a positive personal or family history of migraine, and had E.E.G.s which showed more abnormalities suggestive of latent migraine than those of controls on oral contraceptives who were headache-free. Moreover, these abnormalities persisted in those who had repeat E.E.G.s after discontinuing the pill, which suggests that the vascular abnormalities pre-existed.[1] In view of Dr. Grant's finding of prominent arterioles in 16% of pre-treaunent endometrial biopsies, it would seem reasonable to postulate a widespread vascular hyperreactivity, which frequently manifests as headache on oral contraceptives.

My findings do not show the same specificity of response to the particular oestrogen/progesterone combination as do Dr. Grant's. In my series, the incidence of severe headache on Anovlar (norethisterone acetate, ethinyloestradiol) was 3.2% (compared with Dr. Grant's 40%); 1.7% with Lyndiol (lynoestrenol, mestranol) (Dr. Grant 32%) and 6.2% with Ovulen (ethynodiol acetate, mestranol) (Dr. Grant 13%). Moreover, headaches frequently persisted despite changing to another brand with a different combination once (23%), twice (15%), three or more times (7%) in an effort to overcome the headaches.—I am, etc.,

Cheam, Surrey. JOY WEST.

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SIR,—There are a few comments which I would like to make about the paper by Dr. Ellen C. G. Grant on the relation between headache, oral contraceptives, and the incidence of well-developed endometrial arteries (17 August, p. 402).

One of the major difficulties of studies into the incidence of subjective symptoms is in the collection of adequate and carefully regulated control data. It is well known that patients do not retain an accurate memory for symptoms of the more common type over a long period, and that such data can prove exceedingly unreliable when related to side-effects of oral contraceptives.[1] However, in this paper the only control material available[2] relates to patient's history—retrospective—and is compared to a prospective analysis of greater depth, at least two interviews over the year of study, a procedure which can give rise to highly misleading results.[1] In addition, such methods of obtaining control data have the great disadvantage of alerting the patients to the possibility of headache on drug therapy. Adequate control material can only be obtained by running a group concurrently with the one undergoing medication, that is, perhaps, with an intrauterine device, etc., the interviewer remaining blind to the treatment the patient is receiving. It is not possible for the patient to be blind because of the nature of medication, that is either you are on the pill or you are not on the pill. A placebo group would be ruled out for obvious reasons. Only by this method can the spontaneous development of headache be taken into consideration and observer bias removed. Patient bias, unfortunately, would still remain.

The method of collecting data has given rise to another difficulty created by the method of expressing the results, namely the headache incidence, as a percentage of women receiving treatment in the first year. It is unlikely that pretreatment interview relates to a history of more than a few months' duration. If we take the spontaneous incidence of a woman complaining of headache from one interview as 17%, two interviews over the period of a year would give an overall frequency of at least 30% if expressed as above. This figure is the one to which comparison shall be made. As stated before, it is not possible to be exact about this percentage without an adequate control procedure being followed. However, it would mean that only four out of the 16 trial combinations would materially fall above this. In addition, this estimate is likely to be on the low side because of the lack of knowledge about a spontaneous development of headache in a population so fraught with emotional overtones as that requiring family planning. Would one, therefore, be justified in stating that Ovulen (ethynodiol acetate), Ortho-Novin (norethisterone, mestranol), Lyndiol 2.5 (lynoestrenol, mestranol), and Ovran (norgestrel) caused a considerable decrease in headache incidence compared with that present in the non-treated female population, as is suggested by some investigators ?[1]

In addition it is unclear whether the diagnostic groupings of headache in the pre-treatment assessment, namely migraine and premenstrual headache, both of which are fairly well defined clinically, can be compared with those obtained on treatment, where it would appear that "headaches" generally were included. Were only "typical pill headaches" included or were other types such as psychologically induced tension headaches excluded? Headache as a clinical term contains so many different conditions of different aetiologies, ranging from migraine to meningitis or mercurial poisoning, that some differentiation into the type of headache should be endeavoured. In essence, therefore, no valid conclusion can be drawn from material of this type without adequate control data being available, and some attempt at categorizing the all-embracing term of headache into something which is more clinically meaningful.—I am, etc.,

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E.C.G. and Tricyclic Antidepressive Drugs

SIR,—It is known that the tricyclic antidepressive drugs imipramine[1 2] and amitriptyline[3] may produce arrhythmias and E.C.G. changes in cases of poisoning, and with imipramine these changes have also been reported during therapeutic use.[4] The effects produced comprise various A–V arrhythmias, widening of the QRS complex, and displacement of the S–T segment. Recently Drs. R. J. Barnes, S. M. Kong, and R. W. Y. Wu (27 July, p. 222) have suggested a diagnostic application of these findings to distinguish poisoning by the tricyclic antidepressive agents from other types of drug poisoning. However, there are both animal and clinical data which suggest that this diagnostic aid may not be generally applicable, because the cardiac action of the related, but indole-based, tricyclic drug iprindole[5] appears to differ from that of imipramine and amitriptyline.

