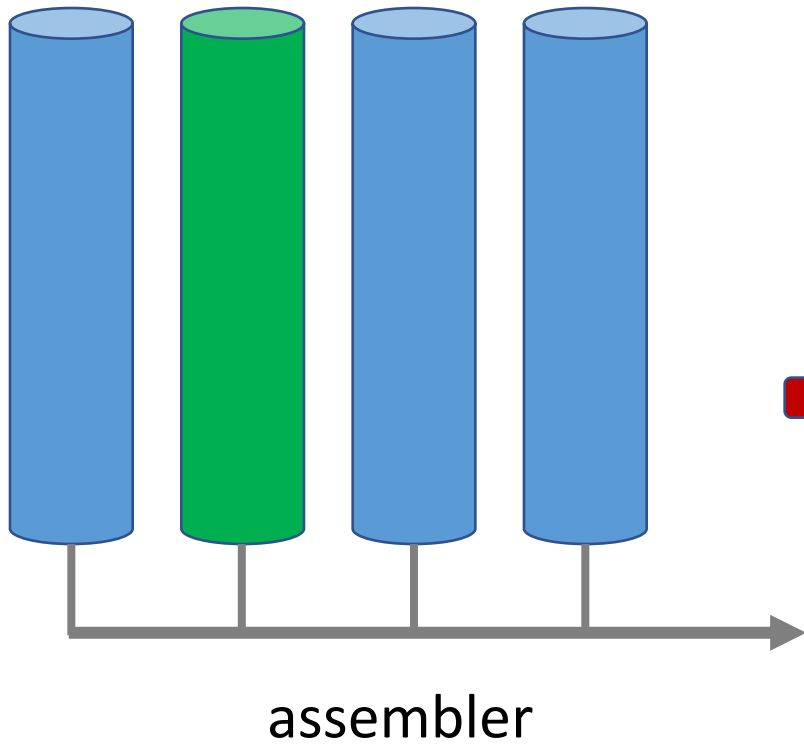


Assembly into
tetramers

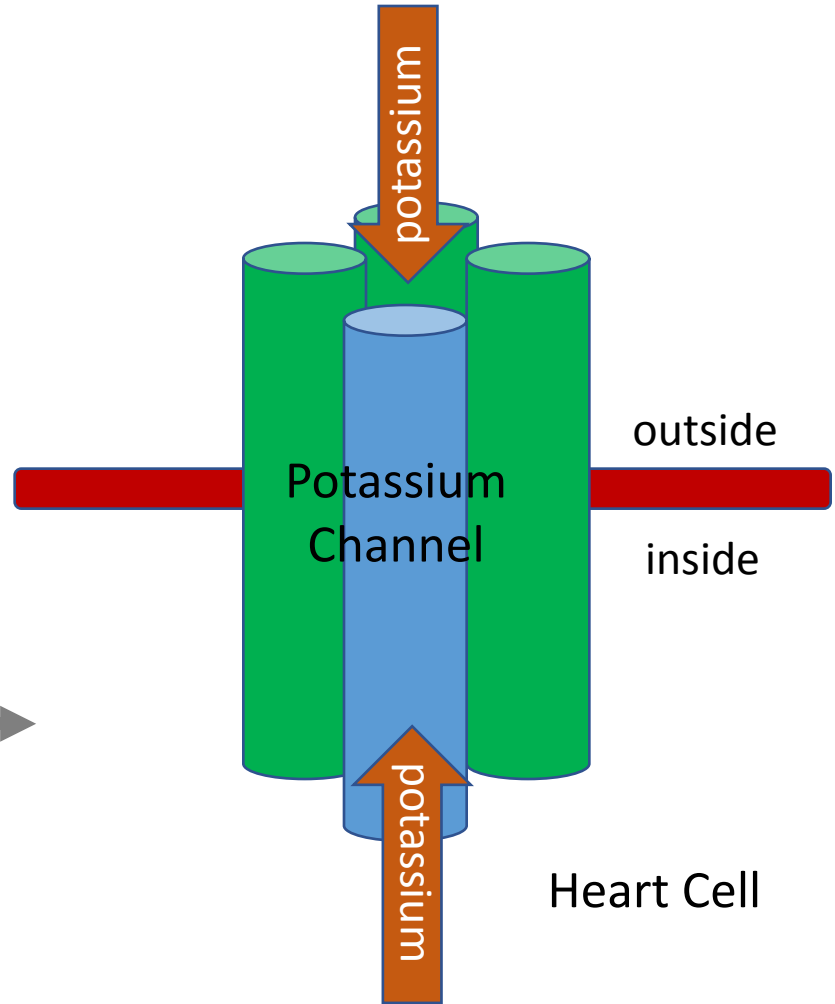
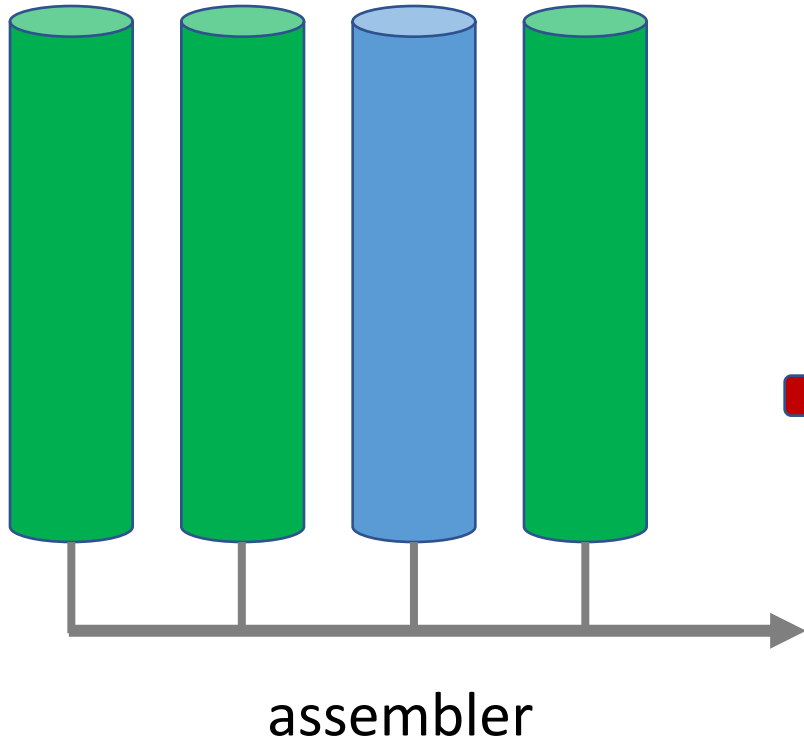


Lots of normal subunits – better channel function – shorter QT

Bad QT Channels



Better QT Channels



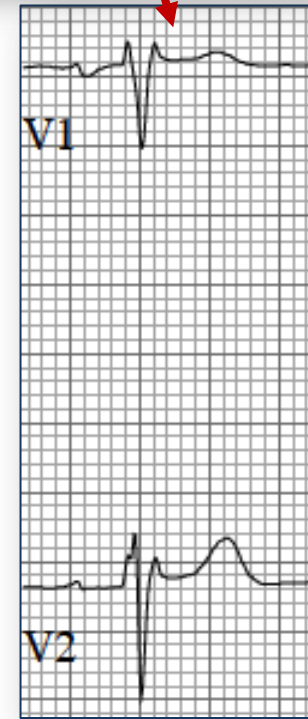
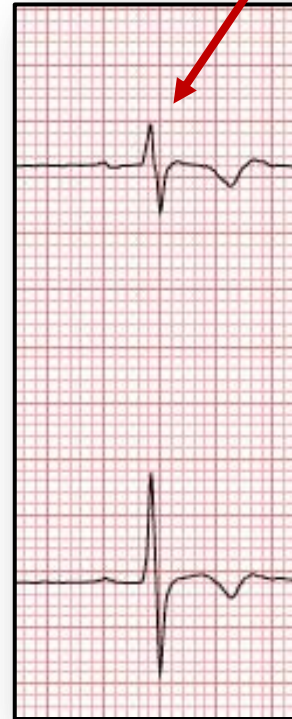
And our usual confusing story



- 27 year old “street” person
- Collapses on the street and brought in, has a cardiac arrest in the emergency room, nothing recorded
- Lives in a shelter, no family contact, using marijuana, previous cocaine use, EKG shows long QT
- EKG gets better, gets an ICD, sent home
- Back in hospital with shocks from his ICD, drug overdose
- Care team calls the genetic team because the QT is long
- Has genetic testing which does not show anything
- Put on beta blockers, tells us to our face he won’t take them
- Does he have Long QT?

