

Electrocardiographic Changes in Infectious Diseases

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Electrocardiography is a valuable, noninvasive graphical representation of the heart's electrical activity. Augustus D. Waller, a physiologist from London, published a description of the first human electrocardiogram (ECG) in 1887,¹ and since then, the ECG has evolved as a useful tool in diagnosing coronary artery disease, rhythm abnormalities, and certain medical conditions. In addition, the ECG can play an important role in the assessment of the severity of illness in a variety of infections and may at times serve as a marker of cardiac involvement or cardiac complications from infection and provide information on prognosis.² The ECG manifestations of infections are oftentimes insignificant but can represent a life-threatening complication, such as para-aortic valve abscess in endocarditis. ECG abnormalities in infections can be caused by multiple factors, including direct invasion by the microorganism, the effects of the organism's toxin, and electrolyte, metabolic, or autonomic system abnormalities caused by the infection. Unfortunately, the ECG is often overlooked in the evaluation of patients with an infectious disease. This article highlights electrocardiographic findings that are associated with bacterial, viral, spirochetal, and parasitic infections and that occur as side effects of antimicrobial therapy (Table 1).

VIRAL INFECTIONS

HIV Infection

Cardiac involvement is seen predominantly in the advanced stages of HIV-1 infection, and in most cases the etiology of HIV-related cardiac disease is unclear.³ CD4+ T lymphocyte counts of 100 cells/ μ L or less can be a risk factor for the development of cardiac manifestations in patients with HIV infection.³ Cardiovascular abnormalities that can be detected on ECG include sinus tachycardia, left ventricular (LV) systolic dysfunction, right ventricular dilatation,⁴ dilated car-

TAKE HOME POINTS

- In patients diagnosed with an infectious disease, electrocardiography can be used to evaluate for cardiac involvement, provide information on prognosis, and assess the effect of treatment.
- Abnormalities on the electrocardiogram (ECG) of a febrile patient in whom late-stage Lyme disease is suspected can point to the diagnosis; conduction and rhythm disturbances are the most common ECG findings.
- In a patient with known endocarditis and persistent fever despite appropriate therapy, heart block on repeated ECG may indicate the presence of complicated valve abscess.
- Myocarditis is caused by many infectious agents and may produce a number of ECG abnormalities: Adams-Stokes syndrome, conduction disturbances, pseudoinfarction pattern, ST-segment and T-wave abnormalities, and premature ventricular contractions.
- Physicians should know the QTc interval in a patient to be treated with a quinolone or macrolide as these agents have proarrhythmic effects.

diomyopathy, pericardial effusion, bacterial endocarditis, mitral valve prolapse, myocarditis,⁵ low-voltage QRS complex, nonspecific ST-segment and T-wave changes, poor R-wave progression, and prolonged QTc interval. An asymptomatic prolonged QTc interval is associated

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Table I. Common Electrocardiographic Changes in Infectious Diseases

Disease/ Condition	ECG Abnormalities
HIV infection	Sinus tachycardia, LV systolic dysfunction, right ventricular dilatation, low-voltage QRS complex, nonspecific ST-segment and T-wave changes, poor R-wave progression, and prolonged QTc interval
Rubella	Abnormal ST-segment and T-wave changes and axis deviations
Lyme disease	First-degree AV blocks, shorter duration of Q, and deeper S wave
Leptospirosis	First-degree AV heart block and pericarditis
Chagas' disease	RBBB, left anterior hemiblock, heart blocks
Trichinosis	Transient nonspecific ventricular repolarization disturbance, nonspecific changes from pericarditis
Diphtheria	Myocarditis, PR-interval prolongation, T-wave changes, intraventricular blocks, and AV conduction blocks
Tetanus	Sinus tachycardia, prolonged QT interval, nonspecific ST-segment and T-wave changes, and P-wave changes
Pertussis	Sinus node and AV nodal blocks
Rheumatic fever	First-degree heart block
Invasive streptococcal infections	ST-segment and T-wave changes
Typhoid	Myocarditis, PR-interval prolongation, QTc prolongation, ST-segment depression, T-wave inversion
Pericarditis	PR depression, ST-segment elevation, then normalization of the ST segment, T-wave inversion, and finally normalization of all changes
Myocarditis	Adams-Stokes syndrome, conduction disturbances, pseudoinfarction pattern, ST-segment and T-wave changes, and premature ventricular contractions
Endocarditis	Sinus tachycardia, low QRS voltage, varying degrees of heart blocks
Mycoplasmosis	T-wave inversion, bradycardia, prolonged PR interval and narrow QRS complex
Increased intracranial pressure	Tall P waves, prominent U waves, inverted U waves, ST-segment and T-wave changes (eg, depression or elevation), notched T waves, sinus bradycardia
Macrolides, quinolones	Prolonged QT interval

AV = atrioventricular; ECG = electrocardiogram; LV = left ventricular; RBBB = right bundle branch block.

with increased cardiovascular mortality in HIV infection, and the prevalence of this finding increases as the patient's immune system deteriorates.⁶

Arrhythmias are uncommon in both children and adults with HIV infection. The arrhythmias commonly seen are benign and include sinus tachycardia, first-degree heart block, junctional escape rhythm, and

premature atrial beats. These arrhythmias rarely progress to supraventricular or ventricular tachycardia,⁷ second-degree heart block, right bundle branch block, and prolonged QTc, which have high mortality rates.⁸ Right ventricular hypertrophy is the most common electrocardiographic finding in HIV-related pulmonary hypertension.⁹

Rubella

Rubella, or German measles, is an acute exanthematous viral infection that occurs mainly in children. The incidence of rubella is low due to use of the vaccine targeting this virus. The number of rubella cases in United States has dropped since 2001: 23 cases in 2001, 18 in 2002, 7 in 2003, and 9 in 2004.¹⁰ The clinical manifestations of the disease are fever, adenopathy, and maculopapular rash that begins on the face and moves downward. Myocardial injury is a complication of rubella that is seen rarely due to widespread vaccination of children. Abnormal ST-segment and T-wave changes and axis deviations are often seen on ECG.¹¹ Rubella infection with abnormalities on ECG is associated with increased morbidity. Superior left axis deviation in rubella represents either temporary or permanent damage to the left bundle branch fascicles and is associated with hemodynamic changes.¹²

