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The rate of blood loss from skin punctures during the Ivy bleeding time test

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SYNOPSIS The rate of blood loss from skin punctures during the performance of the Ivy bleeding time test has been measured by a simple technique in normal individuals, in patients without defects of the haemostatic or coagulation system, and in patients with known haemorrhagic disorders.

A wide range was found in normal individuals, but repeated tests on a single individual showed a smaller variation. Nearly half of the tests on patients with von Willebrand's disease, thrombocytopenia, 'capillary type' of bleeding, or haemorrhagic renal failure gave abnormally high rates of blood loss. Haemophilic, Christmas disease, and Dinedevan-treated patients gave low volumes and rates of blood loss.

A group of patients has been encountered in whom the bleeding time was normal but the rate of blood loss was increased. The majority of these had haemorrhagic symptoms and other evidence of a defective haemostatic or coagulation system. It is suggested that a consideration of the rate of blood loss in those patients with a normal bleeding time gives additional help in interpreting the Ivy test. A high rate may indicate the need for further investigation of the haemostatic and coagulation system.

During the performance of the Ivy bleeding time test (Ivy, Shapiro, and Melnick, 1935) it can be seen that there is considerable variation in the amount and rate of blood loss from the skin punctures in different patients. This is so even when care is taken to avoid puncturing superficial veins. The possibility was recognized that a consideration of this blood loss might prove a useful adjunct to the Ivy bleeding time as a test of haemostasis.

TECHNICAL METHODS

HAEMOGLOBIN ESTIMATIONS These were performed using an Eel photoelectric colorimeter and oxyhaemoglobin as described by Dacie (1956) (100% is equivalent to 14·8 g. %).

IVY BLEEDING TIME This was performed as described by Biggs and Macfarlane (1957), using a spring lancet set to a depth of 3 mm. and taking care to avoid superficial veins. The skin punctures were blotted every quarter of a minute with Whatman No. 1 filter paper from a roll of width 1 cm. The normal range was taken to be a mean (from three punctures) of up to six minutes.

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MEASUREMENT OF VOLUME OF BLOOD LOST FROM SKIN PUNCTURES The blood was eluted from the roll of filter paper used for blotting the skin punctures by placing it in a 100 ml. stoppered conical flask containing 50 ml. of ammoniated '0·04%' distilled water and agitating on a rotary mixer for 30 minutes. After centrifugation the haemoglobin concentration in the supernatant was estimated with an Eel photoelectric colorimeter. When the amount of blood loss was very great an appropriate dilution had to be made before estimation.

Since haemoglobin estimations are normally performed on a 1 in 200 dilution of blood a reading of '100%' in the eluate (referred to above) corresponds to a volume of blood equal to 1/200 × 50 ml. or 250 c.mm. Thus each '1%' on the haemoglobin scale corresponds to 2·5 c.mm. of blood lost from the skin punctures. If the patient was anaemic a proportionate correction was applied, depending upon the haemoglobin concentration of the capillary blood, *i.e.*, volume of blood loss in c.mm.

$$= \text{'\%' of haemoglobin in eluate} \times 2{\cdot}5 \times \frac{100}{\text{patient's Hb\%}}.$$

Results have been expressed as c.mm. of blood lost. The rate of blood loss per minute per puncture was calculated by dividing the total volume by the sum of the bleeding time, in minutes, from the three punctures.

TESTS OF THE COAGULATION SYSTEM These, including platelet counts, Quick's one-stage prothrombin time, Lee and White's clotting time, Merskey's prothrombin

consumption index, and Hess's tourniquet test, were performed as described by Biggs and Macfarlane (1957). The antihaemophilic globulin assay was that of Biggs (1957).

SELECTION OF SUBJECTS

NORMAL VOLUNTEERS These were drawn from the technical and medical staff over a period of two years. Forty-seven tests were made on 16 males and 43 tests on 17 females. None was known to have haemorrhagic symptoms.