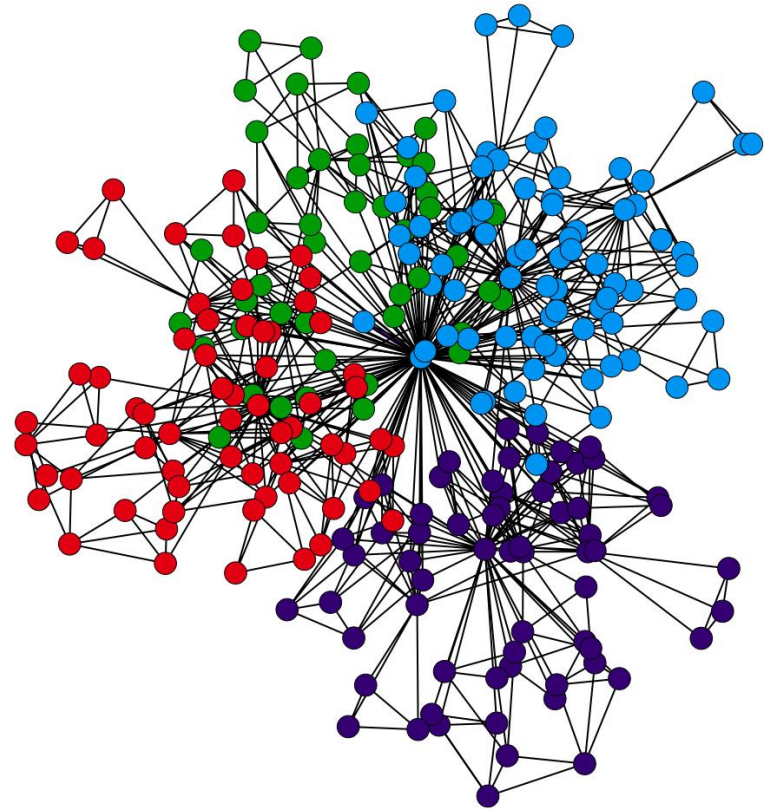
Other Kinds of Complicated

- 18 year old athlete faints during basketball practice
- Tests show lots of skipped beats called PVCs
- Diagnosed with arrhythmogenic right ventricular cardiomyopathy (ARVC)
- Family check shows Mom has Brugada!!!
- Genetic testing is negative
- This is called “Overlap Syndrome”