SPIROCHETAL INFECTIONS

Lyme Disease

Lyme disease is caused by the spirochete *Borrelia burgdorferi*, which is spread by the *Ixodes scapularis* tick (deer tick). Approximately 20,000 cases of Lyme disease are diagnosed each year in the United States.¹³ Lyme disease affects the cardiovascular, musculoskeletal, and nervous systems. The clinical manifestations are categorized into early and late diseases. Stage 1 of early disease occurs a few days to 1 month after the tick bite, stage 2 and 3 of early disease occur a few days to 10 to 12 months after the tick bite, and late disease occurs months to years after the tick bite. Stage 1 of early disease manifests as localized infection and an erythematous rash with central clearing at the site of the tick bite, called erythema migrans. Stage 2 of early disease is characterized by multiple annular skin lesions with fatigue, headache, fever, chills, regional lymphadenopathy, and sometimes mild encephalopathy. If untreated at this stage, patients can develop neurologic symptoms (eg, meningitis, encephalitis, cranial neuritis, radiculoneuritis, mononeuritis multiplex) and cardiovascular symptoms (eg, fluctuating atrioventricular [AV] blocks, myopericarditis, LV dysfunction, left axis deviation, cardiomegaly, LV

dysfunction, sinus arrhythmia, sinus bradycardia, ST-segment and T-wave abnormalities, wandering atrial pacemaker, ectopic atrial bradycardia, and ventricular ectopy).¹⁴⁻¹⁶ Stage 3 is characterized by intermittent joint pains and swelling primarily in large joints as a result of the immune response to the infection; chronic neurologic changes are seen in approximately 5% of people with the disease.

The incidence of cardiac involvement in Lyme disease is estimated to be 8% in adults; conduction and rhythm disturbances are the most common findings.¹⁴ The cardiovascular manifestations usually occur within the first 21 days of exposure to *B. burgdorferi*.¹⁷ Heart block in Lyme disease is generally self-limited, responds to intravenous ceftriaxone, and rarely requires a permanent pacemaker.¹⁶ Although erythema migrans alone is rarely associated with electrocardiographic changes, the manifestations that may be seen are first-degree AV blocks, shorter duration of Q, and deep S waves.¹⁸ An ECG can be a useful screening test for detecting cardiac involvement in suspected Lyme disease as suggested by a study that found that 3 of 10 children with probable Lyme disease had an abnormal ECG.¹⁹

Leptospirosis

Leptospirosis is caused by a spirochete of the genus *Leptospira*. The incidence of leptospirosis in the United States is 128 cases per 100,000 persons based on a surveillance study conducted in 1992; this study found that the highest incidence was in Hawaii.²⁰ Leptospirosis is an occupational hazard for people who work with animals and a recreational hazard for people who engage in activities near contaminated water. This disease is acquired by direct or indirect contact with urine or tissues of infected animals and is characterized by sub-clinical illness followed by self-limited systemic illness in most patients. However, approximately 10% of infected persons will progress to a severe, potentially fatal form of leptospirosis called Weil's syndrome, which is associated with renal failure, liver failure, pneumonia, and hemorrhagic diathesis. The common ECG findings seen in leptospirosis include first-degree AV block and changes due to acute pericarditis (*see* Infections of Heart Structures).²¹ Electrocardiographic abnormalities in leptospirosis represent definite involvement of the myocardium, and are possibly caused by interstitial myocarditis; they indicate a poor prognosis.²²

Tick-borne Relapsing Fever

Tick-borne relapsing fever is caused by *B. hermsii* and *B. turicatae*. It is characterized by recurrent high fevers that have a sudden onset and are followed by an

afebrile period. The febrile episodes last for 3 to 6 days and are accompanied by headache, arthralgias, myalgias, neck stiffness, and nausea. Cranial nerve abnormalities can be present. Myocarditis is rarely seen, and these patients present with prolonged QTc interval.²³

PARASITIC INFECTIONS

Chagas' Disease

Chagas' disease is caused by infection with the parasite *Trypanosoma cruzi*, which is spread by triatomine bugs (or "kissing" bugs). Commonly seen in South and Central America, Chagas' disease has a worldwide prevalence of 16 to 18 million patients. Chagas' disease frequently affects the cardiovascular, nervous, and gastrointestinal systems and includes acute, intermediate, and chronic stages. The acute phase is seen 1 week after the triatomine bug bite and lasts for 1 to 2 months. It is characterized by fatigue, fever, hepatosplenomegaly, and enlarged lymph nodes. Young children can present with convulsions and meningo-encephalitis when it affects the brain. Patients are asymptomatic during the intermediate phase, which lasts for 20 to 30 years. The chronic phase consists of enlargement of the heart, esophagus, or large bowel (megacolon) from the inflammatory response, cellular lesions, and fibrosis induced by the parasite.

Cardiac manifestations can be seen in all phases of the disease and range from mild changes on ECG to sudden death. The common changes observed in Chagas' disease are generally conduction abnormalities such as right bundle branch block, left anterior hemiblock, first-degree block, and complete AV block. The prevalence of ECG abnormalities increases with age and the presence of *T. cruzi* antibodies in the serum, with a 44% incidence in patients with antibodies and a 15.1% incidence in patients without antibodies.²⁴ Serious conduction abnormalities such as complete AV blocks and sudden death are noted if reinfection with *T. cruzi* occurs during the acute phase rather than during the chronic phase, a finding confirmed by an experimental study in mice.²⁵⁻²⁷ Mortality is 3 times higher in patients with abnormal T-wave changes than in patients without electrocardiographic changes.²⁸ Other electrocardiographic changes that predict increased risk for death in Chagas' disease include altered ventricular repolarization, prolonged maximum QTc interval duration, and increased QT dispersion.²⁹

Trichinosis

Trichinosis develops following consumption of undercooked meat contaminated with *Trichinella* larvae. The incidence of the disease is less than 100 cases

per year in the United States. The clinical symptoms of trichinosis consist of fever, myalgia, headache, skin rash, nausea, vomiting, diarrhea, leg edema, cough, and subconjunctival and subungual splinter hemorrhages. Trichinosis has an incubation period of 8 to 15 days, and the disease results from invasion of the intestinal wall by the juvenile larvae. During this invasive phase, ECG abnormalities are seen, most commonly a transient nonspecific ventricular repolarization disturbance (with ST-segment and T-wave changes), which is seen especially with pericarditis.^{30,31} The incidence of cardiac involvement in trichinosis has been reported to range from 21% to 75%, but a recent study reported an incidence of 13%.³⁰

