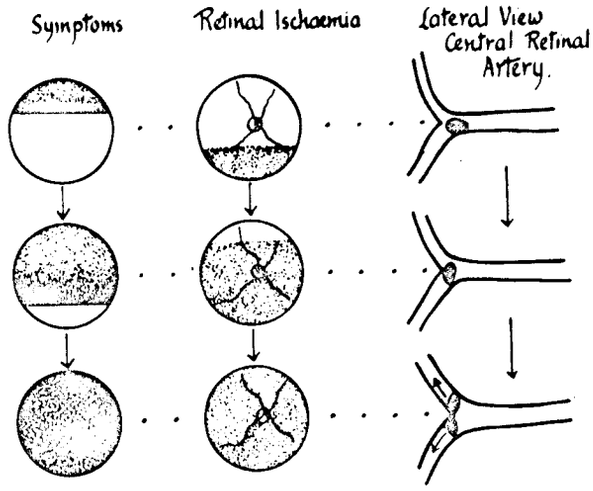

Fig. 2—Retinal ischæmia in amaurosis fugax due to embolism. Hypothetical picture of progress of visual loss and recovery as embolus breaks up. The lower retina is ischæmic longest and the last to recover. The " blind " moves up.

However, the temporal retinal vessels may be affected more often than the nasal and the upper more than the lower. Visual loss described as a blind being pulled across the eye is quite likely to be embolic and suggests ipsilateral carotid disease; angiography may therefore be justified. A younger patient describing attacks of monocular blindness is unlikely to be suffering from such disease and angiography may throw no light on the problem.

The origin of these attacks is obscure; some may be migraine equivalents, others may be embolic. The striking feature emphasised by Dr. Eadie, and his colleagues is their benign course.

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SEVERE HEAD INJURIES

SIR,—Pituitary changes, especially necrosis of the anterior lobe, should be included in any discussion on severe head injuries such as your leading article (March 9, p. 514) especially since you emphasise mortality and survival rates as well as sequelæ of brain injury. The first reference to this complication of head injury was published in 1959.[1] Two years later Daniel and Treip collected more cases and suggested a pathogenetic mechanism.[2] In 1966, unaware of this earlier work, I reported a series of 102 cases of head injury with a high incidence of anterior-lobe-pituitary necrosis.[3] Proceeding along a very different line of thought, I reached the same conclusion about the pathogenesis of the lesion as did Daniel and Treip—namely, amputation of the stalk of the pituitary, either anatomical or functional at time of trauma, with derangement in the blood-supply to the anterior lobe. What is important to emphasise is that pituitary necrosis may be the leading cause of, or at least a very important factor in, death during the three to ten days after injury. Also, some of the post-traumatic ill-effects of head injury could represent subclinical or minor degrees of hypopituitarism. These publications do not seem to have had the impact they deserve since they are notably absent from the reference lists in most studies of head injury, as your leading article illustrates.

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LYSERGIDE AND CHROMOSOMES

SIR,—Less desirable effects of the use of lysergide (L.S.D.) and similar drugs have received considerable editorial attention [1–3] in what we take to be attempts to discourage their widespread and irresponsible use. While that is a worthy object, many of the " darker possibilities " [1] claimed for lysergide on the basis of its ability to damage chromosomes are not well founded. We are concerned that a premature and possibly erroneous condemnation might discourage the responsible use of these drugs—for example, in psychiatry where they show promising therapeutic value.

It is reasonably well established that chromosomal abnormalities appear in cultured leucocytes from persons who have taken lysergide, although in most cases also with other drugs.[4–6] This ability to damage chromosomes has been taken also to indicate mutagenic, leukæmogenic, and teratogenic properties of lysergide.

Many agents, particularly radiation and the radiomimetic chemicals, cause both chromosome breakage and gene mutation, but it is by no means certain that all chromosome-breaking agents are mutagenic. Many common viruses and chemicals, unlike irradiation and the radiomimetic agents, cause damage predominantly in heterochromatic regions of the chromosome, and the apparently non-random breakage caused by lysergide suggests that it belongs to this class. It is believed that many of the breaks and other effects in heterochromatin probably do not reflect a specific action of the causal agents but a response of the chromosome to non-specific environmental alteration,[7] since these manifestations in heterochromatin can also result from various physical and chemical manipulations such as calcium deficiency, fixation treatment, and low temperature.[8] It is unlikely that the chromosome damage resulting from these causes, and possibly from many viruses and chemicals, is associated with gene mutation which may be harmful to future generations. At least the mutagenic potential of these agents including lysergide can be tested readily by experiments on the mouse or fruit fly.

