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Julie Goodfellow

Specialist Nurse Inherited Cardiac Condi

Cardiac Family History Service
Freeman Hospital

# Inherited Arrhythmia…

# Estimated Prevalence for ICCs - commoner than you think!



| | ***Estimated*** prevalence | % Genetic |
|---|---|---|
| Hypertrophic cardiomyopathy | 1 in 500 | >50% |
| Dilated cardiomyopathy | 1 in 2500 | 40 – 50% |
| Long QT syndrome | 1 in 5000 | 100% |
| Brugada Syndrome | 1 in 2000 | 100% |
| CPVT | 1 in 10000 | 100% |
| Arrhythmogenic right ventricular cardiomyopathy | 1 in 5000 | 100% |
| Familial hypercholesterolaemia | 1 in 500 | 100% |
| Marfan syndrome | 1 in 5000 – 1 in 10 000 | 100% |
| Progressive cardiac conduction defect (PCCD) | Rare | 100% |

# Why do we carry out family screening for ICCs?



Growing awareness of ICCs in recent years (NSF CHD Chapter 8 2008 - Arrhythmias & SCD)

*Mostly… inheritance is autosomal dominant and so 50% FDRs at risk…..Lives can be saved through screening of at-risk individuals*

- Evaluation of families who may have ICC takes place in a dedicated clinic
- Staff trained in diagnosis, management & support
- Genetic counselling & further testing available if appropriate

# Why do we carry out family screening?



- Around half of DCM & HCM inherited
- Channelopathies & ARVC are inherited
- Lives can be saved through screening of at-risk individuals inheritance autosomal dominant – 50% FDRs affected!
- Early detection may decrease severity & increase treatmen choices
- Decrease uncertainty
- Increase knowledge & control
- Opportunity to educate & support affected people

