(Lewis and Maxfield, 1954). Pleural and pulmonary complications have been noted to follow enucleation; also hiatus hernia and oesophagitis when resection has been performed.

Summary and Conclusion

Leiomyomas of the oesophagus were once incidental post-mortem findings, but recently they have usually been diagnosed and removed surgically. In cases of long-standing dysphagia, without loss of weight in young and middle-aged patients, this tumour has to be considered. Investigations, particularly barium-swallow examination, lead to the diagnosis. The diagnosis of the tumour is important because most, if not all, leiomyomas of the oesophagus can be cured by enucleation.

We have presented two cases, pre-operatively diagnosed and surgically treated by enucleation.

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BIBLIOGRAPHY

- Buckstein, J. (1953). *The Digestive Tract in Roentgenology*, 2nd ed., vol. 1. Lippincott, Philadelphia.
 Chalmot, Faivre, and Lochard (1951). *Poumon*, 7, 19.
 Johnston, J. B., Clagett, O. T., and McDonald, J. R. (1953). *Thorax*, 8, 251.
 Kenworthy, R. A., and Welch, C. S. (1948). *Surgery*, 23, 745.
 Lewis, B., and Maxfield, R. G. (1954). *Int. Abstr. Surg.*, 99, 105.
 Lortat-Jacob, J. L. (1949). *Sem. Hôp. Paris*, 25, 1709.
 Ohsawa, T. (1933). *Arch. Jap. Chir.*, 10, 605. Cited by Storey and Adams (1956).
 Piacentini, L. (1955). *J. thorac. Surg.*, 29, 296.
 Sauerbrück, F., and O'Shaughnessy, L. (1937). *Thoracic Surgery*, p. 333. Arnold, London. Cited by Storey and Adams (1956).
 Schatzki, R., and Hawes, L. E. (1942). *Amer. J. Roentgenol.*, 48, 1.
 Schlager, J., and Arcomano, J. (1956). *Amer. J. Surg.*, 91, 852.
 Storey, C. F., and Adams, W. C. (1956). *Ibid.*, 91, 3.

METASTATIC CARCINOMA OF THE PROSTATE AND BLEEDING

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The phenomenon of fibrinolysis and the presence of hypofibrinogenaemia in metastatic carcinoma of the prostate, if searched for, is not infrequent; for example, Tagnon, Whitmore, Schulman, and Kravitz (1953) found six cases showing fibrinolysis in their series of 48. The knowledge of the mechanism of fibrinolysis is still limited, but has been diagrammatically represented by Stefanini (1953). Tagnon *et al.* (1946) state that fibrinolysis is present when the clot of whole blood or diluted plasma disappears completely in less than 24 hours at 37° C. Furthermore, Tagnon *et al.* (1952) believe that the mechanism of fibrinolysis in prostatic cancer may be different—that is, that the prostatic cancer itself may be the source of the enzyme responsible for the dissolution of the blood clot. Huggins and Vail (1943) demonstrated such a fibrinolytic enzyme in prostatic tissue. Ratnoff (1952) demonstrated fibrinolysis and hypofibrinogenaemia in cancer of the head of the pancreas, but he did not think the process was due to release of pancreatic trypsin. McKay *et al.* (1953) described a case of mucinous carcinoma of the body of the pancreas with hypofibrinogenaemia and multiple fibrin thromboses, but did not carry out tests for fibrinolysis.

The relationship between metastatic carcinoma of the prostate and bleeding is of interest in that the bleeding, which may be dangerous (Swan *et al.*, 1957), may be due to fibrinolysis and fibrinogenolysis, or to the more frequent finding of thrombocytopenia secondary to bone-marrow involvement. Clinically, the bleeding sites, which are particularly from the nose and urinary and gastro-intestinal tracts, as well as in the skin or after minor trauma, may be identical. Tagnon, Whitmore, Schulman, and Kravitz (1953) report that the platelet count may be depressed in metastatic carcinoma of the prostate with fibrinolysis, but haemorrhagic manifestations in association with fibrinolysis occur despite the presence of a normal level of platelets.

The following report concerns a case of metastatic carcinoma of the prostate with fibrinolysis, hypofibrinogenaemia, hypoprothrombinaemia, and thrombocytopenia, and the response to stilboestrol therapy; and it is contrasted with another case with thrombocytopenia and bleeding secondary to bone-marrow involvement.

Case 1

A man aged 68 was admitted to hospital on May 10, 1957, complaining of anorexia, loss of weight, and low back pain; immediately before admission he had a brisk rectal haemorrhage, passing about 1½ pints (850 ml.) of bright red blood.

On examination he was pale and ill, with many ecchymoses and purpuric spots over the limbs and trunk. It was noted later that there was moderately severe oozing from venepuncture sites. Rectal examination revealed a hard, irregular prostate and the presence of bright red blood. He had several moderately severe rectal haemorrhages during the first few days after admission and he had to be transfused with four pints (2.3 litres) of whole blood. The blood sent for cross-matching remained in a fluid state, any clot that had originally been present having disappeared on reaching the laboratory.

