

the presence of viral genomes in the heart can identify a population with dilated cardiomyopathy that would not improve with immunosuppression. Patients with viral genomes that were detected on cardiac biopsy were excluded from the recently reported Tailored Immunosuppression in Inflammatory Cardiomyopathy (TIMIC) trial.<sup>3</sup> Multicenter, randomized trials are still needed to assess the effect of immunosuppression on clinically meaningful end points, such as the rate of death and heart transplantation in patients with chronic, persistently symptomatic dilated cardiomyopathy.

I strongly agree with Szabo et al. that specific infections and toxins contribute substantially to the burden of myocarditis, particularly in the developing world. Since many of these specific causes have been addressed in other recent review articles, I chose to use the limited space in my article to focus primarily on viral and select noninfectious, autoimmune cardiac conditions. The authors cite a letter to the Editor concerning two patients with Chagas' cardiomyopathy who responded to levosimendan. At this time, the use of levosimendan for myocarditis is not established.

I agree with Ammar and Fouda that carditis

from post-streptococcal rheumatic fever is a major cause of cardiomyopathy, particularly in the developing world. Frequently the long-term effects of post-streptococcal endocarditis, including atrial fibrillation and stroke, garner more attention than the long-term effects of myocarditis in this disorder. The Gates Foundation is sponsoring an ongoing project on the Global Burden of Disease that should help to separate the long-term morbidity of rheumatic carditis on the basis of major sequelae, including dilated cardiomyopathy.

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## Calculation of Number Needed to Treat

**TO THE EDITOR:** The number of patients who would need to be treated to prevent a given adverse outcome in one patient, called the number needed to treat, is often used in randomized trials and observational studies to provide a simple measure of the effect of a treatment. The computation of the number needed to treat can, however, be inaccurate and its interpretation misleading in trials with varying follow-up times. In this case, the cumulative incidence of an outcome cannot simply be calculated as a proportion of subjects but must instead be estimated over time by means of the Kaplan–Meier approach that accounts for varying follow-up times.

Trials that based the computation of the number needed to treat on the simple proportion of patients with the outcome, rather than the Kaplan–Meier estimates, may have distorted values of the number needed to treat.<sup>1-3</sup> Other trials have ac-

counted for varying follow-up times by using, instead, the incidence rate computed as the number of patients with the outcome divided by the total amount of person-time.<sup>4,5</sup> However, the corresponding number needed to treat, although based on the incidence rates, was interpreted as the number needed to treat to prevent one occurrence of the outcome among patients treated for a given period, which may be incorrect.

For example, in the recent trial of 3845 elderly patients who had hypertension, with follow-up times varying from 0 to 6.5 years, the incidence rate of stroke was 12.4 per 1000 patient-years for active treatment compared with 17.7 per 1000 patient-years for placebo.<sup>5</sup> These rates were converted to 2-year rates and the number needed to treat was computed as  $1 \div (0.0354 - 0.0248) = 94.3$ , interpreted as “1 stroke being prevented because 94 patients were treated for 2 years.”<sup>5</sup> This inter-

pretation is not accurate, since this number needed to treat does not represent patients, but rather patient-years. Indeed, 94 patients treated for 2 years is not necessarily the same as 188 patient-years: the former implies 94 distinct patients treated for 2 years, whereas the latter can equally imply 188 patients treated for 1 year or 47 patients treated for 4 years. The study in fact provided the Kaplan–Meier curves for the cumulative incidence of stroke, which resulted in a 2-year cumulative incidence of stroke of around 2.2% for active treatment and 3.8% for placebo. These values correspond to a more accurate number needed to treat of 63 patients needing to be treated for 2 years to prevent 1 stroke, rather than the reported 94 patients.

Although the number needed to treat is a simple and intuitively appealing measure of the effect of a treatment, its computation must be performed with care in trials with varying follow-up times.

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## Muscle Glycogenesis Due to Phosphoglucomutase 1 Deficiency

**TO THE EDITOR:** Muscle glycogen storage diseases are rare inborn diseases caused by errors of metabolism associated with either dynamic, exercise-related symptoms or permanent muscle weakness. The most common glycogen storage disease, McArdle's disease (glycogen storage disease type V), is caused by myophosphorylase deficiency and characterized by cramps and muscle pain elicited by sudden vigorous exercise, which may lead to rhabdomyolysis and myoglobinuria. Diagnosis can be suggested by the absence or blunting of the increase in lactate level and the exaggeration of the ammonia response in venous effluent blood in the forearm of a person who is exercising. One exception is that lactate and ammonia responses may be normal in patients with phosphorylase *b* kinase deficiency (glycogen storage diseases type VIII).<sup>1</sup>

A 35-year-old man was referred for investigation of recurrent cramps provoked by exercise. He was the second child of nonconsanguineous, healthy parents who had no family history of a muscle disease. He had two episodes of dark-brown urine after strenuous exercise, suggesting rhabdomyolysis. No second wind occurred dur-

ing exercise. Neurologic examination showed mild weakness of the pelvic-girdle muscles. The creatine kinase level at rest was 300 U per liter, but it increased by a factor of 10 to 20 after strenuous exercise. Needle electromyography showed a myopathic pattern in the vastus medialis. A standardized forearm-exercise test<sup>2</sup> showed that the patient was able to perform isometric, nonischemic exercise at 70% of the maximum voluntary contraction force for 30 seconds. The increase in plasma lactate level was normal, but ammonia release was four times the expected increase (Fig. 1A and 1B).

<sup>13</sup>C-magnetic resonance spectroscopy of the gastrocnemius muscle revealed a normal glycogen-to-creatine ratio. After performing 160 seconds of aerobic plantar flexion, producing 1680 joules, muscle acidification was normal.<sup>3</sup> During recovery, the myoglobin reoxygenation rate was normal, as was the perfusion profile.

The patient performed a constant workload test for 20 minutes, followed by an incremental exercise test until exhaustion on a cycle ergometer (Tunturi Oy); normal increases in the plasma lactate level during submaximal and maximal