

dramatically and CPK levels were normal in spite of the fact that he had resumed taking lovastatin.

With the patient's consent we challenged him with diltiazem; again, myopathy and very high CPK levels developed. When diltiazem was discontinued the patient's symptoms cleared rapidly; elevated CPK levels returned to normal over the ensuing 5 days. Results of the challenge, dechallenge, and rechallenge attest that the diltiazem was the culprit in inducing the myopathy. The manufacturer has received reports of diltiazem-induced myopathy, and it is listed as a possible side effect in their package insert. Nevertheless, to my knowledge this article appears to be the first published about a patient with this drug-induced myopathy. In view of this clinical observation, I suggest that diltiazem therapy be added to the list of drugs considered to be potential causes of a drug-induced myopathy.¹

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ARTERIAL THROMBOSIS IN THROMBOCYTHEMIA

To the Editor:

Erythromelalgia is a typical thrombotic manifestation of primary thrombocythemia or thrombocythemia in association with polycythemia vera, occurring at platelet counts in excess of $400 \times 10^9/L$.¹⁻³ The painful erythromelalgic burning and red congestion of toes, fingers, or soles of the feet frequently progress to painful ischemic acrocyanosis and peripheral gangrene if left untreated. The specific histopathology of erythromelalgic lesions shows a thrombotic occlusion of the acral arterial microvasculature without evidence of preexisting vascular disease.^{1,2} From 1978 to the present, we documented 59 consecutive cases of primary thrombocythemia and 26 cases of thrombocythemia associated with polycythemia vera. The specific manifestations in 55 symptomatic patients were erythromelalgia in 43, cerebrovascular disease in 23, and coronary artery disease in nine patients. To exclude polycythemia vera as a contributory factor in arterial vascular disease, the presenting coronary, neurologic, and visual ischemic symptoms in 22 patients with primary thrombocythemia were studied.

Coronary events in nine cases were myocardial infarction in four and unstable angina pectoris in five. Cardiac catheterization was performed in eight patients. Two patients with myocardial infarction had normal coronary arteries. A third patient with myocardial infarction had a totally occluded coronary artery but no other signs of atherosclerosis in the remaining coronary and peripheral arteries. The five patients with unstable angina pectoris had coronary disease (one-vessel disease in two and two-vessel disease in three) and underwent coronary bypass surgery. Nineteen patients presented neurologic or visual ischemic symptoms. Eleven patients had focal symptoms: transient monocular blindness in three, transient monoparesis or hemiparesis in six patients, and both in

one; migraine in one, and partial stroke in one. Nonfocal symptoms occurred in 14 patients: transient postural instability in 13, dysarthria in eight, and scintillating scotomas in five. The transient focal and nonfocal neurologic and visual symptoms all had a sudden onset, occurred in a progression rather than all at once, lasted for a few seconds to several minutes, and were usually associated with or followed by a dull or pulsatile headache. This clinical presentation is very atypical of transient ischemic attacks caused by atherosclerosis, but the striking similarity with migraine supports the crucial role of platelets in the pathogenesis of ischemic circulation disturbances in primary thrombocythemia. Only four of the patients with primary thrombocythemia had one or more of the known risk factors for vascular disease: hypertension, hypercholesterolemia, diabetes, or a family history of arterial thrombosis. Smoking was the single risk factor in four cases. The peripheral arterial pulses were normal in all patients, indicating absence of clinical relevant atherosclerosis. However, an arterial thrombotic tendency was present in 12 patients, in whom erythromelalgia caused by platelet-mediated thrombosis¹⁻³ preceded or followed the coronary artery disease or the transient cerebral or ocular ischemic attacks.