# ICCs affect all ages, but disproportionately the young




# Cardiac Family History Service – set up in 2009

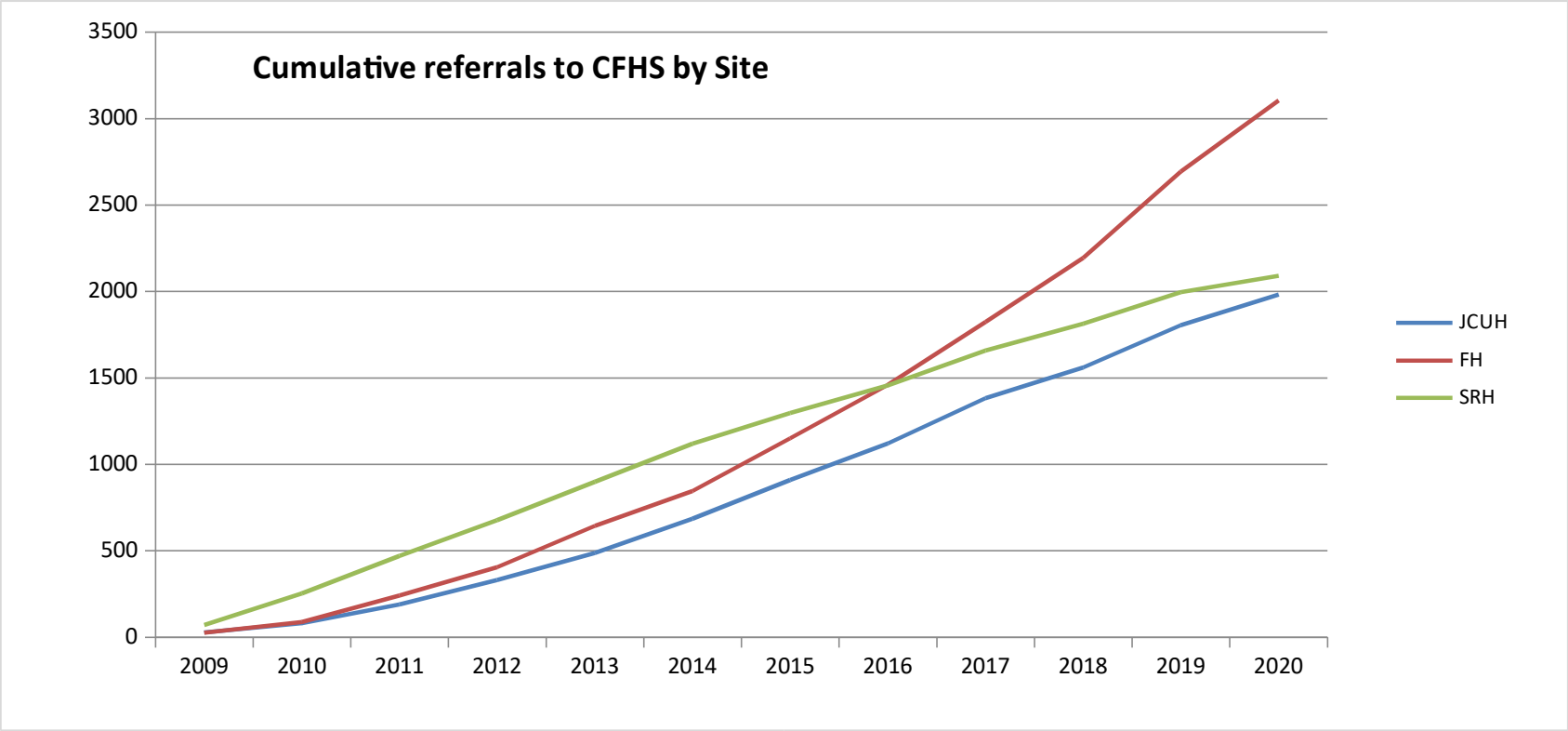


# Cardiac Genetics Nurses



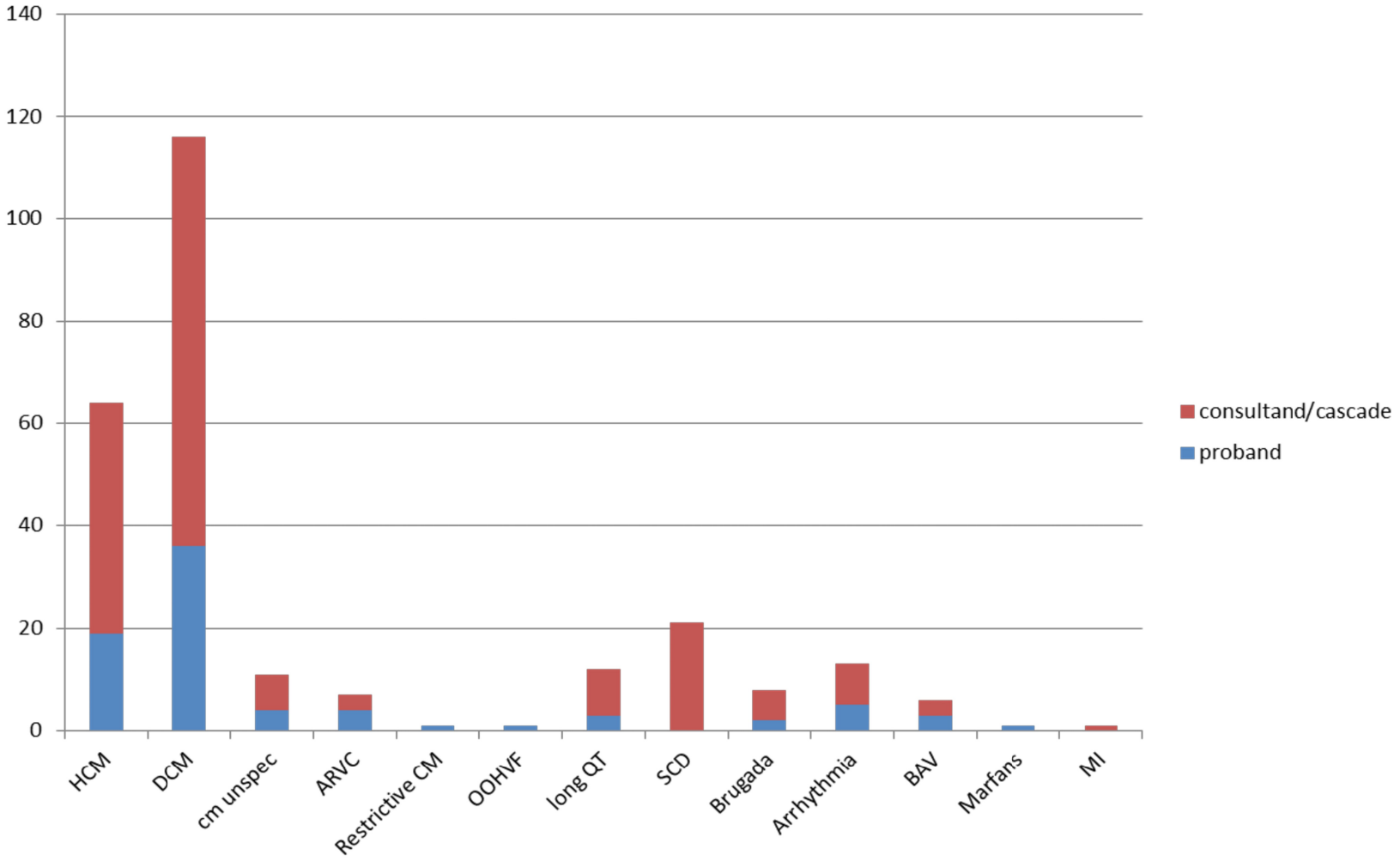
- Support & investigate families with suspected inherited cardiac disease
- Provide counselling, information, pedigrees, organise & carry out family investigations, cardiac tests, results & advise about implications
- Detailed phenotyping important
- Discuss the science and inheritance patterns
- work out the probability of  inherited cardiac disease:
  - Cardiomyopathies
  - Inherited arrhythmias
  - **Sudden cardiac deaths…..sadly this is sometimes the first symptom ICC!**

# Referrals to CFHS 2009 - 2020



# Types of referrals to CFHS at FH 2019





# Sudden cardiac deaths



- 100,000 SCD per year in UK: mostly coronary HD
- 500 unexplained deaths (structurally normal heart, toxicology NAD) due to Sudden Arrhythmic Death Syndrome (SADS)
- Most of these affect are young adults and teenagers
- ***Up to 50% of their relatives are at risk of SCD***