BACTERIAL INFECTIONS

Diphtheria

Diphtheria is caused by *Corynebacterium diphtheriae*, a sporulating, nonmotile, noncapsulated, gram-positive bacillus. It is spread by airborne respiratory droplets and direct contact with respiratory secretions and exudates from infected skin or fomites. Five or fewer cases per year have been reported in the United States since 1980 (www.cdc.gov). An outbreak of diphtheria occurred in Russia during the early 1990s, with 50,425 cases reported in 1995 at a yearly rate of 17.3 cases per 100,000 persons. Mass immunization, early identification, and management of cases has reduced this rate to 0.6 cases per 100,000 persons since 1999.³²

Diphtheria can affect multiple organs. Infection of the anterior nares leads to serosanguinous or purulent nasal discharge, and involvement of the posterior structure of the mouth leads to the development of a membrane, which is initially white and later changes to gray with patches of green or black necrosis on one or both tonsils. The infection can be seen on the soft palate, oropharynx, nasopharynx, and larynx. Risk factors for involvement of the heart in diphtheria include older age, low socioeconomic status, and extensive involvement of the respiratory tract.³³ Two thirds of patients with diphtheria demonstrate subtle evidence of myocarditis, 10% to 25% demonstrate cardiac dysfunction,³⁴ and others demonstrate ST-T segment depression.

The ECG findings associated with diphtheria are broadly categorized under 2 groups, with the asymptomatic group consisting of PR-interval prolongation and T-wave changes, and the symptomatic group consisting of intraventricular blocks and AV conduction blocks.³⁵ The ECG abnormalities in severe diphtheria last for several days after the disappearance of the clinical symptoms.³⁵ ECG abnormalities (eg, ST-segment

and T-wave changes) were observed in guinea pigs after diphtheria-tetanus-pertussis vaccination.³⁶

Cardiac damage is the leading cause of mortality in adults with diphtheria, accounting for approximately one third of all deaths from this infection.³⁷ Diphtheria toxins cause severe acute myocarditis leading to cardiac damage.³⁸ Kneen and colleagues³⁹ showed that the use of 24-hour electrocardiography on admission improved the ability to predict diphtheritic cardiomyopathy by 57%. The risk of cardiac involvement is higher in patients presenting with fever, toxic disease, and membranous disease.³³ Findings that indicate a worse prognosis for heart disease in diphtheria are ventricular ectopy on presentation,^{35,40} aspartate transaminase levels exceeding 80 U/L, white blood cell count exceeding 25,000 cells/ μ L, and membrane extending to at least 2 anatomic sites.⁴¹

Tetanus

Tetanus is caused by the anaerobic gram-positive bacillus *Clostridium tetani*. Between 35 and 70 cases of tetanus are reported to the Centers for Disease Control and Prevention each year (www.cdc.gov). Tetanus is classified as generalized, localized, cephalic, and neonatal. Generalized tetanus is associated with trismus (lockjaw), risus sardonicus (increased tone in orbicular oris), and generalized spasms. The localized form of tetanus consists of rigidity of muscles at the site of spore inoculation. Cephalic tetanus is seen with head wounds and affects the cranial nerves. Neonatal tetanus occurs as a result of contamination of the umbilical stump with *C. tetani* spores following childbirth if mothers are not adequately immunized. Cardiac involvement occurs more often in generalized tetanus and is marked by sinus tachycardia, prolonged QT interval, nonspecific ST-segment and T-wave abnormalities, and P-wave changes on ECG.⁴² Higher mortality is seen in patients with spatial QRS-T angle widening.⁴³

Pertussis

The small coccobacillary organism *Bordetella pertussis* causes pertussis. During the years 2001 to 2003, 28,998 cases of pertussis were reported from the 50 states and the District of Columbia (7580 in 2001; 9771 in 2002; and 11,647 in 2003); 69% of these cases were reported as confirmed.⁴⁴ The disease consists of catarrhal, paroxysmal, and convalescent phases. The catarrhal phase is characterized by low-grade fever, malaise, conjunctival redness, rhinorrhea, and lacrimation. The paroxysmal phase is characterized by dry cough with paroxysms, vomiting with thick mucus plugs, and watery secretions. The convalescent phase is associated with a decrease in the

intensity of cough and the frequency of the paroxysms. Complications of pertussis include secondary infections as well as central nervous system and cardiac involvement. The common electrocardiographic changes seen in pertussis with cardiac involvement are sinus node and AV nodal blocks.^{45,46} These changes occur as a result of depression of the cardiac muscle secondary to activation of the potassium conductance channels by the guanine nucleotide binding protein in the pertussis toxin.^{45,46}

Streptococci

Streptococci can affect the heart by producing inflammatory lesions and myocarditis in rheumatic fever and by direct involvement of bacteria or toxin in other streptococcal infections.⁴⁷ Rheumatic fever is caused by group A beta-hemolytic streptococci. First-degree heart block is the common cardiac manifestation and is included in the Jones criteria as a minor criterion for the diagnosis of rheumatic fever. The other changes involving the heart consist of sinus tachycardia, P-wave changes, T-wave inversion, cardiomegaly, congestive heart failure, appearance of new mitral or aortic regurgitation murmur, and ectopic beats. Rheumatic fever is rarely associated with other conduction abnormalities such as complete heart block or Wenckebach block.⁴⁸

ECG abnormalities associated with invasive streptococcal infections mostly involve the ST-T segment region. Group B streptococcal myocarditis is associated with low voltage in the limb leads and can mimic acute myocardial infarction on ECG.⁴⁹ Streptococcal tonsillitis is associated with acute myopericarditis. The electrocardiographic changes seen with invasive streptococcal infections will usually disappear on treatment with intravenous penicillin.⁵⁰ Diffuse ST-segment elevation attributed to purulent pericarditis caused by group G streptococcus has been reported.⁵¹

Typhoid

Typhoid is caused by *Salmonella typhi* and has an estimated incidence of 16 million cases worldwide, with 600,000 cases resulting in death each year. The symptoms of typhoid include fever with relative bradycardia, chills, diarrhea, rose spots, and hepatosplenomegaly. Complications are seen in the fourth week of the disease and commonly include intestinal obstruction, ulceration, and perforation. Electrocardiographic changes in typhoid can be seen in both the acute (lasting up to 4 weeks) and convalescent periods (lasting up to 2 months). They may be observed up to the convalescent period due to structural damage to the heart caused by invasion of the myocardium by *Salmonella* or its toxins. Cardiac enzymes are elevated only in the

