Table 1. Serologic characteristics of idiopathic thrombocytopenic purpura patients at the time of diagnosis

Rheumatoid factor*	<1:20
C3/C4 levels (mg/dl), mean ± SD†	112 ± 30/26 ± 10
Anti-DNA antibodies‡	<20%
Positive antinuclear antibodies	
Diffuse	2/18 (titer 1:80)
Speckled	4/18 (titers 1:160–1:640)

* Latex fixation test.
† Radial immunodiffusion technique. Normal levels: C3, 70–140 mg/dl; C4, 16–30 mg/dl.
‡ Farr technique. Normal level: 15–20% binding.

The serologic characteristics of this group of patients are presented in Table 1. None of the patients had circulating rheumatoid factor (IgM) in their serum. Serum levels of C3 and C4 were within normal limits, and circulating antibodies to double-stranded DNA were undetectable.

Six of the 18 patients had positive ANA determinations. Two had the diffuse pattern of immunofluorescence (with titers of 1:80), and 4 had speckled pattern ANA with titers ranging between 1:160–1:640. Of the 4 patients with speckled pattern ANA, 1 had high-titer antibody to Sm, while another had high-titer antibody to RNP. The remaining 2 patients had negative Sm and RNP determinations. Only 1 patient had a serologic marker (Sm antibody) that might be considered characteristic of SLE (6).

Thus, 6 of 18 patients (33%) with the diagnosis of ITP had positive ANA determinations. It should be emphasized, however, that none of these patients had signs or symptoms of SLE at the time of initial consultation.

Four patients later developed SLE. The mean time from the initial diagnosis of ITP to the development of SLE was 2.3 years (range 8 months–4 years). All of the patients who developed SLE had presented initially with high-titer, speckled pattern ANA. The 2 patients presenting with diffuse pattern ANA had not developed any signs or symptoms of SLE at the followup examination 3 years later.

Thus, this pilot prospective study suggests that ITP patients who have high-titer, speckled pattern ANA at the time of initial diagnosis may be at risk of developing SLE. Recently, a similar (but larger) study that supports our findings was reported in abstract form. Peebles et al (7) reported on the significance of ANA in patients with immune thrombocytopenia. Twenty-four of 117 patients with ITP (20%) were found to have positive ANA, a frequency similar to ours. Five of the 24 patients with positive ANA had the speckled pattern, with antibodies directed against various nuclear antigens. Four of these 5 patients developed SLE. Furthermore, SLE did not develop in the remaining 19 patients with positive ANA. These findings are almost identical to those reported here.

Given the association between these 2 diseases (1,2), the presence of a serologic marker that would allow the identification of the subset of ITP patients who are at risk of developing SLE may be of prognostic significance. Large, controlled studies are needed in order to determine the precise incidence of ANA positivity in ITP patients, and the percent of those patients who will develop SLE.

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Autoantibodies during captopril treatment

To the Editor:

In a recent brief report, Reidenberg et al described the development of antinuclear antibody (ANA) in patients treated with high doses of captopril (1). They concluded that this was not a result of any linkage between the gene for susceptibility to ANA development and the gene for slow acetylation.

In a prospective study conducted at this institution (2), we described the development of ANA in 13 of 89 patients treated with captopril. The ANA were mainly of the IgM class, did not fix complement, and were transiently present. In addition, low avidity anti–double-stranded DNA antibodies, exclusively of the IgM class and not complement-fixing, developed in 3 patients. In 5 patients, perinuclear factors developed during captopril treatment (3).

Based on these data, we hypothesize that captopril induces dose-related alterations in immunoregulation, resulting in autoimmune phenomena, as has been shown for methyldopa (4). Indeed, alterations in lymphocyte reactivity during captopril treatment have been demonstrated (5,6). In agreement with the data of Reidenberg et al, we did not find an association between captopril-induced side effects and ANA development (2). In a report on cutaneous side effects, captopril-induced in vitro lymphocyte transformation and positive findings of intracutaneous skin test were described in patients with skin rashes due to captopril (7), indicating drug-specific allergic reactions.

In conclusion, treatment with high doses of captopril seems to result in immunoregulatory disturbances such as the development of multiple autoantibodies, and some of the side effects of captopril are associated with a drug-specific immune response.

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Systemic lupus erythematosus and Down's syndrome

To the Editor:

The recent report by Yancey et al (1) describes an inflammatory arthropathy associated with Down's syndrome. Their estimated prevalence of arthritis in Down's syndrome appeared to be much higher than the prevalence of juvenile rheumatoid arthritis (JRA) in the general population. It remains uncertain whether this arthropathy represents JRA occurring in a genetically predisposed population, or a separate illness occurring as a result of the known genetic and immunologic abnormalities in Down's syndrome (2). Previously described abnormalities in Down's syndrome include chronic active hepatitis and multiple serologic abnormalities (3), psoriatic arthritis (4), gouty arthritis (5), an increased incidence of thyroid antibodies (6), and an increased incidence of alopecia areata (7). We recently treated a patient with Down's syndrome who developed an inflammatory polyarthritis with additional clinical and serologic features of SLE.

The patient is a 20-year-old white woman with Down's syndrome, congenital heart disease, and suspected Eisenmenger's syndrome with pulmonary hypertension. In August 1981, she was hospitalized with congestive heart failure. Daily temperatures elevated to 39°C were noted. Multiple blood cultures revealed no abnormalities. Daily fevers persisted, and in November 1981, she developed a gradual onset of pain and swelling in multiple joints. Evaluation revealed moderate swelling of the proximal interphalangeal, metacarpophalangeal, wrist, elbow, ankle, and subtalar joints bilaterally. Mild ulnar drift was noted. There were flexion contractures of both elbows and limited mobility of the shoulders. Effusions were present in both knees and there was metatarsophalangeal tenderness. Persistent malar erythema and patchy alopecia were present without mucous membrane lesions. There was mild axillary adenopathy. The lungs were clear. P_2 was increased, and there was a grade 3/6 systolic mumur at the left sternal border. There was no abdominal organomegaly.

Laboratory studies revealed the following values: a hemoglobin of 10.8 gm/dl, hematocrit 32.7%, white blood cells (WBC) 7,400/mm^3 with 7% bands, 84% segmented neutrophils, and 9% lymphocytes. Persistent leukopenia was subsequently noted with the WBC count ranging from 2,800–4,200 cells/mm^3. Erythrocyte sedimentation rate was increased at 67 mm/hour. A test for antinuclear antibodies was positive at a titer of 1:160 with a homogenous pattern. Anti-DNA antibody (*Crithidia luciliae* method) was positive at a titer of 1:10 initially and subsequently increased to 1:80. Lupus erythematosus cell preparation was positive. Complement C3 and C4 levels were normal. Rheumatoid factor was negative. Direct Coombs' test result was negative. Liver enzyme values and renal function were normal. Radiographs of the hands and wrists revealed fusiform swelling of the proximal interphalangeal joints and periarticular demineralization without erosive changes or periostitis.

She was treated with salicylates with marked symptomatic improvement evidenced by diminished articular swelling and resolution of the daily fevers. Her course was complicated by gastrointestinal bleeding necessitating the cessation of aspirin. She has subsequently been treated with choline magnesium trisalicylate and hydroxychloroquine and has continued to do well.

The patient fulfilled 5 of the 11 American Rheumatism Association revised criteria for SLE (8). One hundred sixty-one patients with Down's syndrome were evaluated at the