of cases is less than the expected number in the last period only (1948-9); the actual number exceeds the expected in each of the other periods. The probability of this difference being due to chance is only 1 in 50.

From the above it seems to be quite clear that the number of women immunized by a transfusion was greater before the end of 1947 than after this period. With and without transfusion, a certain number of rhesus-negative mothers are bound to become immunized if the foetus is rhesus-positive, but the figures will be much higher if precautions are not taken to prevent artificial immunization by transfusion in the rhesus-negative population.

Discussion

Though the figures show a definite improvement in the two years under review as compared with previous years, they seem to be still too high to be accepted with complacency. It would appear to be imperative to adopt effective measures to reduce these figures still further, and no case of immunization by transfusion in a female should ever occur. As the great majority of transfusions are "cold" transfusions there is usually enough time to group and type the patient so that homologous blood can be given. Most hospitals have by now a blood bank run by the pathological laboratory; blood grouping and typing has reached in most parts of the country a very high standard indeed, and technical mistakes are very rare.

With regard to emergency transfusions, a simple procedure would serve to prevent immunization and at the same time save the rare rhesus-negative blood, particularly of Group O: a female patient admitted in an emergency is treated, to start with, as if she was rhesus-negative, and rhesus-negative blood is given. If the group is known or if there is enough time at least to determine the group, rhesus-negative blood of the same ABO group may be given if available. Before the transfusion is begun an adequate sample of blood from the patient is put into a test-tube and sent immediately to the laboratory, where grouping, typing, and cross-matching can be performed. If further blood is needed for the patient, this can then be given as homologous blood, and rhesus-positive patients will receive positive blood. The great amount of antenatal care and the issue of grouping cards by the transfusion centres have further increased the safety of transfusion treatment. The flying squad, for instance, in Birmingham during 1946 and 1947 was issued with rhesus-negative blood only. Lately it has been found possible to make use of rhesus-positive blood, as many emergency patients can now produce their blood-grouping cards on request. If the patient has been typed as rhesus-positive, homologous rhesus-positive blood is given.

The scarcity of anti-rhesus serum, which at one time seemed to limit a further expansion of antenatal typing, will, it is hoped, be overcome in the future if pathologists and clinicians realize the importance of its availability and will help to persuade immunized mothers to contribute some serum to the common pool.

Conclusion and Summary

Using the figures obtained from the records of the Regional Transfusion Service in the Midlands, it has been shown that the percentage of immunization among rhesus-negative mothers due to previous transfusions has gone down significantly in the two years 1948 and 1949 as compared with previous periods. It is felt, however, that no immunization should ever occur if simple precautions are taken in the treatment of girls and women of pre-child-bearing or child-bearing age.

REFERENCES

- Diamond, L. K. (1946). "Physicochemical and Immunological Character of Rh Antibodies." Paper read at International Haematology and Rh Conference, Dallas, Texas, November 15, 1946.
Medical Research Council (1943). Memorandum No. 9. London.

INFECTIOUS MONONUCLEOSIS WITH THROMBOCYTOPENIC PURPURA

BY

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A tendency to abnormal bleeding in patients with infectious mononucleosis has been noted for many years, but a true thrombocytopenic purpura has been recognized only since Magner and Brooks (1942) reported a case. Accounts of nine other cases have now been published, six of these during the past two years. Despite this increased recognition of the condition, only one instance has been reported in the European literature (Finlayson, 1951). Thrombocytopenia is not mentioned in many recent accounts of infectious mononucleosis published in this country, but it is still quoted as diagnostic evidence of acute leukaemia in the differentiation of this condition from infectious mononucleosis. We describe a further case of thrombocytopenic purpura in infectious mononucleosis and review the literature on this complication.

Case Report

An unmarried girl aged 20 was admitted to the Liverpool Royal Infirmary as a case of purpura on May 11, 1951. She complained of lassitude, sore throat, swollen glands, and a rash on her arms and chest. Her previous health had always been good, and neither the patient nor her family had ever shown abnormal bleeding tendencies. She had not recently taken drugs in any form and was not exposed to toxic substances at her work.

On admission she stated that she had felt tired and "run-down" for about a month but had remained at work. For the same period she had been aware of enlarged glands behind her right ear; these had not altered in size. Three days before admission red spots appeared over the neck, the upper part of the chest, the upper arms, and the radial border of the left forearm. This rash developed in about 48 hours and gradually faded during the ensuing fortnight. On the day of admission she complained of sore throat, which remained for about a week. A menstrual period two weeks before the rash appeared was not excessive.