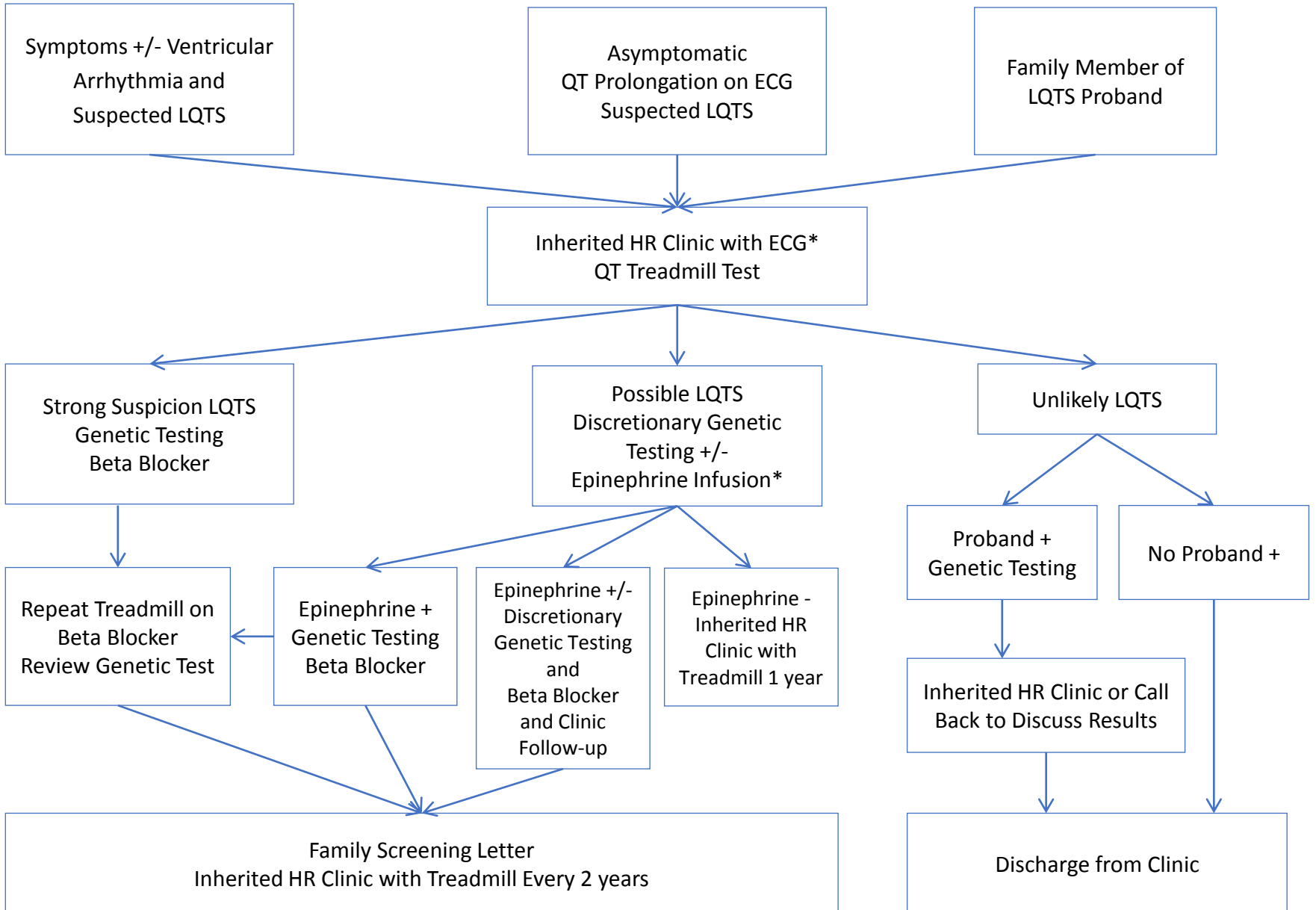


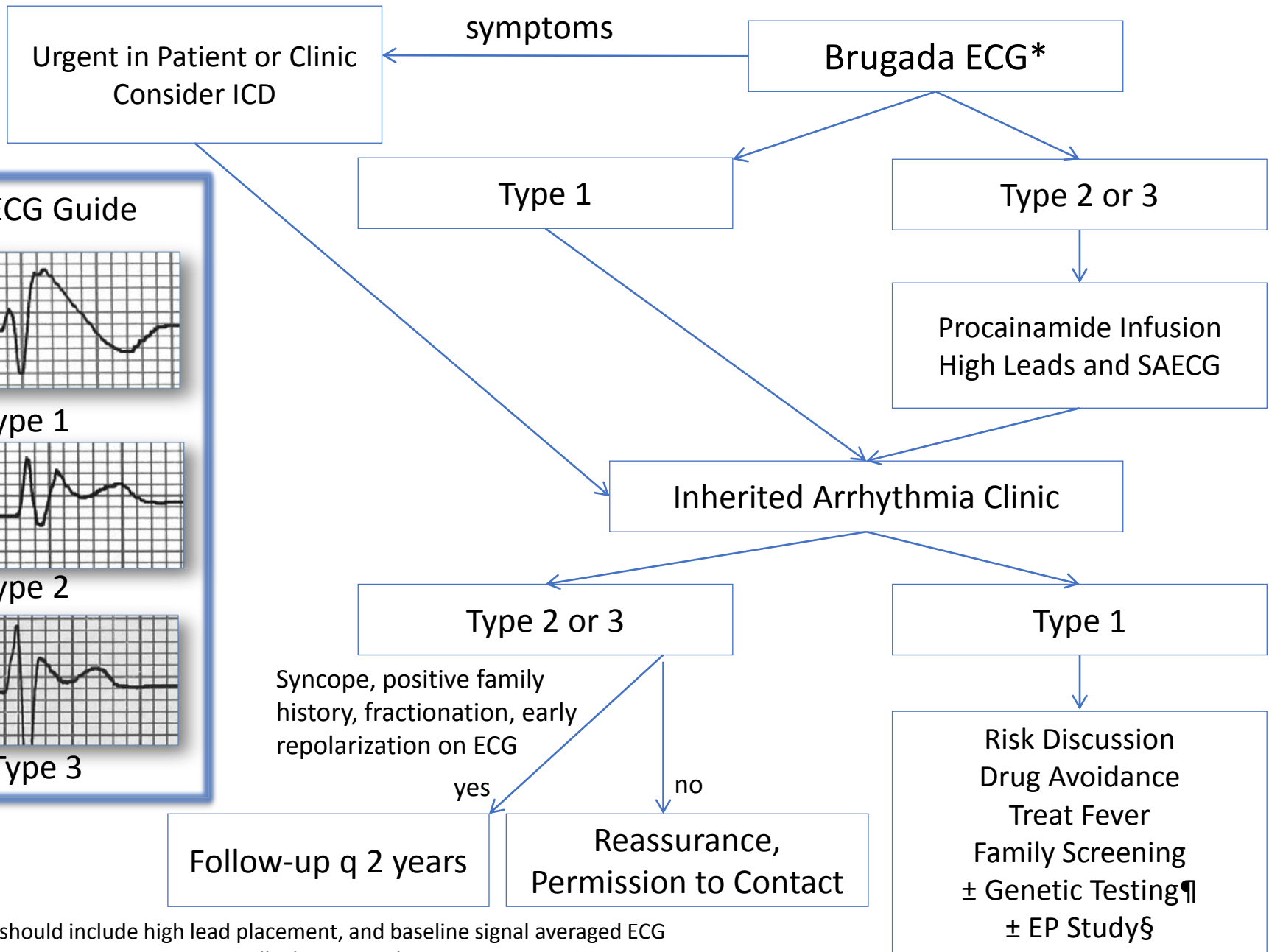
Sources of “Complicated”

