pre-existing heterologous antibody may show an increased response to a given type, while those with pre-existing homologous antibody give a "booster" response.

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HAEMOLYTIC ANAEMIA FOLLOWING THROMBOCYTOPENIC PURPURA

BY

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Primary thrombocytopenic purpura associated with red-cell sensitization was originally described by Evans *et al.* (1951). In their group of five patients presenting with primary thrombocytopenic purpura together with evidence of red-cell sensitization, one developed a haemolytic anaemia following splenectomy.

In the case described below an acute haemolytic anaemia developed after apparent spontaneous recovery from primary thrombocytopenic purpura.

Case Report

A 58-year-old man was referred to the dermatological out-patient department with varicose eczema, which had been present for 10 years. Four months later extensive purpura appeared on the legs, thighs, and trunk. Inquiry elicited that similar attacks with occasional epistaxis had occurred at irregular intervals over the preceding 10 years. He had taken no drugs likely to produce haematological effects.

Examination on January 3, 1956, revealed a heavily built man with healed varicose ulceration covering an extensive area of both legs. There was a purpuric eruption over the legs, thighs, and trunk. Neither the spleen nor the liver was palpable.

Investigation showed: Haemoglobin, 13.3 g./100 ml., red blood cells, 4,500,000/c.mm.; platelets, 15,000/c.mm.; white cells 7,000/c.mm., with a normal differential count. Reticulocytes were less than 1%, and the bleeding-time was nine minutes. Examination of the marrow showed some maturation arrest of the thrombocytic series. The tourniquet capillary fragility test was positive, and capillary microscopy showed tortuosity and varied calibre, with defective contractility of the capillaries on trauma. The patient was group O, rhesus negative. Serial dilution anti-human-globulin test was positive to a titre of 128, with pan- and auto-agglutinins in saline and albumin at 4° C. No rhesus, Kell, or platelet antibodies active at 37° C. were detected.

Five months later he was admitted to a medical ward with symptoms suggestive of coronary thrombosis. Examination showed that the purpura had cleared and there were no abnormal findings on examination of the cardiovascular system.

In view of the history of purpura the haematological investigations were repeated on June 6: haemoglobin, 12.6 g./100 ml.; red blood cells, 3,800,000/c.mm.; platelets,

200,000/c.mm.; white blood cells 2,000/c.mm. (band cells, 2%, neutrophil polymorphs 40%, eosinophil polymorphs 16%, basophils 0.1%, lymphocytes 20%, and monocytes 22%).

Over the next three weeks the haemoglobin fell to 9.8 g./100 ml., but the platelet and white-cell counts remained constant. As the patient was suspected of having sustained a small coronary thrombosis without electrocardiographic changes he was discharged home after three weeks' bed rest. In view of his apparent recovery from primary thrombocytopenic purpura and the leucopenia which had developed, it was decided to keep him under observation.

Three months later he was readmitted because of rapidly increasing anaemia. Examination showed marked pallor with mild icterus. The spleen was just palpable. Haemoglobin, 8 g./100 ml.; red blood cells, 2,420,000/c.mm.; platelets, 250,000/c.mm.; white blood cells 3,000/c.mm. (neutrophil polymorphs 54%, eosinophil polymorphs 2%, lymphocytes 40%, monocytes 4%). The reticulocyte count was 18% and the erythrocyte sedimentation rate was 138 mm. in the first hour (Westergren). The urine contained excess urobilin and urobilinogen, and the total faecal urobilinogen was 731 mg./100 g. of faeces.

Marrow examination showed greater activity of normoblasts and macronormoblasts than noted previously. Haemolysis continued, and three weeks later the haemoglobin was 5.6 g./100 ml. and the red cells numbered 1,670,000 per c.mm. The direct antiglobulin test was positive in serial dilution. The antibody coating of the erythrocytes appeared to be a mixture of gamma- and not-gamma-globulins. The acid haemolysin test was negative; there was a strong auto-agglutinin active at 37° C., 20° C., and 4° C., and a pan-agglutinin at 4° C. active in saline and albumin.

The direct antiglobulin test on the platelets was negative; platelet antibodies were not demonstrable by the methods of Stefanini *et al.* (1953) and Dausset *et al.* (1952), or by the indirect antiglobulin test. No antibodies could be eluted from the red cells after elution at 56° C. for 10 minutes. A preparation of stroma from three-times-washed red blood cells, eluted at 56° C. with 8% albumin, reacted with all group O cells tested.

At this point treatment with corticotrophin was begun, and was followed by a rapid rise in haemoglobin to 12.4 g./100 ml., and in red blood cells to 3,850,000/c.mm. The platelet count rose to 620,000/c.mm., and the white cell count to 8,000/c.mm. (see Table). Maintenance therapy with prednisone was continued until the time of report.

Date	Hb. (g. 100 ml.)	R.B.C. (10 ⁶ c.mm.)	W.B.C. per c.mm.	Retics.	Platelets Lempert per c.mm.	Direct Anti- globulin Test
3/1/56 ..	13.3	4.5	7,000	1%	15,000	+
6/6/56 ..	12.6	3.8	2,000		200,000	
25/6/56 ..	10.4	3.01	2,000		200,000	
3/10/56 ..	8.0	2.42	3,000	18%	250,000	+
23/10/56 ..	5.6	1.67	3,400		570,000	
Corticotrophin, 120 u. daily						
29/10/56 ..	8.3	2.55	4,000	20%	620,000	+
7/11/56 ..	12.4	3.85	8,000	18%		
Prednisone, 30 mg. daily						
22/11/56 ..	13.9	4.25	7,000	2%	130,000	+
6/12/56 ..	13.3	3.8	8,000		280,000	+
Prednisone, 20 mg. daily						
20/12/56 ..	14.8	4.8	—	4%	280,000	+
3/1/57 ..	15.0	5.0	9,000	4%	300,000	+
Prednisone, 10 mg. daily						
23/1/57 ..	14.5	4.4	8,000		340,000	+
Prednisone 5 mg. daily						
21/2/57 ..	14.8	4.5	6,000	3%	400,000	
29/12/57 ..	14.8	4.8	6,000	1%	190,000	+

The antiglobulin test in serial dilution remained strongly positive after treatment was started. Further attempts to demonstrate platelet antibodies were unsuccessful.

