Familial Arrhythmia Network Scotland (FANS)
FANS Paediatric Pathway for Inherited Arrhythmias

The pathway is based on the HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes

(A Document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013) This international consensus statement is the collaborative effort of three medical societies representing electrophysiology in North America, Europe and Asian-Pacific area: the Heart Rhythm Society (HRS), the European Heart Rhythm Association (EHRA) and the Asia Pacific Heart Rhythm Society. The objective of the consensus document is to provide clinical guidance for diagnosis, risk stratification and management of patients affected by inherited primary arrhythmia syndromes.

The consensus statement is directed to all health care professionals who are involved in the management of:

1) Individuals who survived a cardiac arrest at a young age (usually defined as <40 years) in the absence of a clinical diagnosis of cardiac disease, despite extensive clinical assessment

2) Family members of individuals who died suddenly at young age with a negative autopsy

3) Patients and family members in whom the diagnosis of a channelopathy is clinically possible, likely, or established

4) Young patients with unexplained syncope.

Long QT Syndrome (LQTS):
(In the absence of a secondary cause for QT prolongation) is diagnosed:

1) In a patient with a pathogenic mutation in a LQTS gene

2) QTc ≥500 ms in repeated 12-lead ECG

3) In the presence of an LQTS risk score ≥3.5 (Schwartz criteria), LQTS can be diagnosed in the presence of a QTc between 480–499 ms in repeated 12-lead ECGs in a patient with unexplained syncope

Management:
All patients with LQTS should be seen by clinical genetics who will arrange cascade molecular testing where a pathogenic gene mutation has been found in the family

If no pathogenic mutation is identified then clinical genetics recommend first degree relatives undergo clinical screening.
1. The following lifestyle changes are recommended in all patients with a diagnosis of LQTS:
   a) Avoidance of QT-prolonging drugs (www.qtdrugs.org)
   b) Identification and correction of electrolyte abnormalities, e.g. during diarrhoea, vomiting, metabolic conditions or imbalanced diets for weight loss.

2. Beta-blockers are recommended for patients with a diagnosis of LQTS:
   a) Propranolol 1mg/Kg three times daily in < age 2 years
   b) Nadolol 1mg/Kg per day in:
      - A single daily dose in > age 2 years
      - Two divided doses, age < 2 years
   A cardioselective betablocker such as atenolol or bisopropol may be prescribed if asthma worsens with noncardioselective betablockers.

3. ICD implantation is recommended in the following situations:
   a) Patients with LQTS who are survivors of a cardiac arrest.
   b) Patients who experience recurrent syncopal events secondary to LQTS, while on beta-blocker therapy.

4. Left Cardiac Sympathectomy may be considered
   In patients who are intolerant of or who have contraindication to beta-blockers.

5. The following LQTS patients should be referred to a clinical expert
   a) Survivors of a cardiac arrest.
   b) Patients who wish to engage in competitive sports - for evaluation of risk.
   c) Patients who experience breakthrough events while on therapy with beta blockers/ICD.
   d) Patients with LQT3

Catecholaminergic Polymorphic ventricular tachycardia (CPVT) is diagnosed:

1) In the presence of a structurally normal heart, normal ECG, and unexplained exercise or catecholamine-induced bidirectional VT or polymorphic ventricular premature beats or VT in an individual <40 years of age

2) In patients who have a pathogenic mutation for CPVT

3) In family members of a CPVT index case, with a normal heart who manifest exercise-induced premature ventricular contractions (PVCs) or bidirectional/polymorphic VT

4) In the presence of a structurally normal heart and coronary arteries, normal ECG, and unexplained exercise or catecholamine-induced bidirectional VT or polymorphic ventricular premature beats or VT in an individual <40 years of age.

