their walls. The rate of absorption of any given substance is a measure of the permeability of the vascular wall to such substance. The pressure in the unsupported veins of the subarachnoid space cannot be much below that of the C.S.F., or they would be completely collapsed; but dural sinuses into which they drain are at a lower pressure because they are held open by the rigid and inelastic dura mater. So long as the blood in these sinuses does not occupy the total potential volume of the sinus (as in hydrocephalus) it is possible for their pressure to be below that of their tributary veins. Thus the true pressure gradient exists not between the C.S.F. and the veins which it immediately bathes, but between the unsupported (pial) veins and the dural venous sinuses.

Such a mechanism demands that all the subarachnoid veins be in the same phase of vascular systole or diastole. If, for example, the cerebral veins were dilated while the spinal veins were compressed, and vice versa, there would merely result a flow of C.S.F. from cranial to spinal subarachnoid spaces and back again. This would happen during the phases of respiration of the cranial subarachnoid veins drained into the superior caval system and the spinal into the inferior. But Howarth and Cooper (1949) showed that a radioactive local analgesic injected into the lumbar subarachnoid space is subsequently found in much higher concentration in the azygos vein than in any other systemic veins. Bowsher (1954) demonstrated that in six representative mammals (including man) the intradural and extradural veins of the vertebral canal drain into the azygos system and thence into the superior vena cava. Hence the total venous drainage of the cranial and spinal subarachnoid spaces is into the superior caval system in the thorax, and thus venous volume changes in subarachnoid vessels induced by the phases of respiration will be in the same direction throughout the subarachnoid system.

Summary

A semi-collapsed semi-permeable tube in a rigid water-jacket can increase in volume, up, to a circular cross-sectional area, by absorbing the contents of the jacket.

In the closed C.S.F. system, increase in volume of the intrathecal veins results in increased absorption of C.S.F., whereby the total volume of intrathecal liquid is equilibrated.

So long as there is no expansion of the total circumference of the vascular walls in the subarachnoid space, as opposed to change in cross-sectional area, there will be little or no change of pressure accompanying volumetric changes in these blood vessels.

The rhythmic changes in volume of the subarachnoid vessels due to cardiac action, and especially those due to respiration, are an important factor in the purely mechanical absorption of C.S.F.

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SEVERE POST-OPERATIVE THROMBOCYTOPENIC PURPURA

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Generalized haemorrhage in the post-operative period, especially after a major operation, is an alarming occurrence. Among a number of conditions which may cause this is thrombocytopenic purpura. Many drugs (Ackroyd, 1955) have been described as able to cause a severe thrombocytopenia, of which the reaction to "sedormid" (Ackroyd, 1949) is the classical example. It has been shown that both phenobarbitone (Andel and Groen, 1937) and allylisopropyl barbituric acid (Wintrobe, 1942) can cause this condition.

In the case here described hypersensitivity to butobarbitone developed; it was rapidly recognized by a positive patch test, and later by the effects of a test dose of the drug. The widespread use of pre-operative sedation, and the ease with which sedative drugs can be obtained, make it imperative that this condition be recognized early, for, though a rare complication, its effects may be fatal.

Case Report

A man aged 65 was admitted to hospital with a four-months history of abdominal pain and loss of weight. He was found to have a carcinoma of the stomach. Examination of the chest revealed no abnormality, and x-ray examination showed no active disease there. His blood pressure was 138/75; haemoglobin, 67% (9.9 g./100 ml.), blood group A, Rh negative. He was transfused with 1 pint (570 ml.) of packed cells, group A, Rh negative, and next day a partial gastrectomy was performed.

At operation a growth 2 by 2 in. (5 by 5 cm.) was found in the pyloric part of the stomach, and enlarged glands were present in the adjacent mesentery, none distant from the stomach. There was no growth in the liver or peritoneum. Histologically the growth proved to be a well-differentiated papillary adenocarcinoma. No growth was seen in the glands present in the operation specimen. For the next few days progress was uneventful.

