The haemorrhagic condition responded rapidly to vitamin K₁, first intravenously and then intramuscularly. By the third day haematuria had ceased and there was no further bruising. 48 hours after treatment the prothrombin time was 24 seconds (control 18 seconds), and after a further seven days it was 19 seconds.

Folic acid and calciferol were given orally and he was put on a gluten-free diet with normal allowance of fat and protein. Within four weeks the anaemia had cleared up: haemoglobin, 102% (15.1 g./100 ml.); red cells, 4,930,000/c.mm.; packed cell volume, 43%; white cells, 5,300/c.mm., with a normal differential count.

When seen nearly nine months later (October 23) he had gained considerably in weight and reported a normal bowel habit, the blood picture was normal, and serum calcium was 10.3 mg./100 ml.

Discussion

It was decided that this case should be published, in spite of the absence of detailed studies of the coagulation deficiency, to draw attention to the importance of haemorrhagic manifestations in the malabsorption syndrome. Though this complication is fairly well recognized, many regard the incidence as slight. In a symposium on disorders of the small intestine at the Royal Society of Medicine the only brief reference to a bleeding tendency due to deficient vitamin-K absorption was by Avery Jones (1959); Pullan (1959) also mentioned that the fat-soluble vitamins (A, D, E, and K) are likely to be imperfectly absorbed in the presence of steatorrhea.

It appears that haemorrhage associated with malabsorption has received greater emphasis in America. At a symposium on the malabsorption syndrome in New York Bossak *et al.* (1957), reporting their observations on 94 patients with idiopathic sprue, noted haemorrhagic manifestations in 26.6% of cases, varying from skin petechiae to fulminating gastro-intestinal haemorrhage. In those patients in whom the prothrombin time was determined it was prolonged to more than 3 seconds above the control in 70.2%. Wang and Bossak (1957), at the same symposium, recorded haemorrhagic manifestations in idiopathic sprue in 25 cases in a review of 82 patients seen during a period of 25 years, with an average follow-up of 5.1 years. All were considered to be due to hypoprothrombinaemia. In 13 out of 14 of these patients at the time of abnormal bleeding the prothrombin time varied between 21 seconds to over 3 minutes (control 12 seconds), in all patients the prothrombin time returned to normal after treatment with vitamin K.

Douglas (1958) investigated the coagulation deficiency in vitamin-K deficiency regardless of its pathogenesis. He found a deficiency of factor II (prothrombin), factor VII, and factor IX (Christmas factor).

Hoffman and Hewlett (1959) carried out detailed coagulation studies in a patient with idiopathic steatorrhea and severe haemorrhagic manifestations. They confirmed Douglas's findings—that is, a deficiency of prothrombin, factor VII, and Christmas factor—and also found a deficiency of Stuart (Prower) factor. After a single intravenous injection of vitamin K₁ all four factors returned to near normal in 24 hours and to normal in five days.

Summary

A case is described of an acute haemorrhagic illness which was proved to be an idiopathic steatorrhea; there was a greatly prolonged prothrombin time, which

became normal after vitamin-K₁ therapy, and the haemorrhagic condition rapidly cleared.

Some of the literature relevant to this condition is reviewed and reference is made to the specific coagulation factors which are defective.

It is considered that further emphasis should be placed on this serious complication in idiopathic steatorrhea.

I thank Dr. E. C. Warner for access to this patient under his care at Charing Cross Hospital.

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POSSIBLE ASSOCIATION OF MALIGNANT NEOPLASM WITH IRON-DEXTRAN INJECTION

A CASE REPORT

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Recent reports of the carcinogenic properties of iron-dextran in rats and mice by Richmond (1959) and Haddow and Horning (1960) have aroused interest in the possibility of similar effects in humans. The following is a report of a patient who recently was found to have a sarcoma at the site of previous iron injections.

Case Report

A 74-year-old white spinster, known to have had a hypochromic anaemia since 1955, was investigated in hospital on three occasions: in 1955, 1959, and 1960. Frequent stool examinations revealed the presence of blood, but several series of upper and lower gastro-intestinal x-ray films and sigmoidoscopy failed to explain the blood loss adequately. Gastric analysis was normal. On recent admissions the prothrombin time, which was prolonged, responded once to vitamin K₁ oxide, and on another occasion the response was equivocal. Otherwise coagulation factors were normal. There was neither hepatic nor splenic enlargement nor lymphadenopathy.