Investigations.—Radiography showed osteoplastic deposits involving the right innominate bone and lumbar vertebrae. Haemoglobin, 5.1 g./100 ml. (35% Haldane). White blood count, 6,000/c.mm. (polymorphs 65%, lymphocytes 24%, monocytes 1%, eosinophils 1%, myelocytes 2%, metamyelocytes 7%). The blood film showed some macrocytes, occasional megaloblasts, and 24 nucleated red blood cells per 100 leucocytes. Serum alkaline phosphatase, 40 K.-A. units.* Total serum acid phosphatase, 6.3 K.-A. units. Alcohol stable fraction, 3.5 units. Serum bilirubin, 0.6 unit. Thymol turbidity, 0.8 unit. Platelet count (Lempert), 40,000/c.mm. Prothrombin activity (Quick's one-stage), 40% of normal control. Plasma fibrinogen level, 100 mg./100 ml. Whole-blood clotting-time (Lee and White), 6 minutes. Plasma recalcification time, 2 minutes. Capillary whole-blood clotting-time, 4 minutes. Factor 5, no deficiency. Factor 7, no deficiency. Clot retraction test (Biggs and Macfarlane, 1953): the clot was formed in normal time but was gradually lysed, thus rendering the test impossible to carry out.

Test for Fibrinolysis.—A standard fibrin clot was formed from equal quantities of normal plasma, brain thromboplastin, and M/40 calcium chloride at 37° C. The standard clot was washed free from thrombin with physiological saline and was suspended in the patient's plasma and placed in a water bath at 37° C. At the same time controls were set up, using a similar fibrin clot and normal plasma. The fibrin clot suspended in the patient's plasma was completely lysed and disappeared after four hours. Those in the control tubes were intact up to at least 48 hours.

Two-stage prothrombin time (Biggs and Douglas, 1953): true prothrombin was 70% of normal control. Sternal marrow examination: mainly normoblastic but late megakaryoblasts were seen; no neoplastic cells seen. Fractional test meal with histamine showed the presence of free acid. A

The patient was discharged from hospital on August 1 on stilboestrol, 15 mg. t.d.s. His haemoglobin had risen to 12.9 g. (87%) and the clot retraction was found to be within normal limits, a firm clot being formed which did not lyse. He attends the out-patient department and has remained well, free from symptoms; there has been no recurrence of the haemorrhagic diathesis.

Post-mortem Findings.—Carcinoma of the prostate was found with metastases in the iliac and para-aortic lymph nodes, lumbar vertebrae, and sternum. The brain showed multiple recent haemorrhages, the largest being in the right occipital lobe. Histological examination of the bone marrow showed many groups of undifferentiated neoplastic cells. Megakaryocytes were very scanty.

Tagnon, Whitmore, Schulman, and Kravitz (1953) have shown in cases of metastatic carcinoma of the prostate with fibrinolysis that the platelets may be normal or reduced. If the platelets are within normal limits the cause of the bleeding is due to the fibrinolysis, with or without hypofibrinogenaemia, and this alters the blood coagulation factors in such a way that the prothrombin time becomes prolonged. There is some difficulty when the platelets are reduced. The bleeding tendency due to a "leuco-erythroblastic" or myelophthisic" type of anaemia with severe thrombocytopenia is illustrated by Case 2. In Case 1 the haemorrhagic manifestations were almost certainly due to the fibrinolytic mechanism. In this particular case the thrombocytopenia was probably due to the associated

Graph of Case 1. ■ = Complete lysis of the suspended standard fibrin clot in four hours. ▣ = Complete lysis of the suspended standard fibrin clot in 12 hours. □ = No fibrinolysis up to 24-48 hours.

"leuco-erythroblastic" anaemia. However, Tagnon, Whitmore, Schulman, and Kravitz (1953) and Swan *et al.* (1957) have reported cases of metastatic carcinoma of the prostate with fibrinolysis and thrombocytopenia, where the explanation of the latter is not clear. The clinical presentation of these two cases was very similar, and if operative procedures are contemplated this differentiation is important.

In Case 1 oestrogen therapy alone quickly abolished the patient's symptoms and the haemorrhagic diathesis, during which time a transurethral biopsy prostatectomy was performed with minimal bleeding. The resulting disappearance of fibrinolysis, improvement of the fibrinogen levels, and to a less extent the prothrombin activity can be seen from the Graph. There was no need to give corticotrophin or human fibrinogen in this case. Corticotrophin has been claimed to diminish the lysis, and the response was more rapid than with oestrogens (Stefanini *et al.*, 1953), but, if used, it should be given in conjunction with oestrogens. Tagnon, Schulman, Whitmore, and Leone (1953), however, showed that the addition of testosterone to a maintenance dose of oestrogens caused an increase in the patient's symptoms and serum acid phosphatase level, as well as the reappearance of fibrinolysis. Orchidectomy does not seem to be justifiable in Case 1 at the present time. However, if fibrinolysis and hypofibrinogenaemia should return, then bilateral orchidectomy, with probably the addition of human fibrinogen, may be required. Swan *et al.* (1957) have recommended fractionated fibrinogen or triple-strength reconstituted dried plasma as the only type of emergency therapy. This has not been necessary in Case 1.