On the seventh post-operative day a slight blood-stained discharge appeared from the stab wound into which a drainage-tube had been inserted at operation. On the 10th day the sutures were removed and the wound appeared satisfactory. The next day a slight greenish discharge from the wound was noted, and "crystamycin" therapy was started. On the 12th post-operative day a small epistaxis occurred, and the following day a slight blood-stained discharge from the wound was noticed. At this time, also, some purpuric spots in the region of the wound in the abdominal wall appeared; these were thought to be due to bruising resulting from the use of adhesive strapping to cover the wound. On the 14th post-operative day bright-red blood was oozing from the wound and stab hole and from the stitch holes. The blood was fluid and showed no evidence of fibrin formation. Gross haematuria then appeared for the first time. Purpura was now extensive, being evident over the trunk, arms, legs, and heels. Bleeding from the face after shaving was difficult to control.

Haematological investigation at this time showed: haemoglobin 58% (8.6 g./100 ml.); red cells, 3,560,000 per c.mm.; colour index, 0.8; white cells, 19,100 per c.mm. (polymorphs 87%, lymphocytes 8%, monocytes 5%); bleeding-time grossly prolonged (over 10 hours); clotting-time, 10 minutes (room temperature); platelets, 35,000 per c.mm. (method of Lempert); prothrombin index, 100% of normal; capillary fragility test, strongly positive; blood

fibrinogen, 320 mg. per 100 ml. The significant findings were a greatly reduced platelet count, prolonged bleeding-time, and increased capillary fragility. The thromboplastin generation test was not therefore proceeded with.

Inquiry elicited the following: the patient had received 3 gr. (0.2 g.) of butobarbitone on the night of admission, pethidine and atropine pre-operatively, crystamycin during the post-operative period, with further 3-gr. (0.2-g.) doses of butobarbitone on the third, fourth, and fifth post-operative days. Patch tests as described by Ackroyd (1955), containing butobarbitone, penicillin, and streptomycin, were accordingly applied.

A slow drip transfusion was started and continued for the next 48 hours, and vitamin K₁ therapy was begun. The next day the patch test with the butobarbitone was found to be positive; the rest were negative. Sternal puncture was performed, but no malignant cells were found in films or sections of the marrow aspirate. In the meantime haemoptysis had appeared, the wound continued to ooze bright-red blood without any fibrin formation, and the urine still contained a large amount of blood. Although the fibrinogen levels had been determined on successive days, the level never became low enough to account for the haemorrhage, and the normal prothrombin time also excluded the possibility of haemorrhage due to fibrinopenia. The platelets continued to decrease, levels of 63,000 and 49,000 per c.mm. being found on successive days.

Since it was now clear that the bleeding diathesis was due to a platelet defect, and since this was likely to be due to hypersensitivity to butobarbitone, treatment with prednisolone was begun.

Twelve hours after the first dose of prednisolone was given the platelets were 31,000 per c.mm.; six hours later they were 164,000 per c.mm. Fibrin clot appeared in the blood on the dressing of the wound. Within 48 hours of starting prednisolone therapy the urine was clear macroscopically and contained only scanty red cells in the spun deposit. The haemoptysis had ceased. Thereafter there was a steady improvement in the patient's condition. The platelet level, bleeding-time, and capillary fragility tests became normal. All bleeding ceased, and the wound healed satisfactorily. Prior to his discharge to a convalescent home, three weeks after the bleeding episode had started, the patient was given a test dose of approximately 1/20 of a tablet (5 mg.) of butobarbitone, with no effect on his platelet level, as shown below:

9.30 a.m.	..	Platelets, 255,000 per c.mm.
9.40 a.m.	..	Test dose 1/20 tablet butobarbitone.
10.40 a.m.	..	Platelets, 245,000 per c.mm.
11.40 a.m.	..	" 251,000 " "
12.40 p.m.	..	" 250,000 " "
2.40 p.m.	..	" 261,000 " "
3.40 p.m.	..	" 239,000 " "
4.40 p.m.	..	" 234,000 " "

