illness in two. In one patient there was a history of a previous non-puerperal depressive attack. In two patients symptoms had begun in mild form during one puerperium and a further childbirth had had an aggravating effect. In one case the starting-point had been an abortion at three months.

Patients with milder symptoms enjoyed well-being for periods up to three months. Those with more severe symptoms had only occasional "good days."

There was a relation of symptoms to the menstrual cycle in six patients; in five of these there was worsening during the premenstrual phase, in one worsening at ovulation time.

Irregularity of menstruation or oligomenorrhoea of the same duration as the psychiatric symptoms occurred in five patients.

There was clinical evidence of disturbed water balance in two patients.

In the majority the pre-morbid personality showed some cyclothymic traits, but on the whole these women were well-integrated people who had reached a good all-round level before they fell ill.

Discussion

Diagnosis.—The history of puerperal depression as the starting-point of the illness could be established without leading questions in all these patients, but, largely on account of their preoccupation with current problems, some persistence was necessary to get them to give a satisfactory account of the onset. This history is the main pointer to the diagnosis, since the symptoms themselves are not of a specific kind.

Differential Diagnosis.—The majority of these patients had been regarded by their family doctors as psychoneurotic, one or two as "ordinary" depressives. The personality, history, and symptomatology are, however, quite different from what is characteristic of the neurotic: "ordinary" recurrent depressives usually enjoy much longer symptom-free periods than do these post-puerperal patients. Depression in psychopaths and epileptics may have some resemblance in frequency and brief duration of attacks to what is found in the post-puerperal group, but the history of fits or of lifelong personality disorder suffices to distinguish them.

Aetiology.—In the absence of knowledge of the nature of the depressive state and of the neuro-endocrine effects of the puerperal involutional processes one cannot go far towards a physiological understanding of this disorder, or, for that matter, of those puerperal depressions which run a self-limiting course. The condition may, on clinical grounds, be regarded as a variant of manic-depressive disorder combined with features of the premenstrual tension syndrome. Pre-menstrual tension and its relation to disturbed water metabolism has been adequately discussed by Stieglitz and Kimble (1949), Bickers and Woods (1951), and Linford Rees (1953). Hemphill (1953) has referred to "the acute alteration in the physiological state associated with childbirth operating on a susceptible personality" . . . appearing "to activate . . . puerperal depression." Rees's (1953) remark about the precipitation of premenstrual tension by the puerperium has already been quoted. On the basis of the material under consideration it would appear that two alternative interpretations might be made: either that a relatively irreversible reinforcement of the manic-depressive diathesis may occur, or that some other alteration in the constitution—for example, tendency to premenstrual water intoxication—may supervene which increases susceptibility to depressive attacks.

Course and Prognosis.—No women of post-menopausal age have been seen suffering from this illness, and the possibility exists that the menopause may lead to an improvement in these patients. Two patients had shown slow spontaneous improvement over the years but were still far from recovery. In the others there had been little or no change, even when the environment had improved.

Response to Treatment.—Dextro-amphetamine produces a dramatic symptomatic relief in some patients and a useful improvement in others. Acetylcholine shock therapy had no effect on the one patient on whom it was tried. Electric convulsion therapy produced no lasting benefit on two patients who received it. Its known effect in alleviating a depressive attack without touching the diathesis may explain its failure here. Hormone therapy and measures to control water-retention have not been adequately explored.

Summary

A syndrome is described in which recurrent depression, irritability, and tension dating from an attack of mild but typical puerperal depression are the leading features.

The symptoms tend to be worse in the premenstrual phase.

A pyknic body build appears to be typical.

The condition follows a chronic course, and treatment is problematical.

Serious disturbance of the life of the family is a secondary effect of the illness.

The condition appears to be related to the premenstrual tension syndrome.

It is a common and important condition and is at present insufficiently recognized.

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ALPHA-PROTHROMBOPLASTIN DEFICIENCIES (HAEMOPHILIA) OF DIFFERING DEGREES IN A MOTHER AND SON

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There are a number of reports in which female bleeders are described as haemophiliacs. However, it has been realized that, despite clinical similarity, the "haemophilic" syndrome can be caused either by a deficiency of any one of several essential clotting factors, or it can be due to the presence of an inhibitor of blood-clotting. Although haemophilia has been connected by most workers with a derangement of the blood thromboplastin complex, in the last few years it has been found that it consists of several components. Clinical manifestations are therefore insufficient to establish the diagnosis of haemophilia. As the various components of the clotting system have been separated from plasma,

it seems logical to apply biochemical nomenclature to haemorrhagic disorders. Since it is customary to refer to hypoprothrombinaemia or to fibrinogenopenia it has been suggested (Fantl and Sawers, 1954a, 1954b) that haemophilia be called alpha-prothromboplastin deficiency, and the related condition, known as P.T.C. deficiency (Aggeler *et al.*, 1952) or Christmas disease (Biggs *et al.*, 1952), be called beta-prothromboplastin deficiency.