Table 2. Infectious Causes of Myocarditis

Bacteria	Fungi
<i>Borrelia burgdorferi</i>	<i>Aspergillus</i>
<i>Brucella</i>	<i>Blastomyces</i>
<i>Campylobacter</i>	<i>Candida</i>
<i>Chlamydia pneumoniae</i>	<i>Coccidioides immitis</i>
<i>Chlamydia psittaci</i>	<i>Cryptococcus</i>
<i>Clostridium perfringens</i>	<i>Histoplasma capsulatum</i>
<i>Corynebacterium diphtheriae</i>	Parasites
<i>Coxiella burnetii</i>	<i>Trypanosoma cruzi</i>
<i>Ehrlichia</i>	<i>Trypanosoma gambiense</i>
<i>Legionella pneumophila</i>	<i>Trypanosoma rhodesiense</i>
<i>Listeria monocytogenes</i>	<i>Toxoplasma gondii</i>
<i>Mycobacterium tuberculosis</i>	Virus
<i>Mycoplasma pneumoniae</i>	Coxsackievirus A and B
<i>Neisseria meningitidis</i>	Cytomegalovirus
<i>Rickettsia</i>	Echovirus
<i>Salmonella</i>	Epstein-Barr virus
<i>Shigella</i>	Hepatitis B, C
<i>Staphylococcus aureus</i>	HIV
<i>Streptococcus pyogenes</i>	Paramyxovirus
<i>Vibrio cholerae</i>	

acute period.⁵² The severity of manifestations of myocarditis in typhoid depends on systemic factors such as anemia, preexisting cardiovascular disease status, and nutritional status.⁵³ The common ECG abnormalities seen in typhoid fever are those of myocarditis, such as PR prolongation, QTc prolongation, ST-segment depression, and T-wave inversion. Abnormalities on ECG in typhoid myocarditis can be confused with inferior wall myocardial infarction, especially in patients with underlying structural abnormalities such as Wolff-Parkinson-White syndrome.^{54,55} Although relative bradycardia is a common entity, sinus bradycardia is rare. Several cases of sinus bradycardia secondary to sick sinus syndrome in typhoid fever have been reported.^{56,57} Sinus bradycardia in typhoid fever is refractory to atropine and improves as the disease course improves.^{56,57}

INFECTIONS OF HEART STRUCTURES

Myocarditis

The electrocardiographic and pathologic changes that develop during acute myocarditis may be due to the infectious agent invading the myocardium or to secondary changes related to the infection (fever, hypokalemia, vitamin deficiencies, and drugs). Myocarditis is caused by many different infectious agents (Table 2),

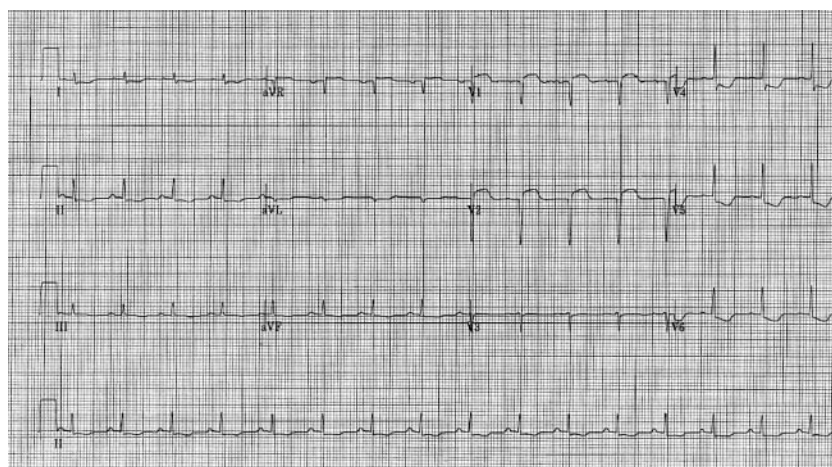


Figure 1. ST-T wave elevation in myocarditis.

Table 3. Common Causes of Infectious Pericarditis

Bacteria	Virus
<i>Haemophilus influenzae</i>	Coxsackievirus A and B
<i>Mycobacterium</i>	Echovirus
<i>Neisseria gonorrhoeae</i>	Epstein-Barr virus
<i>Neisseria meningitidis</i>	HIV
<i>Salmonella</i>	Influenza virus
<i>Staphylococcus aureus</i>	Paramyxovirus
<i>Streptococcus pneumoniae</i>	Parvovirus B19
Fungi	
<i>Aspergillus</i>	
<i>Blastomyces</i>	
<i>Candida</i>	
<i>Coccidioides immitis</i>	
<i>Cryptococcus neoformans</i>	
<i>Histoplasma capsulatum</i>	

although viruses are the most common causes, especially enteroviruses such as coxsackieviruses. Because the location of the viral infection in the heart is influenced by local or systemic hypoxia, viral infections have a predilection for the subendocardium. The manifestations of viral infections of the myocardium are influenced by the strain of the organism as well as by the hormonal and immunologic state of the host. Intrauterine infection of the fetus with rubella, paramyxovirus, and coxsackievirus can induce congenital cardiac defects.⁵⁸ Myocarditis is associated with many ECG abnormalities, including Adams-Stokes syndrome (transient loss of consciousness usually associated with partial or complete heart block), conduction disturbances, pseudoin-

farction pattern, ST-segment and T-wave abnormalities (**Figure 1**), and premature ventricular contractions.⁵⁹

Pericarditis

Pericarditis is an inflammation of the pericardium that can be caused by many infectious agents (**Table 3**), some of which affect both the pericardium and endocardium. PR depression is seen in the early phase of pericarditis^{60,61} and is followed by changes such as ST segment elevation (**Figure 2**), normalization of the ST segment, T-wave inversion, and normalization of all changes over several days to weeks.⁶² Low-voltage complexes are seen in pericarditis with pericardial effusion (**Figure 3**).

