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# Cardiac Conduction Defects in the Context of Cardiac Diseases: From Basics to Practice

[1]Ismail Alsuz, FICMS (Cardiol), CABM (med.), MBChB , Nasiriyah Heart Center, Dhi Qar, Iraq

[2]Mahdi Al-Zaidi, FICMS (Cardiol), FICMS (med.), MBChB, Ibn Al-Bitar Cardiac Center, Baghdad, Iraq

**Corresponding Author:** Ismail Alsuz, FICMS (Cardiol), CABM (med.), MBChB , Nasiriyah Heart Center, Dhi Qar, Iraq

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**Abstract**

Aim of this review is to explore the basic components of cardiac conduction system and to address how myocardial ischemia and other cardiac diseases can impact cardiac conductive properties with focusing on the conduction disorders that faced frequently in modern cardiology practice.

**Keywords:** Conduction, Heart block, AV node, Ischemia.

## Anatomy of the Sinus Node and Conduction System

### Sino atrial Node

In humans, the Sino atrial node is a spindle-shaped structure composed of a fibrous tissue matrix with closely packed cells [(1)]. Normal electrical activation of the heart arises from the principal pacemaker cells that spontaneously depolarize, located laterally in the epicardial groove of the sulcus terminals, near the junction of the right atrium and the superior vena cava where they envelop the SA nodal artery. The sinus node in adult measures approximately 1 to 2 cm long and 0.5 mm wide. The SA node is composed of a cluster of small fusiform cells the central zone of the sinus node containing the principal pacemaker cells is small and located within a fibrous tissue matrix. The SA node is structurally heterogeneous, but the central prototypic nodal cells have fewer distinct myofibrils than the surrounding atrial myocardium, no intercalated disks visible on light microscopy, a poorly developed sarcoplasmic reticulum, and no T-tubules. [(1)]

In the periphery of the node along the crista terminals, transitional cells with pacemaker function are also present. Experimental and clinical evidence now suggest that the sinus node region is less defined than previously appreciated [(3)]. The principal pacemaker site within this region may migrate, resulting in subtle alterations in P-wave morphology. Once the impulse exits the sinus node and the perinodal tissues, it traverses the atrium to the AV node [(5)]. The conduction of impulses from right to left atrium has been postulated to occur preferentially via Bachmann bundle, and secondarily across the musculature of the coronary sinus [(6)].

### Atrioventricular Node

Once the sinus node impulse activates the atrium, electrical activation continues through the AV node, with a conduction delay ensuring complete atrial contraction before initiation of ventricular conduction [(2)]. The AV conduction axis is structurally complex, involving the atria and ventricles as well as the AV node. Unlike the SA node, the AV node is a

subendocardial structure. The AV nodal complex is considered to have three related regions:

1- The transitional cell zone, 2- the compact AV node, and 3- the penetrating AV bundle. The transitional cell zone composed of aggregates of cells in the posterior-inferior right atrium [4]. The compact AV node (~1, 3, 5 mm) is shaped like a half oval and is located beneath the right atrial endocardium at the apex of the triangle of Koch.

The triangle of Koch is defined by the coronary sinus ostium posteriorly, the septal tricuspid valve annulus anteriorly, and the tendon of Todaro (formed by the extension of the eustachian valve into the central fibrous body)