Management:
All patients with CPVT should be seen by clinical genetics who will arrange cascade molecular testing where a pathogenic gene mutation has been found in the family

If no pathogenic mutation is identified then clinical genetics recommend first degree relatives undergo clinical screening.
1. The following lifestyle changes are recommended in all patients with diagnosis of CPVT:
   a) Limit/avoid competitive sports
   b) Limit/avoid strenuous exercise
   c) Limit exposure to stressful environments

2. Beta-blockers are recommended
   a) In all symptomatic patients with a diagnosis of CPVT
      – advise nadolol 1-2mg/Kg/day – may require higher dose
   b) In carriers of a pathogenic CPVT mutation

3. Flecainide can be a useful addition to beta-blockers
   If recurrent syncope or polymorphic/bidirectional VT while on beta-blockers.

4. ICD implantation:
   a) In patients with CPVT who experience cardiac arrest,
   b) In patients with CPVT who have recurrent syncope or polymorphic/bidirectional VT
despite optimal medical management, and/or Left Cardiac Sympathectomy (LCSD).

   NB ICD as a standalone therapy is not indicated in an asymptomatic patient with a
diagnosis of CPVT.

5. Left Cardiac Sympathectomy may be considered
   a) In patients with a diagnosis of CPVT who experience recurrent syncope or
      polymorphic/bidirectional VT/appropriate ICD shocks while on beta-blockers
   b) In patients who are intolerant of or who have contraindication to beta-blockers.

**Brugada Syndrome (BrS)** is diagnosed:

1) In patients with ST-segment elevation with type 1 morphology ≥2 mm in ≥1 lead among
   the right precordial leads V1, V2, positioned in the 2nd, 3rd or 4th intercostal space
   occurring either spontaneously or after provocative drug test with intravenous
   administration of Class I antiarrhythmic drugs

2) In patients with type 2 or type 3 ST-segment elevation in ≥1 lead among the right
   precordial leads V1, V2 positioned in the 2nd, 3rd or 4th intercostal space when a
   provocative drug test with intravenous administration of Class I antiarrhythmic drugs
   induces a type I ECG morphology.

**Management:**
All patients with BrS should be seen by clinical genetics who will arrange cascade molecular
testing where a pathogenic gene mutation has been found in the family

If no pathogenic mutation is identified then clinical genetics recommend first degree relatives
undergo clinical screening.

1. The following lifestyle changes are recommended in all patients with diagnosis of
   BrS:
   a) Avoidance of drugs that may aggravate BrS (Brugadadrugs.org),
   b) Avoidance of excessive alcohol intake.
   c) Immediate treatment of fever with antipyretic drugs.
2. **ICD implantation** is recommended in patients with a diagnosis of BrS who:
   a) Are survivors of a cardiac arrest.
   b) Have documented spontaneous sustained VT with or without syncope.
   c) Have a spontaneous type I ECG and history of syncope judged to be likely caused by ventricular arrhythmias.
   d) Develop VF during programmed electrical stimulation (inducible patients).

ICD implantation is not indicated in asymptomatic BrS patients with a drug-induced type I ECG with family history of Sudden death alone.

3. **Quinidine can be useful in BrS**
   a) In a patient with arrhythmic storms (i.e. > 2 episodes of VT/VF in 24 hours).
   b) In patients who qualify for an ICD but have a contraindication to an ICD or refuse ICD.
   c) Have a history of documented supraventricular arrhythmias that require treatment.
   d) In asymptomatic patients with a diagnosis of BrS and a spontaneous type I ECG.

4. **Isoproterenol infusion can be useful** in suppressing arrhythmic storms

5. **Catheter ablation may be considered** in patients with arrhythmic storms or repeated appropriate ICD shock

**Progressive cardiac conduction disease (PCCD)** is diagnosed when the following 4 criteria are fulfilled:

1) Presence of unexplained progressive conduction abnormalities
2) Age < 50 years
3) Structurally normal heart
4) No skeletal myopathy

*Especially*, if there is a family history of PCCD.

All patients with PCCD should be seen by clinical genetics who will arrange cascade molecular testing where a pathogenic gene mutation has been found in the family.

If no pathogenic mutation is identified then clinical genetics recommend first degree relatives undergo clinical screening.

