ly understood in 1971. T cells had been identified, but their role in arenavirus infection was not well understood. Lassa virus was unknown, and the arenaviral hemorrhagic fever syndrome was not well described in the English-language literature. Also, there were experiments in mice indicating that LCMV infection could lead to the regression of lymphoid tumors, thus providing an experimental basis for undertaking this experiment in humans.[3]

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Biventricular Pacing

TO THE EDITOR: The article by Jarcho (July 20 issue)[1] summarizes the usefulness of biventricular pacing in the setting of chronic heart failure. Randomized clinical trials have shown a significant improvement in left ventricular function and remodeling after the placement of a biventricular pacemaker in patients with moderate-to-severe chronic heart failure and a large QRS interval,[2] and a positive effect on survival has recently been reported.[3] This approach should be considered for patients with chronic heart failure in New York Heart Association functional class III or IV who are receiving optimal medical therapy. Nevertheless, medical therapy too often is not optimized before pacemaker implantation.

In the clinical vignette described by Jarcho, a patient who reports shortness of breath with mild exertion is treated with an angiotensin-converting–enzyme inhibitor, a diuretic, and a beta-blocker and is described as being optimally treated and therefore a candidate for biventricular pacing. I disagree, since medical treatment for this kind of patient should also include an aldosterone antagonist, as indicated by the international guidelines on chronic heart failure,[4] and digitalis, which does not affect survival but may be initiated to reduce symptoms, avoid hospitalization, control rhythm, and enhance exercise tolerance. Considering that the magnitude of clinical effects, in terms of survival and left ventricular remodeling,[2-5] is similar with spironolactone and with biventricular pacing, it is not of secondary importance that a substantial difference in economic burden exists between aldosterone antagonism and biventricular pacing.

Including a vignette in which a patient with chronic heart failure receives suboptimal therapy and then receives a biventricular pacemaker may promote the misleading concept that an invasive strategy is superior to drug therapy and may encourage readers to skip important steps in the evaluation and treatment of these patients.

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TO THE EDITOR: In his article on biventricular pacing, Jarcho states that he would wait until the highest doses of lisinopril and carvedilol proved ineffective in patients with severe heart failure before implanting a biventricular pacemaker. In my opinion, this approach would make the job tougher for both the patient and the cardiologist who is implanting the pacemaker. These patients are sick, are hemodynamically compromised, and invariably have systemic blood pressures on the lower side. The implantation procedure therefore becomes that much more complicated. Once the patient satisfies the criteria of a low left ventricular ejection fraction (<35%) and mechanical dyssynchrony, it would be preferable not to wait

too long before inserting a biventricular pacemaker.

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TO THE EDITOR: In his review of biventricular pacing, Jarcho states that the atrioventricular pacing delay should be short, in order to maximize ventricular pacing. However, his assertion that the preferred pacing scheme is right atrial pacing, in addition to right and left ventricular pacing, is controversial. All the major biventricular-pacing trials have used programming modes that ensured atrial sensing and ventricular pacing.[1] Native (nonpaced) atrial contraction is preferred, since atrial pacing induces intraatrial conduction delay, which can lead to alterations in the optimal atrioventricular delay and reduced overall effectiveness of biventricular pacing.[2] Most clinical electrophysiologists program biventricular devices to sense changes in the atrium and provide pacing in the ventricles, with pacing in the atrium provided only if the patient has an indication for this, such as sinus-node dysfunction.

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THE AUTHOR REPLIES: Cicoira notes that no mention was made of the use of either an aldosterone antagonist or digitalis in defining optimal medical therapy for the patient before the insertion of a biventricular pacemaker was recommended. In discussing the therapeutic approach, I was reflecting to some degree the analysis provided by Strickberger et al. in their 2005 American Heart Association Science Advisory (cited in my review), which states that "in general, the CRT [cardiac-resynchronization therapy] trials included patients . . . [receiving] optimal medical treatment for heart failure, including β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and diuretics."[1] However, the authors of the advisory certainly did not specifically confine their recommendation of "optimal medical therapy" to these agents alone, and I must agree with Cicoira that in general, all medical therapy for heart failure should be implemented and adjusted for optimal effect before biventricular pacing is considered. I thank Cicoira for calling attention to this important omission.

In so noting, I must then disagree with Natarajan in his assertion that refining medical therapy before device implantation is too demanding a criterion. It is true that many patients with advanced heart failure do not tolerate high doses of angiotensin-converting–enzyme inhibitors or beta-blockers, which is why I specifically advised that doses should be increased to the "maximum tolerated." If the patient remains symptomatic and a decision is made to implant the device, it is reasonable to reduce the doses of medication temporarily to prevent undue hypotension during the procedure. But to recommend biventricular pacing for all patients who meet the ejection fraction and dyssynchrony criteria is to set too low a threshold. Such a recommendation disregards the precision of the trial data and the potential risks of the procedure, and will probably result in a lower incidence of clinical benefit than the 70 to 80% currently reported.[2,3] The temptation to use a dramatic (and lucrative) interventional approach as a substitute for meticulous clinical management should be avoided by the conscientious practitioner, and I am sorry if I implicitly endorsed the use of such an approach by providing an insufficiently rigorous description of the appropriate medical therapy.

Henrikson's comments with regard to atrial pacing are entirely correct. The wording in the article is a result of my own editing error and does not convey my actual view of the subject, which is more clearly stated in the letter by Henrikson.

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