Examination revealed a lively and well-nourished girl showing no pallor or jaundice. Her temperature on three evenings during the first week in hospital was 100-101° F. (37.8-38.3° C.), and thereafter remained normal. Crops of petechiae were found on the left arm and breast, and larger purpuric areas on the right upper arm and left thigh. Hess's test for capillary fragility was negative. Firm, discrete mobile lymph nodes were palpated behind the upper part of the right sternomastoid, and one node was felt in a similar position on the left side. Inguinal and axillary lymph nodes were normal and the spleen was not palpable. The faucial pillars were injected and a mucous exudate partially covered the tonsils, but the mucous membranes were otherwise normal and no haemorrhagic lesions were seen in the mouth. The examination revealed no other abnormal features.

A blood examination on admission showed no anaemia. There were changes in the white cells typical of infectious mononucleosis, and this diagnosis was confirmed by a strongly positive Paul-Bunnell reaction. A platelet count revealed a marked thrombocytopenia (the haematological findings are enumerated in the accompanying table).

TABLE

Date	Haemoglobin %	White Blood Cells per c. mm.	Polymorphs %	Lymphocytes %	Monocytes %	Eosinophils %	Basophils %	Atypical Mononuclears %	Platelets per c.mm.	Bleeding Time (Duke's Method)	Clotting Time (Wright's Method)
11/5/51	100	14,000	13	59	2.5	—	0.5	25	12,000		
16/5/51	—	—	—	—	—	—	—	—	130,000		
21/5/51	—	5,000	27	56	13	1	1	2	350,000	1 min.	3½ min.
22/6/51	—	—	—	—	—	—	—	—	270,000		
27/6/51	97	6,000	43	48	8	1	—	—	260,000	1½ min.	
8/1/52	100	7,000	60	33.5	4	1	—	1.5	295,000	2 min.	4½ min.

A differential count on a specimen of sternal marrow obtained on May 16 was as follows (400 cells were counted): reticulo-endothelial cells, 0.25%; blast cells, 0.25%; haemocyto blasts, 0; proerythroblasts, 0.25%; normoblasts: early 0.75%, intermediate 3.5%, late 20.0%; megaloblasts, 0; promyelocytes, 7.25%; myelocytes, 4.5%; eosinophil myelocytes, 0.75%; metamyelocytes, 18.25%; eosinophil metamyelocytes, 0.5%; polymorphs, 6.75%; lymphocytes, 18.75%; eosinophils, 0.75%; basophils, 0; monocytes, 9.75%; plasma cells, 1.75%; atypical monocytes, 5.0%; unidentified cells, 1.0%. The myeloid erythroid ratio was 1.5:1. Platelets were very scanty in the marrow films and no megakaryocytes were seen when counting 400 cells. When the films were examined under the ¼-in. objective, megakaryocytes, although present, were fewer than normal, and while some were normal mature cells others were much smaller with a large kidney-shaped nucleus almost filling the whole cell, and appeared to be young immature forms.

On May 15 the Paul-Bunnell reaction was positive to a titre of 14,000 with both the unabsorbed and the guinea-pig-kidney absorbed serum, but only to 1/28 with the serum absorbed with ox cells. Six weeks later, June 27, the titre was 7,000 and on January 9, 1952, 1/112. The blood Kahn test was negative on June 27, 1951.

Vincent's organisms were not demonstrated in direct smears of throat swabs, and cultures yielded *Neisseria* and *Streptococcus viridans* only. No abnormality was found in the urine. The van den Bergh reaction, the serum alkaline phosphatase, and the flocculation tests for liver function were within normal limits. The chest radiograph was normal.

The patient recovered without treatment and was discharged free from symptoms after 12 days in hospital. The rash disappeared during this time and no fresh petechiae were noted. One month later she reported that several bruises had appeared on her legs. She had otherwise remained well and a menstrual period had been normal. Physical examination was negative, a platelet count was normal, and the blood picture now showed only a slight predominance of lymphocytes. No further symptoms had developed up to the time of writing, and on January 8, 1952, no clinical or haematological abnormality was found.

Review of Literature

Haemorrhage (epistaxis) was observed in a case of infectious mononucleosis in 1895, and many other instances of mucosal bleeding—epistaxis and haematuria especially—have been reported since that time. In 1921 Tidy and Morley found haematuria in 6% of 270 patients, and in 1945 Read and Helwig reported mucosal haemorrhages (from the nose, mouth, or lung) in 4% of their series.

Cutaneous purpura was first reported in a case of infectious mononucleosis by Downey and McKinlay (1923), but Tidy (1934) could find only four other instances in the literature. Bernstein (1940) quoted two further cases, and a third in which infectious mononucleosis had exaggerated a pre-existing haemorrhagic state. Recently, purpura has been reported more often in infectious mononucleosis, but it is not common; it was found in only 1 of 290 cases reviewed by Halcrow *et al.* (1943), in 9 of Read and Helwig's (1945) series of 300, and in 3 out of 556 cases reported by Wechsler

et al. (1946). Rosenthal (1939), reviewing the aetiology of 153 cases of purpura, mentions that in four "the picture resembled mononucleosis."