In anaesthetized animals a comparison has been made of the effects of iprindole, imipramine, and amitriptyline administered intravenously in cumulative doses of 1 to 5 mg./kg. in rats and 1 to 25 mg./kg. in cats. In both species all three compounds reduced the blood pressure and caused temporary apnoea, and, particularly in the rat, there was also transient bradycardia with A–V block and occasional premature atrial systoles lasting less than two minutes. The bradycardia and arrhythmias were most pronounced with iprindole, but imipramine and amitriptyline were more respiratory depressant and were lethal to both rats and cats in lower doses. Apart from its transient effect on cardiac rhythm, iprindole had little or no effect on the configuration of the electrocardiogram, whereas both imipramine and amitriptyline had an additional and almost immediate effect in increasing the S wave voltage of lead II, with widening of the Q–T interval and displacement of the S–T segment lasting up to one hour in the cat. These findings suggest that although iprindole shares with imipramine and amitriptyline the ability to produce transient changes in cardiac rhythm, perhaps associated with an effect on the autonomic innervation of the heart, it does not share their ability to produce those changes in the cardiac muscle responsible for alterations in the electrical complex itself.

In therapeutic use iprindole has approximately the same antidepressive potency as imipramine, but it produces fewer anticholinergic side-effects and has not been observed to cause electrocardiographic changes. Imlah[6] has described the effects of iprindole in two groups of four patients treated continuously with daily doses of 45 and 90 mg. for more than 12 months, but no changes were found in the E.C.G.; similarly, no electrocardiographic changes were found in six patients treated with daily doses of 90 mg. iprindole for six weeks.[7] Although no case of poisoning with iprindole alone has yet been reported, the evidence indicates that the drug is unlikely to produce those changes in the electrocardiographic configuration which Dr. Barnes and his colleagues described as diagnostic for poisoning with other tricyclic antidepressive agents.—We are, etc.,

B. J. ALPS.
T. V. A. HARRY.
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Purpura and Paracetamol

SIR,—In view of the rarity of untoward side-effects from therapeutic doses of paracetamol, the following case report may be of interest.

A 63-year-old woman had been receiving adequate therapy of cyanocobalamin and thyroxine for some years following a well-substantiated diagnosis of pernicious anaemia and hypothyroidism. In addition, for five

months the patient had been taking Distalgesic (dextropropoxyphene with paracetamol) for intermittent headaches, and estimated her intake to be approximately six tablets per week. With no other significant history she presented with thrombocytopenic purpura. Physical examination and all laboratory investigations failed to reveal any underlying cause. The patient's platelet count rose spontaneously to 142,000/cu. mm. after seven days, and with a provisional diagnosis of drug-induced thrombocytopenia she was allowed to return home with instructions not to take Distalgesic. Four days later the patient was seen again with a recurrence of purpura and a platelet count of 16,000/ cu. mm. She said she had taken two tablets of paracetamol 48 hours previously, and denied having taken any other medication. The count again rose spontaneously, and after it had remained normal for three days the patient was given two tablets of paracetamol as a "challenge" test. Thrombocytopenic purpura appeared within eight hours, and a spontaneous recovery of the platelet count to normal levels again followed in a period of seven days. Attempts were made to demonstrate that the patient was sensitive to paracetamol by examining the effect of the drug in vitro on platelet agglutination and clot retraction.[1 2] Positive results were not obtained.

The diagnosis of paracetamol-induced thrombocytopenia in this patient was based on the precipitation of thrombocytopenic purpura within hours of ingesting the drug, followed by spontaneous recovery of the platelet count to normal levels within a period of 10 days. Both these features seem typical of platelet destruction induced by the drug-antibody-platelet mechanism[3] and the negative results from studies on platelet agglutination and clot retraction do not necessarily invalidate this explanation.[4]

I am grateful to Professor R. H. Girdwood for permission to report this case, and to Dr. S. H. Davies for the investigations for platelet antibodies.

—I am, etc.,

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A Sort of Psychodrama

SIR,—Dr. Griffith Edwards's review (7 September, p. 613) of the play at the Congress of the World Federation of Mental Health is excellent, so far as it goes, but why has he made no reference to what seems to me the *principal* criticism, that the whole theme has been given, for far too long, a generality its obscure folklore origins simply do not justify?

And why the omission of any reference to what gives the "Touching is sin" theme, in the second act, its significance, that it is its association with *the worship of the Goddess* (which is such anathema to the "General") which is its *raison d'être*, and which I thought was admirably brought out in the play itself? Again, one wonders, why has Dr. Edwards passed over without comment the liberty Adrian Mitchell has taken in the script, either in deference to his audience or from his own inner anxieties, in making Lucifer a tart? To my mind this obscures not only the recognition of the "General's" isolation, violence, and misogyny, so illuminating to his madness, but the fact that the whole theme is a homosexual, and possibly onanistic, fantasy. To introduce a *woman* into the "upper level" is to fail to appreciate that this is just what the folklore exists to avoid.

