Our use of serum, rather than plasma or whole blood, may call for brief comment here. Both Christmas factor and Factor VII are stable in stored blood, plasma, or serum for considerable periods (Biggs *et al.*, 1952). We have found Christmas factor to be stable in stored oxalated plasma and normal serum for three weeks. Therefore, any of these fractions may be used in the treatment of Christmas disease, Factor VII deficiency, or a combination of these defects. In the course of work carried out by us on another patient with uncomplicated Christmas disease, we have found that 1 ml. of serum is approximately equivalent in therapeutic effect to 10 ml. of A.C.D.-stored plasma. Because of this finding, and because serum provided a supply of both deficient factors in this patient, it was used exclusively in this case, with good results.

Family History

The presence in this patient of a combined deficiency, apparently of a congenital nature, called for an effort to test all available members of his family. This proved only

Family tree of patient. The numbers refer to the subjects (see Table II). □ Male, non-bleeder. ■ Male, bleeder. ○ Female. ▨ Male, reported bleeder, not studied.

moderately successful owing to distant residence, unwillingness on the part of some members, and death of others. The accompanying genealogical tree is based on information received from several members of the family. The patient's maternal grandmother could not be tested; his grandfather and both his father and stepfather were dead. An apparently unaffected uncle, a bleeder brother, and two sisters were not available for testing. Only males showed a bleeding diathesis. The principal clinical manifestations in all affected males were haemarthroses and subcutaneous haematomata.

In Table II are summarized the results of tests performed on the members identified in the family tree by numerals. Since these tests had to be done either in the patient's home

TABLE II.—Results of Tests in Members of Family

Subject	Bleeder	Clotting-Time (min.)	Pro-thrombin Consumption (3 Hours)	I-Stage Pro-thrombin (% of Normal)	Factor VII (% of Normal)	Peak Thromboplastin Generation (% of Normal)	Correction by Plasma or Serum
1	—	8	(sec.) 48.2	65	65	98	—
2	—	9	34.9	75	75	93	—
3	—	7	64.5	72	72	80	—
4	—	8.5	93.0	100	100	80	—
5	—	8	43.3	50	50	93	—
6	+	18	24.8	45	45	12	Serum
(patient)	+	17	25.8	46	45	10	—
7	+	17	28.2	48	50	11	—
8	+	17	28.2	48	50	11	—

or two hours later on return to the laboratory, their range had to be limited, and normal controls were subjected to similar conditions.

Discussion

This investigation is reported in order to draw attention to the existence of combination forms of isolated coagulation factor deficiencies. In this family the most striking

feature seems to be that, whereas both sexes showed deficiencies of Factor VII, only some of the males had Christmas disease as well; all of the clinical "bleeders" belonged to this latter group. From these results it would appear that the critical haemorrhagic level of Factor VII is less than 40% of normal and that it was the deficiency of Christmas factor which determined the tendency to bleed. It is interesting to note that the serum of the mother (a female carrier of Christmas disease) was as effective in the correction of the abnormal thromboplastin generation tests as normal human serum, providing further evidence of the inability to demonstrate a laboratory defect in the female carrier of this disease.

Summary

A survey is made of a family, some of whose members exhibit a combination of Christmas disease and Factor VII deficiency. Pathological bleeding was confined to those showing both defects.

The advantage of serum in the clinical management of such patients is illustrated.

We wish to thank Sir Lionel Whitby for providing the facilities for this study, and Miss S. C. Tomlin for valuable technical assistance. We are indebted to Mr. D. J. Martin for referring to us the patient whose case is reported in detail.

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A CASE OF PHAEOCHROMOCYTOMA

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As comparatively few cases of phaeochromocytoma are described in the literature of this country the following case is recorded. The number of cases of successful removal of the chromaffin tumour of the adrenal is smaller still, many of the reported cases having been found at necropsy (Crowther, 1951; Jelliffe, 1952; Davies, 1952; Priest, 1952). A review of the world literature up to 1949 is given by Graham (1951).

Phaeochromocytoma is probably a commoner condition than the literature would lead one to believe, and it is likely that many cases remain undiagnosed. By publishing details of these cases the condition will become better known and take its proper place in the diagnostic field. An additional reason for publication is that most new cases still present special difficulties in diagnosis and surgical treatment.

Case Record

A married woman aged 52 was admitted to hospital with sweating attacks following a respiratory infection. There were few signs in the chest, however, no pyrexia, and x-ray examination showed that her chest was normal. She then volunteered that she had suffered from these sweating

attacks for some two years. During these attacks, many of which occurred during her stay in hospital, there was no associated headache, dizziness, or definite pallor of the skin. She had no other complaints, but it is interesting to note that she had been treated at home for the past seven or eight years for high blood pressure. There was no other significant illness.

On examination she presented a normal appearance for a woman of her age, and her general condition was average. There was a sense of fullness in the right lumbar region, but no definite tumour could be felt. Manipulation of this region did not produce an attack of sweating. Her blood pressure at the time of admission was 180/110, but frequent estimations showed that it varied between 250/150 and 160/100.

Unresolved pneumonia was at first thought to be a possible diagnosis. Thyrotoxicosis was considered and the B.M.R. at this time was +39%. In view of this it is of interest that Davies's case (1952) simulated thyrotoxicosis. At this stage, however, a sweating attack was observed by one of us and the possibility of a phaeochromocytoma was considered. Special investigations were undertaken with this diagnosis in mind.