Endocarditis

Electrocardiographic changes are common in endocarditis and indicate invasive disease, thereby predicting high morbidity and mortality.⁶³ Conduction abnormalities can also suggest that the disease is extending into the perivalvular region.⁶⁴ ECG abnormalities are seen commonly in patients with prosthetic valves. No prospective studies have evaluated the electrocardiographic changes in endocarditis. An autopsy study reported that sinus tachycardia is the most common finding, seen in approximately 53% of patients.⁶⁵ Other observed findings are low QRS voltage (44%), varying degrees of heart blocks (**Figure 4**; 9%), ST elevation, atrial fibrillation, ventricular tachycardia, and supraventricular tachycardia. In patients with infective endocarditis who have persistent fever and onset of symptoms such as chest pain or shortness of breath despite appropriate therapy, heart blocks signal the presence of complicated aortic valve disease, which require consideration of surgical intervention (**Figure 5**).⁶⁵

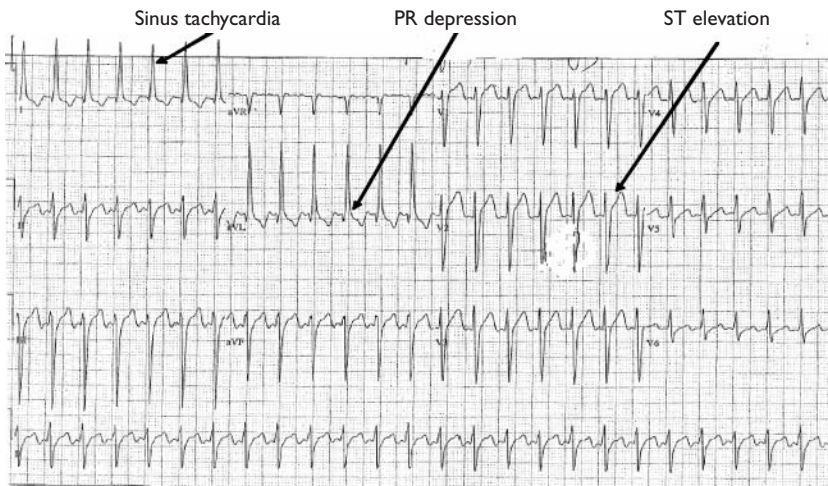


Figure 2. Tachycardia, diffuse ST elevation, and PR depression in pericarditis.

Figure 3. Low-voltage complex in pericardial effusion.

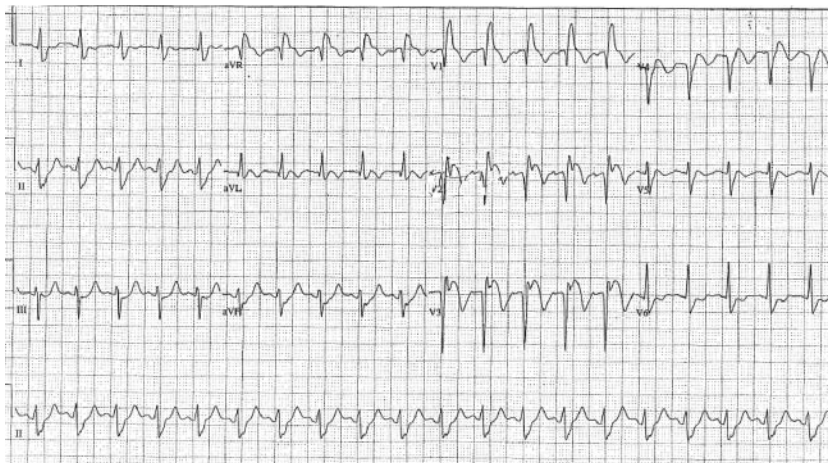
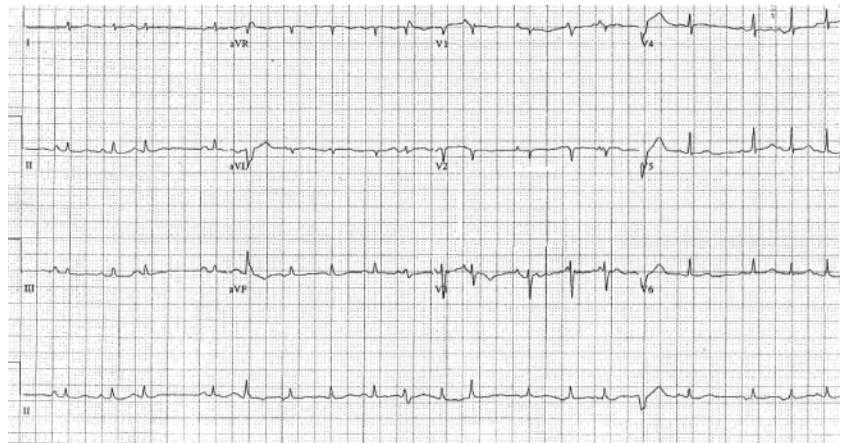


Figure 4. Endocarditis with right bundle branch block (QRS duration > 120 msec, terminal R wave in lead V₁, slurred S wave in leads I and V₆) and left anterior hemiblock (QRS deflection in lead II is negative).

MYCOPLASMOSIS

Infection with *Mycoplasma pneumoniae* is asymptomatic in 20% of the population, and it involves the upper respiratory tract more than 70% of the time.⁶⁶ Epidemics are common in closed populations such as

prisons and military population.⁶⁶ Cardiac involvement is rare. The changes commonly seen in patients with symptomatic mycoplasmosis are alterations in the end portion of the ventricular ECG complex such as T-wave inversion, bradycardia, prolonged PR interval, and

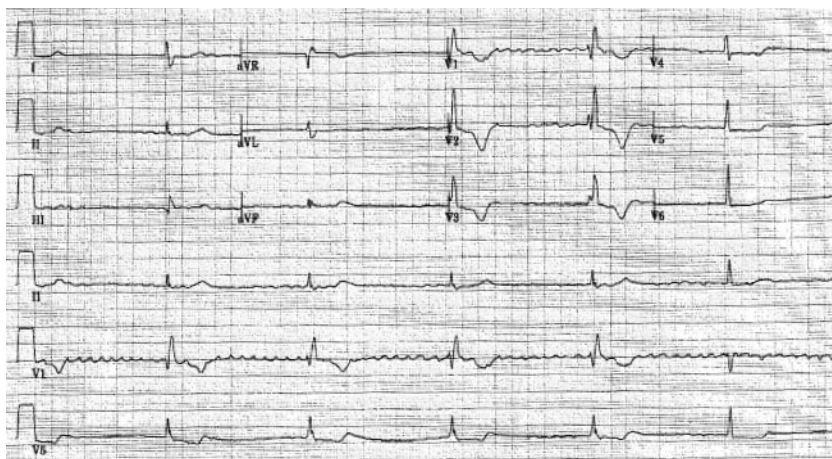


Figure 5. Complete heart block in infective endocarditis with valve abscess. The ventricular rate is slower than the atrial rate, the atrial and ventricular rhythms are regular, and the PR interval is variable.

