Easy bruising and recurrent ecchymoses in the female, primarily involving limbs, may be found in such fairly well-characterized conditions as anaphylactoid purpura, hypergammaglobulinemic purpura, amyloidosis, pseudoxanthoma elasticum, Ehlers-Danlos syndrome, histamine purpura, and cutaneous hypersensitivity to DNA\textsuperscript{1,2} and to hemoglobin.\textsuperscript{3} The condition is also encountered in two poorly understood syndromes: auto-erythrocyte sensitization purpura\textsuperscript{4} and purpura factitia.

In auto-erythrocyte sensitization purpura, crops of apparently spontaneous, painful, inflammatory bruises sometimes occur in women who have sustained unrelated physical injuries. The bleeding continues for some time until it stops spontaneously, only to recur if additional trauma produces new ecchymotic lesions. Hemorrhagic manifestations may also involve internal organs. It is postulated that the patient becomes sensitized to her own erythrocytes as a result of injury and that subsequent extravasation of blood, due to unrecognized trivial traumas, produces inflammation and purpura. The intracutaneous injection of whole blood or red blood cell (RBC) stroma from the patient may reproduce the typical bruises,\textsuperscript{5} which confirm this diagnosis. A fixed-tissue antibody may react with the RBC stroma to produce edema and increased capillary permeability,\textsuperscript{6} although other evidence militates against the role of immunologic mechanisms in this syndrome. The condition is benign and may eventually disappear.

In purpura factitia, on the other hand, ecchymoses are usually not preceded by unexpected pain. Skin testing with the patient’s blood is negative if the test is done in inaccessible areas; protection by a cast prevents bleeding in the covered area.\textsuperscript{7} Specific histologic findings are not present. Nevertheless, the practical differentiation of auto-erythrocyte sensitization purpura from purpura factitia remains difficult, since both conditions have a strong psychiatric or hyperemotional background. Moreover, skin tests in auto-erythrocyte sensitization purpura fluctuate in positivity from time to time and may be positive in some areas but not in others at the same time.

We are reporting our observations of a case of purpura factitia. It is hoped that they might be of use in the differentiation of purpura factitia from auto-erythrocyte sensitization purpura.

**Report of a Case**

A 31-year-old woman had a history of swelling of the right knee of one month’s duration, following accidental trauma. The affected joint appeared swollen and reddened. Urinalysis, blood cell count, biochemical studies, and x-ray films of the affected joint disclosed no abnormalities; aspiration of the joint yielded no fluid. Improvement came with rest, but symptoms reappeared soon after discharge. A cast was then applied from the right thigh to lower leg. One month later, the patient returned to have the cast removed and the covered area was found to be free of hemorrhage. However, a few days later local heat, swelling, tenderness, and redness in the right patellar region recurred. X-ray films of the knee were again normal. After a tentative diagnosis of chronic, recurrent, prepatellar bursitis, exploration of the knee joint showed only some fibrotic tissue holding down the prepatellar bursa to adjacent structures. Recovery seemed uneventful, but three weeks later swelling and redness of the right patellar region were again noted and a diagnosis of thrombophlebitis was made. Anticoagulation with heparin sodium and bed rest brought improvement. Two weeks

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From the Department of Pathology, Saint Elizabeth Hospital, Danville, Ill; and the University of Illinois College of Medicine, School of Basic Medical Sciences, Urbana-Champaign.

Reprint requests to Department of Pathology, St. Elizabeth Hospital, 600 Sager Ave, Danville, Ill 61832 (Dr. Stefanini).
after discharge from the hospital, the patient’s symptoms recurred, and swelling, purpura, and discoloration of the right knee area were accompanied by ecchymoses of the dorsal surface of both hands. A consultant submitted a diagnosis of collagen disease, although a biopsy specimen of the anterior aspect of the lower third of the left arm (the site of a hemorrhagic area at that time) showed only minimal, nonspecific vasculitis. On the basis of this tentative diagnosis, the patient received courses of treatment with prednisone (10 mg three times a day for one month) azathioprine (Imuran) (40 mg three times a day for four weeks), and chloroquine (500 mg daily for two weeks and 250 mg daily for two additional weeks). During the course of treatment, the patient continued to develop marked ecchymoses, involving primarily the arms and legs, without demonstrable trauma.