Treatment consisted of whole-blood transfusions and oral iron. Between October 30 and December 4, 1956, six injections of iron-dextran ("imferon"), 2 ml. (100 mg.) each,

were administered in the left deltoid region. In February, 1960, at the time of her last admission, a moderately soft, oval, non-tender lump was noted over the left deltoid, measuring 1 by 1½ in. (2.5 by 3.8 cm.). This tumour had been observed by the patient a few weeks previously. A biopsy was taken on February 6, 1960, and the tumour was completely excised on February 15.

Pathology Reports

Biopsy (February 6). Surgical tissue specimen S 60-1910. An irregular portion of reddish white tissue of firm consistency 1.1 by 1 by 0.8 cm. surmounted by a narrow ellipse of epithelium. On section it presented a fleshy, yellowish white cut surface.

Excision Biopsy (February 15). Surgical specimen S 60-2373. An ellipse of skin 2.5 by 1.2 cm. containing a well-healed biopsy incision. It surmounted an ovoid portion of firm fibro-fatty tissue measuring 2.5 by 1.2 by 3 cm. Section through this area revealed a fleshy subcutaneous tumour

FIG. 1.—Soft-tissue sarcoma, deltoid area. ($\times 150$.) Perl's iron stain, haematoxylin counterstain. Blue-staining pigment appears as dark agglomerations. (See arrows.)

FIG. 2.—Soft-tissue sarcoma, deltoid area. (H. and E. $\times 100$.)

nodule 1.5 by 1 cm., not encapsulated, yellow-white in colour, and firm in consistency, its deepest margin very close to the deep site of resection. The overlying skin was in juxtaposition to the tumour but was movable over the tumour surface.

Microscopically, both the biopsy S 60-1910 and the excision biopsy S 60-2373 showed the tumour to be composed predominantly of spindle-shaped cells, most of them hyperchromatic. Mitotic figures were not especially numerous. Many cells contained fat vacuoles. Mononuclear giant cell forms with abundant cytoplasm and irregular vesicular nuclei were observed, along with occasional multinucleated giant cells. The stroma was relatively scanty and of a fibro-fatty type. The tumour infiltrated the investing fibro-fatty tissue and was not encapsulated. Finely divided Prussian-blue-positive particles were scattered throughout the tumour but were most abundant in the deep peripheral areas and the superficial corium. Only in rare instances did the particles appear to occur in histiocytes. The pigment was present in both S 60-1910 and S 60-2373.

A diagnosis of "undifferentiated sarcoma, soft tissues of left upper arm" was applied.

A random 5-mm. punch biopsy of skin and subcutaneous tissue was taken from the corresponding deltoid area of the other arm and was reported (S 60-9138) as normal. Serial sections were stained by Prussian-blue method for iron and all were negative.

Discussion

Although the evidence in this case may seem to weigh in favour of an aetiological interrelationship, the possibility of a sarcoma developing coincidentally at the site of the iron-dextran injection must be considered. Sarcomas of the upper extremity and shoulder areas are by no means uncommon (Lieberman and Ackerman, 1954; Weder, 1955; Pack, 1956), and none reported has been preceded by iron injection.

We have examined sections prepared from tumours in rats produced by iron-dextran. Those examined were fibrosarcomas and differed considerably in appearance from the case under discussion. More iron appeared to be present in the animal tumours.

Slides of tissue removed from areas reputedly injected with iron-dextran up to two years previously were also reviewed (Golberg and Smith, 1960), and these demonstrated retention of iron in amounts appreciably in excess of that demonstrated in the present case.

Conclusive proof that the tumour was primary, and not a metastasis from an occult lesion elsewhere, cannot be provided at the present time.

Summary and Conclusions

A 74-year-old woman received six injections of iron-dextran (imferon) between October 30 and December 4, 1956. It is not known whether these were administered intramuscularly or subcutaneously. All were given in the deltoid area of the left arm.

A tumour mass estimated to be 2.5 by 3 cm. was first observed in February, 1960, approximately three years after her last injection of iron-dextran in the area, and was reported as an undifferentiated soft-tissue sarcoma.

Iron-dextran as a carcinogenic agent in experimental animals has been reported, and its potential as a factor in human carcinogenesis has been reviewed editorially in the *British Medical Journal* (1960) and the *Canadian Medical Association Journal* (1960).