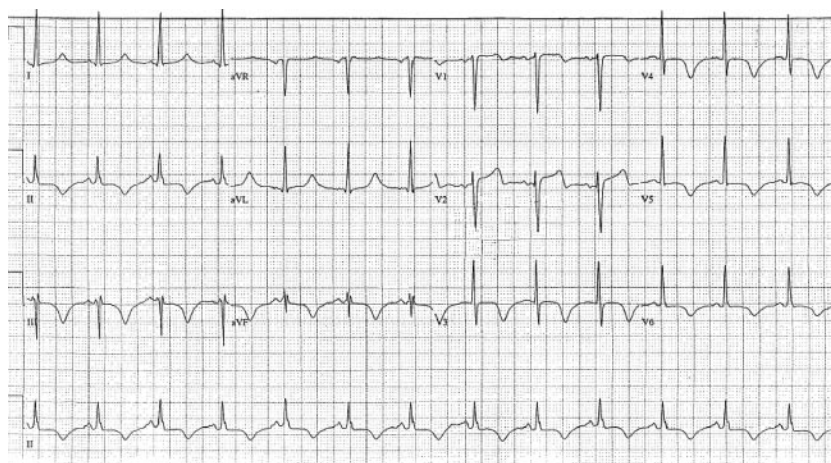


Figure 6. Diffuse T-wave inversion in meningitis/cerebrovascular accident/intracranial process.

narrow QRS complex.^{67,68} Nonspecific ECG abnormalities are seen in patients without cardiac symptoms.^{67,68} The patient's underlying cardiac status does not affect the ECG findings in mycoplasmosis.^{69,70}

INCREASED INTRACRANIAL PRESSURE

Electrocardiographic changes may occur in patients with increased intracranial pressure caused by tumors, subarachnoid hemorrhage (SAH), or meningitis. The mechanisms of these changes in patients with raised intracranial pressure depend on the underlying etiology and include increased sympathetic and vagal activity in the acute phase of SAH;⁷¹ release of large amounts of norepinephrine and epinephrine from intracranial tumors;⁷² and electrolyte abnormalities in meningitis and arrhythmogenic effects of lesions of limbic structures in cerebral tumors.⁷³ Hypokalemia caused by tumors, hemorrhage, and stimulation of the autonomic nervous system in the brain also produce ECG abnormalities.⁷⁴ The common changes seen in patients with raised intracranial pressure are tall P waves, prominent

U waves, inverted U waves, ST-segment and T-wave changes, notched T waves, and sinus bradycardia (**Figure 6**).^{72,74}

ANTIMICROBIAL DRUGS

Antimicrobial drugs can block cardiac potassium channels, resulting in a longer duration of cardiac repolarization and QTc prolongation on ECG.⁷⁵ Intravenous pentamidine can result in QTc prolongation with increased risk of torsades de pointes.⁷⁶ Fluoroquinolones can rarely cause proarrhythmic effects such as prolongation of the QTc interval, including torsades de pointes. The proarrhythmic effects of fluoroquinolones are more prominent in patients with an electrolyte imbalance (eg, hypomagnesemia, hypokalemia, hypocalcemia); alcoholics; and patients taking class I antiarrhythmics, especially quinidine, and class III antiarrhythmics. The effects normalize on cessation of the drugs.⁷⁷ Sparfloxacin is more commonly associated with prolonged QT interval (14.5 cases/million treatments) than ciprofloxacin (1 case/million

treatments) and clarithromycin (3 cases/million treatments). The azoles, antifungal agents, also cause QT prolongation.⁷⁸ Ketoconazole causes QTc prolongation in combination with antihistamines such as loratadine, terfenadine, and ebastine.⁷⁹ Macrolides can cause proarrhythmic effects, such as prolonged QT interval. Erythromycin is more potent at provoking arrhythmia, followed by clarithromycin, roxithromycin, and azithromycin.⁸⁰

CONCLUSION

Electrocardiographic changes that occur during the course of various infections can be caused by direct effects of the infectious agent as well as by electrolyte, metabolic, or autonomic system abnormalities resulting from the illness. In some situations, electrocardiography can augment the diagnostic work-up of a suspected infection, such as in Lyme disease. Much more frequently, however, it is used to evaluate for cardiac involvement in patients already diagnosed with an infectious disease, provide information on prognosis of the disease, and assess the effect of treatment. Many antimicrobial drugs have proarrhythmic effects, and physicians should know the patient's QTc interval prior to treating with a quinolone or macrolide. **HP**

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REFERENCES

1. Waller AD. A demonstration on man of electromotive changes accompanying the heart's beat. *J Physiol* 1887; 8:229–34.
2. Berul CI, Aronovitz MJ, Wang PJ, Mendelsohn ME. In vivo cardiac electrophysiology studies in the mouse. *Circulation* 1996;94:2641–8.
3. Steffen HM, Schrappe-Bacher M, Muller R, et al. [Cardiac involvement within the scope of HIV-1 infection: preliminary results of echocardiography study.] [Article in German.] *Z Kardiol* 1990;79:83–8.
4. Lubega S, Zirembuzi GW, Lwabi P. Heart disease among children with HIV/AIDS attending the paediatric infectious disease clinic at Mulago Hospital. *Afr Health Sci* 2005;5:219–26.
5. De Castro S, Migliau G, Silvestri A, et al. Heart involvement in AIDS: a prospective study during various stages of the disease. *Eur Heart J* 1992;13:1452–9.
6. Sani MU, Okeahialam BN. QTc interval prolongation in patients with HIV and AIDS. *J Natl Med Assoc* 2005; 97:1657–61.
7. Saidi AS, Moodie DS, Garson A Jr, et al. Electrocardiography and 24-hour electrocardiographic ambulatory recording (Holter monitor) studies in children infected with human immunodeficiency virus type 1. The Pediatric Pulmonary and Cardiac Complications of Vertically Transmitted HIV-1 Infection Study Group. *Pediatr Cardiol* 2000;21:189–96.
8. Kocheril AG, Bokhari SA, Batsford WP, Sinusas AJ. Long QTc and torsades de pointes in human immunodeficiency virus disease. *Pacing Clin Electrophysiol* 1997;20:2810–6.
9. Mehta NJ, Khan IA, Mehta RN, Sepkowitz DA. HIV-Related pulmonary hypertension: analytic review of 131 cases. *Chest* 2000;118:1133–41.
10. Centers for Disease Control and Prevention. Achievements in public health: elimination of rubella and congenital rubella syndrome—United States, 1969–2004. *MMWR Morb Mortal Wkly Rep* 2005;54:279–282.
11. Rowe RD. Cardiovascular disease in the rubella syndrome. *Cardiovasc Clin* 1973;5:61–80.
12. Halloran KH, Sanyal SK, Gardner TH. Superiorly oriented electrocardiographic axis in infants with the rubella syndrome. *Am Heart J* 1966;72:600–6.
13. Dennis DT, Hayes EB. Epidemiology of lyme borreliosis. In: Gray J, editor. *Lyme borreliosis: biology, epidemiology, and control*. New York: CABI Pub.; 2002:251.
14. Horowitz HW, Belkin RN. Acute myopericarditis resulting from Lyme disease. *Am Heart J* 1995;130:176–8.
15. Steere AC, Batsford WP, Weinberg M, et al. Lyme carditis: cardiac abnormalities of Lyme disease. *Ann Intern Med* 1980;93:8–16.
16. Rosenberg R. Medical mystery: bradycardia—the answer [letter]. *N Engl J Med* 2005;353:430–2.
17. Lo R, Menzies DJ, Archer H, Cohen TJ. Complete heart block due to lyme carditis. *J Invasive Cardiol* 2003;15: 367–9.
18. Pikelj-Pecnik A, Lotric-Furlan S, Maraspin V, et al. Electrocardiographic findings in patients with erythema migrans. *Wien Klin Wochenschr* 2002;114:510–4.
19. Woolf PK, Lorsung EM, Edwards KS, et al. Electrocardiographic findings in children with Lyme disease. *Pediatr Emerg Care* 1991;7:334–6.
20. Sasaki DM, Pang L, Minette HP, et al. Active surveillance and risk factors for leptospirosis in Hawaii. *Am J Trop Med Hyg* 1993;48:35–43.
21. Watt G, Padre LP, Tuazon M, Calubaquib C. Skeletal and cardiac muscle involvement in severe, late leptospirosis. *J Infect Dis* 1990;162:266–9.
22. Ramachandran S, Perera MV. Cardiac and pulmonary involvement in leptospirosis. *Trans R Soc Trop Med Hyg* 1977;71:56–9.
23. Wengrower D, Knobler H, Gillis S, Chajek-Shaul T. Myocarditis in tick-borne relapsing fever. *J Infect Dis* 1984; 149:1033.
24. Zicker F, Netto JC, Zicker EM, et al. *Trypanosoma cruzi* infection and electrocardiographic findings among active