# SCD in young (<40)



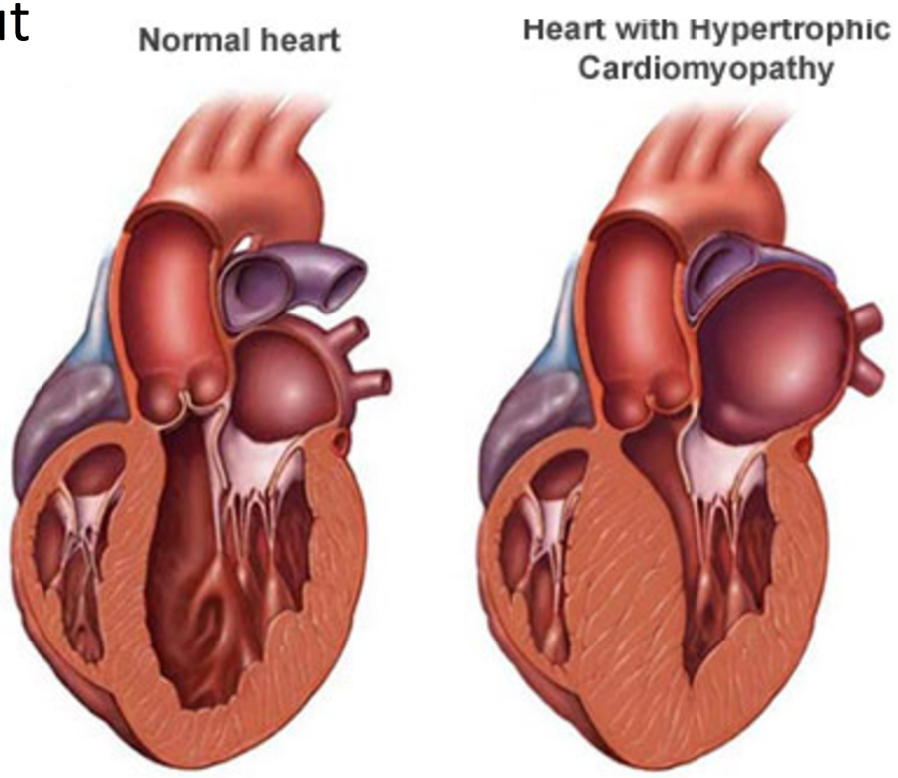
About 50 SCD in region annually

- IHD - Familial hypercholesterolaemia
- Aortic dissection
  - connective tissue disorder
  - Familial thoracic aortic aneurysm
- Heart muscle disorders – cardiomyopathies
- SADs due to Inherited arrhythmias – Brugada Syndrome, long QT Syndrome CPVT, PCCD

# Hypertrophic cardiomyopathy HCM



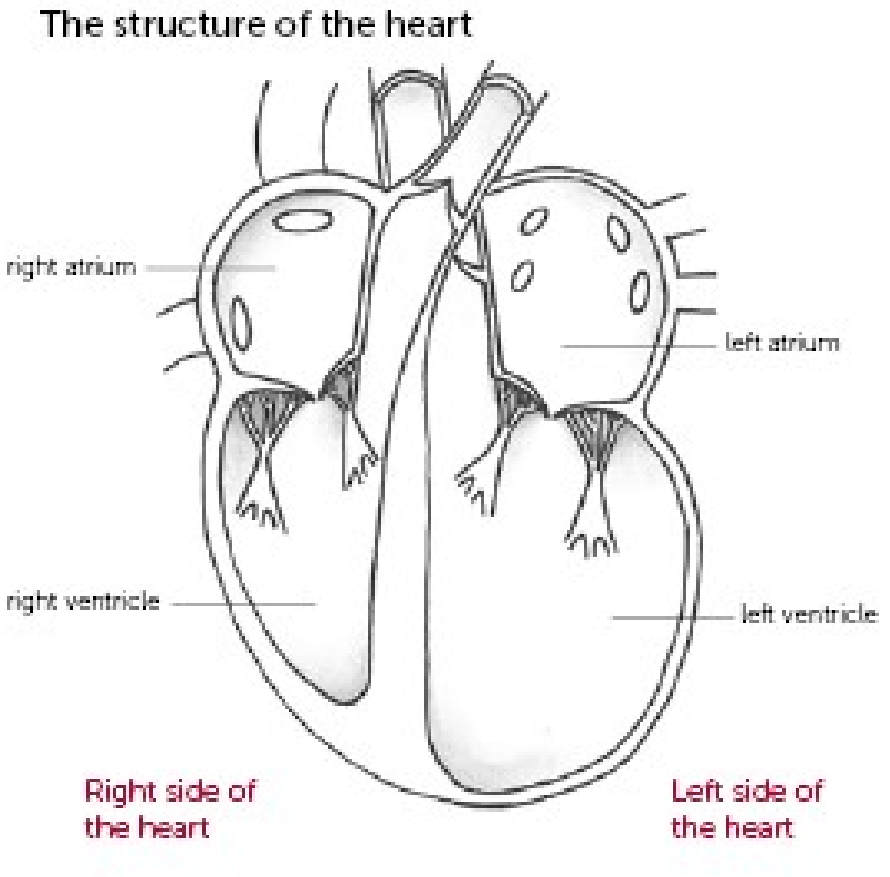
- Mutation present from birth, but usually doesn't develop until puberty or later
- Usually autosomal dominant inheritance
- SOB
- Chest pain
- **Palpitations**
- **Syncope**
- **Sudden death**
- Myocyte disarray / fibrosis



# Dilated cardiomyopathy DCM



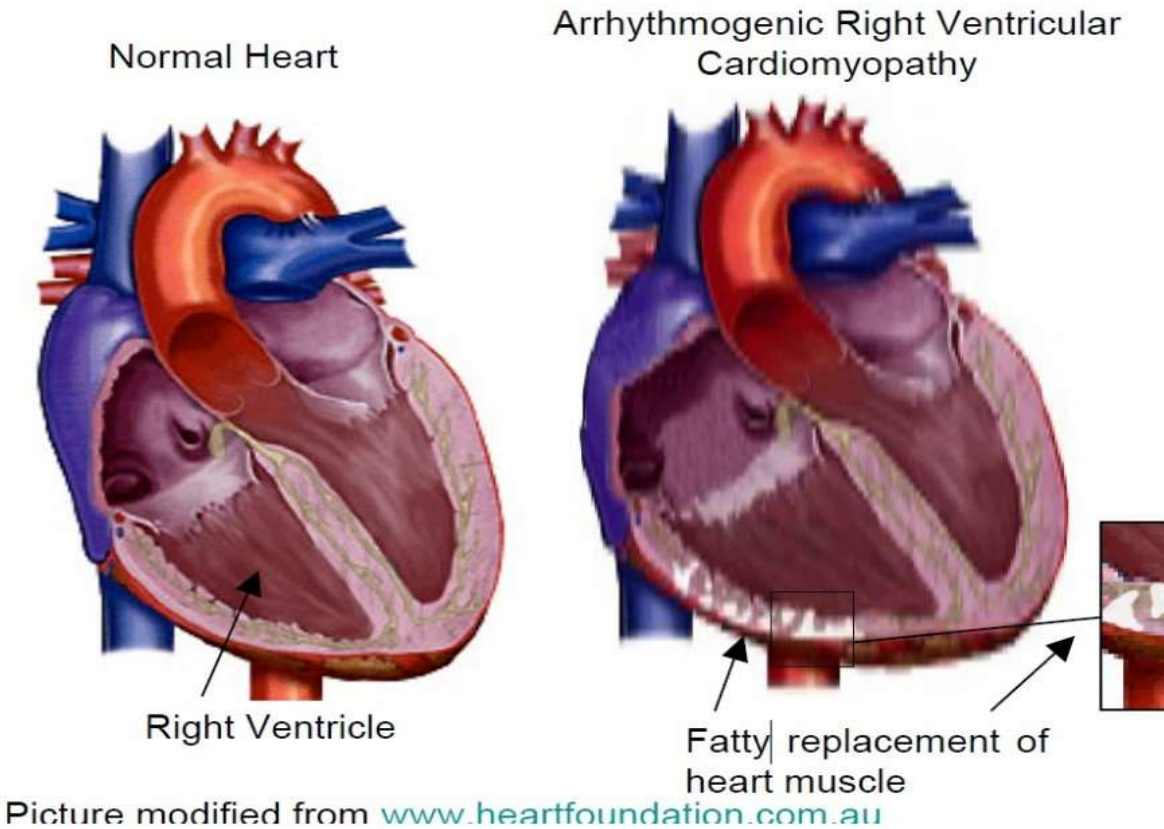
- LV dilated, weak & “floppy”
- May also be mitral regurgitation
- SOB, ankle & abdo. swelling, tired, lethargic
- **Palpitations & arrhythmias**
  - **AF**
  - **VT & VEs**
  - **heart block**
- Chest pain, blood clots
- Heart murmurs, endocarditis
- **Sudden death**
- Usually autosomal dominance