The above case report is presented as a possible example. We make no claim that the iron pigment

identified in the tumour is injected iron-dextran and not haemosiderin. A random biopsy of skin from the deltoid area of the other arm contained no iron. The possibility that the tumour developed coincidentally at the inoculation site has been considered. It has not been proved that the tumour is primary.

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Medical Memoranda

Huntington's Chorea in Northamptonshire

The incidence of Huntington's chorea in Northamptonshire was investigated by Pleydell (1954), who found eight affected families in the county. The following year (Pleydell, 1955) a further choreic family came to light, making nine such families in Northamptonshire, with a total of 17 living affected members, and giving an incidence of 6.5 cases per 100,000 population.

Yet another family has recently been found, and, as the affected members were in fact suffering from Huntington's chorea at the time of Pleydell's original investigation, this memorandum is presented in order to amend that author's figures. The family is also of interest because all ascertained cases of the disease occurred in the same generation.

I 1.—Free from disease. Alive, aged 81. Her mother and father both left the district, and it is thought that her mother died at the age of 45, though the cause of death could not be ascertained. Where and when her father died is likewise unknown.

I 2.—Died aged 79. Cause of death was coronary thrombosis and arteriosclerosis. No suggestion of Huntington's chorea. Both parents of this man lived till beyond the age of 80 and neither was apparently affected.

II 1.—Onset of disease at 33. Admitted to hospital and diagnosed as suffering from disseminated sclerosis. Death ascribed to cerebral haemorrhage. Hospital notes record, just before death—that is, 10 years after onset of disease—that the reflexes were not obviously exaggerated and that the Babinski plantar response was not present. Had to be nursed in a cot. True diagnosis almost certainly Huntington's chorea.

II 7.—Served in 1939–45 war. Onset of chorea at 34, and has been unemployed since shortly after that time. Now has classical signs of the disease, including gross ataxia and disturbed speech.

Pedigree of family. O=Age at onset. D=Age at death. A=Present age.

II 8.—Worked in shoe factory till onset of chorea at 31 or 32. When admitted to hospital after an accident at the age of 33, was recorded as mentally defective. Has steadily gone downhill, and at age 39 was falling about the house, required constant attention, and was suffering from advanced dementia. Speech was restricted to incomprehensible grunting sounds.

COMMENT

Although it is not shown in the accompanying pedigree, none of the three affected patients married, whereas, of their eight normal siblings, only one has remained a bachelor. The remaining seven all have families, and, while most of their children are still below the most likely age of onset, none has so far developed any signs of Huntington's chorea.

Unlike the nine families reported by Pleydell, all the cases of the disease in the present family have occurred in the same generation. The father of these patients died at the age of 79, and his family doctor states that there was no evidence of chorea at that time. The mother is still alive and remarkably healthy at the age of 81. This state of affairs is extremely uncommon. In only 6 of the 151 pedigrees quoted by Bell (1934) did the parents of one or more affected offspring live to old age without themselves developing evidence of Huntington's chorea.

Reconstructing the full family tree, only the relevant portion of which is published, was not easy. In addition to Huntington's chorea, the stigma of illegitimacy entered into the picture at various stages, and this combination made some of those who were interviewed reluctant to give information. Despite the evidence before her own eyes, the elderly mother of the affected brothers would not accept that all three were victims of the same condition. In the case of the youngest living affected member (II 8), she insisted that his condition was the result of a fall from his bicycle. Reluctance on the part of a parent to admit to the presence of a disease which affects several members of her family is perhaps understandable, as admission would no doubt be accompanied by unjustified feelings of guilt.

In conclusion, it would appear that at the time of Pleydell's investigation there were at least ten choreic families in Northamptonshire. By tracing their pedigrees a total of 72 cases were found, and at the time in question 19 patients were alive in the county, giving an incidence of 7.2 cases per 100,000 population.

I am grateful to Dr. C. M. Smith, Dr. G. O'Gorman, and Dr. M. J. Pleydell for their advice and help, and to the staff of the mental health section of the County Health Department for their assistance in establishing the pedigree.

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The Morison Medals, which are awarded by the Royal College of Physicians of Edinburgh to members of the nursing staffs of mental hospitals in Scotland in recognition of long and meritorious service, were presented at a recent College meeting to Miss Margaret D. Morrison (matron-superintendent, Broadfield Institution, Port Glasgow, Renfrewshire) and Mr. Andrew S. Wisley (chief male nurse, Murray Royal, Perth).