Time lapses of thrombotic or ischemic events ranged from 1 to 7 years. Recurrent thrombotic or ischemic events of the coronary or cerebral circulation were recorded in five patients while they were receiving adequate warfarin treatment. During continuous treatment with low doses of aspirin (250 to 500 mg/day) for 1 to 9 years, there was no recurrence of vascular events in 14 patients with primary thrombocythemia at platelet counts of 520 to $1380 \times 10^9/L$. Eleven patients maintained remissions of primary thrombocythemia (platelet counts less than $350 \times 10^9/L$) for 3 to 7 years after treatment with busulfan and remained asymptomatic. It is concluded that thrombocythemia is a main risk factor for arterial thrombosis.^{4,5} Moreover, our observations indicate that in thrombocythemia platelets are primarily involved in the etiology of the thrombotic occlusions of the acral arterial microvasculature as well as the coronary and cerebral circulation. In contrast, thrombotic events are rare or not observed in patients with reactive thrombocytosis. We therefore prospectively performed kinetic studies of ⁵¹Cr-labeled autologous platelets in 10 patients with thrombocythemia complicated by erythromelalgia (E+), in 10 asymptomatic patients with thrombocythemia (E-), and in 10 control subjects with reactive thrombocytosis (RT).⁶ The mean survival (MS) of platelets in the E+ group was significantly decreased compared with both the E- and RT groups ($p < 0.001$), indicating platelet consumption in symptomatic patients with thrombocythemia and erythromelalgia. Continued treatment with 500 mg of aspirin per day normalized the MS of E+ patients ($p < 0.001$) by suppressing platelet consumption, resulting in complete relief of erythromelalgic distress and restoration of the ischemic and thrombotic circulation disturbances. These findings indicate that an intrinsic platelet defect may underlie the observed thrombotic predisposition in thrombocythemia.

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CHAGAS' DISEASE IN NORTH AMERICA

To the Editor:

American trypanosomiasis (AT) or Chagas' disease is a zoonosis indigenous and still limited to America, caused by the hemoflagellate *Trypanosoma cruzi*, which infests the blood and tissues of mammalian hosts. It causes a chronic heart disease that still has no effective treatment. A high prevalence of AT has been reported in South America, where 24,000,000 people are infected. The disease occurs from latitude 36° North to 36° South, that is from Tijuana at the U.S.-Mexican border to Bariloche in Argentina, sparing only the high mountains and the Amazonian basin.^{1,2} Although Mexican cases have been described since 1940 as parasitemic disease and heart involvement has been recognized several times since 1965, for many years it was thought that AT was a rare condition in North America, including Mexico. A general concept was that North American strains of *T. cruzi* were less pathogenic than South American ones, and no information in regard to the presence of chronic chagasic cardiopathy existed in Mexico until the late 1970s.³⁻⁸

To ascertain the incidence of immunoglobulin G (IgG) antibodies to *T. cruzi* in people admitted to our Institute with dilated cardiomyopathy, a diagnosis that represents 2.5% of all yearly admissions and 2.8% of necropsies, we surveyed for reactive serum antibodies in an enzyme-linked immunosorbent assay (ELISA) against a crude saline extract obtained from the epimastigote stage of Mexican isolates of *T. cruzi*, as well as for antibodies reactive with epimastigotes in an indirect immunofluorescent assay. The presence of antibodies against *T. cruzi* in sera positive on both tests was confirmed by a Western blot assay. These tests were previously validated in our population and by external controls.⁹ Thirty-seven patients were studied; all of them had a definite diagnosis of dilated cardiomyopathy of unknown origin and 15 of them (40%) had antibodies against *T. cruzi*. There was no difference in the clinical picture between patients with or without anti-*T. cruzi* antibodies; however, a significant difference was present between both groups in regard to rural origin and residence, poor housing, and vector recognition ($p < 0.01$). Our results suggest that Chagas' disease could be a relatively common cause of chronic chagasic cardiopathy (CCC). In fact, dilated cardiomyopathy is a well-known expression of Chagas' disease, and these cases are considered idiopathic if serologic testing is not performed. Besides

and perhaps more important, is the fact that most people infected with *T. cruzi* do not develop CCC or any other clinical feature; they are asymptomatic and only the presence of serum-specific antibodies allows their recognition as so-called "indeterminate" chagasic individuals.¹⁰ These people may be a source of infection through blood or even organ donation for transplantation. A definite risk for iatrogenic spreading of this deadly condition does exist and the search for anti-*T. cruzi* antibodies in the blood of organ donors should be mandatory. Because of the continuing social phenomenon of migration to the United States and Canada, this disease may be a potential problem in North America that needs to be measured accurately.

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U.S. TRENDS IN RHEUMATIC FEVER AND HEART DISEASE

To the Editor:

Articles and editorials have described the decline in acute rheumatic fever and trends in chronic rheumatic heart disease in the United States.¹ More recently reports have appeared that suggest that a resurgence of acute rheumatic fever took place in the mid 1980s.¹ Therefore I examined recent morbidity and mortality statistics from the National Center for Health Statistics. In 1988 through 1990 an estimated 16,792 hospital discharges had any diagnosis of acute rheumatic fever. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM) codes 390 through 392, compared to 18,791 in 1985 through 1987. However, the number of such cases is too small to permit accurate es-