Thrombocytopenia, with or without purpura, would appear from the earlier literature to be a very rare event in infectious mononucleosis. Bernstein (1940) was able to quote four references to thrombocytopenia without purpura, while Minot's (1936) four patients with thrombocytopenic purpura and an "atypical white cell response" were not thought by the author to be cases of infectious mononucleosis. It should be noted, however, that platelet counts are rarely performed in infectious mononucleosis and are even omitted from early accounts of purpura in this condition. In recent years platelet counts have been done more often; Angle and Alt (1950) found a mild thrombocytopenia (100,000–200,000 per c.mm.) in five out of seven cases of infectious mononucleosis without purpura or haemorrhage, and 10 cases of thrombocytopenic purpura complicating proved infectious mononucleosis have been published since 1942 (Magner and Brooks, 1942; Lloyd, 1944; Read and Helwig, 1945; Goldbloom and Denton, 1948; Angle and Alt, 1950; Wallerstein and Madison, 1950; Kutzer and Allen, 1950; Thompson, 1950; Finlayson, 1951).

Except for the various purpuric manifestations, the clinical and pathological findings in these cases are not significantly different from those found in uncomplicated infectious mononucleosis. Haemorrhagic features appeared in each case during the first fortnight of the illness, and subsided within one to four weeks. The purpura was seen most often on the legs, and also occurred in the mouth in the majority of patients. Spontaneous mucosal bleeding was reported in all but two cases, haematuria and epistaxis being the most frequent. When reported, the clotting-time was normal, clot retraction defective, and the bleeding-time and capillary fragility were usually, but not invariably, increased. Anaemia was never present at the onset of the illness, but appeared later in two patients. (The case reported by Read and Helwig was unusual in that there was a progressive fall in the red cells, white cells, and platelets, followed by a gradual return to normal.) The platelet count fell to below 100,000 per c.mm. in every case, and in five patients did not return to a normal level for more than six weeks; the severity of the haemorrhage could not be correlated with the number of circulating platelets. The bone marrow was examined in five cases, and in two the megakaryocytes were reduced in number. All the patients made a complete clinical and haematological recovery; only two were regarded as seriously ill and two required blood transfusions. Death due to a ruptured spleen has been recorded in a similar case by Smith and Custer (1946), but the Paul-Bunnell reaction in this patient was negative.

Comment

Various explanations of this rare complication of infectious mononucleosis have been offered. Bethell *et al.* (1946) suggested that a sulphonamide drug might be responsible in some cases, but in fact only two of the patients in this series were given a sulphonamide. Read and Helwig postulated an infective granulomatous infiltration of the bone marrow, but their case showed anaemia and leucopenia as well as a fall in platelets. Lloyd (1944) attributed the purpura to

an acute infection leading to capillary damage with loss of circulating platelets at the purpuric sites. In other acute infective conditions with purpura, however, the patient is usually gravely ill. Several of the authors quote Dameshek and Grassi's (1946) case, in which there was a dramatic response to splenectomy, and attribute the purpura to hypersplenism. Although this theory may be correct, it should be noted that Dameshek and Grassi's patient had suffered from a haemorrhagic condition for two years before it was aggravated by infectious mononucleosis, and is thus not strictly comparable to the cases under discussion. Whereas the spleen was "considerably enlarged" in Dameshek and Grassi's case, it was not palpable in half the patients in this series, and in the remainder it was only slightly enlarged.

Lymphatic hyperplasia seems to be a factor common to a number of cases of thrombocytopenic purpura in which no other cause for the platelet reduction has been found (Minot, 1936; Cooley, 1938; Lytle and Ward, 1937). In Cooley's patient, for example, greatly enlarged abdominal lymph nodes were found at necropsy. He remarked upon the identical microscopical appearances of the lymph nodes and spleen, and thought that the lymph nodes were taking part with the spleen in platelet destruction. In the case of infectious mononucleosis which we have reported the immediate cause of the thrombocytopenia appeared to be a deficiency of the megakaryocytes in the bone marrow; this finding was also recorded by Wallerstein and Madison (1950).

Conclusion

We would suggest that in patients presenting with purpura, especially children and young adults, infectious mononucleosis should be excluded by means of the Paul-Bunnell reaction. A wrong diagnosis of acute leukaemia or "essential thrombocytopenia" may otherwise be made, and this may lead in the first case to the neglect of life-saving measures and in the second to unnecessary splenectomy. The absence of anaemia at the onset of the purpuric phase is a constant finding in infectious mononucleosis, and will help to exclude acute leukaemia.

We wish to thank Dr. Robert Coope, Dr. W. S. Sutton, and Dr. T. Black for their helpful criticism and for permission to publish this case.