# Arrhythmogenic right ventricular cardiomyopathy ARVC



- Affects RV, but LV can also be affected
- Thin ventricle with fibrofatty replacement of myocardium
- Altered myocytes with vacuoles
- Atria not affected
- Usually autosomal dominant (can be autosomal recessive)
- mostly mutations in desmosomal genes




Picture modified from www.heartfoundation.com.au

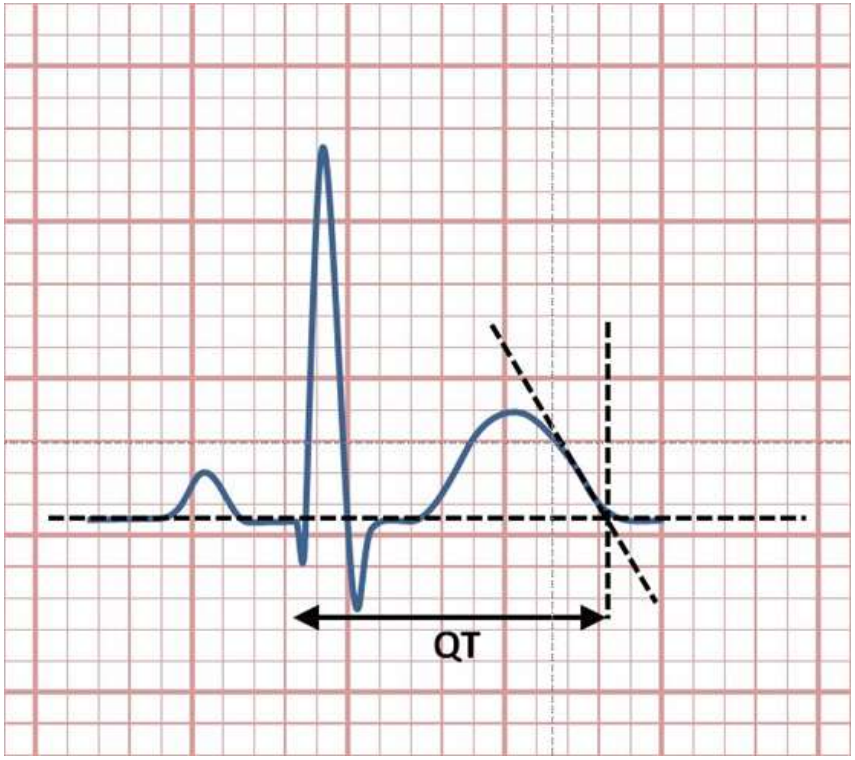
# Long QT Syndrome



- Ion channelopathy, which affects repolarisation of the cells
- 1 in 5000 people
- Caused by pathogenic gene variants affecting ion channels in cardiac cells – usually K+ &
- Ion channels are the routes that ions take in and out of the heart muscle cells, regulating electrical charge of the cells
- If the channels do not behave normally, electrical function is abnormal -> arrhythmias
- Blackouts, palpitations, seizures, sudden death