- manual workers. A population-based study in central Brazil. *Int J Epidemiol* 1990;19:182–6.
25. Bustamante JM, Rivarola HW, Palma JA, Paglini-Oliva PA. Electrocardiographic characterization in *Trypanosoma cruzi* reinfected mice. *Parasitology* 2004;128(Pt 4):415–9.
 26. ElMunzer BJ, Sallach SM, McGuire DK. Cardiac chagas disease masquerading as an acute myocardial infarction. *Cardiol Rev* 2004;12:69–72.
 27. Maguire JH, Hoff R, Sherlock I, et al. Cardiac morbidity and mortality due to Chagas' disease: prospective electrocardiographic study of a Brazilian community. *Circulation* 1987;75:1140–5.
 28. Salles GF, Xavier SS, Sousa AS, et al. T-wave axis deviation as an independent predictor of mortality in chronic Chagas' disease. *Am J Cardiol* 2004;93:1136–40.
 29. Salles G, Xavier S, Sousa A, et al. Prognostic value of QT interval parameters for mortality risk stratification in Chagas' disease: results of a long-term follow-up study. *Circulation* 2003;108:305–12.
 30. Lazarevic AM, Neskovic AN, Goronja M, et al. Low incidence of cardiac abnormalities in treated trichinosis: a prospective study of 62 patients from a single-source outbreak. *Am J Med* 1999;107:18–23.
 31. Puljiz I, Beus A, Kuzman I, Seiwerth S. Electrocardiographic changes and myocarditis in trichinellosis: a retrospective study of 154 patients. *Ann Trop Med Parasitol* 2005;99:403–11.
 32. Dittmann S, Wharton M, Vitek C, et al. Successful control of epidemic diphtheria in the states of the Former Union of Soviet Socialist Republics: lessons learned. *J Infect Dis* 2000;181 Suppl 1:S10–22.
 33. Lumio JT, Groundstroem KW, Melnick OB, et al. Electrocardiographic abnormalities in patients with diphtheria: a prospective study. *Am J Med* 2004;116:78–83.
 34. Boyer NH, Weinstein L. Diphtheritic myocarditis. *N Engl J Med* 1948;239:913–9.
 35. Ledbetter MK, Cannon AB 2nd, Costa AF. The electrocardiogram in diphtheritic myocarditis. *Am Heart J* 1964;68:599–611.
 36. Dymnicka S, Zoltowska A. Myocardial changes after chronic immunization of guinea pigs with diphtheria-tetanus-pertussis (DTP) vaccine. *Cor Vasa* 1977;19:458–64.
 37. Rakhmanova AG, Lumio J, Groundstroem K, et al. Diphtheria outbreak in St. Petersburg: clinical characteristics of 1860 adult patients. *Scand J Infect Dis* 1996;28:37–40.
 38. Gore I. Myocardial changes in fatal diphtheria. A summary of observations in 221 cases. *Am J Med Sci* 1948;215:257–66.
 39. Kneen R, Nguyen MD, Solomon T, et al. Clinical features and predictors of diphtheritic cardiomyopathy in Vietnamese children. *Clin Infect Dis* 2004;39:1591–8.
 40. Bethell DB, Nguyen Minh Dung, Ha Thi Loan, et al. Prognostic value of electrocardiographic monitoring of patients with severe diphtheria. *Clin Infect Dis* 1995;20:1259–65.
 41. Havaladar PV, Sankpal MN, Doddannavar RP. Diphtheritic myocarditis: clinical and laboratory parameters of prognosis and fatal outcome. *Ann Trop Paediatr* 2000;20:209–15.
 42. Panciera DL, Baldwin CJ, Keene BW. Electrocardiographic abnormalities associated with tetanus in two dogs. *J Am Vet Med Assoc* 1988;192:225–7.
 43. Mitra RC, Gupta RD, Sack RB. Electrocardiographic changes in tetanus: a serial study. *J Indian Med Assoc* 1991;89:164–7.
 44. Centers for Disease Control and Prevention. Pertussis—United States, 2001–2003. *MMWR Morb Mortal Wkly Rep* 2005;54:1283–6.
 45. Adamis D, Boyer NH, Weinstein L. An electrocardiographic study of uncomplicated pertussis. *J Pediatr* 1956;49:567–9.
 46. Bohm M, Schmitz W, Scholz H, Wilken A. Pertussis toxin prevents adenosine receptor- and m-cholinoceptor-mediated sinus rate slowing and AV conduction block in the guinea-pig heart. *Naunyn Schmiedebergs Arch Pharmacol* 1989;339:152–8.
 47. Putterman C, Caraco Y, Shalit M. Acute nonrheumatic perimyocarditis complicating streptococcal tonsillitis. *Cardiology* 1991;78:156–60.
 48. Mohindra R, Pannu HS, Mohan B, et al. Syncope in a middle aged male due to acute rheumatic fever. *Indian Heart J* 2004;56:668–9.
 49. von Kurnatowski HA, Sierra-Callejas JL, Henkel W, Diedrich KW. [Rapidly fatal myocarditis due to group B streptococci (author's transl).] [Article in German.] *Dtsch Med Wochenschr* 1977;102:439–41.
 50. Karjalainen J. Streptococcal tonsillitis and acute nonrheumatic myopericarditis. *Chest* 1989;95:359–63.
 51. Kim NH, Park JP, Jeon SH, et al. Purulent pericarditis caused by group G streptococcus as an initial presentation of colon cancer. *J Korean Med Sci* 2002;17:571–3.
 52. Nand N, Sharma M, Bhutani M, et al. Cardiac status in typhoid fever. *Angiology* 1996;47:1095–100.
 53. Choudhary S. Myocarditis in enteric fever. *J Assoc Phys India* 1974;22:251–4.
 54. Pelupessy JM, Sangka P. Electrocardiographic pattern of typhoid fever in children. *Paediatr Indones* 1989;29:215–20.
 55. Akdeniz H, Tuncer I, Irmak H, Demiroz AP. Salmonella myocarditis in a patient with Wolf-Parkinson-White syndrome that was confused with an inferior myocardial infarction. *Clin Infect Dis* 1997;25:736–7.
 56. Rajeshwari K, Yadav S, Puri RK, Khanijo CM. Sick sinus syndrome—a rare complication of typhoid fever. *Indian Pediatr* 1994;31:995–8.
 57. Mathur SL. Sino-atrial block in typhoid fever [letter]. *J Assoc Physicians India* 1990;38:243–4.
 58. Levine HD. Virus myocarditis: a critique of the literature from clinical, electrocardiographic, and pathologic standpoints. *Am J Med Sci* 1979;277:132–43.
 59. Hayakawa M, Inoh T, Yokota Y, et al. A long-term follow-up study of acute myocarditis an electrocardiographic and echocardiographic study. *Jpn Circ J* 1984;48:1362–7.
 60. Marinella MA. Electrocardiographic manifestations and differential diagnosis of acute pericarditis. *Am Fam*