superiorly [7]. The distal end of the compact AV node enters the central fibrous body to become the penetrating bundle where it immediately traverses the central fibrous body and is in close proximity to the aortic, mitral, and tricuspid valve annuli; thus, it is subject to injury in the setting of valvular heart disease or its surgical treatment. Then it continues in the membranous septum as the bundle of His. The speed of conduction through the AV nodal complex is at 0.03 m/s, whereas the His-Purkinje fibers conduct at 2.4 m/s. The AV node is highly innervated with postganglionic sympathetic and parasympathetic nerves (8). The bundle of His and distal conducting system are minimally influenced by autonomic tone. The cells that comprise the AV node complex are heterogeneous with a range of action potential profiles. In the transitional zones, the cells have an electrical phenotype between atrial myocytes and cells of the compact node. Atrionodal transitional connections may exhibit decremental conduction, defined as slowing of conduction with increasingly rapid rates of stimulation. Fast and slow AV nodal pathways have been described, but controversy remains as to whether these two types of pathway are anatomically distinct or represent functional heterogeneities in different regions of the AV nodal complex. Myocytes that comprise the compact node are depolarized (resting membrane potential ~ −60 mV); exhibit action potentials with low amplitudes, slow upstrokes of phase 0 (10 V/s), and phase 4 diastolic depolarization; high-input resistance; and relative insensitivity to external [K]. The action potential phenotype is explained by the complement of ionic currents expressed. AV nodal cells lack IK1 and INa; ICa-L is responsible for phase 0; and phase 4 depolarization reflects the composite activity of the depolarizing currents If, ICa-L, ICa-T, and INCX and the repolarizing currents IKr and IKACh. Electrical coupling between cells in the AV node is tenuous due to the relatively sparse expression of gap junction channels (Predominantly connexin-40) and increased extracellular volume [10].

**His-Purkinje System**

The penetrating part of the AV bundle continues through the annulus fibrosis into the membranous septum, along the crest of the left side of the interventricular septum for 1 to 2 cm, and then divides into the right and left bundle branches. The right bundle branch continues intramyocardially along the right side of the interventricular septum and emerges subendocardially beneath the anterior papillary muscle of the right ventricle. The left bundle begins as a sheet of fascicles and runs along the left side of the inter-ventricular septum and soon separates into anterior and posterior sheets (most anatomists agree it is a trifascicular system with a substantial septal branch) corresponding to the papillary muscles [11]. In many hearts, the left bundle may appear more as a network rather than a well-defined bifascicular system. The

terminal Purkinje fibers arising from the bundle branches form interweaving networks on the endocardial surface of both the right and left ventricles. The rapid conduction of electrical impulses across this network results in near simultaneous activation of both right and left ventricles. The His bundle and bundle branches are insulated from ventricular myocardium. The most rapid conduction in the heart is observed in these tissues. The action potentials exhibit very rapid upstrokes (phase 0), prolonged Plateaus (phase 2), and modest automaticity (phase 4 depolarization). Gap junctions, composed largely of connexin-40, are abundant but bundles are poorly connected transversely to ventricular myocardium [(12)]. The blood supply to the penetrating AV bundle is from the AV nodal artery [(11)].

**Blood Supply**

The sinus node receives its blood supply from the sinoatrial (SA) nodal artery arising from the right coronary artery in 59% of patients, from the left circumflex artery in 38%, and from both arteries with a dual blood supply in 3%. The AV node is supplied by the AV nodal artery arising from the right coronary artery in 90% of patients, whereas the left circumflex artery provides it in the remaining 10% of patients. The bundle of His is supplied by both the AV nodal artery and first septal perforator of the left anterior descending coronary artery. The bundle branches also have a dual blood supply from the septal perforators of the left anterior descending coronary artery and branches of the posterior descending coronary artery [(11)].

The left bundle has a rich blood supply from the AV nodal artery, posterior descending artery, and branches of the left anterior descending artery.

**Atrioventricular (AV) block** is defined as a delay or interruption in the transmission of an impulse from the atria to the ventricles due to an anatomical or functional impairment in the conduction system. The conduction disturbance can be transient or permanent, and it can have many causes.

The conduction can be delayed, intermittent, or absent. The commonly used terminology includes first degree (slowed conduction without loss of atrio-ventricular synchrony), second degree (intermittent loss of atrio-ventricular conduction, often in a regular pattern, e.g., 2:1, 3:2, or higher degrees of block), and third degree or complete AV block.

**Physiologic and Pathophysiologic Av Block**

**Increased vagal tone** — enhanced vagal tone due to sleep, athletic training, pain, carotid sinus massage, or hypersensitive carotid sinus syndrome can result in slowing of the sinus rate and/or the development of AV block.