# Measuring QTc

## Tolerances:  Male > 440ms, female > 460ms



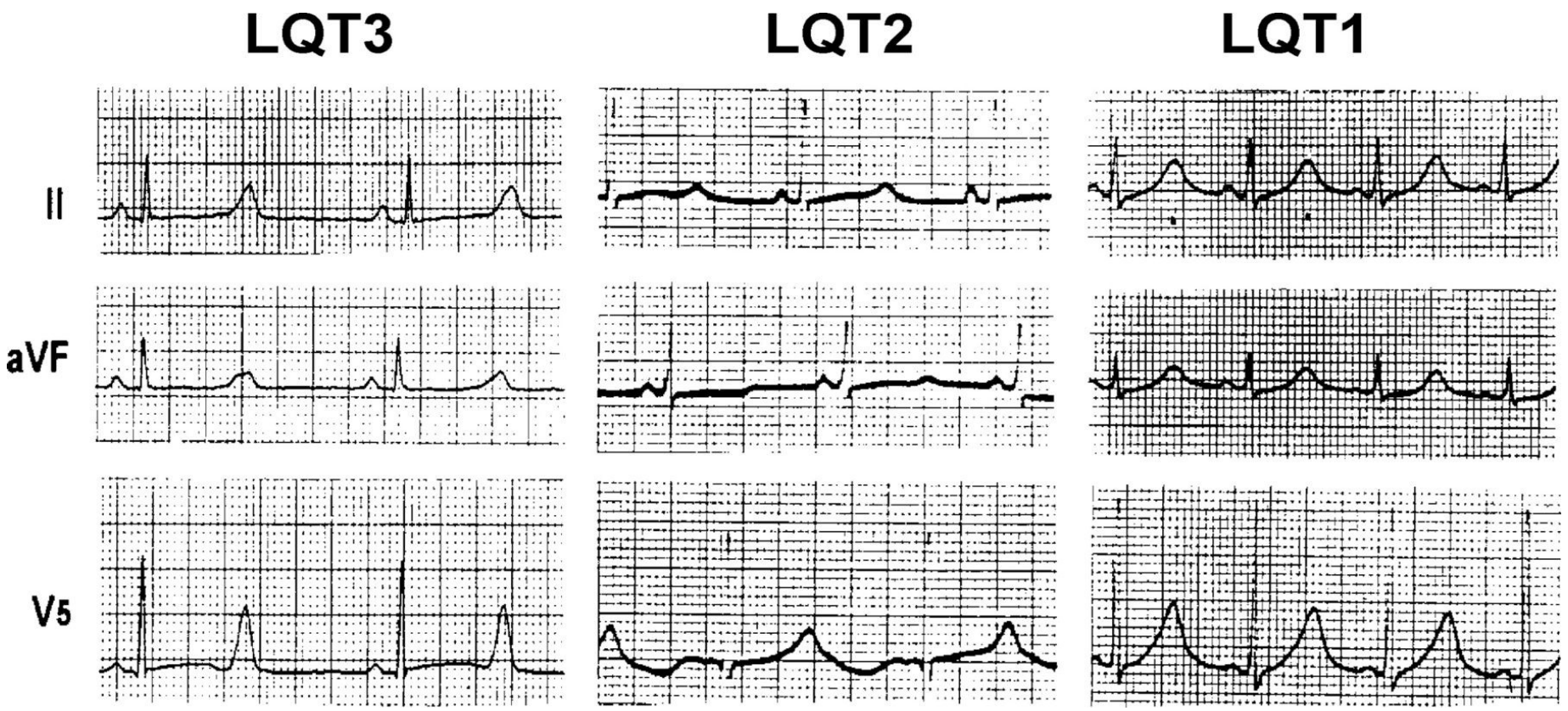

Bazett's formula

$$QTc = \frac{\text{QT interval in seconds}}{\sqrt{\text{cardiac cycle in seconds}}} = \frac{QT}{\sqrt{RR}}$$

https://www.crediblemeds.org/

# Long QT syndrome





# Long QT syndrome – management / lifestyle



Can be specific according to type:

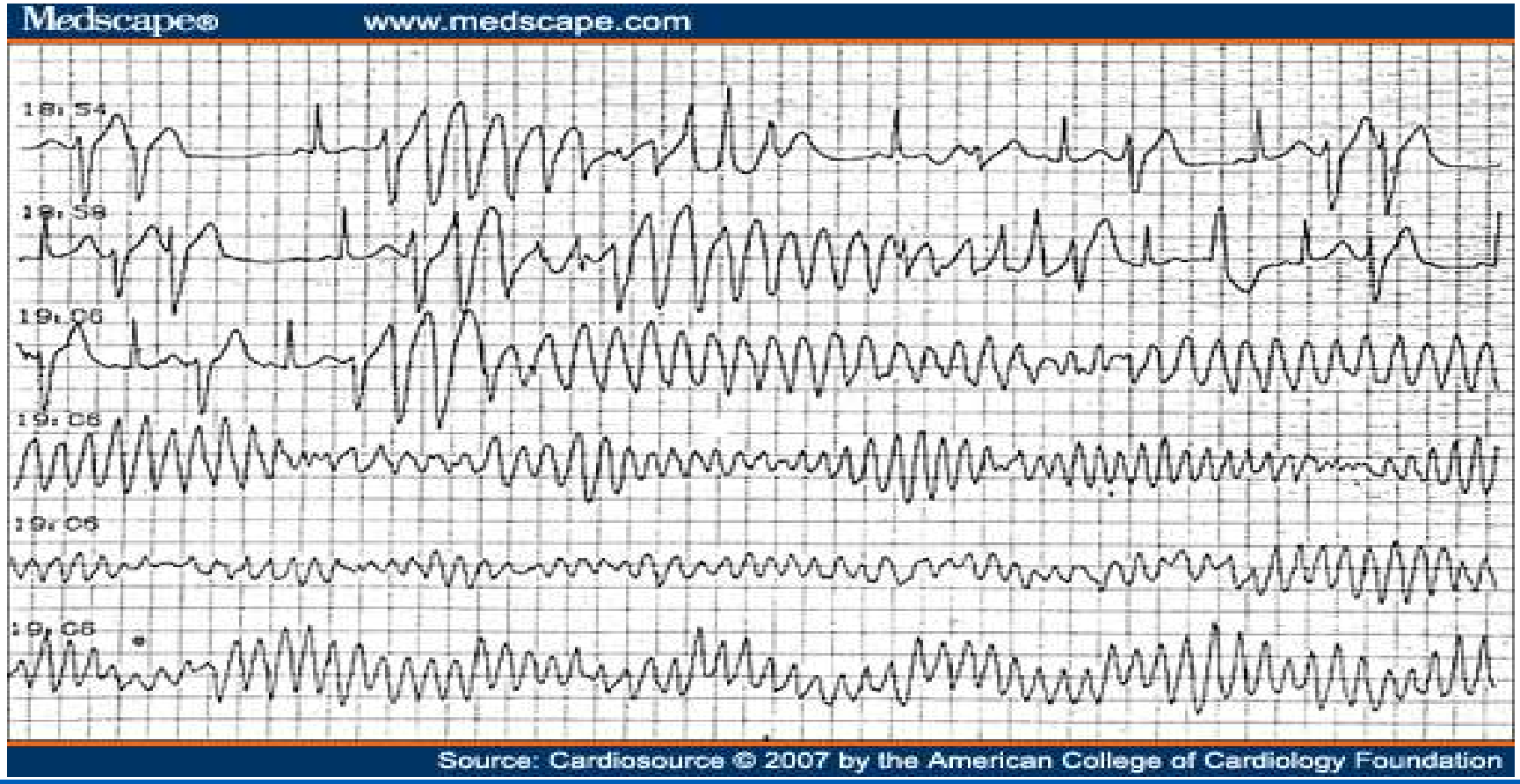
- Type 1 – swimming & exercise
- Type 2 – loud noises, startle, sudden arousal
- Type 3 – sleep