PATIENTS WITHOUT HAEMORRHAGIC SYMPTOMS OR DISORDERS OF COAGULATION SYSTEM These patients were suffering from hypertension, renal disease, or urinary tract abnormalities but enquiry and examination gave no evidence of a haemorrhagic tendency. Also the bleeding time, coagulation time, prothrombin time, prothrombin consumption index, and platelet counts were normal. Twenty-seven tests were made on 25 patients.

VON WILLEBRAND'S DISEASE Patients included in this group had a prolonged bleeding time, normal platelet count, and either a low antihaemophilic globulin (AHG) level or there was a prolonged bleeding time in a close relative (parent, sibling, or child). Sixteen tests were made on seven patients.

'CAPILLARY TYPE' OF HAEMORRHAGIC STATE Patients included in this group had a prolonged bleeding time and normal platelet count, coagulation time, prothrombin time, and prothrombin consumption index. All had haemorrhagic symptoms affecting the mucous membranes. A conclusive family history of a bleeding tendency was not demonstrable. Eleven tests were performed on 10 patients.

THROMBOCYTOPENIA Patients included in this group had a platelet count of less than 100,000 per c.mm. in the absence of any other known defect of the coagulation system. The causes were idiopathic thrombocytopenic purpura, leukaemia, aplastic anaemia, nitrogen mustard treatment, and liver failure. Fifteen tests were performed on 12 patients.

RENAL FAILURE WITH HAEMORRHAGIC SYMPTOMS Patients in this group had persistently raised levels of blood urea but normal platelet counts, coagulation times, and prothrombin times. The bleeding time was usually prolonged and prothrombin consumption impaired. All had haemorrhagic symptoms affecting the skin or mucous membranes. Thirty tests were performed upon 20 patients.

HAEMOPHILIA AND CHRISTMAS DISEASE These patients were diagnosed or investigated by Dr. Rosemary Biggs. Eight tests were performed on seven haemophiliacs and two tests on two patients with Christmas disease.

DINDEVAN-TREATED PATIENTS Three patients were tested in whom the 'prothrombin and proconvertin' percentages were 5, 13, and 13·5 (Owren and Aas, 1951). They did not have haemorrhagic symptoms and the bleeding times were normal.

THROMBOCYTHAEMIA Two patients with platelet counts of 680,000 and 1,035,000 per c.mm. were tested. The primary conditions were polycythaemia rubra vera and chronic myeloid leukaemia. The bleeding times were prolonged in both cases.

ACUTE DEFIBRINATION SYNDROME An obstetric patient with a severe haemorrhagic diathesis, investigated by Dr. A. A. Sharp of the Radcliffe Infirmary, was tested on three occasions. The platelet counts at these times were 94,000, 318,000, and 335,000 per c.mm. The bleeding times were prolonged on each occasion. The whole blood clotting time was greater than six hours initially.

RESULTS

Table I shows the range and mean values for bleeding time and rate of blood loss from 20 repeated tests on a single individual (M.J.A.).

TABLE I

RESULTS OF 20 REPEATED BLEEDING TIME TESTS ON A SINGLE NORMAL INDIVIDUAL

Measurement	*Mean*	*Range*
Bleeding time (min.)	3·6	1·5 to 7·2
Rate of blood loss (c.mm./min.)	6·8	1·4 to 13·0

Table II shows the rates of blood loss found in a group of normal volunteers, patients without haemorrhagic symptoms, and in groups of patients with different haemorrhagic states. In general higher rates were found in patients with von Willebrand's disease, 'capillary type' of bleeding, thrombocytopenia, or haemorrhagic renal failure than in normal volunteers, patients without haemorrhagic states, or in patients with plasma coagulation defects. The few tests on patients with thrombocythaemia or acute defibrination also gave high rates of blood loss.

Brief details are given in Table III of 15 patients with a probable haemorrhagic tendency, normal bleeding times and platelet counts, but a rate of blood loss from skin punctures which was higher than that usually encountered in normal individuals.

