forced to abandon conservatism in such a case; for, as both Noble and White have reported, some patients even of this unfavourable type have been completely relieved. At present, however, we are reasonably convinced that the intubated jejunostomy, perhaps by its decompression function, or perhaps by the merit of providing a more orderly pattern for the intestine, is a most effective means of dealing with recurrent post-operative obstruction where the cause is recent peritonitis.

Summary

Many cases of recurrent small-intestinal obstruction are not at present treated adequately.

Intubation of the whole small bowel at operation, via a jejunostomy, after suction decompression, proved to be successful in the treatment of the three cases described.

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REPAIR OF CARDIAC DEFECT IN PATIENT WITH EHLERS-DANLOS SYNDROME AND DEFICIENCY OF HAGEMAN FACTOR

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Congenital defects of the cardiac septa usually have no known cause, but an incidence of 20–30% in arachnodactyly (Marfan syndrome) and mongolism has been observed (Wood, 1956). Congenital heart disease of all kinds is apparently rare in patients with Ehlers–Danlos syndrome, a hereditary disorder of connective tissue. We have found only one report of such an association, in which the patient had tetralogy of Fallot (Wallach and Burkhart, 1950).

The essential manifestations of the Ehlers–Danlos syndrome are friability of the skin and blood-vessels, undue mobility of the joints, and excessive distensibility and elasticity of the skin. The syndrome is transmitted as a Mendelian dominant character and has often been observed together with other anomalies (Johnson and Falls, 1949; Summer, 1956; Macfarlane, 1959; Zaidi, 1959). McKusick (1959) has stressed how little knowledge we have of the visceral abnormalities which may occur in this condition.

Hageman trait is a rare defect of blood-clotting which does not cause abnormal bleeding, despite a severe coagulation defect which is detectable in laboratory tests (Ratnoff and Margolius, 1957).

The occurrence of partial persistent atrio-ventricular canal in a patient with both Ehlers–Danlos syndrome and deficiency of Hageman factor must therefore be exceedingly rare. Such a combination and relevant observations are reported in the following case.

Case Report

A boy aged 11 years had been regarded as normal until the age of 8 years, when a heart murmur was detected by the school medical officer and he was referred to the cardio-thoracic unit of the Alfred Hospital. He had the clinical features of an atrial septal defect with left axis deviation in the electrocardiogram, suggesting the diagnosis of partial persistent atrio-ventricular canal. Two and a half years later his poor muscular development was noted, and he had developed symptoms of exertional dyspnoea. Cardiac catheterization and femoral-artery puncture performed without incident indicated a left-to-right shunt at both the atrial and ventricular levels, and the pulmonary blood flow to be four times greater than the systemic flow. The original diagnosis was retained, and he was admitted to hospital for repair of the defect three years after the first examination.

The patient, his mother, and at least 15 of her relatives (Fig. 1) had experienced abnormally easy bruising; the size

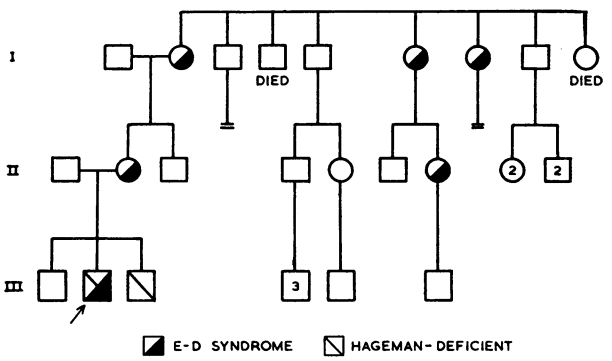

FIG. 1.—Part of family tree of the patient, who is shown by the arrow. Died indicates died in infancy.

of the ecchymoses was small (up to 4 cm. diameter). All had experienced large lacerations (5 cm. or more in length) requiring suturing of the knees and lower legs after minor traumata. Healing occurred without difficulty but resulted in broad scars of tissue-paper thinness. Excessive bleeding never occurred from these wounds or from accidental incised wounds. The affected relatives and the patient had not suffered from bleeding from mucous membranes, or into the joints and deeper tissues or from the uterus. The skin over the knees and elbows of the patient and his mother was unduly extensible; it could be pulled out to 4–5 cm. and felt elastic. On release the skin immediately resumed its normal contour. Apart from numerous large scars over the knees, the skin felt and appeared normal. Their wrist- and finger-joints were excessively mobile, so that they could be bent dorsally and almost touch the forearm. These features indicated that the patient had the Ehlers–Danlos syndrome of a mild-to-moderate severity.