Tagnon, Whitmore, *et al.* (1952), and Tagnon, Whitmore, Schulman, and Kravitz (1953) found no constant correlation between the occurrence of fibrinolysis and the level of acid phosphatase in the serum. There appears to be no satisfactory explanation for this. They also state that the test for the level of acid phosphatase in the serum cannot be replaced by that of fibrinolysis, since the latter occurs in only approximately 12% of patients with metastatic carcinoma of the prostate. In Case 1 the correlation between the serum acid phosphatase levels and the occurrence of fibrinolysis is variable (see Graph). This lack of correlation has still to be fully explained.

Summary

A case of metastatic carcinoma of the prostate with a haemorrhagic diathesis secondary to a circulating fibrinolysin (Case 1) is reported, and is contrasted with Case 2, with thrombocytopenia and bleeding secondary to bone-marrow involvement.

Therapy with stilboestrol alone caused the fibrinolysis to disappear in Case 1, with subsequent improvement of the fibrinogen level and prothrombin time. A transurethral biopsy prostatectomy was carried out during oestrogen control.

No correlation was found in Case 1 between the occurrence of fibrinolysis and the level of acid phosphatase in the serum.

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REFERENCES

- Biggs, R., and Douglas, A. S. (1953). *J. clin. Path.*, **6**, 15.
 — and Macfarlane, R. G. (1953). *Human Blood Coagulation and its Disorders*. Blackwell, Oxford.
 Huggins, C., and Vail, V. C. (1943). *Amer. J. Physiol.*, **139**, 129.
 McKay, D. G., Mansell, H., and Hertig, A. T. (1953). *Cancer (N.Y.)*, **6**, 862.
 Ratnoff, O. D. (1952). *J. clin. Invest.*, **31**, 521.
 Stefanini, M. (1953). *Amer. J. Med.*, **14**, 64.
 — Campbell, E. W., Pittman, G. I., and Salomon, L. (1953). *Bull. New Engl. med. Cent.*, **15**, 23.
 Swan, H. T., Wood, K. F., and Daniel, O. (1957). *Brit. med. J.*, **1**, 495.
 Tagnon, H. J., Levenson, S. M., Davidson, C. S., and Taylor, F. H. L. (1946). *Amer. J. med. Sci.*, **211**, 88.
 — Schulman, P., Whitmore, W. F., and Leone, L. A. (1953). *Amer. J. Med.*, **15**, 875.
 — Whitmore, W. F., and Shulman, N. R. (1952). *Cancer (N.Y.)*, **5**, 9.
 — Schulman, P., and Kravitz, S. C. (1953). *Ibid.*, **6**, 63.

ACUTE RADIATION NEPHRITIS IN CHILDHOOD

BY

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The following case of acute radiation nephritis associated with a uraemic haemolytic anaemia is reported because of the interest aroused by the annotation in the *British Medical Journal* of May 3, 1958 (p. 1053), on the effect of x-irradiation on the kidney.

Case Report

The patient, a pale normally developed girl of 2½ years, was first seen in January, 1957, when a large firm mass was found filling the whole of the left side of the abdomen. This was removed surgically and found to be a Wilms's tumour. She made an uneventful post-operative recovery, and a four-weeks course of radiotherapy (3,250 r) was given

FIG. 1.—Blood film showing "burr" cells, anisocytosis, and polychromasia. ($\times 500$.)

to the left renal area. She remained well until October, when a metastasis was discovered in the right perirenal fat. This could be treated only by a second course of radiotherapy (3,000 r) to the right renal area over a period of three weeks, after which the abdominal mass could no longer be palpated. On January 17, 1958, it was noted that the child, although still pale, was gaining weight, but when seen on February 7 she showed marked pallor, ankle and face oedema, full and bounding pulse, and enlargement of the heart in the transverse diameter. The B.P. was 130/85 mm. Hg. The urine showed albumin ++, R.B.C. ++, pus cells +, and a moderate number of granular and hyaline casts. The blood urea was 140 mg./100 ml. and the haemoglobin 6.2 g./100 ml. Blood films showed marked anisocytosis, polychromasia, and poikilocytosis with numerous "burr" cells of the type usually associated with the haemolytic anaemia of uraemia in childhood (Fig. 1). The white-cell count was 19,000, with a normal differential.

The child's condition deteriorated rapidly, and the blood pressure fluctuated between 135/80 and 170/110 mm. Hg. The blood urea rose progressively to 320 mg./100 ml., and she died on February 13, six days after the onset of the symptoms of acute nephritis.

Post-mortem Findings

The body was that of a pale, ill-nourished female child showing severe anasarca and extensive purpura. The heart (160 g.) showed marked left ventricular hypertrophy and