DISCUSSION

These results show that abnormally high rates of blood loss from skin punctures are common in those types of haemorrhagic states attributed to a capillary or platelet abnormality. Defects of the plasma coagulation factors, such as occur in haemophilia, Christmas disease, or after treatment with Dindevan,

TABLE II

RATE OF BLOOD LOSS FROM SKIN PUNCTURES IN C.MM. PER MINUTE

Group of Subjects	*Range*	*Mean*	*No. of Tests Over 25 c.mm./min.*	*No. of Tests Under 52 c.mm./min.*
Normal volunteers	1·0-161·0[1]	12·6	12	78
Non-haemorrhagic patients	1·5- 24·0	11·6	0	27
Haemophilia, Christmas disease, Dindevan-treated patients	1·2- 11·0	6·1	0	12
			12	117
von Willebrand's disease	3·6- 92·0	34·1	5	5
Capillary type of bleeders	7·5- 53·4	24·1	4	7
Thrombocytopenia	3·5- 50·0	19·0	4	11
Haemorrhagic renal failure	7·0-108·0	29·8	16	14
Thrombocythaemia	36·3-100·0	68·2	2	0
Acute defibrination syndrome	11·3- 88·0	41·5	2	1
			33	38

[1]The next highest value in this group was 47·6 c.mm./min.

TABLE III

GROUP OF PATIENTS WITH PROBABLE HAEMORRHAGIC STATES BUT NORMAL BLEEDING TIME AND PLATELET COUNTS

	No. of Patients	*Rates of Blood Loss from Skin Punctures (c.mm./min.)*
Menorrhagia + bruising or epistaxis	4	30, 32, 42, 80
Repeated haemorrhages after dental extractions	2	32, 40
Chronic nephritis + epistaxis ± bruising	3	31, 40, 108
Purpura while recovering from subacute bacterial endocarditis	1	55
Recovering from attack of idiopathic thrombocytopenic purpura	1	48
Haematemesis and melaena, hepatosplenomegaly	1	43
Gastrointestinal bleeding, ? 'capillary bleeder'	1	35
Excessive bleeding from skin trauma	1	55
Mother of a patient thought to have von Willebrand's disease	1	66
	15	Mean 48·7

do not appear to result in an increased rate of blood loss from skin punctures.

In addition a number of patients with suspected haemorrhagic states have been found to have a normal bleeding time but an unusually high rate of blood loss, *i.e.*, 30 c.mm. or more per minute. These 15 cases are listed in Table III. Haemorrhagic symptoms, present in all but one, were confined to the skin and mucous membranes and were generally mild in character. This clinical pattern of the bleeding suggested an abnormality of capillary or platelet function. In some cases it was partially confirmed by a positive tourniquet test or by a prolonged bleeding time on a different occasion. In another instance the patient's daughter had a long bleeding time. The four cases with renal failure all had impaired prothrombin consumption due to a qualitative platelet defect (Willoughby, 1960).

In the presence of a normal bleeding time the finding of a high rate of blood loss suggests defective cutaneous haemostasis where it might not otherwise be suspected. In the presence of a prolonged bleeding time it provides confirmatory evidence. Because of the imperfections of available tests of haemostasis this information proves useful in practice. The two tests are complementary to each other and the measurement of rate of blood loss cannot replace the bleeding time since, as shown in Table II, the mean rate is often within the normal range in patients with a long bleeding time.

The only other report that has been found in which consideration is given to the amount of blood loss is that of Adelson (1956). He reported that Dextran infusion in large amounts caused a haemostatic defect which could be demonstrated by using a 'modification of the Ivy technique whereby the bleeding was measured by volume of blood as well as by duration'. No figures for the volumes of blood were given. It is of interest that Dextran appears to produce this haemostatic defect by becoming adsorbed on to the surface of platelets (Rothman, Adelson, Schwebel, and Langdell, 1957) and

inhibiting their participation in the early stages of blood coagulation (Jacobaeus, 1955).

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