Figure 1. Biopsy sample of nonlesional skin from a patient with systemic lupus erythematosus before treatment with intravenous immunoglobulin. There is diffuse immunofluorescence staining at the dermal–epidermal junction.

Figure 2. Biopsy sample of nonlesional skin from the same patient as in Figure 1, after 3 cycles of monthly infusions of intravenous immunoglobulin (each cycle consisted of 400 mg/kg/day for 5 consecutive days). The immunofluorescence staining has shifted to a focal papillary pattern.

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Familial primary antiphospholipid antibody syndrome

The majority of cases of arteriovenous thrombosis (AVT) that arise from the presence of IgG antiphospholipid antibodies (aPL) are of idiopathic origin or else occur in the setting of systemic lupus erythematosus (SLE) (1). On rare occasions, several family members with SLE have been documented as having symptomatic aPL (2). Moreover, relatives of patients with SLE have been reported to have a high incidence of aPL (3) or lupus anticoagulants (4). To our knowledge, familial idiopathic primary aPL syndrome (APS) has not been previously reported. In the present report, we describe a family in which 5 members were found to have IgG-aPL. These were symptomatic in 2 family members and presumed to be the cause of a fatal massive pulmonary embolism in another member.

The patient described herein, a 25-year-old woman who was not taking an oral contraceptive pill and who had no

history of AVT or fetal loss, was identified by her hospital admission for an angiographically confirmed femoral vein thrombosis. Test results for IgG anticardiolipin antibodies (IgG-aCL) were negative on admission, but, at 2 months and 6 months after admission, the results were significantly positive for aCL ("moderate" titer, defined by the Second International Anticardiolipin Standardization Workshop as equivalent to 32–70 GPL units/ml). A search for inherited causes of AVT was initiated, since one of the patient's sisters had experienced a fatal pulmonary embolism in the previous year at age 21. Both parents, 6 of 8 siblings, and 5 of 8 nephews and nieces who were >1 year old, agreed to be tested for aCL. Significant moderate titers of IgG-aCL were observed on 2 consecutive occasions (at least 6 months apart), in 2 male siblings (ages 35 and 30), and in 1 nephew and 1 niece (ages 6 and 5, respectively). Except for the older IgG-aCL–positive male sibling who previously had a large thrombophlebitis of the left calf and had evidence of venous thrombosis on histologic examination, no other surviving family member had features associated with APS or SLE. Serum levels of anti–thrombin III, and protein C and S, were normal in all aCL-positive individuals in whom there was no factor V resistance to either activated protein C or the lupus anticoagulant. These individuals also had normal findings for levels of hemoglobin, blood film examination, and platelet count. Clinical and laboratory evidence of complement deficiency was absent, and test results for antinuclear antibodies and antibodies to double-stranded DNA, smooth muscle, mitochondria, parietal cells, and extractable nuclear antigens were negative. Symptoms suggestive of connective tissue disease were notably absent in each family member, and all adult patients had a negative VDRL result for treponemal infection.

Recently, the frequency of aPL in healthy individuals was estimated to be approximately 2% (5). Thus, the probability that 5 family members would have aPL purely by chance was extremely small (1 in 50^5). In contrast to previous reports of familial APS (6) and Sneddon's syndrome (7), this family demonstrated an inherited tendency to develop aCL in isolation of other autoantibodies and clinical features of autoimmune disease. In addition, there was no evidence of the Bernard-Soulier syndrome in any family member (8). Symptoms appeared to have been more severe in the female members of this family, and were completely absent in 1 of the 2 male siblings with aCL. Both the nephew and niece are, at present, fairly young and, therefore, are likely to have little vascular endothelial damage, which may be an additional cofactor in the etiology of thrombotic symptoms in individuals with aPL. Identification of the pediatric members of this family who had elevated aCL titers will allow documentation of the natural history of this rare event in childhood. While the tendency to develop aPL in this family was clearly autosomal, the exact pattern of inheritance remains unclear.

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Mannose-binding protein in Chinese patients with systemic lupus erythematosus

The etiology of systemic lupus erythematosus (SLE) is unknown, but genetic factors have been implicated. Inherited homozygous deficiencies of C1, C4, and C2 have been associated with a high incidence of SLE (1), and heterozygous deficiency of C4 shows a similar association with more than half of the patients with SLE having a C4AQ0 allele. This is true both for Caucasians, in whom most examples of C4AQ0 occur on an HLA background with A1, B8, and DR3, and for Orientals, in whom this haplotype does not occur (1). C4A null alleles may predispose to SLE by impairing clearance of immune complexes (1).

Mannose-binding protein (MBP) is a C-type serum lectin that is synthesized by the liver as an acute-phase protein (2). MBP functions as an opsonin after it binds to microbial glycoproteins that are terminated with mannose and *N*-acetylglucosamine (2). It can activate the classical complement pathway independent of antibody and C1q or through a novel C1s-like serine protease (3). MBP is a multimeric molecule of up to 6 subunits, each of which is a triple helix of 3 identical 32-kd polypeptides. MBP deficiency in Eurasians has been associated with a common opsonic defect (4). The molecular basis of MBP deficiency has been shown to be due to a single point mutation at codon 54 (GGC→GAC), resulting in the substitution of glycine by an aspartic acid residue (4). The gene frequency of this codon 54 mutation was estimated to range from 0.11–0.17 in Caucasians, Chinese, and Eskimos (5–7).

Since complement deficiencies have been implicated in the pathogenesis of SLE, and increased frequency of the codon 54 mutation has also been reported recently in white patients with SLE (8), we investigated the frequency of the codon 54 mutation and compared the serum MBP levels in 111 Chinese patients with SLE and 123 controls.