A 60-year-old man with a history of remote myocarditis and residual mild left ventricular dysfunction presented with syncope. Before admission, the patient was not taking any regular medications. Medical history was otherwise unremarkable. Examination at presentation was unremarkable, apart from slow atrial fibrillation (AF). ECG on presentation demonstrated AF with slow ventricular response and a complete left bundle-branch block (Figure 1). Inpatient telemetry demonstrated episodes of nonsustained ventricular tachycardia (VT). Cardiac catheterization with coronary angiography was normal. Echocardiogram demonstrated mild left ventricular dysfunction (ejection fraction 50%) but was otherwise unremarkable.

An electrophysiological study showed a hisoventricular interval of 75 ms during AF at a rate of 75 beats per minute. No spontaneous pauses or infranodal phase 4 atrioventricular (AV) block was spontaneously observed. Programmed stimulation from the right ventricular apex was unremarkable at a 600-ms cycle length. At a 400-ms cycle length, a sustained monomorphic VT at 165 beats per minute with left bundle-branch block morphology and an inferior axis (Figure 2) was induced with a single extrastimulus (S2=270 ms). After 35 seconds, the VT spontaneously terminated. Despite the persistence of AF, the termination of VT was followed by a prolonged complete infrahisian AV block (Figure 3). After 8.5 seconds of ventricular asystole, AV conduction resumed. In addition, spontaneous premature ventricular complexes were observed (Figure 4). Those originating from the left anterior septum were associated with transient infrahisian AV block (Figure 4A). In contrast, those originating from the right ventricular apex were not associated with AV block, despite an identical coupling interval (Figure 4B). A single-chamber cardioverter-defibrillator was successfully implanted, and the patient subsequently remained asymptomatic.

This case demonstrates an uncommon cause of syncope in a patient with persistent AF and mild cardiomyopathy. Although paroxysmal infrahisian AV block may be observed in patients with underlying conduction disease, the mechanism of block in this case is fairly unique. Specifically, fatigue phenomenon of a diseased His-Purkinje system (HPS) is a rarely observed mechanism of infranodal atrioventricular AV block, whereby transient but sustained anterograde A V block, which is not inducible by rapid anterograde stimulation, occurs after rapid retrograde stimulation (either by ventricular burst pacing or by spontaneous ventricular arrhythmias).1,2

Irrespective of the underlying cause, a depression of infranodal conduction is a prerequisite, usually as a result of ischemic injury, but also nonischemic (as in this case) or idiopathic fibrosis, and once established acts as the substrate for high-degree
block when combined with the appropriate clinical circumstance. In patients with a narrow baseline QRS complex, the block always occurs within the common His bundle, whereas in those with pre-existing bundle-branch block, the location of block may be in the remaining fascicle.

The underlying electrophysiological mechanism of the fatigue phenomenon is complex and potentially multifactorial. Specifically, the observation that the duration and the degree of block are directly related to the rate and duration of ventricular pacing suggest that time-dependent and rate-dependent changes in conduction properties are at least partially responsible.

**Mechanism 1: Overdrive Suppression**

Fatigue phenomenon has to do with overdrive suppression of a diseased conduction system. In this case, it is postulated that fatigue may result from an accumulation of intracellular sodium or calcium and the accumulation of extracellular potassium. Thereafter, the resultant reduction of transmembrane sodium or calcium concentration gradients and the decreased cell-to-cell coupling secondary to intracellular calcium accumulation further reduce the excitability of these already depressed cells. Finally, the subsequent normalization of conduction is time dependent, whereby the decreased phase 0 upstroke or reduced resting membrane potential results in a prolonged period of functional block.

In this case, the longer duration of tachycardia facilitates a more dramatic reduction of transmembrane concentration gradients, the combination of which resulted in an increased HPS refractoriness with resultant prolonged anterograde block (Figure 3). Conversely, single premature ventricular complex only triggered a short duration of block (Figure 4A).

This mechanism also depends on the site of stimulation. It has been demonstrated that pacing proximal to the His bundle lesion (atrial or direct His bundle pacing) may not trigger fatigue phenomenon, whereas direct pacing of the left bundle branch just distally to the lesion does. The underlying mechanisms of these anisotropic specific properties of disease HPS remain unclear, but in our case one may also suppose that relatively slow conduction through the AV node may have initially protected the diseased HPS from overdrive suppression. The persistent AF did not allow us to assess further more anterograde properties of AV conduction in this patient.

**Figure 2.** A sustained left bundle-branch block morphology ventricular tachycardia was induced by ventricular pacing protocol, probably originating from the anterior midseptum. Twelve-lead ECG at a sweep speed of 25 mm/s.