- All of our tests are imperfect
- Lots of overlap between normal and abnormal
- Genetic testing is more capable but MUCH more complicated
- It can be hard to get a whole family picture
- These conditions are different between family members, and vary from day to day in the same person
- The number of parts in play is likely 100s to 1000s!

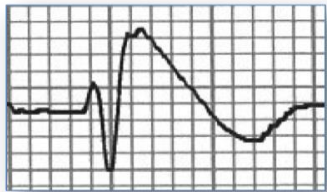


Approach to Long QT

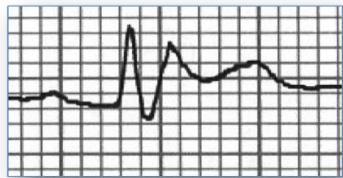




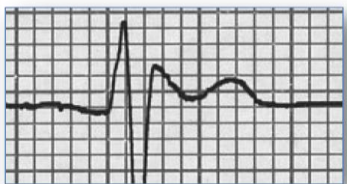
*** ECG Guide**



Type 1



Type 2



Type 3

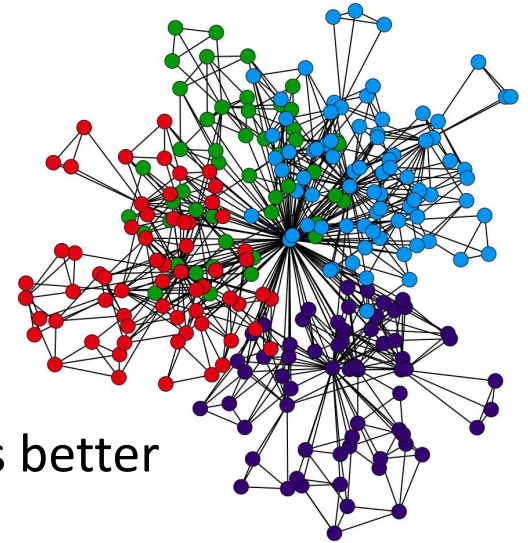
* ECG should include high lead placement, and baseline signal averaged ECG

§ Discretionary EP testing, generally discouraged

¶ CCS Guidelines recommend genetic testing when there is a positive family history or phenotypically affected first degree relative

Comments and Conclusions

- We all need to be open minded and humble
- So much to learn
- Philosophy: “More and better information begets better decisions”
- We are a lot further ahead than 10-20 years ago with systems that are helpful 90% of the time
- Half the time its “clean cut”
- Teams think and work together to help understand the complicated ones
- Communication, research, exchange



I am an open access person – for slides, e mail akrahn@mail.ubc.ca