punch-grafting¹ confirms this and lends support to the suggestion that the factors concerned in male hereditary-type baldness are due to a change in hair pattern due to genetic and endocrine factors. The fact that normally the tonsure of the scalp is not susceptible to baldness whatever the hair pattern or cycle and that when transplanted remains so would seem to suggest a genetically unsusceptible region of scalp which is also not susceptible to whatever the hormone situation happens to be. In fact what is inherited genetically is hormone susceptibility of the rest of the scalp.

Furthermore, this seems to be confirmed by clinically observing the influence of hormones in treating excess loss of hair. It is noted that oestrogens do not influence the hair pattern in females. I am surprised that no reference is made to the generalized thinning of hair complained of by the menopausal female. No doubt this is due to endocrine changes affecting the hair cycle.

Preliminary work, in both males and females, of injecting 0.1 mg. oestradiol monobenzoate at monthly intervals serially over the whole area of the crown of the scalp, in the females supplementing with 0.625 mg. Premarin (conjugated equine oestrogen) daily for 21 days of each cycle, suggests very beneficial results. After three to four months of such treatment patients are reporting much less fall-out of hair, which would suggest a decrease in the telogen phase or an overall increase in anagen-telogen ratio. This would also seem to apply to males under treatment, and so far there is no change in pattern but the cycle is advantageously effected. These patients have been undergoing treatment for varying periods up to seven months and confirm reports from Dr. Orentreich,² whose series now includes cases treated for 15 months.

No doubt the more readily available methods of hormone estimation and scalp biopsy in patients before and undergoing treatment will provide valuable material in establishing the results of this research, and thanks are due to Dr. Rook's stimulating lecture for drawing attention to investigating hair cycles in man.—I am, etc.,

London W.1.

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Porphobilinogen-like Chromogens in Urine of Epileptics

SIR,—M. Markovitz¹ reported the presence of porphobilinogen-like chromogens in urine from 47 out of a total of 91 epileptic patients. Though weak positives have been reported with the Watson-Schwartz test by Townsend² in the urine of general hospital patients, the proportion was much smaller—59 in 1,000 routine specimens. It seemed worth confirming the work of Markovitz and possibly identifying further the substances responsible for the weak positive results he reported.

A group of 93 Maudsley Hospital patients with epilepsy was examined. The series of patients consisted of 53 males and 40 females. The age range was from 13 to 65 years, with an average age of 30 years. There were 34 patients with temporal-lobe epilepsy, 43 with petit-mal and grand-mal epilepsy, 14 with focal cortical epilepsy, and 2 cases of epilepsy of uncertain aetiology. The diagnosis had been confirmed in

most cases by electro-encephalogram and neuro-radiological methods as well as by history and clinical examination. The patients were treated with phenobarbitone, phenytoin, primidone, tridione, methoin, acetazolamide, ethosuximide, and sulthiame, usually two of the drugs in combination. A single specimen of urine was examined from each patient—an early-morning specimen in the case of in-patients and a random specimen from out-patients.

The Watson-Schwartz test³ was performed as follows: 5 ml. of Ehrlich's aldehyde reagent was added to an equal volume of fresh urine; 10 ml. of saturated solution of sodium acetate was then added followed by 5 ml. of chloroform. The mixture was shaken and inspected. The test was considered negative if the aqueous layer was colourless—i.e., all the pink colour had been extracted from the aqueous phase. If, however, any pink colour remained in the aqueous phase butanol extraction was carried out, as discussed by Watson *et al.*⁴ Not a single positive result was obtained even in the chloroform extraction, hence butanol extraction was not required.

These findings do not agree with those of Markovitz despite the similarity of the patient sample and the technique used. No satisfactory reason can be given for the contradiction; however, it seems that such a discrepancy is more likely to be related to variation in technique than the epileptics examined.

Thanks are due to Dr. D. W. Liddell, physician, Maudsley Hospital, for the use of his cases, and to Dr. R. C. Wilcox for his advice, and to his staff for performing the tests.