Laboratory investigations are necessary to find the particular deficiency. Blood from alpha-prothromboplastin-deficient patients shows several characteristic features. There is a slightly to grossly delayed whole-blood clotting time, which can be corrected *in vitro* by the addition of blood or plasma from a beta-prothromboplastin-deficient patient. If this is not available, such plasma can be prepared from normal human oxalated plasma by adsorbing the beta factor with alumina gel or barium sulphate (Ba plasma). Further, the patient's deficiency should not be corrected by the addition of stored plasma or serum which are devoid of the alpha factor. Another indication of the clotting defect is the prothrombin content remaining in serum after clotting has taken place. In the serum of normal persons this is very low, whereas thromboplastin-deficient blood examined 60–150 minutes after clotting contains more than 12% of the plasma prothrombin. In addition to the tests which are necessary to establish the diagnosis it is desirable to estimate the degree of the deficiency. This can be carried out by the determination of the rate of thrombin formation in diluted blood in the presence of pyrocatechol, which acts as a thrombin stabilizer. The theoretical basis and the experimental details for this technique have been given by Fantl (1954b).

The Investigation

The clinical examination and laboratory investigation of a mother and her son, which we record here, show that both are suffering from alpha-prothromboplastin deficiency, although of differing degree. The mother is in fact a true haemophiliac.

Mrs. M, aged 30, stated that she bruised much more easily and extensively than the other members of her family. She suffered heavy menstrual loss, the bleeding often lasting eight days. She bled consistently after teeth extractions, the oozing often beginning one week after extraction and continuing for another week. After the birth of each of her two children she had severe post-partum haemorrhage, which on the first occasion lasted one week and was associated with a cervical tear. She submitted to radium sterilization, following which she again bled severely and required a blood transfusion. Apart from the haemorrhagic tendency no other pathological lesions have been found. So far as it was possible to trace her family history, no abnormal haemorrhages were noted except for a vague story of excessive bleeding after teeth extractions in her maternal great-uncle, who died at the age of 80 (see Fig. 1).

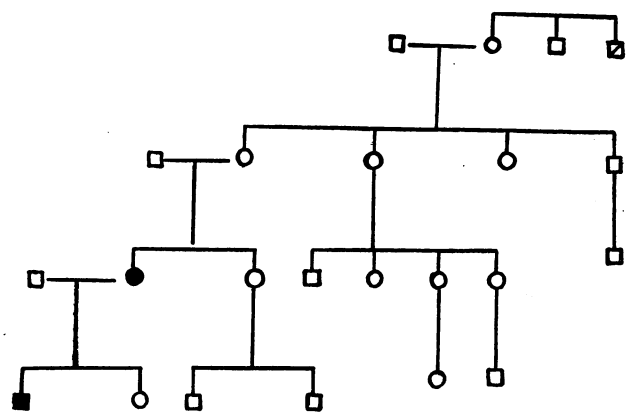

FIG. 1.—Family tree. ● Refers to Mrs. M. ■ Refers to her son. ◪ Refers to the maternal great-uncle of Mrs. M, who is believed to have had abnormal haemorrhages. All the other relatives gave no indication of abnormal bleeding.

Mrs. M's daughter, born in 1951, does not show any bleeding tendency. Her son was born in 1952. He was first admitted to the Royal Alexandra Hospital for Children, Sydney, at the age of 14 months with severe bruising of head and buttocks. The parents stated that after circumcision at the age of 10 days the child bled for one week, and could only be controlled with difficulty with several blood transfusions. Repeated attacks of extensive bruising had been observed since the age of 6 months. Primary dentition was accompanied by oozing from the gums. The child was admitted to the above hospital six times with bleeding episodes, and received several blood transfusions. The clinical symptoms of the mother are much less severe than those of her son. Table I gives the results of laboratory investigations.

