

## **Clinical overview of inherited heart disease**

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Given the complex interplay of ionic current and myocardial structure required for normal cardiac rhythm, it is remarkable that the heart should beat – ordered, consecutive, synchronous – over a life time. However, it is now known that multiple inherited disorders can interrupt this mechanism and manifest with tragic consequence in utero to very late age. Broadly, such conditions may be considered ionic or structural – a useful distinction in the clinic and laboratory, though an over simplification. Ionic inherited arrhythmia syndromes result from mutations in genes encoding ion channels or their structural components. The most common include: long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia, Brugada syndrome, progressive cardiac conduction disease, atrial fibrillation, and early repolarisation disorder. The structural disorders predisposing to cardiac arrhythmia represent both a morphologic and clinical phenotype and include: hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy (or dysplasia), and myocardial non-compaction. After two decades of intensive research, the genetic underpinnings of these disorders have to a large extent been identified. The advance has been so great that genetic testing is now established in the clinical setting where it is used for the confirmation of a diagnosis and in cascade family screening. Increasingly, family members are identified without a clinical phenotype but who harbour a pathogenic mutation. Preliminary work suggests that such early identification allows intervention whether by lifestyle change or drug therapy that may prevent a clinical phenotype from manifesting. Yet the greatest advances are to come as advance in our knowledge of the underlying molecular mechanisms enables the development of targeted and gene-specific therapy.