The patient was then admitted to our institution. Her history revealed a strong psychiatric background, culminating in commitment to mental institutions because of acute anxiety states. The patient had received treatment with chlorpromazine (Thorazine) at least one year prior to the appearance of purpura and occasionally used aspirin. On physical examination, multiple ecchymotic areas were present over both forearms and legs, but were limited to areas accessible to the patient. Laboratory values included the following: urine, traces of mucus; erythrocyte count, 4.8 million/cu mm; hemoglobin, 14.2 gm/100 ml; hematocrit reading, 43%; leukocyte count, 5,500/cu mm, with 2% eosinophils; platelets, 450,000/cu mm (direct method), with normal structure. The VDRL test for syphilis was nonreactive. lupus erythematosus and fluorescent nuclear antibody tests were negative. Serum lactic dehydrogenase and alkaline phosphatase levels were 350 (normal, 250 to 450) and 19 (normal, 12 to 35) international units, respectively. Values for the following were also included: blood glucose, 65 mg/100 ml; blood urea nitrogen, 12.5 mg/100 ml; serum creatinine, 0.75 mg/100 ml; serum uric acid, 2.8 mg/100 ml; serum cholesterol, 271 mg/100 ml; total serum protein, 6.6 gm/100 ml; with an albumin-globulin ratio of 1.6. Electrophoretic and immunoelectrophoretic patterns of serum were normal. Concentration of serum immunoglobulins was as follows: IgA, 115 mg/100 ml; IgG, 1,370 mg/100 ml; IgM, 24 mg/100 ml; and IgD, 4 mg/100 ml. Extensive investigation of the hemostatic and fibrinolytic mechanisms showed no significant findings (Table 1).

No manifestations of bleeding were noted when a heavy bandage was applied to the right leg and frequently checked. Later removal of the bandage was followed promptly by recurrence of ecchymoses in the area.

After discharge from the hospital, the patient has suffered from repeated attacks of ecchymoses in the right knee, right thigh, and many other easily accessible areas of the body.
Materials and Methods

Hematologic and chemical factors, results of which are given in the preceding history, were studied using standard techniques. Concentrations of immune globulins and levels of blood histamine were obtained with the methods stated by Noah and Brand. Multiple skin tests were carried out with modifications of the techniques described by Schwartz et al.  

Test solution (0.1 ml) was injected intracutaneously with a disposable 25-gauge needle and disposable tuberculin syringe in order to raise a small bleb in the skin. The patient was informed of the presumable nature of the solution injected and told the expected result of the test.

Red blood cell stroma and leukocyte extracts were prepared as follows: Venous blood was aspirated in a 20-ml heparinized syringe containing 4 ml of a sterile 6% solution of 0.9% sodium chloride and dextran 75. After the contents were mixed, the syringe was capped and held upright in a clamp for an hour. The leukocyte-rich plasma area was removed and centrifuged at 1,600 g at 4°C for 30 minutes; the cell-free plasma was drawn off and frozen. The button of leukocytes was suspended in 1 ml of 0.15M saline solution and subjected to ten cycles of alternate freezing and thawing. The remaining RBC sediment was suspended in 0.15M saline solution to a final hematocrit value of 60%, and frozen and thawed in dry ice. These blood fractions were used in skin testing without further manipulations.

Preparations of yeast RNA and DNA from calf thymus and from Escherichia coli were obtained. Each reagent was dissolved in 0.05M tromethamine containing 0.0075M magnesium sulfate. All solutions were filtered through Seitz filters into sterile containers immediately before testing.

Attempts to demonstrate humoral or cell-bound antibodies were also carried out, utilizing double-agar diffusion, immunofluorescent methods, passive cutaneous anaphylaxis, and the Prausnitz-Küstner reaction. In each experiment, the antigen employed was a solution of about 50 µg of calf thymus DNA per milliliter of solution or of 100 µg of phosphodiesterine from autologous RBC stroma per milliliter of solution which was prepared using a modification of a standard method. The antibody used was the patient's serum.

