Pregnancy, Hair Loss, and the Pill

SIR,—It is not uncommon for diffuse hair loss, telogen effluvium, to occur two to four months after pregnancy. A similar type of hair loss has been described occurring approximately two months after the cessation of oral contraceptive therapy. Since oral contraceptives induce a "pseudopregnancy" it has been suggested that these types of alopecia have a similar pathogenesis.[1] However, little work has been carried out on the effects of oral contraceptives on the human scalp hair cycle and thus this possibility remains unproved.

We have recently seen a patient who developed diffuse hair loss after stopping oral contraceptive treatment and again after a subsequent pregnancy. She was a 27-year-old married woman. She took Ovulen (ethynodial and mestranol) for two years from 1967 until summer 1969. Two months after stopping this she noticed increasingly severe hair loss from the scalp particularly evident in the fronto-parietal regions after washing and combing. On examination at this stage no abnormality was detected, the hair loss not having progressed to alopecia. Nine months after stopping Ovulen she became pregnant and the hair loss decreased to normal amounts. She subsequently gave birth to a full-term normal child. Two months after delivery, severe hair loss recommenced. A count of hairs shed during one 24-hour period at this stage totalled 480 (normal maximum approximately 100 hairs/day). Of 60 hairs plucked from the mid-parietal region 39 (65%) were in telogen compared with normal approximately 10% in telogen. Four months later the patient was still losing excessive amounts of hair and had developed slight fronto-parietal thinning.

At no stage during either period of hair loss was any abnormality detected on general clinical examination; repeated Hb, blood film, W.B.C. and differential, E.S.R., serum thyroxine, and serum iron were normal. She took iron and folic acid supplements during pregnancy but otherwise took only an occasional aspirin for headache during the period 1967 to the present.

The similarity in type and timing of the excessive hair loss after stopping Ovulen therapy and after pregnancy we feel supports the idea that the pathogenesis is the same in both situations. It also suggests the possibility that excessive hair loss after the "pill" may presage a similar occurrence after any subsequent pregnancy.—We are, etc.,

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1 Cormia, F. E., *Journal of the American Medical Association*, 1967, **201**, 635.

Depression from a Physical Symptom

SIR,—A well-built male patient aged 36 suffered from severe headaches and depression. The headaches were attributed to a hypertension of 200/110 mm Hg, which, in spite of drug therapy, remained unaltered. The patient became more and more depressed.

On examination here, as well as the headaches he complained of weakness of his legs—"legs like jelly, and pins and needles in the toes after walking 200-300 yards" in his own words—which caused him great anxiety and worry. His wife corroborated his story and said that he had similar complaints even as a youth.

Drug-induced depression as a diagnosis was quickly eliminated as the depression continued even after stopping hypotensives. The possibility that coarctation of the aorta could be the cause of his symptom complex was considered, and a further examination showed that femoral pulses as well as blood pressure recording in the lower limbs were unobtainable. A systolic murmur was heard all over the precordium, and chest *x*-ray showed characteristic rib notching and dilatation of the ascending aorta.

The patient was referred for surgery, and resection of the coarctation was performed with dramatic results. The headaches disappeared as well as the weakness of the legs as soon as the femoral pulse reappeared. The depression was a thing of the past, and the patient was able to go back to work three months after surgery. When last seen his brachial blood pressure was 130/90 mm Hg.—I am, etc.,

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Effects of Anticonvulsant Drugs on Chromosomes

SIR,—Recently there have been reports of teratogenic effects of certain anticonvulsant drugs on mice[1] and man.[2-4]

Studies carried out in vitro have revealed no significant statistical differences between the incidence of chromosomal aberrations in a batch of mice treated with an anticonvulsant drug (ethotoin) and a control group.[5] Some resemblance between the chemical structure of these drugs suggested that, like barbiturates, diphenylhydantoin could have an aberrant effect on cultured human lymphocytes in vitro.[6] We have reported a marked aberrant effect induced by diphenylhydantoin in vitro which proved to be similar to that of barbiturates.[7]

A batch of six A_2G female mice were treated by diphenylhydantoin dissolved in propylene glycol and administered in doses of 0·2 mg/kg body weight over a period of 10 days before the coupling of the animals. Mated immediately after the conclusion of treatment, these animals did not become pregnant; the six control animals littered a number of 41 young, all alive and apparently normal.