Pre-operative blood examinations gave the following results: haemoglobin, 14.8 g./100 ml.; white cells, 9,000/c.mm.; platelets, 280,000/c.mm. Skin bleeding-time and capillary resistance tests were normal. Blood-clotting studies are given in Tables I and II.

From the coagulation tests it is seen that the blood-clotting time and the partial thromboplastin time were prolonged. Prothrombin time was normal. From these results it seems that there was a defect in the early stages of blood coagulation. Thromboplastin generation tests

showed only abnormal results when both $BaSO_4$-treated plasma and serum from the patient's blood were used. When one of these components was obtained from normal blood the results were normal. Tests using the partial thromboplastin time were used to establish the coagulation defect, and the results are given in Table II.

The results in Table II show that the clotting-time of the patient's plasma could not be reduced by the addition of suspensions of kaolin or bentonite, but was reduced to normal figures by the addition of normal serum and adsorbed plasma, and serum from a patient with complete Factor IX deficiency (haemophilia-B). These results are characteristic of a coagulation defect due to lack of Hageman factor or P.T.A. (plasma thromboplastin antecedent) (Margolis, 1958). Addition of the patient's plasma to that from a patient (S.) with Hageman-factor deficiency showed that the patient's plasma had only little effect in correcting the Hageman-factor deficiency. This establishes the diagnosis of Hageman-factor deficiency in the present patient. Assuming that S. plasma had a complete deficiency of Hageman factor, our patient had in his plasma not more than 1–2% Hageman-factor activity.

Operation was performed, using total body perfusion with a Kay–Cross disk oxygenator. It was observed that the septal leaflets of both ventral and tricuspid valves were cleft and that there was a low atrial septal defect 3 cm. in diameter. No ventricular septal defect was found. The clefts in the valves were closed with interrupted sutures, and a plastic prosthesis was sewn into the atrial septal defect. The patient (weight 28 kg., height 145 cm., body area 1.08 sq. m.) received 6,000 units of heparin intravenously and 5,400 ml. of heparinized blood (4 units heparin/ml.) during the extracorporeal circulation. The by-pass lasted 40 minutes. The observed heparin concentrations in the patient's blood are given in Fig. 2. It is seen that approximately 100 minutes after the protamine sulphate injection the patient's blood was free of heparin, and coagulation tests, including fibrinogen determination and platelet count (185,000/c.mm.), were normal. The total drainage from the chest in the post-operative period was 290 ml. This figure is in the low range for this type of surgery.

The gradual disappearance of Hageman-factor activity from the patient's blood was determined by the partial thromboplastin-time technique, and results are given in Fig. 3. It is seen that the disappearance of Hageman factor from the patient's circulation followed an exponential curve and the half-life of Hageman factor was approximately two days. The chest wound healed in normal time, but the scar was somewhat broader than normal. Nine months after the operation he won the following events: 80 yards sprint, the hop, step, and jump, and the broad jump, and he became senior athletic champion at the primary school he was attending.

TABLE I.—*Coagulation Data of Venous Blood*

	Patient	Normal
Blood-clotting time (mins.), glass 35° C.	27–54	12–20
,, ,, ,, ,, silicone 35° C.	120–160	40–80
Clot retraction	Normal	—
Partial thromboplastin time (secs.) ..	390–600	75–85
Prothrombin time (secs.)	13	12–13
Platelet count/c.mm.	150,000	100,000–300,000
Thromboplastin generation (secs.) with:		
Patient's Ba-plasma and patient's serum	25–28	10–11
,, ,, ,, normal ,,	10	—
Normal ,, ,, patient's ,,	10	—