Lastly, why no criticism of Mitchell's glaring omission of the figure of Abraham, and the "Frankenstein theme," for it is this which gives meaning to the whole, that the "General" is the creation of *Abraham's* madness, the "monster" of *his* invention, loosed upon a world too much in fear and awe of it to recognize that the "General" is really only an elaborate, if devastating, puppet it has adopted—a kind of Hebraic "wooden horse" imported into saner realms. —I am, etc.,

London N.W.3. N. A. CHISHOLM.

Vas Deferens in Hernioplasty

SIR,—In large or recurrent herniae in elderly people it is justified to undertake an orchidectomy, and I have found that the vas deferens can be used as a most suitable suture material for repairing the inguinal canal. The maximum length which can usually be obtained is about 15 cm., provided the vas is carefully dissected from low down from off the epididymis. If preferred, the testicle can be left in situ with the other structures of the cord and the vas deferens dissected off, leaving its proximal end still attached. Rather than mount the vas on a Gallie's needle, which is rather traumatic to tissues, it is better to use a Cleveland ligature carrier with which to suture. I have used the vas deferens on numerous occasions and have always found it much easier than taking fascia from the thigh.—I am, etc.,

Bath. PATRICK SAMES.

Waiting for Doctor

SIR,—I would like to correct a point of fact in Dr. D. J. Pereira Gray's letter (7 September, p. 615). Data on waiting time for admission to hospital have been published in the annual *Report on Hospital Inpatient Enquiry, Part I*, from 1962 onwards. Table 6 shows the mean and median waiting time in weeks by region of residence of the patient, sex, and detailed diagnostic group. A similar table will appear in the 1966 *Report* to be published shortly, and careful consideration is given by the Ministry of Health or the General Register Office to requests for information in advance of publication.

In addition, the *Annual Report of the Ministry of Health* publishes national figures by specialty of the number of patients on the waiting list, compiled from returns for individual hospitals. More detailed information, for example analyses by region, are available in the Ministry of Health and consideration will always be given to requests for these.—I am, etc.,

D. EVANS.

Statistics and Research Division, Ministry of Health, 14 Russell Square, London W.C.1.

SIR,—I am interested in your leading article "Waiting for Doctor" (24 August, p. 447) and Dr. D. J. Pereira Gray's letter (7 September, p. 615).

I have recently done some research on an opposite problem, for example, outpatients who fail to keep their appointments. At a Coventry psychiatric clinic 28% of booked appointments during a study period of six months were missed. Seven out of 99 non-attenders studied were admitted urgently to the mental hospital prior to the date of appointment. All other non-attendances were, strictly speaking, avoidable. The corresponding figure for non-attendances at a medical outpatient at the same hospital during a study period of three months was 15.1%.

Overcrowded, overworked outpatient clinics with patients too ill to wait on the one hand, and patients dropping out, creating unpredictable gaps of inactivity and wastage of precious clinic time on the other: a paradoxical situation. Could the gaps be filled with the more urgent cases? Perhaps a penalty for voluntary non-attendance without previous cancellation within a specified period (say, one week before attendance) will ensure a pool of vacancies which can be advantageously used for the more urgent cases at an opportune moment. In a recent perusal of the medical literature[1 2] I could find no work on non-attendance at medical (non-psychiatric) outpatients in this country.—I am, etc.,

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Acute Epiglottitis

SIR,—I read with interest the paper by Dr. J. D. Andrew and others (31 August, p. 524) referring to the fulminating nature of acute epiglottitis. We recently had such a case in a healthy dairy-farmer of 22, where a prompt tracheostomy was life-saving.

This patient had been previously healthy until he awoke at 5 a.m. with a sore throat and malaise. Within an hour he developed severe stridor and was admitted to a local cottage hospital. Shortly after admission he collapsed unconscious with complete respiratory obstruction. Fortunately a colleague was present who performed an immediate tracheostomy, and the patient was transferred to the district hospital. At that time he was febrile (102° F., 39° C.), and a blood count showed 9,600 cells, with 84% neutrophils, 6% monocytes, and 9% lymphocytes.

Cultures from the pharynx and trachea showed a predominant growth of *Ps. pyocyanea* with a few colonies of *Neisseria*. This must represent a most unusual infecting organism in upper respiratory tract infections. He was treated with chloramphenicol and made a rapid and complete recovery.—I am, etc.,

M. K. G. HUDSON.

Beaminster, Dorset.

SIR,—We were most interested in the paper by Dr. J. D. Andrew and others (31 August, p. 524). We agree that there is a need for widespread awareness of this condition so that prompt treatment may be instituted.

We were disappointed, however, that mention was not made of the benefits to be derived from nasotracheal intubation. In acute epiglottitis rapid resolution usually