—I am, etc.,

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Blackboard Drawing in Medical Teaching

SIR,—Mr. A. Barabas in his article (20 March, p. 782) is quite correct when he states that blackboard drawing is still the most useful visual aid in a lecture. It is about time that the disadvantages of magic lantern slides and moving pictures were exposed. Mr. Barabas has mentioned some of these. A very large number, if not the majority, of people who attend international meetings fall asleep before the end of each lecture. This is due to the fact that the audience has to sit in darkness in an overheated and sometimes very badly ventilated lecture hall. Would not the audience learn more if they got a chance of staying awake in a room full of sunshine and fresh air? Undergraduates certainly do.—I am, etc.,

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"Break-through" Bleeding and Cervical Cancer

SIR,—Recent correspondents have suggested that, despite weighty pronouncements to the contrary, oral contraceptives may predispose to thromboembolic phenomena. Another and equally grave danger is that these drugs may be conditioning many women (and, even worse, their doctors) towards accepting intermenstrual bleeding as "break-through" in type and relatively unimportant.

A recent case shows just how dangerous this thinking can be. The 30-year-old patient had been on oral contraceptives for 17 months after her fifth pregnancy, when she developed intermenstrual "spotting." The complaint was dismissed by her doctor as "break-through" bleeding and the brand of tablet changed twice in order to obviate the trouble. Five months after the initial symptom, by which time the bleeding had become post-coital in type and was no longer to be ignored, she was seen at the hospital clinic. A clinical diagnosis of cervical cancer was easily made and subsequently confirmed by histology. It seems clear that the contraceptive therapy led directly to unnecessary delay in diagnosis. It is possible that this delay was contributed to by (but still not excused by) the fact that a year before the intermenstrual bleeding began a cervical smear had been reported as negative.

Having envisaged the possibility of such a case arising, I once suggested to a well-known drug firm that packages of contraceptive tablets should carry a suggestion to patients to have regular smear tests and to report any unusual bleeding. This was declined as being liable to create more difficulties (? commercial ones) than it would solve. It is regrettable that even when a patient does report intermenstrual bleeding it can be casually dismissed as a side-effect of "the pill."—I am, etc.,

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Chromosome Mosaicism in Stein-Leventhal Syndrome

SIR,—My attention has recently been drawn to a letter by Mr. N. P. Bishun and Dr. W. R. M. Morton (7 November, p. 1200) which records the results of chromosome studies in three cases of the Stein-Leventhal syndrome. While studying in the pathology department in Cambridge in 1962 I studied the chromosomes of a similar case.

The patient, a short, dark, somewhat hirsute female with some degree of virilization had complained of infrequent irregular periods since the menarche at the age of 21 years. She was 27 at the time of investigation. Vaginal examination revealed a small, hypoplastic, anteverted uterus, and moderate bilateral ovarian enlargement. She was admitted to Addenbrooke's Hospital under the care of Mr. O. Lloyd. At laparotomy both ovaries were found to be about twice the normal size and to contain multiple follicular cysts. Bilateral wedge resections were performed, and samples of fluid from the cysts were obtained. Analysis of the follicular fluid by Dr. R. V. Short (Department of Veterinary Clinical Studies, University of Cambridge) showed absence of oestrone and oestradiol, but the levels of 17-hydroxyprogesterone and androstenedione were considerably higher than those found in normal women.

Urinary excretion of steroids was not studied in detail. Studies of nuclear chromatin in buccal cells from the patient had given variable results, but most reports had shown less than 20% of cells to have Barr bodies. Two samples of blood were cultured by the leucocyte method of Hungerford *et al.*¹ Most of the 94 cells considered satisfactory for study came from the first culture. Of these, two cells had 43, two had 44, 39 had 45, and the remaining 44 cells had 46 chromosomes each. The cells with 46 chromosomes all had normal karyotypes. At least 37 of the cells with 45 chromosomes showed a loss of a chromosome from the group 6-12;