TABLE I.—*Laboratory Data of the Haemorrhagic Defect of Mother and Son*

	Mother	Son	Normal
Whole-blood clotting time of 2 ml. at 37° C. in minutes ..	14–30	40–>100	9–19
Skin bleeding-time in minutes. Technique (Copley and Lalich, 1942)	3	3	1·5–3
Plasma prothrombin. Technique (Quick, 1951), in seconds ..	10	10	10–12
Prothrombin assay. Technique, Fantl (1954a) in units per ml. oxalated plasma	530	420	440–600
Serum prothrombin:			
1 hour after clotting	10	9·5	14– ∞
2 hours „ „	14	9·5	20– ∞
Technique, modified Quick in seconds			
Serum prothrombin:			
1 hour after clotting	31–43	—	0–12
2 hours „ „	17–31		
Technique, Fantl in units per ml. serum as % of plasma prothrombin			
Thrombocytes, indirect. Technique, Fonio per cubic mm. blood	450,000	450,000	>100,000
Clot retraction	Complete	Complete	Complete

The type and degree of the deficiency were determined in the blood of mother and son by the rate of thrombin formation. These results are given in Fig. 2.

Rate of Formation and Yield of Thrombin in Diluted Blood of Mother and Son

The laboratory data show a coagulation defect in Mrs. M's blood in degree consistent with the clinical findings. The whole-blood coagulation time is moderately prolonged; the residual serum prothrombin is well above the upper normal limit (Table I). The thrombin formation in Mrs. M's diluted blood is delayed although the yield is normal (Fig. 2, curve A). The addition to Mrs. M's blood of 10% normal Ba plasma, as a source of alpha-prothromboplastin, converts the rate of thrombin formation to normal (Fig. 2, curve B).

These findings are characteristic of a partial alpha-prothromboplastin deficiency. No evidence of abnormality of other clotting factors or the presence of clotting inhibitors or fibrinolysis was detectable.

There is no doubt that the son is suffering from the same type of deficiency as his mother, but, in contrast to her, his blood is completely devoid of alpha-prothromboplastin (Fig. 2, curve C), the abnormality being again corrected *in vitro* by 10% Ba plasma (curve D), but not significantly by stored plasma (beta-prothromboplastin) (curve E). In the child's case these results corroborate the evidence obtained from plasma clotting times of mixtures of the patient's plasma with that of authentic alpha- and beta-prothromboplastin-deficient patients respectively, as can be seen from Table II.

TABLE II.—*Recalcification Time of Oxalated Plasma Mixtures (0.2 ml. 0.01/M $CaCl_2$ was added at 37° C.)*

	Plasma in ml. of			Normal Serum (ml.)	Clotting Time (Seconds)
	Authentic Alpha-prothrombo-plastin Deficiency	Authentic Beta-prothrombo-plastin Deficiency	Normal Alumina Plasma		
Mother, 0·1 ..	—	—	—	—	130
Son, 0·1 ..	—	—	—	—	>400
,, — ..	0·1	—	—	—	400
,, — ..	—	0·1	—	—	300
,, 0·08..	0·02	—	—	—	480
,, 0·08..	—	0·02	—	—	130
,, 0·08..	—	—	0·02	—	180
,, 0·08..	—	—	—	0·02	300
Normal, 0·1 ..	—	—	—	—	130–200