**Figure 3.** Spontaneous ventricular tachycardia termination was followed by an 8.5-second asystole because of infrahisian block, as proved by the isolated irregular His potentials, before hisio-ventricular conduction eventually resumed. From top to bottom, at a sweep speed of 16 mm/s, tracings are surface ECG leads I, II, aVF, V1, and V6, His catheter proximal and distal bipole, and right ventricular apex (RVA) catheter bipole.
Mechanism 2: Peeling Back

This mechanism has been alternately described as a peeling back of the refractory barrier, whereby an increased tachycardia rate (or degree of prematurity) results in a progressively a deeper retrograde penetration of the impulses into areas of damaged His bundle fibers. This results in the more proximal portion of the diseased His bundle being in the absolute refractory period, thus blocking subsequent conduction from anterograde impulses to the less-damaged His fibers. As such, the combination of shorter tachycardia cycle length and longer arrhythmia duration resulted in an increased degree of HPS refractoriness, with resultant prolonged anterograde block. This would explain why, in our case, short bursts of ventricular pacing at 400 ms were unable to induce sustained AV block; however, sustained VT was able to unmask severe infrahisian conduction disease. In the former, the shorter duration of activation and relatively longer cycle length may have protected the proximal conduction system from ionic overload. In the latter, the shorter cycle length associated with the tachycardia facilitated the retrograde penetration into the more proximal portions of the damaged HPS, whereas the longer duration of tachycardia facilitated a more dramatic reduction of transmembrane concentration gradient.

This mechanism should also depend on the site of stimulation. In this case, VT probably originated from the anterior midseptum (Figure 2), thus more proximal to the diseased HPS than the site of right ventricular pacing (apex). In our case, we observed that a single spontaneous premature ventricular complex originating from the left anterior septum was able to induce transient infrahisian block (Figure 4A). In contrast, spontaneous (or mechanically induced) premature ventricular complexes originating from the right ventricular apex were not associated with subsequent AV block, despite an identical coupling interval (Figure 4B). The explanation may be based on the understanding of the patterns of normal and abnormal retrograde His-Purkinje conduction. Irrespective of the site of origin, it is well described that the preferred retrograde conduction pathway is the left-sided His-Purkinje system, with retrograde block within right bundle branch due to longer refractory period, delayed retrograde concealed conduction into more proximal portions (1), allowing subsequent anterograde impulse to conduct to the ventricles through the right bundle (2). Left, from top to bottom, at a sweep speed of 150 mm/s, tracings are surface ECG leads I, II, aVF, V1, and V6, His catheter proximal and distal bipoles, and right ventricular apex catheter bipolar.

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behaved, electrophysiologically, as if they were left ventricular muscle. This may explain in that case why outflow tract pacing, not apical pacing, allowed a deeper retrograde penetration and subsequently induced AV block.

Although we can only hypothesize on the mechanisms involved in the fatigue phenomenon in this case, it is clear that retrograde ventriculo-atrial conduction patterns are complex, especially in case of diseased HPS, and pacing at different ventricular sites may create different degrees of retrograde penetration (peeling back) and thus improve the probability of inducing overdrive suppression.

Conclusions
This case illustrates how both mechanisms of overdrive suppression and peeling back of a refractory barrier may combine to induce fatigue of the HPS. It also demonstrates that in addition to the rate and the duration of ventricular stimulation, the site of ventricular activation may also play an important role in the manifestation of this phenomenon.

When atrioventricular block is suspected in a patient, prolonged stimulation at a high pacing rate and at different ventricular sites may improve the sensitivity of detecting fatigue phenomenon in patients with infranodal conduction disease compared with standard apical ventricular pacing protocol.

Disclosures
None.

References

Key Words: atrial fibrillation • heart block • tachycardia, ventricular

EDITOR’S PERSPECTIVE
Teaching Rounds in Cardiac Electrophysiology
The purpose of any teaching rounds in medical practice is to encourage discussion and develop insights from clinical events in our patients. This spirit is outstandingly exemplified by Clementy et al in their article, “Unusual Tachycardia-Bradycardia Syndrome During Atrial Fibrillation: What Is the Mechanism?” They noted an intriguing phenomenon where a prolonged pause from infrahisian block was induced by a monomorphic ventricular tachycardia. The phenomenon did not occur following antegrade stimulation at a similar rate. They discuss the possible explanation from the phenomenon of fatigue, and in their explanations, they bring out the importance of maintaining a wide differential diagnosis, seeking physiological explanations, and appreciating differences in activation resulting from different sites of ventricular stimulation.