Discussion

The association of a low platelet count with evidence of red-cell sensitization led Evans *et al.* (1951) to suggest the existence of immuno-thrombocytopenic purpura. Dausset

et al. (1952), Miescher *et al.* (1952), Stefanini *et al.* (1953), Harrington *et al.* (1953), Kissmeyer-Nielsen (1953), Tutein Nolthenius *et al.* (1953), Sauer and van Loghem (1954), Jaeger-Draafsel *et al.* (1956), and Tullis (1953) have developed techniques for the detection of platelet antibodies, and have applied these techniques to the study of platelet antibodies in thrombocytopenic purpura. In the cases in which Dausset *et al.* (1952) found platelet antibodies there had been a history of concomitant disease, or of previous transfusions which had complicated the interpretation of the platelet antibody.

In the above case there seems to have been three phases of destruction or suppression of the cellular elements of the blood. The patient presented with an illness which was indistinguishable from thrombocytopenic purpura. Spontaneous recovery from this ensued, and was followed by a period of symptomless leucopenia. Subsequently he developed the haemolytic anaemia which had been anticipated from the inception of his illness because of the strongly positive Coombs test.

When the patient was first seen the platelet count was too low for a direct antiglobulin test to be performed on the platelets according to the technique of Nelken and Gurevitch (1956). Following the development of the haemolytic anaemia the direct antiglobulin test was performed on the platelets on several occasions with negative results, and the serum was not found to contain a complete or an incomplete platelet antibody. Despite this, wide variations in the platelet count have occurred.

Evans *et al.* (1951) claimed that the immune globulin coating of the red cell was the critical factor for haemolysis. The fact that a strongly positive antiglobulin reaction was observed before the onset of haemolysis and during the phase of recovery does not support this view. This is borne out in other cases by the failure of the antiglobulin reaction to become negative even after long periods of treatment with steroid hormones and despite the successful control of the haemolytic process (Dameshek and Reeves, 1956). While "anti-red-cell" antibody production has not been suppressed the abnormal destruction of the sensitized red cells has been arrested by steroid therapy.

The period between the appearance of thrombocytopenia and haemolytic anaemia seems to have been characterized by leucopenia when the other formed elements were not affected. The process of cell destruction seems to have affected one series at a time and does not appear to have been associated with a specific antibody.

The strongly positive antiglobulin test, together with the asynchronous depression of the three formed elements of the blood, makes it unlikely that these features of the patient's illness result from hypersplenism alone.

The possibility that this patient had lupus erythematosus, as in the cases reported by Dameshek and Reeves (1956), was considered. Repeated attempts to demonstrate the L.E. cell phenomenon failed, but, as these workers showed, this phenomenon may not appear until splenectomy has been performed.

Summary

A case is described in which there was spontaneous recovery from idiopathic thrombocytopenic purpura, followed after an interval of several months by the development of an acquired haemolytic anaemia.

The significance of a strongly positive antiglobulin test accompanying thrombocytopenic purpura is discussed.

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GREASE-GUN INJURY TO THE HAND

VALUE OF EARLY TREATMENT

BY

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Increasing automation and speed in the lubrication services available for motor-cars is making injury by high-pressure injection of grease into the hand and fingers less uncommon. When it occurs a distressing and crippling reaction ensues. References to the injury are becoming more numerous; Mason and Queen (1941) recorded two cases and brought an interesting literature together, and more recently Rank and Wakefield (1953) and Bunnell (1956) have brought it to some prominence in textbook form.

The air-compressors which are used to provide the force behind the grease have an output, in most garages, of 100–200 lb. per square inch (7–14 kg. per square cm.), and, while this in itself may not be sufficient to cause penetration, the pressure of the grease coming through the small orifice of the grease-gun may be anything from three to twenty times as great (600 lb. per square inch (42 kg. per square cm.) seems to be an average figure). Grease nipples on the steering connecting rods or on the propeller shafts have the annoying habit of turning away as soon as pressure is applied (the owner who carries out such servicing by himself appreciates this through the loss of skin from knuckles). It is often necessary to steady the nipple with the free hand, but if the gun slips and high-pressure lubrication is in use, the reaction of the finger on the trigger is not in time to avert the injection of grease or oil into the other hand or fingers which the nozzle may come up against.

From the moment of injury the stages of surgical pathology and the clinical features follow in dreadful succession. Owing to the unyielding attachment of skin to deep fascia by the fibrous septa (also well known for the anatomical basis of the aetiology of blisters), the part is tightly distended by the grease, some of which may be forced along those fascial compartments occupied by digital nerves and vessels. Pressure necrosis and gangrene may therefore occur. Tenseness, numbness, and pallor are present, and through a small pin-point or laceration grease may ooze or be expressed.

It is the delay in obtaining an immediate release of the entrapped grease under tension which results in the gangrene and loss of the part or, if not this, the development of a chronic granuloma (an oleoma). The chemical properties of the grease (so often a soap or paraffin salt, with addition of lime salts) set up an inflammatory response with islands of grease surrounded by fibrous tissue, foreign-body giant cells, and lymphocytes. Superadded infection is common. Function is lost.

Lastly, the development of contractures, ulcers, recurrent infection, even elephantiasis and cancer, seems to be the outlook over the years.