Accordingly, the following day, half a tablet, or 47 mg., of butobarbitone was given, which caused a small but definite drop in the platelet level, as shown below:

9.30 a.m.	..	Platelets, 259,000 per c.mm.
	..	Test dose 1/2 tablet butobarbitone given.
10.40 a.m.	..	Platelets 259,000 per c.mm.
11.40 a.m.	..	" 290,000 " "
12.40 p.m.	..	" 233,000 " "
2.40 p.m.	..	" 219,000 " "
3.40 p.m.	..	" 175,000 " "
4.40 p.m.	..	" 170,000 " "
5.40 p.m.	..	" 272,000 " "
6.40 p.m.	..	" 285,000 " "

The urine deposit contained scanty red cells.

One month later the bleeding-time, clotting-time, platelets, and capillary fragility tests were all normal. A gain in weight of 3 lb. (1.4 kg.) was recorded, and the patient felt well.

Discussion

The appearance of a haemorrhagic condition after operation may be due to the presence of a congenital defect of the clotting mechanism, or an acquired defect. In the present

case it seemed unlikely that the defect could be congenital, since no haemorrhage had occurred for 10 days following operation.

Fibrinolysis has been described (Dyggve, 1947; Soulier *et al.*, 1952) as a cause of post-operative haemorrhage, but this was discounted by the presence of a moderately reduced but nevertheless significant blood fibrinogen level and a normal prothrombin time. Fibrinolysis due to general dissemination of carcinoma was made unlikely by the absence of malignant cells in the sternal marrow.

The most significant finding was a gross reduction in the platelets, accompanied by a prolonged bleeding-time and increased capillary fragility. It is well recognized (Williams *et al.*, 1955) that thrombocytopenia occurs and is sustained for three to four days after surgical operation, and that the pre-operative platelet level is regained by the seventh post-operative day, so that it appeared that the thrombocytopenia in this case could not be due to the operation *per se*. Massive transfusions have been shown (Krevans and Jackson, 1955) to cause thrombocytopenia, and to be unaffected by cortisone therapy, but the transfusions have to be of at least 5 litres and given rapidly. The present case had received 560 ml. of blood by slow drip.

A positive patch test seemed to implicate butobarbitone as the sensitizing agent in producing the thrombocytopenia, and this was confirmed by subsequent test-dosing when the patient was well and had recovered from his haemorrhagic episode.

Since this case showed an immunological response, large doses of prednisolone were given, with remarkably dramatic results.

Summary

A case of thrombocytopenic purpura developing post-operatively is described.

The cause has been identified as due to sensitization to butobarbitone.

Prednisolone was found to be remarkably effective in controlling the condition.

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A day-school for physically handicapped children—the Franklin Delano Roosevelt School—was opened in London on October 3 by Sir EDWARD BOYLE, Parliamentary Secretary to the Minister of Education. The school, an L.C.C. establishment in Avenue Road, Hampstead, is stated to be the first day-school for physically handicapped children to be built in London since the second world war. Originally an all-age school in Paddington, which was reorganized and divided in 1944, the school was renamed the Franklin Delano Roosevelt in 1950; the transfer to the new building was made in January this year. The new school is for 160 boys and girls, whose ages range from 2 to 16. Among the pupils are children suffering from cerebral palsy, heart diseases, anterior poliomyelitis, tuberculosis of the bones and joints, and haemophilia. In addition to the headmistress, Mrs. E. K. SELICK, there are eight full-time teachers and one part-time, and a part-time nursing sister. A remedial exercises room is provided, in which visiting physiotherapists give treatment; speech therapy is also available when required. Children attend the school from west and north-west London, Middlesex, and Hertfordshire.