Syncope and Atrial Fibrillation, Not Always What It Seems
Patients with atrial fibrillation (AF) and syncope are common, largely reflective of the frequent occurrence of both these conditions. AF is rarely a sole cause of hemodynamic compromise significant enough to result in loss of consciousness. AF with preexcitation, conversion to atrial flutter and 1:1 ventricular conduction, in the setting of critical aortic stenosis, or severe ventricular relaxation abnormality in a sick patient are exceptions. Paroxysmal AF in the setting of severe sinus node dysfunction may produce a sinus pause resulting in syncope. Typically, a permanent pacemaker is required, as complete eradication with any known technique or medication of paroxysmal AF is uncertain.

Although a rare cause for the pause is illustrated by Clementy et al, a second tachyarrhythmia, such as the monomorphic VT seen in the electrophysiology laboratory, is also a possible cause of syncope. The irregular conduction through the AV node in AF may, similar to an “EP study,” induce VT in patients with the existing VT substrate. In addition, rapid AF may further compromise ventricular function, and in the context of prior myocardial infarction further accentuate the possibility of a tachycardia (AF) inducing a tachycardia (ventricular tachycardia [VT]).

“The EKG Shows AF… What Is the Diagnosis?”
In past years, a common occurrence on teaching rounds was for a senior physician to select from the patient’s record an EKG, hemodynamic tracing, or an auscultation finding, and asking for a “spot” diagnosis. For a student queried about the EKG in Figure 1 the diagnosis is not AF alone. The slow ventricular rates, left bundle branch block, and PVC need to be considered. In the absence of significant doses of AV nodal blocking agents, slow AF signifies conduction system disease (sick sinus syndrome). This in turn should raise concern for sinus pauses should the AF convert or chronotropic incompetence from poor AV nodal and infranodal conduction. Left bundle branch block in the context of slow ventricular responses with AF may be similar to situations where one considers trifascicular delay. In patients with prolonged P-R intervals and bifascicular block, the possibility that all major fascicles have conduction delay is present, and complete AV block should be strongly considered as a cause for syncope. Further, whenever slow AF is seen, one must look for regularization of the R-R intervals, signifying complete heart block with a junctional, fascicular, or ventricular escape rhythm. Antegrade penetration into the junction from AF may cause variation in the junctional escape and thus inexact regularization despite complete AV block. The PVC seen in the EKG is consistent with outflow tract origin and is likely similar to the induced VT that provoked the pause described subsequently. In the setting of left bundle branch block, a critically timed PVC may cause block in a diseased right bundle and produce a pause. PVCs in the setting of slow AF and left bundle branch block raises concern for monomorphic VT causing symptoms, retrograde penetration of the right bundle or AV node producing either block or facilitation of antegrade conduction, which in turn may be symptomatic. A sudden pause with mechanism possibly similar to that described by the authors may also occur from a fascicular ectopic beat or tachycardia, or tachycardia arising from the compact AV node itself. Paroxysmal concealed tachycardia, for example, even when it is present and ongoing, can result in complete atrioventricular block and without an escape rhythm.
Regional Anatomy and Arrhythmia Induction

The authors discuss possible reasons why the patient’s monomorphic VT induced pauses, but pacing near the right ventricular apex at a similar rate did not. Entrance into the conduction system from ventricular stimulation is a complex process and difficult to predict. Because of the insulation consisting of extensions from the fibrous skeleton of the heart that surrounds the His bundle and proximal infranisian conduction system, the ventricular entrance or exit is actually relatively closer to the apex than the base. Thus, pacing from the right ventricular apex will excite the His bundle earlier than pacing at a similar coupling interval from the annular myocardium. The situation is more complex with the outflow tract because of the possible presence of superior branches of the right bundle that may be present and active or represent “dead end” conduction tracts. Further, the arrangement of myocardial fibers, interventricular myocardial breakthrough sites, and the complexity of regional conduction velocity changes within the infranisian conduction system itself can coalesce to produce exquisitely specific requirements for regionality in induction of an arrhythmogenic phenomenon that depends on entrance to the conduction system.

The careful study that stems from an actual patient encounter provides some of the most stimulating and enlightening experiences in clinical medicine. Clementy et al’s discussion of VT producing prolonged infranisian block not only revisits the past for us but, as is typical of bedside rounds, will inspire future investigation and discovery by students of cardiac electrophysiology.
Unusual Tachycardia-Bradycardia Syndrome During Atrial Fibrillation: What Is the Mechanism?
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