**Idiopathic progressive cardiac conduction disease** — Fibrosis and sclerosis of the conduction system accounts for about one-half of cases of AV block and may be induced by several different conditions which often cannot be distinguished clinically (14). Progressive cardiac conduction defects, referred to as Lenegre's or Lev's disease, are characterized by progressive impairment of the conduction system:

- The term Lenegre's disease has been traditionally used to describe a progressive, fibrotic, sclera-degenerative affliction of the conduction system in younger individuals. It is frequently associated with slow progression to complete heart block and may be hereditary.
- Lev's disease has referred to "sclerosis of the left side of the cardiac skeleton" in older patients, such as that associated with calcific involvement of the aortic and mitral rings [(15)]. It is caused by fibrosis or calcification extending from any of the fibrous

structures adjacent to the conduction system into the conduction system [16].

Fibrosis of the top of the muscular septum is a common cause of right bundle branch block (RBBB) with left anterior fascicular block in the elderly patient. Involvement of the mitral ring or the central fibrous body, for example, may be the most common cause of complete heart block with a narrow QRS complex in the elderly. Aortic valve calcification, on the other hand, can invade the bundle of His, the right and/or left bundle branch as well as the left anterior fascicle. Thus, the QRS complex may be prolonged.

Ischemic heart disease — Ischemic disease accounts for about 40 percent of cases of AV block (14). Conduction can be disturbed with either chronic ischemic disease or during an acute myocardial infarction (MI) [18]. It is estimated that approximately 20 percent of patients with an acute MI develop AV block: 8 percent with first degree; 5 percent with second degree; and 6 percent with third degree [19].

Intraventricular conduction disturbances (IVCDs), including bundle and fascicular blocks, also occur in 10 to 20 percent of cases of acute MI [20]. Left bundle branch block (LBBB) and RBBB with left anterior fascicle block are most common, each occurring in about one-third of patients with an IVCD (22). RBBB with or without left posterior fascicular block and RBBB alternating with LBBB are less frequently seen, while isolated left anterior or posterior fascicle block is most unusual.

Second-degree and higher-grade AV block tends to occur more often in inferior rather than anterior acute MI; however, the level of block in inferior

MI tends to be in the AV node with more stable, narrow escape rhythms.

In contrast, acute anterior MI is associated with block in the distal AV nodal complex, His bundle, or bundle branches and results in wide complex, unstable escape rhythms and a worse prognosis with high mortality.

**Cardiomyopathy and myocarditis** — AV block can be seen in patients with cardiomyopathies, including hypertrophic obstructive cardiomyopathy and infiltrative processes such as amyloidosis and sarcoidosis, and in patients with myocarditis due to a variety of causes including rheumatic fever, Lyme disease, diphtheria, viruses, systemic lupus erythematosus, toxoplasmosis, bacterial endocarditis, and syphilis [16]. The development of AV block in myocarditis is often a poor prognostic sign.

**Congenital heart disease** — congenital complete heart block may be an isolated lesion or may be associated with other types of congenital heart disease.

**Familial disease** — Familial AV conduction block, characterized by a progression in the degree of block in association with a variable apparent site of block, may be transmitted as an autosomal dominant trait. One form of AV conduction block has been mapped to a genetic locus at chromosome 19q13 and the other to chromosome 3p21, where the cardiac sodium channel, SCN5A, is encoded. Several SCN5A mutations have been associated with AV conduction block [16].

Some of these mutations produce AV block in childhood, while others present in middle-age and have been called hereditary Lenegre's disease. In the latter setting, it has been proposed that haploinsufficiency combined with aging leads to a progressive decline in conduction. Consistent with this hypothesis is the observation in a mouse model of SCN5A-linked hereditary Lenegre's disease of progressive impairment of atrial and ventricular conduction with aging in association with myocardial fibrosis; these changes

occurred without a change in left ventricular systolic or diastolic function.

In some families with SCN5A mutations, AV block or other conduction abnormalities are present with or without associated dilated cardiomyopathy.

