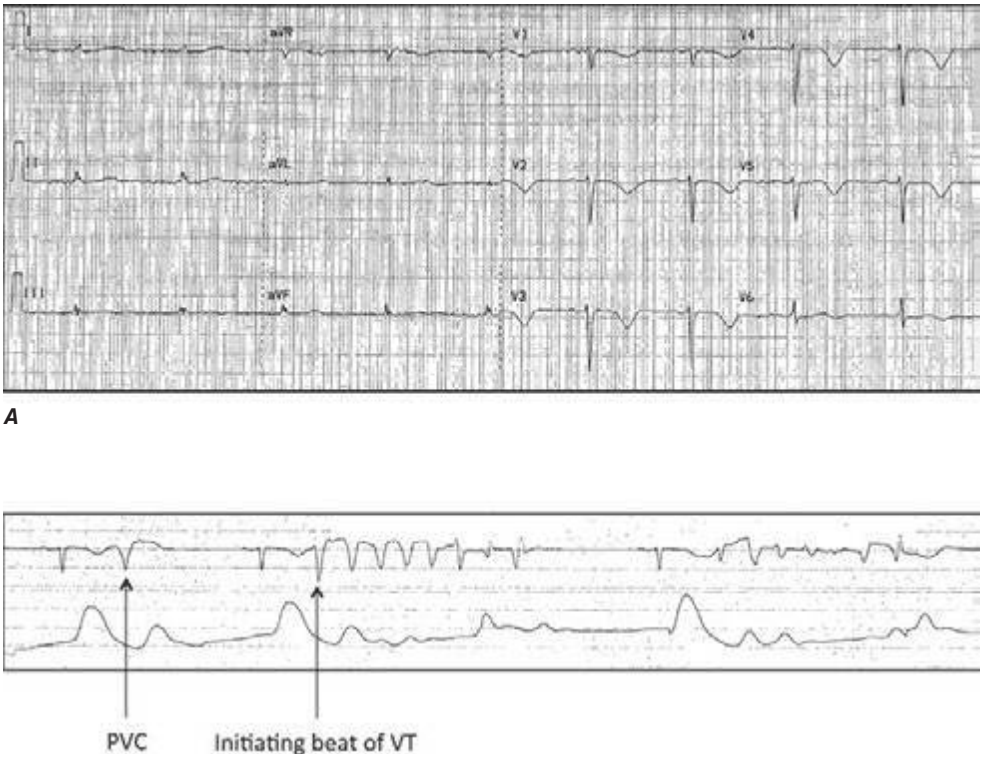

FIGURE 277-8 Electrocardiogram (ECG) of a patient with prolonged QT and episodes of torsade de pointes ventricular tachycardia (VT). ***A.*** Twelve-lead ECG showing a heart rate of 54, anterior wall T inversion, and QT interval of 600 ms. The corrected QT interval (QTc) is 585 ms. ***B.*** Telemetry ECG tracing with digital pulse waveform demonstrating bursts of torsade de pointes VT. The initiating sequence of the VT is characteristic, with a PVC inducing a pause followed by a sinus beat that had a longer QT and interruption of the T wave by a PVC that is the first beat of VT. The VT is self-terminating in this case.

REPOLARIZATION ABNORMALITIES AND GENETIC ARRHYTHMIA SYNDROMES • Acquired long QT Abnormal prolongation of the QT interval is associated with the polymorphic VT Torsade de Pointes (Fig. 277-8). The VT often has a characteristic initiation sequence of a premature ventricular beat that induces a pause, followed by a sinus beat that has a longer QT interval and interruption of the T wave by the PVC that is the first beat of the polymorphic VT. This characteristic initiation is termed "pause-dependent" (Fig. 277-8). Causes of QT prolongation include electrolyte abnormalities, bradycardia, and a number of medications that block repolarizing potassium currents, notably the antiarrhythmic drugs sotalol, dofetilide, and ibutilide, but also a number of other medications used for noncardiac diseases, including erythromycin, pentamidine, haloperidol, phenothiazines, and methadone (Table 277-3). Individual susceptibility may be related to genetic polymorphisms or mutations that influence repolarization.