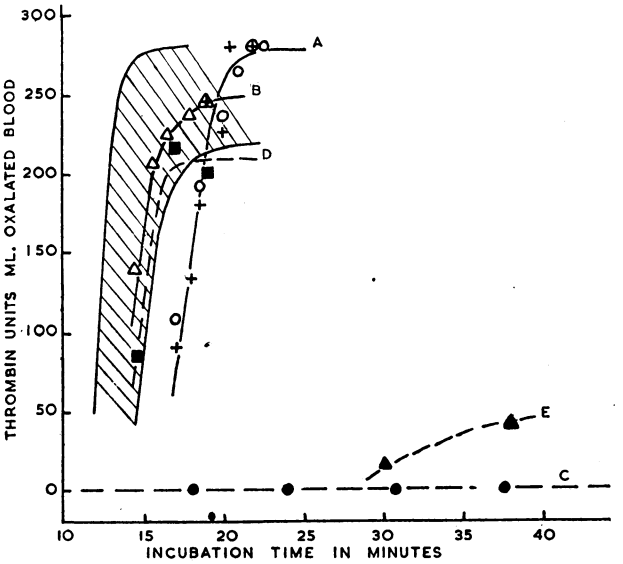

FIG. 2.—A 20% dilution of venous oxalated blood with 0.15/M sodium chloride was made immediately after collection. Mixture 1 consisted of 0.2 ml. 20% diluted blood added to 1.5 ml. of a solution containing 0.6 ml. 0.025/M $CaCl_2$, 0.6 ml. 0.15/M NaCl, 0.3 ml. 0.18/M pyrocatechol in veronal buffer *p*H 7.4. Temperature 28° C. Thrombin was measured according to the technique of Fantl (1954a). Curves, full line (A, B), were obtained from Mrs. M's blood. Curve A +——+, o——o indicate mixture 1 plus 0.1 ml. 0.15/M NaCl. Curve B △——△ indicates mixture 1 plus 10% Ba plasma. Dotted line curves C, D, and E were obtained from son's blood. Curve C ●— — —● indicates mixture 1 plus 0.1 ml. 0.15/M NaCl. Curve D ■— — —■ indicates mixture 1 plus 10% Ba plasma. Curve E ▲— — —▲ indicates mixture 1 plus 10% stored plasma. The shaded area presents the normal range.

Discussion

A critical review of the literature dealing with female bleeders, believed to be haemophiliacs, has been made by Merskey (1951) and by Israëls *et al.* (1951). Both groups of workers produce good evidence for the existence of congenital haemophilia in females, although the possibility that some of the cases may have suffered from beta-prothromboplastin deficiency must be considered. In both instances the homozygous state in the affected women has been established.

Additional reports of female haemophiliacs have been published (Koller *et al.*, 1950; Graham *et al.*, 1953; Quick and Hussey, 1953). With the exception of the latter, who described a sporadic case in a girl in whom the hereditary nature of the condition could not be established, the other females showed both clinically and on laboratory evidence the same degree of deficiency as their affected male relatives. Graham *et al.* (1953) have postulated the existence of a series of allelic genes which decide the plasma level of the anti-haemophilic factor in individual families. This is usually constant within an affected family, and breeds true according to the degree of the defect. Generally the inherited prothromboplastin-deficiency diseases show the recessive sex link type of inheritance, but there is some evidence that the trait may not be completely recessive in female members of a pedigree.

Most of the haemophilic carrier women have not given any laboratory evidence of a clotting defect (Merskey and Macfarlane, 1951).

There is little doubt that Mrs. M and her son suffer from a well-defined congenital defect. Unfortunately the genetic features remain puzzling and unsolved. They are unique in that the mother suffers from a relatively mild haemorrhagic disorder. She is a true haemophiliac, her plasma exhibits a partial alpha-prothromboplastin deficiency, whereas her son is a very severe haemophiliac, whose blood is completely devoid of alpha-prothromboplastin. So far as can be ascertained there is no likelihood of consanguineous marriages in Mrs. M's family. Her husband and his family are free of bleeding tendencies. If the doubtful story of bleeding in the maternal great-uncle is accepted as a manifestation of mild haemophilia, it does not explain the severity of the condition in the child. It appears most probable that Mrs. M is heterozygous in respect of the gene responsible for her son's condition, but in her own case the trait is incompletely recessive. Although other possibilities could be considered, no useful deductions could be made, and it is therefore best to refrain from further speculations concerning the genetic features of the presented cases.

Summary

A congenital haemorrhagic tendency of moderate severity in a mother was shown to be due to a partial alpha-prothromboplastin deficiency (haemophilia) in her blood. Her daughter has no bleeding tendency. The son is a very severe bleeder. His blood is completely devoid of alpha-prothromboplastin. Puzzling genetic features in the presented cases are pointed out.

It is desired to acknowledge the co-operation of Dr. J. M. Alexander, under whose care the patient was. The laboratory investigations were carried out in the pathology department of the Royal Alexandra Hospital for Children, Camperdown, Sydney (director, Dr. R. D. K. Reye). One of us (P. F.) as guest worker enjoyed the hospitality and generous co-operation of Dr. Reye and his staff.

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Prostitution is the subject of a pamphlet published by the British Social Biology Council (*Occasional Paper*, No. 8, price 1s. 6d.), with the object of providing the general reader with some reliable information on the subject. The author, Eleanor French, points out that the young prostitute and the "spiv" are figures of at least equal importance in their anti-social potentialities, and yet study of the former is neglected: "The 'Teddy Boy' is accepted as a respectable subject for interest, and receives far more help and study than does the prostitute." After presenting briefly what little is known about the prostitute and her clients—"the prostitutes who have been studied by research workers have in practically all cases been the failures"—the author discusses what could be done in the way of rehabilitation and prevention. There is also a note on the legal position.