Different SCN5A mutations are associated with other cardiac abnormalities including congenital long QT syndrome type 3, the Brugada syndrome, familial sick sinus syndrome, and familial dilated cardiomyopathy with conduction defects and susceptibility to atrial fibrillation.

Other genetic forms of familial AV block have been described, including a progressive form mapped to a locus on chromosome 19q13 and a form associated with congenital heart disease for which a point mutation has been identified in the cardiac transcription factor CSX/NKX2-5. Targeted deletion of the NKX.2-5 gene in mice causes hypoplasia of the cardiac conduction system and progressive heart block [17].

**Others** — AV block can also occur in a variety of other disorders:

- Hyperkalemia, usually when the plasma potassium concentration is above 6.3 meq. /L.
- Infiltrative malignancies, such as Hodgkin lymphoma and other lymphomas, and multiple myeloma.
- Hereditary neuromuscular heredo-degenerative disease such as myotonic dystrophy, Kearns-Sayre syndrome, and Erb's dystrophy.
- Rheumatologic disorders including dermatomyositis and Paget disease.
- Hyperthyroidism, myxedema, and thyrotoxic periodic paralysis.
- Cardiac tumors, cysts, myocardial bridging, and trauma [17].
- Neonatal lupus syndrome, which results from transplacental passage of anti-Ro/SSA or anti-La/SSB antibodies from the mother.

**Iatrogenic Av Block**

**Medications** — a variety of drugs can impair AV conduction, occasionally resulting in AV block. Examples include digitalis, calcium channel blockers (especially verapamil and to a lesser extent diltiazem), amiodarone, adenosine, and ß-blockers. In comparison, antiarrhythmic drugs that modulate the sodium channel, such as quinidine, procainamide, and disopyramide, can produce block in the more distal His-Purkinje system.

Most patients with AV block who are taking drugs that can impair conduction probably have underlying conduction system disease. This was suggested by a study of 169 patients with second- or third-degree AV block not related to acute MI, digitalis toxicity, or vasovagal syncope. Of these, 92 (54 percent) were receiving beta blockers and or verapamil or diltiazem. Drug discontinuation resulted in resolution of AV block in 32 of 79 cases; however, AV block later recurred in the absence of therapy in 18 of these patients [23].

**Cardiac surgery** — AV block may be associated with replacement of a calcified aortic or mitral valve, closure of a ventricular septal defect, or other surgical procedures [17].

**Catheter ablation for arrhythmias** — AV block is a potential complication of catheter ablation of reentrant arrhythmias when the reentrant pathway lies within or near the AV node.

**Transcatheter closure of VSD** — a variety of devices have been used to close muscular ventricular septal defects (VSDs), both congenital and those that occur after myocardial infarction. The Amplatzer ventricular septal defect occluder, for example, completely occluded 28 of 30 VSDs in one report. One patient with

complete left bundle branch block after the procedure progressed to complete heart block at one year. The presumed mechanism is that the right ventricular retention disk overlaps the ventricular conduction system as it passes above or anterosuperiorly to the defect.

**Alcohol (ethanol) septal ablation** — Percutaneous transluminal septal myocardial ablation, also called alcohol (ethanol) septal ablation, transcoronary ablation of septal hypertrophy, and nonsurgical septal reduction therapy, is a nonsurgical treatment for obstructive hypertrophic cardiomyopathy. This intervention consists of infarction and thinning of the proximal interventricular septum via infusion of alcohol into the first septal perforating branch of the left anterior descending coronary artery through an angioplasty catheter. Complete heart block is seen in 14 to 22 percent of patients after this procedure.

**Transcatheter aortic valve implantation (TAVI)** — A very high rate of AV block can be seen after percutaneous TAVI, with up to one-third of patients requiring a permanent pacemaker within 30 days of the procedure Pre-existing disturbances of cardiac conduction, a narrow left ventricular outflow tract, and the severity of mitral annular calcification appear to be predictors of this complication. There may also be a higher rate of heart block observed with self-expanding implanted aortic valves compared with balloon expandable versions [(24)].

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