TABLE II.—*Partial Thromboplastin Time (secs.) of Plasma**

Patient's plasma + NaCl	390–600
,, ,, + 5 mg. kaolin; 0·8 mg. bentonite ..	375–510; 350
,, ,, + normal Ba-plasma	150
,, ,, + ,, serum	82
,, ,, + $Al(OH)_3$-treated normal serum ..	110–150
,, ,, + haemophilia-B plasma	166
,, ,, + ,, serum	177
Hageman-deficient plasma (S.)	900
,, ,, + 50% patient's plasma ..	520

* 0·2 ml. of citrated plasma + 0·1 ml. of phospholipid suspension + 0·05-ml. additions, as indicated, were incubated at 35° C. and 0·2 ml. of 0·025 M calcium chloride added.

Discussion

Cardiac surgery has been carried out successfully in patients with various anomalies associated with their cardiac defect. The Ehlers–Danlos syndrome might be thought to be a condition in which surgery could result in unusual difficulties due to friability of the tissue, and the thin and weak scars which result from wounds. A number of surgical procedures have been carried out on these patients. These include amputation of a leg (Johnson and Falls, 1949), lens extraction (Thomas *et al.*, 1954), appendicectomy (Packer and Blades, 1954), bone grafting (Saemundsson, 1956), skin grafting (Ricketson, 1957), and thoracoplasty (Ross and Dooneief, 1957). Difficulties sometimes encountered during operation were caused by the friability of the tissues, which allowed skin sutures to tear out and haemostats to drop off. Slow healing, which sometimes occurred, resulted in herniation of the iris and failure of skin grafts to take, and might have been the cause for non-union in the case reported by Saemundsson. Excessive bleeding after tonsillectomy in a patient has been referred to by Johnson and Falls (1949). Operation scars have been stated to become broad along almost their whole length. In spite of the foregoing, absence of surgical difficulties in a patient with Ehlers–Danlos syndrome of severe degree were noted by Ross and Dooneief.

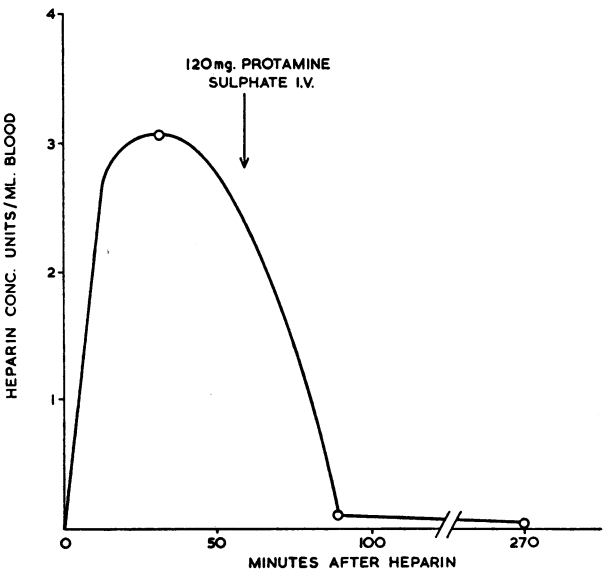

FIG. 2.—Heparin concentration in patient's blood.

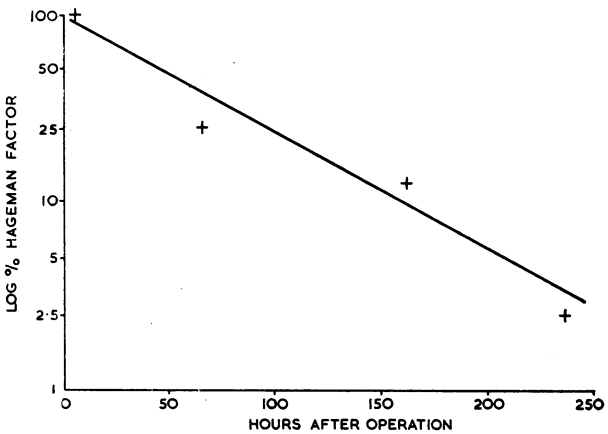

FIG. 3.—Showing disappearance of Hageman factor from the circulation.