- Physician 1998;57:699–704.
61. Baljepally R, Spodick DH. PR-segment deviation as the initial electrocardiographic response in acute pericarditis. *Am J Cardiol* 1998;81:1505–6.
 62. Chan TC, Brady WJ, Pollack M. Electrocardiographic manifestations: acute myopericarditis. *J Emerg Med* 1999;17:865–72.
 63. Meine TJ, Nettles RE, Anderson DJ, et al. Cardiac conduction abnormalities in endocarditis defined by the Duke criteria. *Am Heart J* 2001;142:280–5.
 64. Miyamoto MI, Hutter AM Jr, Blum JH, Torchiana DF. Cardiac conduction abnormalities preceding transoesophageal echocardiographic evidence of perivalvar extension of infection in a case of Salmonella prosthetic valve endocarditis. *Heart* 1997;78:416–8.
 65. Berk WA. Electrocardiographic findings in infective endocarditis. *J Emerg Med* 1988;6:129–32.
 66. Mogabgab WJ. *Mycoplasma pneumoniae* and adenovirus respiratory illnesses in military and university personnel, 1959–1966. *Am Rev Respir Dis* 1968;97:345–58.
 67. Feizi O, Grubb C, Skinner JI, et al. Unusual complications of primary atypical pneumonia due to *M. pneumoniae*. *Br Med J* 1971;4:751.
 68. Chergui K, Fourme T, Veillard-Baron A, et al. *Mycoplasma pneumoniae* and second-degree heart block. *Clin Infect Dis* 1998;27:1534–5.
 69. Bogomolov BP, Mol'kova TN, Deviatkin AV. [Cardiovascular system condition in respiratory mycoplasmosis.] [Article in Russian.] *Klin Med (Mosk)* 2002;80:34–8.
 70. Lim CH, Toh CC, Chia BL, Low LP. Stokes-Adams attacks due to acute nonspecific myocarditis. *Am Heart J* 1975;90:172–8.
 71. Kawahara E, Ikeda S, Miyahara Y, Kohno S. Role of autonomic nervous dysfunction in electrocardiographic abnormalities and cardiac injury in patients with acute subarachnoid hemorrhage. *Circ J* 2003;67:753–6.
 72. Syverud G. Electrocardiographic changes and intracranial pathology. *AANA J* 1991;59:229–32.
 73. Koepp M, Kern A, Schmidt D. Electrocardiographic changes in patients with brain tumors. *Arch Neurol* 1995;52:152–5.
 74. Hersch C. Electrocardiographic changes in subarachnoid haemorrhage, meningitis, and intracranial space-occupying lesions. *Br Heart J* 1964;26:785–93.
 75. Morissette P, Hreiche R, Turgeon J. Drug-induced long QT syndrome and torsade de pointes. *Can J Cardiol* 2005;21:857–64.
 76. Eisenhauer MD, Eliasson AH, Taylor AJ, et al. Incidence of cardiac arrhythmias during intravenous pentamidine therapy in HIV-infected patients. *Chest* 1994;105:389–95.
 77. Prabhakar M, Krahn AD. Ciprofloxacin-induced acquired long QT syndrome. *Heart Rhythm* 2004;1:624–6.
 78. Tholakanahalli VN, Potti A, Hanley JF, Merliss AD. Fluconazole-induced torsade de pointes. *Ann Pharmacother* 2001;35:432–4.
 79. Gras J, Llenas J, Palacios JM, Roberts DJ. The role of ketoconazole in the QTc interval prolonging effects of H1-antihistamines in a guinea-pig model of arrhythmogenicity. *Br J Pharmacol* 1996;119:187–8.
 80. Ohtani H, Taninaka C, Hanada E, et al. Comparative pharmacodynamic analysis of Q-T interval prolongation induced by the macrolides clarithromycin, roxithromycin, and azithromycin in rats. *Antimicrob Agents Chemother* 2000;44:2630–7.

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