REFERENCES

- Angie, R. M., and Alt, H. L. (1950). *Blood*, 5, 449.
 Bernstein, A. (1940). *Medicine*, 19, 85.
 Bethell, F. H., et al. (1946). *Arch. intern. Med.*, 77, 80.
 Cooley, L. E. (1938). *Arch. Path.*, 26, 390.
 Dameshek, W., and Grassi, M. A. (1946). *Blood*, 1, 339.
 Downey, H., and McKinlay, C. A. (1923). *Arch. intern. Med.*, 32, 82.
 Finlayson, R. (1951). *British Medical Journal*, 2, 1563.
 Goldbloom, A., and Denton, R. (1948). *Canad. med. Ass. J.*, 58, 189.
 Halcrow, J. P. A., Owen, L. M., and Rodger, N. O. (1943). *British Medical Journal*, 2, 443.
 Kutzer, M., and Allen, E. G. (1950). *N.Y. St. J. Med.*, 50, 1131.
 Lloyd, P. C. (1946). *Amer. J. med. Sci.*, 207, 620.
 Lytle, C. C., and Ward, D. F. (1937). *J. Iowa St. med. Soc.*, 27, 296.
 Magner, W., and Brooks, E. F. (1942). *Canad. med. Ass. J.*, 47, 35.
 Minot, G. R. (1936). *Amer. J. med. Sci.*, 192, 445.
 Read, J. T., and Helwig, F. C. (1945). *Arch. intern. Med.*, 75, 376.
 Rosenthal, N. (1939). *J. Amer. med. Ass.*, 112, 101.
 Smith, E. B., and Custer, R. P. (1946). *Blood*, 1, 317.
 Thompson, C. A. (1950). *J. Ark. med. Soc.*, 47, 114.
 Tidy, H. L. (1934). *Lancet*, 2, 180, 236.
 — and Morley, E. B. (1921). *British Medical Journal*, 1, 452.
 Wallerstein, R. S., and Madison, L. (1950). *Amer. Practit., Philad.*, 1, 624.
 Wechsler, H. F., Rosenblum, A. H., and Sills, C. T. (1946). *Ann. intern. Med.*, 25, 113, 236.

In a recent address on "Diagnosis in General Practice" the retiring president of the Royal Society of Medicine's Section of General Practice, Dr. J. D. Simpson, divided patients into four classes, depending on their doctors' knowledge of the patient himself, the pathological process, and the patient's environment. His classification was as follows: (1) the old patient with the old disease, where all three were known; (2) the old patient with the new disease, where a pathological process had to be assessed afresh; (3) the new patient with the old disease, where history or previous doctor's notes might help; and (4) the new patient with the new disease.

Medical Memorandum

Use of the Humby Knife in the Excision of Burns

The importance of early excision of the extensive deep burn has become recognized in recent years. The surgical removal of these large full-thickness sloughs may offer the only chance of survival in those once-hopeless cases which, thanks to improved methods of controlled intravenous-fluid therapy, are now being brought through the shock phase in increasing numbers. It is a tedious and time-consuming operation, however, and is often accompanied by considerable blood loss, although this factor may be minimized by the use of methonium drugs in carefully selected cases.

A recent improvement in technique has been found so helpful in this unit that it appeared to warrant publication of this short note.

CASE 1

A female patient aged 38 had suffered severe deep burns involving 60% of her body surface. She was treated by the exposure method,

and on the eleventh day after burning was taken to the theatre for excision and grafting, partly with homografts and partly with her own available skin. In an endeavour to reduce operating time a Humby knife was applied to an extensive slough on the upper part of the back. This was removed with such ease and rapidity that the remaining areas were dealt with in the same manner (see illustration).

CASE 2

A few days later the technique was employed in the case of a female epileptic aged 29 who had sustained a deep "roasting" burn of the trunk and other areas, totalling 32% of the body surface. Excision was performed on the seventh day after burning, autografts being applied and the procedure completed in three-quarters of an hour. In this case a considerable depth of fat was found to be non-viable, and in certain areas it was necessary to remove it in two layers.

COMMENT

The Humby knife used in this procedure is the familiar graft-cutting instrument consisting of a long blade the cutting edge of which is guarded by a roller adjustable according to the depth of skin required. The knife is set to cut more deeply than for ordinary use, and preliminary scalpel punctures of the slough may assist in giving some idea of the required depth. It is difficult to describe the ease and selectivity with which these adherent sloughs are removed at the correct level and the manner in which it is possible to follow difficult contours without damage to neighbouring intact skin. Blood loss is minimal, and an even surface is left which is ready for immediate skin-cover. This technique is now being employed in most cases of severe deep burns, and, together with the use of the electric dermatome, is making excision and grafting at an earlier stage a much more practical proposition.

I wish to thank Sir Harold Gillies for permission to publish this short memorandum.

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