That no technical difficulties were encountered during the operation on our patient was probably in part due to the relative mildness of his connective-tissue disorder. During 10 months since the operation no clinical evidence of breakdown in the repair of his defect or of the tissues divided during the operation has occurred.

An indicator dilution curve was recorded after the injection of indocyanin green into the superior vena cava. This showed no evidence of a significant persisting left-to-right shunt.

The excessively easy bruising experienced by patients with the Ehlers–Danlos syndrome is not a manifestation of an underlying haemorrhagic disorder. These patients, including our own, do not experience symptoms such as epistaxis, menorrhagia, prolonged bleeding from wounds, or joint haemorrhages.

Smith and Hornisher (1954) observed a prolonged blood-clotting time in a patient with Ehlers–Danlos syndrome, but no explanation is given. A detailed study of haemostasis was carried out in three patients with the Ehlers–Danlos syndrome by Frick and Krafchuk (1956), who also reviewed the earlier literature. They found no blood-clotting or platelet abnormality in their patients, but reduced capillary resistance as did some other authors. This was attributed to rupture of the vessels, which became abnormally distended owing to lack of support by the defective collagen. In other reports normal capillary resistance was recorded. The absence of overt bleeding in our patient and his relatives in spite of their easy bruising suggested that no abnormal bleeding would result from connective-tissue disorder during the operation or subsequently, as was later confirmed.

The occurrence of blood-clotting defects in patients with congenital heart disease appears to be more frequent than in other congenital disorders, as indicated by the findings of Favre-Gilly *et al.* (1951), Hartmann (1952), DeWall *et al.* (1956), van Creveld (1958), von Kaulla and Swan (1958), and Fantl and Ward (1960). It is therefore desirable to investigate the coagulation mechanism of such patients prior to operation. The clotting anomaly detected in our patient is almost certainly due to a severe congenital deficiency of Hageman factor. Patients with this anomaly do not experience haemorrhagic symptoms, although their blood-clotting times may be longer than those of many haemophiliacs. The patient and his brother, who had the same coagulation anomaly in the absence of Ehlers–Danlos syndrome, had never suffered from abnormal bleeding. Transfusion with plasma in the post-operative period was therefore not carried out, as would have been necessary in the case of a patient with haemophilia or other coagulation defects.

Summary

An 11-year-old boy with a partial atrio-ventricular canal had the Ehlers–Danlos syndrome of moderate severity and an almost complete deficiency of Hageman factor.

His cardiac defect was repaired. Despite some reports of technical difficulties and poor results with surgical procedures in patients with the Ehlers–Danlos syndrome, no difficulties were encountered in the repair of this patient's cardiac abnormality. He did not show any haemorrhagic tendency or difficulty in haemostasis prior to and after the operation.

The half-life of Hageman factor introduced by transfusion of heparinized blood was approximately two days.

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Requirements for the protection of people employed in factories and other places to which the Factories Act, 1937, applies against ionizing radiations and other hazards arising from the use of unsealed radioactive substances are laid down in a Preliminary Draft of Regulations published by the Ministry of Labour. This draft is a complementary code to the statutory draft of Regulations, published on March 30, dealing with the protection of workers from the dangers arising from the use of "sealed sources" of radioactive substances and from machines which produce ionizing radiations. The proposed Regulations will apply to the whole range of radio-nuclides used in industry, including those used in nuclear reactors, and they will in due course replace the Luminizing Regulations, made in 1947. Unsealed radioactive substances are defined by the Regulations to include nuclear fuel elements. Maximum permissible doses, based on the recommendations of the International Committee on Radiological Protection and supported by the Medical Research Council, are laid down. Provision is made for reliance to be placed on working arrangements that provide intrinsic safety, for the instruction of workers concerned about the hazards involved, and the precautions to be taken, and also for medical supervision. Any observations on these Draft Regulations should be made in writing to the Ministry of Labour, 8 St. James's Square, London S.W.1, by July 31. (Unsealed Radioactive Substances Regulations (Draft), H.M.S.O., price 1s. 3d. net.)