Results

Results of the evaluation of the coagulation and of the fibrinolytic mechanisms are detailed in Table 1. Levels of blood histamine were determined twice during the early and late phases of the appearance of cutaneous hemorrhages. The results were 4.28 µg, 5.01 µg, 3.96 µg, and 4.62 µg per 100 ml, respectively. Levels of blood histamine were also determined twice during a phase of "quiescence" and were 4.92 µg and 2.99 µg per 100 ml, respectively.

Table 2 shows that results of skin testing were positive, irrespective of the antigen used, when the patient thought the physician expected them to be so and when skin testing was done in accessible areas. Ecchymotic areas developed within 6 to 12 hours without any prodromal symptoms. This reaction differed from that of positive reactions in patients with auto-erythrocyte sensitization purpura. The positive reaction in these patients is a painful, burning sensation at the site almost immediately after injection, followed by a reddish-blue area, quite painful at touch, in approximately one hour and followed by an ecchymosis in about 12 hours. All attempts to detect humoral or cell-bound antibodies were unsuccessful.

Comment

Differentiation between auto-erythrocyte sensitization purpura and purpura factitia may be achieved only after careful evaluation. As mentioned, the difficulty in the differential diagnosis stems from the strong emotional and psychiatric backgrounds of both syndromes. In auto-erythrocyte sensitization purpura, hysterical and masochistic characteristics may predominate. Purpura is often related to stressful situations. Although the clinical picture is rather variable, the mental and psychiatric findings remain essentially constant, with the person affected best defined as "psycho-infantile". To further complicate the understanding of the syndrome, hypnotic suggestion can modify symptoms just as it influences quantitatively the response to intradermally injected antigens in allergic subjects.

In our experience, it would seem advisable to limit the diagnosis of "auto-erythrocyte sensitization purpura" to those cases where the following conditions prevail: (1) de-
Table 2.—Result of Skin Testing on Areas of Skin Accessible to Patient

<table>
<thead>
<tr>
<th>Substance Injected</th>
<th>Source</th>
<th>Amount or Volume</th>
<th>Patient Told of an Expected Positive Result</th>
<th>Reaction (Appearance of Echymosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tromethamine</td>
<td>...</td>
<td>0.05M</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>Tromethamine stained with methyl red</td>
<td>...</td>
<td>0.05M</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>Plasma</td>
<td>Autologous</td>
<td>0.1 ml</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Erythrocytes (lysed)</td>
<td>Autologous</td>
<td>0.1 ml</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>RNA</td>
<td>Yeast</td>
<td>10.0µg</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>DNA</td>
<td>Calf thymus</td>
<td>0.4µg</td>
<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>DNA</td>
<td>Escherichia coli</td>
<td>90.0µg</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Lysed leukocytes</td>
<td>Autologous</td>
<td>0.1 ml</td>
<td>No</td>
<td>0</td>
</tr>
</tbody>
</table>

Development of typical echymoses without evidence of trauma, while ordinary bruises continue to develop after accountable trauma; an (2) demonstration of positive response to the patient's own erythrocytes, stroma, or phosphatidylserine, primarily in areas where spontaneous bleeding is observed, proper controls being used at the same time; (3) development of histologic lesions at the site of injection of antigens, consisting of celluli-

tis, with increase of perivascular mononuclears in dermis and epidermis, although variations in the histopathologic picture are often pronounced. Considering these findings, auto-erythrocyte sensitization purpura is probably an organic, possibly immunologic, disease.

On the other hand, none of these criteria applies to purpura factitia. In this condition, histologic findings are noncontributory, and the appearance of purpura is usually not preceded by the development of a painful nodule. Protection of the area by cast or strong bandage assures its immunity from hemorrhage, and skin-sensitivity tests show a predictable, suggestion-induced pattern. On the basis of these findings, the lesions of purpura factitia would seem to be self-inflicted.

Nonproprietary and Trade Names of Drug

Dextran 75—Dextran 6%, Gentran 75.

References