Patients typically present with near-syncope, syncope, or cardiac arrest. Sustained episodes degenerate to VF requiring defibrillation. PVCs and nonsustained VT often precede episodes of sustained VT. Intravenous administration of 1–2 g of magnesium sulphate usually suppresses recurrent episodes. If magnesium alone is ineffective, increasing heart rate with isoproterenol infusion or pacing, to a rate of 100–120 beats/min as required to suppress PVCs, usually suppresses VT recurrences. These maneuvers allow time for correction of associated electrolyte disturbance (hypokalemia and hypocalcemia) and bradycardia and removal of any causative drugs (Table 277-3). Drug interactions that elevate levels of the offending agent are often a precipitating factor. Patients who experience a polymorphic VT induced by QT prolongation should be considered to have a susceptibility to the arrhythmia and should avoid all future exposure to medications known to prolong the QT interval.

Congenital long QT syndrome The congenital long QT syndrome (LQTS) is caused by mutations in genes coding for cardiac ion channels responsible for ventricular repolarization. The corrected QT (QTc) is typically prolonged to greater than 440 ms in men and 460 ms in women. Symptoms are due to Torsade de Pointes VT (Fig. 277-8). Several forms of congenital LQTS have been identified, but three groups of mutations that lead to LQTS type 1 (LQTS-1), LQTS type 2 (LQTS-2), or LQTS type 3 (LQTS-3) account for 90% of cases. The most frequently encountered mutations, *LQTS1* and *LQTS2*, are due to abnormalities of potassium channels, but mutations affecting the sodium channel (*LQTS3*) and calcium channels have also been described (Table 277-3).

Patients often present with syncope or cardiac arrest, usually during childhood. In LQTS-1, episodes tend to occur during exertion, particularly swimming. In LQTS-2, sudden auditory stimuli or emotional upset predispose to events. In LQTS-3, sudden death during sleep is a notable feature. Asymptomatic patients may be discovered in the course of family screening or on a routine ECG. Genotyping can be helpful for family screening and to provide reassurance regarding the diagnosis. Correlations of genotype with risk and response to therapy are beginning to emerge. In most patients with LQTS-1 or LQTS-2, adequate doses of beta blocker therapy (the nonselective agents nadolol or propranolol) are sufficient protection from arrhythmia episodes. Markers of increased risk include QTc interval exceeding 0.5 s, female gender, and a history of syncope or cardiac arrest. Recurrent syncope despite beta blocker therapy or a high-risk profile merits consideration of an ICD. Avoidance of QT-prolonging drugs is critical for all patients with LQTS, including those who are genotype positive but have normal QT intervals.

Short QT syndrome Short QT syndrome is very rare compared to LQTS. The QTc is shorter than 0.36 s, and usually less than 0.3 s. The genetic abnormality causes a gain of function of the potassium channel (I_{Kr}) or reduced inward depolarizing currents. The abnormality is associated with atrial fibrillation, polymorphic VT, and sudden death.

Brugada syndrome Brugada syndrome is a rare syndrome characterized by >0.2 mV of ST-segment elevation with a coved ST segment and negative T wave in more than one anterior precordial lead (V_1–V_3) (Fig. 277-6) and episodes of syncope or cardiac arrest due to polymorphic VT in the absence of structural heart disease. Cardiac arrest may occur during sleep or be provoked by febrile illness. Males are more commonly affected than females. Mutations involving cardiac sodium channels are identified in approximately 25% of cases. Distinction from patients with similar ST elevation owing to LV hypertrophy, pericarditis, myocardial ischemia or MI hyperkalemia, hypothermia, right bundle branch block, and ARVC is often difficult. Furthermore, the characteristic ST-segment elevation can wax and wane over time and may become pronounced during acute illness and fever. Administration of the sodium channel blocking drug flecainide, ajmaline, or procainamide can augment or unmask ST elevation in affected individuals. An ICD is indicated for individuals who have had unexplained syncope or been resuscitated from cardiac arrest.