A second batch consisting of six non-inbred female rats received diphenylhydantoin (phenytoin) orally in doses of 25 mg/100 g body weight daily. In parallel a further six female rats of the same batch were treated with primidone 0·06 mg/100 g body weight daily. The treatment was started on the first day of gestation, and lasted five days. The day after the last dose the animals were killed. Five of them (from the phenytoin batch) were found to have embryos in the course of resorption; one had six embryos in the left oviduct (abnormal metaphases—stickiness), whereas in the right oviduct all the embryos were resorbed. Six rats were found to be sterile—namely, five from the primidone-treated batch and one from the phenytoin-treated one. In the control batch, all embryos were normal, and litters consisted of 8 to 14 young.

The phenytoin-treated animals had an increased number of abnormal bone metaphases (stickiness, interchromatid bridges, and gaps). Fifty metaphases were counted in each case. Further, the phenytoin-treated animals showed 13 (26 ± 1·26%) abnormal metaphases, while those treated with primidone 14 (28 ± 1·08%). The control animals showed only 4 (8 ± 1·75%).

It is remarkable that the increased number of bone metaphases induced by anticonvulsant therapy had returned to normal only seven days after discontinuation of treatment. This may be explained by the relatively rapid dynamics of the bone marrow mitotic cycles which favour chromosomal lesion recovery.

We consider that the chromosomal abnormalities induced by anticonvulsant drugs are caused either by the inhibition of folic acid synthesis,[8] which is one of the precursors of inosine synthesis playing a fundamental role in purine synthesis, or by the inhibition of the synthesis of proteins, constituents of the chromosomal matrix, thus interfering with the normal development of mitosis.—We are, etc.,

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1 Elshove, J., *Lancet*, 1969, **2**, 1074.
2 De Toni, E., Massimo, L., Vianello, M. G., and Bicarelli, F. D., *Annales de Génétique*, 1966, **9**, 99.
3 Meadow, S. R., *Lancet*, 1968, **2**, 1296.
4 Márquez-Monter, H., Ruiz Fragoso, E., and Velasco, M., *Lancet*, 1970, **2**, 426.
5 Brøgger, A., *Lancet*, 1970, **2**, 979.
6 Caratzali, A., and Roman, I. C., *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences, Série D.*, 1969, **268**, 191.
7 Caratzali, A., and Roman, I. C., *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences, Série D.*, 1971, **272**, 663.
8 Mannheimer, E., Pakesch, F., Reimer, E. E., and Vetter, H., *Medizinische Klinik*, 1952, **47**, 1397.

Anaesthetics and Platelets

SIR,—In the leading article on "Anaesthetics and Platelets" (11 September, p. 597) two statements require particular scrutiny. Firstly, "platelets have an essential role in haemostasis. The first defence against a loss of continuity in the wall of a blood vessel is the formation of a plug of platelets stuck to each other and to the vessel wall. This plug is stabilized by fibrin strands." Secondly, "yet although aspirin has been shown to prolong the bleeding time, its use has never been found to be a major surgical hazard."

As early as 1941 Macfarlane[1] stated: "It was perhaps unfortunate that a sweeping generalization of Hayem's view (which introduced the platelet plug theory) should have been applied to the haemostatic process as a whole and accepted almost without criticism." It should be stressed that the fibrin plug concept is a theory, not a fact. The first step in haemostasis is much more likely to be vascular contraction.

That aspirin prolongs the bleeding time, often even in normal subjects as I first established in 1966,[2] is now generally accepted, but the clinical seriousness is still greatly underestimated. Thus, I cannot agree that the use of aspirin has never been "a major surgical hazard." This statement is true only if the patient has no other haemostatic defect, but in haemophilia, in the thrombopathies, in telangiectasia, and other bleeding states aspirin is frequently a major