**Management:**

1. **Pacemaker implantation is recommended** in the presence of:
   a) Intermittent or permanent third-degree or high-grade AV block or
   b) Symptomatic Mobitz I or II second-degree AV block.

2. **Pacemaker implantation can be useful**
   In the presence of bi-fascicular block with or without first-degree AV block.

3. **ICD implantation can be useful**
   In patients with a mutation in the lamin A/C gene with left ventricular dysfunction and/or non-sustained VT.
Family History of sudden death in the following situations:

Definitions:
Sudden unexplained death syndrome (SUDS)
- Unexplained sudden death occurring in an individual older than 1 year of age

Sudden unexplained death syndrome (SUDI)
- Unexplained sudden death occurring in an individual less than 1 year of age (infant)

Sudden arrhythmic death syndrome (SADS)
- Sudden unexpected death with negative pathological and toxicological assessment, presumed secondary to arrhythmia

Sudden unexplained death syndrome (SUDS)

Management:
1) Sudden death victims diagnosed as SUDS at autopsy may be considered for assessment by an expert cardiac pathologist to rule out the presence of microscopic indicators of structural heart disease. At post mortem there should be collection of blood and/or suitable tissue for future molecular autopsy/post mortem genetic testing

2) Referral of first degree relative of SUDS individual to clinical genetics who will collect personal/family history details, circumstances of the sudden death and obtain consent from the next of kin for appropriate molecular testing

3) If a pathogenic mutation in a gene associated with increased risk of sudden death is identified in the SUDS victim then clinical genetics will offer cascade genetic testing to family members

4) If no pathogenic mutation is identified then clinical genetics recommend first degree relatives undergo clinical screening which includes:
   a) Resting ECG with high right ventricular leads* (for Brugada*)
   b) Exercise stress testing or 24 hour ECG
   c) Echocardiography

Prioritise assessment of obligate carriers and relatives with a history of palpitations, arrhythmias or syncope.

Consider evaluation of first-degree relatives of SUDS victims with ambulatory and signal-averaged ECGs, cardiac MRI and provocative testing with Class Ic anti-arrhythmic drugs which may be useful.

Consider evaluation of first-degree relatives of SUDS victims with epinephrine infusion which may be useful.

Follow-up clinical assessment is indicated in young family members of SUDS victims who may manifest symptoms and/or signs of the disease at an older age and in all family members whenever additional SUDS or SUDI events occur.
Sudden unexplained death in infancy (SUDI)
Unexplained sudden death occurring in an individual younger than 1 year of age with negative pathological and toxicological assessment

Management:
1) **Sudden death victims diagnosed as SUDI at autopsy** may be considered for assessment by an expert cardiac pathologist to rule out the presence of microscopic indicators of structural heart disease. At post mortem collection of blood and/or suitable tissue for molecular autopsy is recommended in all SUDI victims.

2) **Consider referral of first degree relative of SUDI individual to clinical genetics** who will collect personal/family history and circumstances of the sudden death and obtain consent from the next of kin for appropriate molecular testing.

3) **If a pathogenic mutation in a gene associated with increased risk of sudden death is identified** in the SUDI victim then clinical genetics will offer cascade genetic testing to family members.

4) **If no pathogenic mutation is identified then**
   a) Evaluation of first-degree relatives of SUDI victims with resting ECG and exercise stress testing may be considered.
   b) Evaluation of first-degree relatives of SUDI victims with a family history of inherited heart disease or other SUDS or SUDI deaths with resting ECG, exercise stress testing and additional tests as indicated may be considered.

Assessment of first-degree relatives with history of arrhythmias or syncope should be prioritised.

Follow-up clinical assessment can be useful in young family members of SUDI victims with a family history of inherited heart disease or other SUDS or SUDI death who may manifest symptoms and/or signs of the disease at an older age and in all family members whenever additional SUDS or SUDI events occur.

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient’s case notes at the time the relevant decision is taken.