Or general

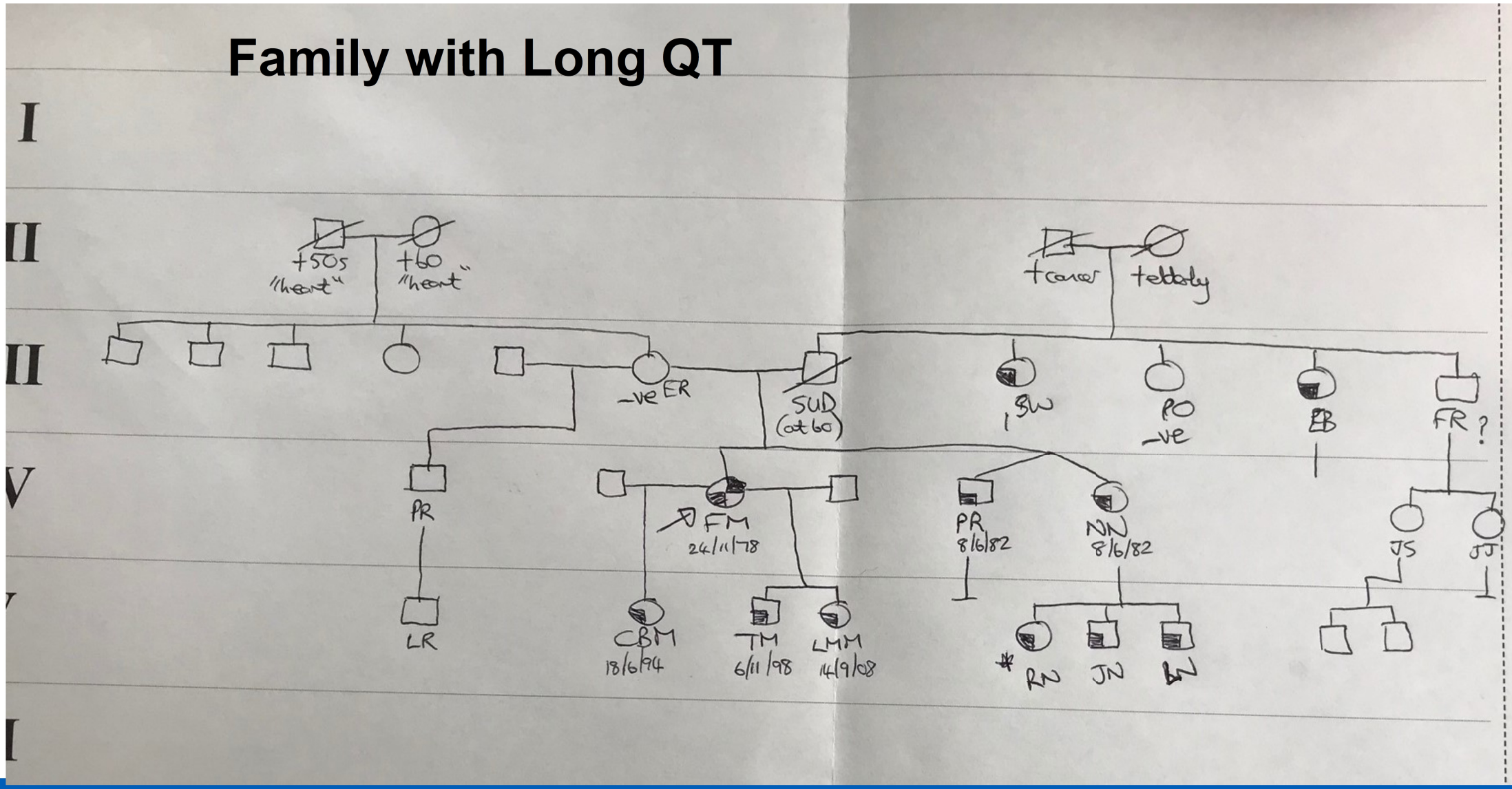
- Medicines to avoid https://www.crediblemeds.org/
- Avoid excessive alcohol / recreational drugs
- Safe rehydration – electrolyte disturbances – Dioralyte
- Betablockers can reduce risk of arrhythmia (but not necessarily QTc) - Nadolol (caution with type 3)
- Devices ICD/PPM for primary/secondary prevention
- Genetic testing to identify pathogenic variant