Special Investigations.—A straight renal and intravenous pyelogram showed some broadening of the lower pole of the right kidney but no other abnormality. A perirenal air insufflation followed by x-ray examination did not show any definite tumour in either kidney region, but, as is usual in our experience, the x-ray films proved difficult to interpret. A piperoxane test showed a definite response, with lowering of the blood pressure from 180/110 to 145/90. This was subsequently repeated, and the blood pressure was lowered from 170/110 to 125/80. The pharmacological tests were reviewed by Swan (1951), who described an illustrative case. In the present case the amount of adrenaline and noradrenaline excreted in the urine before and after operation was ascertained. The pre-operative specimen contained a considerably greater quantity than the post-operative. The pre-operative urine contained 1 mg. of L-noradrenaline per 24-hour output. Three days after operation it fell to the equivalent of 0.5 mg. of L-noradrenaline. Ten days after operation it had fallen to 0.25 mg. An amylobarbitone sedation test, an electrocardiogram, and an x-ray film of the skull showed no significant abnormality.

On the above evidence a diagnosis of phaeochromocytoma was confirmed, and it was thought most likely that the tumour was on the right side, although this was by no means certain. It was decided that if at operation no tumour was found on the right side, then the left side would be explored.

Operation

A right lumbar incision was used, excising the twelfth rib subperiosteally. A spherical tumour about 3 in. (7.5 cm.) in diameter was immediately found in the position of the right suprarenal gland. There was a well-marked line of cleavage between the tumour and the surrounding structures and it was freed along this line without difficulty. The pedicle was then ligated and the tumour removed. The wound was closed in layers with rubber drainage.

Technically, the removal of this tumour presented no problems, but, as is usual with these cases, the problem was to deal with fluctuations of blood pressure throughout the operation. At the beginning of the operation it was 170/90. On incision of the skin it rose to 215/140, and it continued to rise to 235/145 when the tumour was being handled.

Piperoxane, 10 ml., was given immediately before the start of the operation, and this was repeated after 10 minutes. When the blood supply to the tumour had been arrested by ligation the pressure remained unchanged for a period of 15 minutes and then fell to 135/80. It remained at this level until the end of the operation and, coincident with the postural change of the patient, dropped to 60/40. It remained at this level for over an hour, when it rose to 95/65, and continued to rise slowly thereafter. Noradren-

aline was given into the drip as soon as the vascular pedicle of the tumour was clamped, and a noradrenaline drip was continued until the next day.

Throughout the operation there was a marked degree of sweating. Oxygen was given and continued for 1½ hours after the end of the operation. Convalescence from the operation was uneventful and the blood-pressure readings were 120/80 eight days after the operation, and remained round about this figure until her discharge. The piperoxane test was repeated before her discharge and did not demonstrate the previously noted fall in blood pressure, and indeed there was a rise in blood pressure from 125/70 to 160/85.

When seen in the out-patients' department a few weeks after discharge the patient was symptom-free and her sweating attacks had been completely abolished. Her blood-pressure on this occasion was 180/110.

Although she readily agreed to the operation, one interesting personal sidelight was that she was obviously unconvinced that the operation would benefit her. It was not until some little time after the operation that she realized with pleasure that she had indeed been cured of her sweating attacks.

Pathology

The specimen was reported on as a typical chromaffinoma weighing 425 g. The cells were more pleomorphic than usual, and the cytoplasm was plentiful and slightly granular. The nuclei were often large, pale, and with many chromatin dots and an inconspicuous membrane. An estimation of the amount of adrenaline and noradrenaline in the medulla of the tumour was made. The amount of L-noradrenaline was equivalent to 0.46 mg., and the amount of L-noradrenaline was equivalent to 0.85 mg. per g. of medulla.

Summary

A case of phaeochromocytoma is described, illustrating the difficulty in diagnosis of these tumours. Some of the diagnostic investigations are described, together with some of the important points for successful surgical removal of the tumour, which was undertaken in this case.

Our thanks are due to Dr. J. D. Loughrey for the administration of the anaesthetic and the control of the blood pressure during the operation, to Dr. H. E. Vickers for the pathological reports, and to Dr. H. Wilson, of the department of pharmacology, University of Liverpool, for the pharmacological estimations on the urine and tumour.

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"In view of modern knowledge on leprosy, countries have revised their laws against lepers. The present trend in dealing with leper patients does not seem to favour compulsory segregation; this method is becoming obsolete; it has its utility as a check on the spread of disease, but it has also many drawbacks—social, ethical, and administrative—and it certainly does not seem to agree with the modern outlook. It has been ascertained that the ancient system of compulsory segregation may do more harm than good, in causing the early cases to be hidden for fear of lifelong imprisonment, until it is too late for effective treatment and they have already infected members of the household. With modern drugs and modern methods of treatment the course of the disease may be favourably altered, especially if patients seek medical advice early. Forcible segregation has been tried in many countries, but it has given poor results. In the Philippines it was adopted at a great expenditure of money, but it has not proved capable of controlling leprosy, and now the law is being reviewed and amended."—Report of the Chief Government Medical Officer, Malta.