# Long QT – bidirectional VT (Torsades de Pointe)





# Family with Long QT



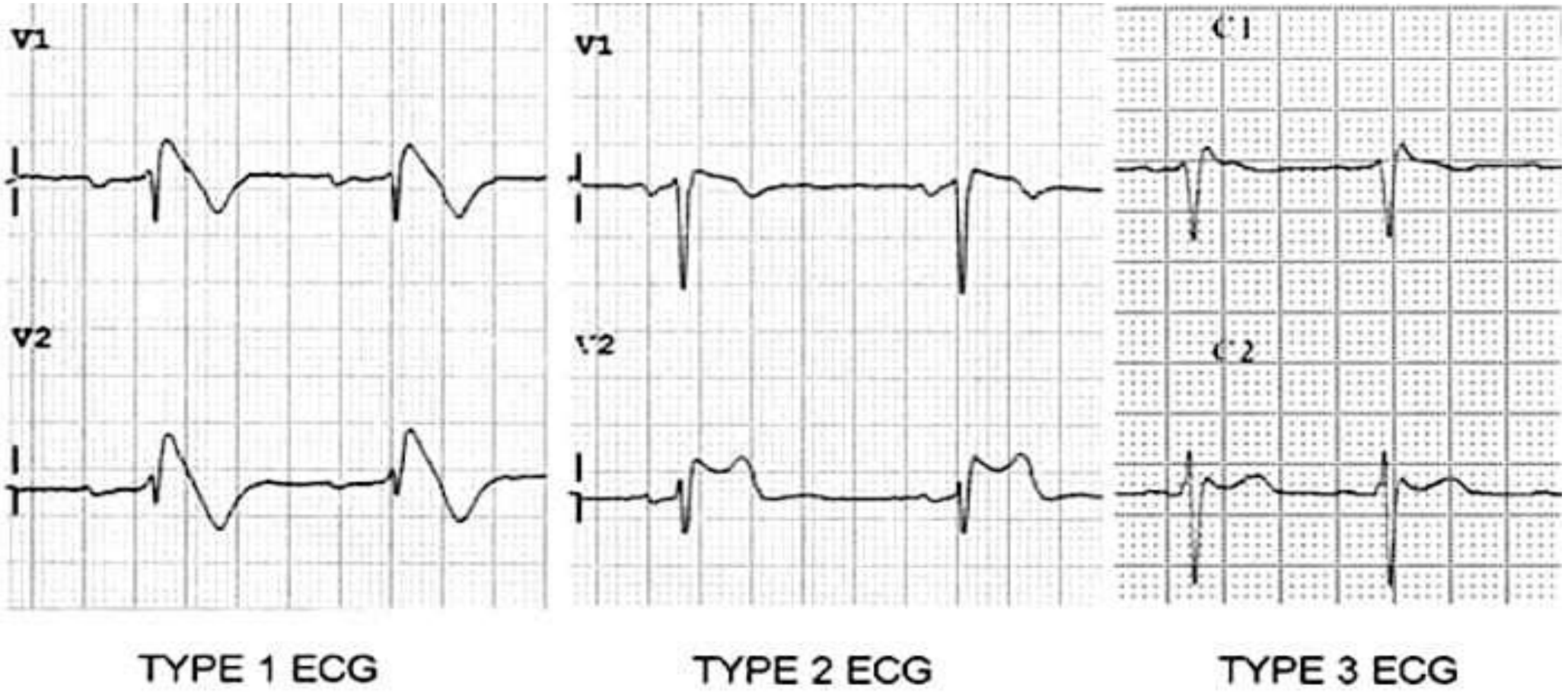
# Brugada Syndrome – Na+ channelopathy.



- First described by Brugada brothers in 1992
- Incidence high in SE Asia – previously Sudden Unexplained Nocturnal Death Syndrome SUNDS
- Sudden death because of ventricular fibrillation
- Often die in sleep / at rest
- Typical ECG patterns – not always spontaneous, unmasked:
  - High lead ECG
  - Ajmaline challenge
  - Fever

# Brugada Syndrome






TYPE 1 ECG TYPE 2 ECG TYPE 3 ECG

# Management / Lifestyle advice for BS



- Genotyping not always helpful – complicated!
- Genotype-phenotype correlations are important
- Family history of SCD, syncope, BS pattern ECG, nocturnal agonal respiration?
- Electrophysiological studies - ? Inducible ventricular arrhythmias
- ICD
- Expert ICC management required – often clinical management decisions under MDT
- Increased risk of arrhythmia with:
  - Fevers
  - Some drugs www.brugadadrugs.org – list of drugs to avoid
  - Electrolyte imbalances – Dioralyte
  - Avoid excess alcohol / recreational drugs

# Catecholinergic Polymorphic VT - CPVT

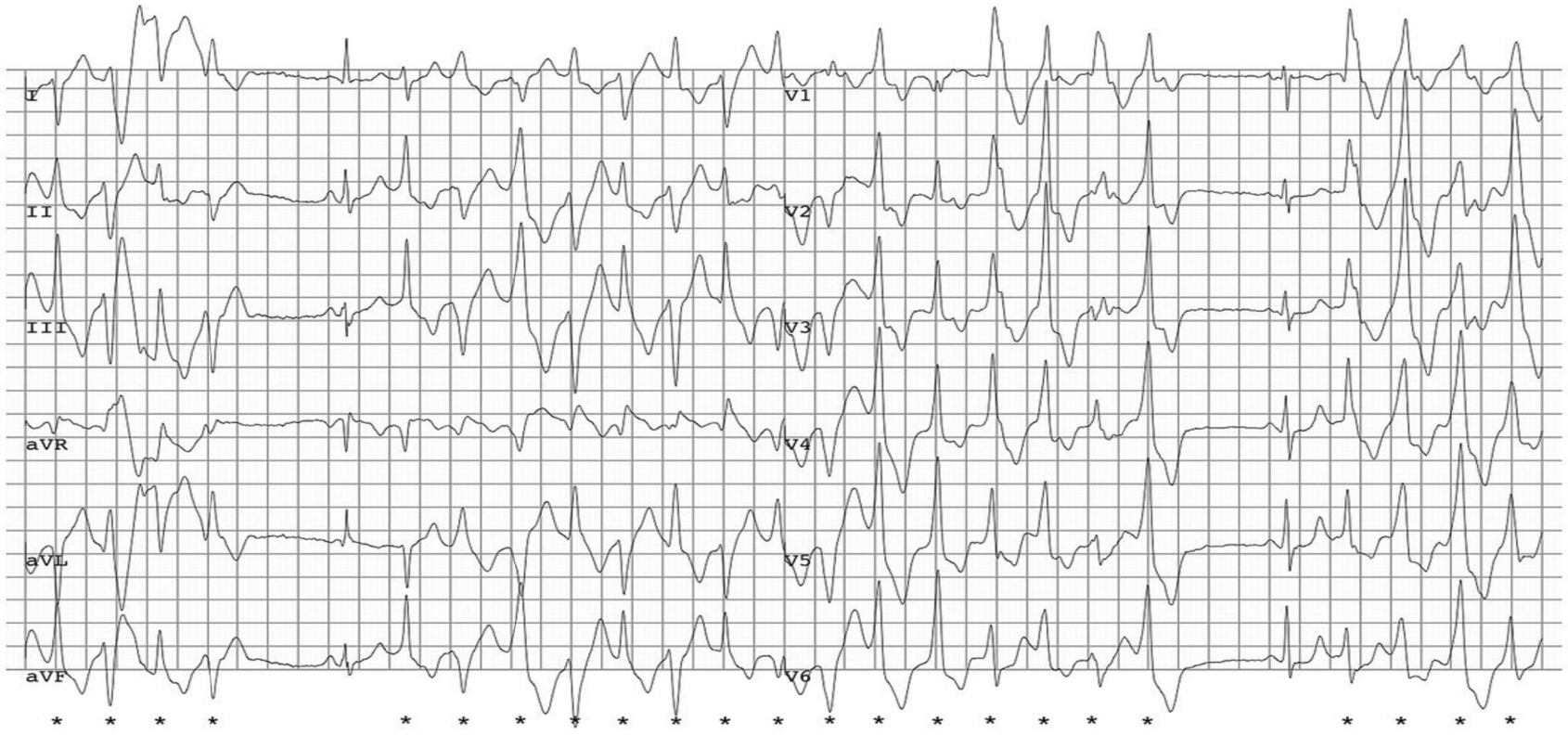


- Emotional or exercise induced syncope
- Palpitations or dizziness
- “epilepsy” / Reflex anoxic seizures
- Mean age presentation 6-10 years, but also SID and up to 40 years (about 75% symptomatic before age 20)
- Nadolol to reduce risk
- ICD with betablockade for cardiac arrest survivors & for those with syncope / sustained VT on betablockade
- Need careful assessment and genotyping
- Thoracic sympathectomy option if betablockade ineffective

# Catecholinergic Polymorphic VT

# CPVT






Courtesy of C. van der Werf, MD, AMC, The Netherlands

ECG PEDIA.ORG

# CPVT family



- John (3) frequent episodes collapse during exercise and normal situations
- Episodes 20-30s typically and up to 3 mins, spontaneous recovery with slight lethargy afterwards
- Probable epilepsy -> sodium valproate -> no help -> normal EEG -> referred cardiology for possible anoxic seizures
- ECG showed inappropriate bradycardia & prolonged QT interval -> admitted
- Collapsed & 72 ambulatory tape showed polymorphic VT
- PPM insertion & c/o Nadolol
- Genotyping confirmed CPVT with RYR2 pathogenic variant
- Brother & parents underwent predictive testing –> normal -> de novo mutation in John

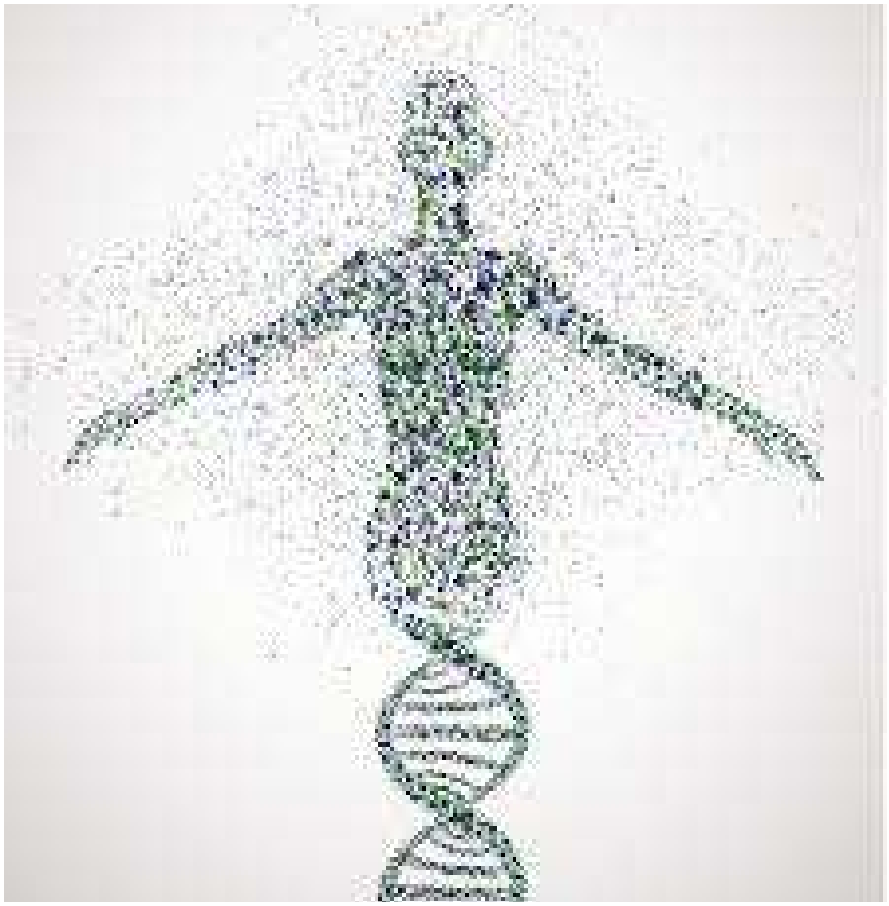
# OK – what next??



Think genetics!

You might be the only one who does!

Refer to us – we'll do the science



# Julie Goodfellow

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Freeman Hospital
0191 223 1307 or extension 31307

*or* julie.goodfellow@nhs.net