Again, some agents—for example, irradiation and benzene —which cause leukæmia also cause chromosome damage, but it is not clear that the chromosome breaks are in any way directly related to the development of the leukæmia. The two may be quite distinct effects. Furthermore there are many chromosome-breaking agents which do not cause leukæmia. To state that " the Philadelphia chromosome seen in myeloid leukæmia " [1] has been found in users of lysergide is hardly justified on the basis of the presumable G-chromosome deletions found in cultured leucocytes.[6] Much attention has also been given to the chromosome breaks in the inherited disorders, Fanconi anæmia, and Bloom's syndrome, but the cause of these breaks is not known, nor whether they have any relation to the subsequent neoplastic developments. Particularly awesome significance has been given to the quadriradial figures in cells from patients with these inherited disorders and in a few cells from lysergide users. It is difficult to see the reason for this if it is not their spectacular appearance. These chromatid rearrangements are known to be caused by many of the antimetabolites, and have been found in the leucocytes of normal persons.[9] The claim has also been made that lysergide " continues to produce chromosome damage many weeks after its ingestion ",[2] but surely this is a misconception based on the persistence of chromosomal damage in dormant small lymphocytes, as was recognised in the experimental reports.[4–6]

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The evidence that lysergide produces embryonic malformation both in humans and in animals is sketchy and contradictory [10 11], and clearly a reliable experimental approach is desirable. Until information from such a study is available, the rule should be followed that only drugs which have been cleared from any teratogenic role by thorough testing are administered to pregnant women, particularly during the first trimester.

When important issues are involved, suspicions, no matter how poorly founded, deserve respect, and any therapeutic use of lysergide should be such as to limit possible ill effects until these are better founded or rejected. The outcry on cytogenetic grounds against lysergide raises a much larger issue however. Several commonly administered agents, such as aspirin, ergometrine maleate [12] and chlorpromazine,[5] are also reported to cause a striking increase in chromosome breakage. But of much greater importance is the fact that in the interests of diagnosis we continue to use levels of irradiation which cause both increased chromosome breakage [13–15] and increased gene mutation. This is particularly important when the fœtus in utero is concerned, and there is also good evidence that this irradiation accounts for a significant proportion of childhood cancers.[16]

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THE HEART IN HYPERTENSION

SIR,—In his interesting and thought-provoking article (April 20, p. 855) Dr. Dickinson says: "We do not yet know the cardiac output in patients with hypertension treated for long periods with propranolol: my guess is that it would be little reduced, if at all." His guess is partially correct: cardiac output is reduced, but more than a little, as found by Frohlich et al.[17] In seven of their hypertensive patients, hæmodynamic studies performed during treatment (after 10 months on average) there was a significant reduction in cardiac output (6130 to 4615 ml. per minute, $P < 0.005$).

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SODIUM-PHOSPHATE FORMATION OF RENAL CALCULI

SIR,—Dr. Bernstein and Dr. Newton[18] gave the pH of the oral sodium-phosphate solution they used ('Phospho-soda', Fleet Co. Inc.) as 7·4.

A request from the stone clinic of the department of urology at this hospital was received by the pharmacy here for some of the solution. Some phospho-soda was purchased, and some solution made in the pharmacy with the same concentration of phosphates as in the Fleet solution, and the pH was taken by means of the pH meter in the pharmacy and independently by the metabolic laboratory staff on their pH meter. The results were 5·2 and 5·18 for the Fleet solution and 5·2 and 5·2 for the home-made solution. A second batch of home-made solution tested on the pharmacy pH meter, but using a different glass electrode, was found to have a pH of 5·3.

In view of these findings, and of the fact that the paper by Bernstein and Newton seems to imply that the Fleet solution was administered without further adjustment of the pH, I feel that confusion is going to arise and that phospho-soda (Fleet) is likely to be administered under the assumption that it has a pH of 7·4.

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PROPHYLAXIS OF INFLUENZA

SIR,—Dr. Beare and his colleagues (April 20, p. 843) report favourably on a synthetic isoquinoline as an influenza prophylactic. I wish to make two criticisms of their paper.

Firstly, patients were deliberately switched between the two treatment groups in an attempt to secure equal susceptibility to infection. Surely stratification should always anticipate randomisation? Acceptable alternatives existed.

Secondly, neither in the text of the article nor in the two papers cited [1 2] is any mention made of precautions to ensure or check that the patients actually took their tablets. There is now extensive evidence to suggest that compliance by both supervised and unsupervised patients can never be assumed. May I make a plea that reports on clinical trials always include evidence that the treatments were in fact taken?

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BACTERIURIA AFTER GYNÆCOLOGICAL SURGERY

SIR,—We read with interest the article by Mr. Mustafa and Professor Pinkerton (April 20, p. 839) and would like to comment on their findings of bacteriuria in patients who were not catheterised, as our experience appears to be so different.

They found that, of 161 patients who were not catheterised, 59 (37%) developed bacteriuria while in hospital. No distinction is drawn between those who had abdominal surgery and those whose operation was vaginal, but as 194 of their 253 patients underwent vaginal surgery it may be assumed that a large proportion of these bacteriuric patients were of the 194. We followed a series of patients who had vaginal repair operations or vaginal hysterectomy with colporrhaphy [3]: 60 of these were not catheterised after leaving theatre and only 1 (1·6%) developed bacteriuria. The discrepancy between these two series may be explained, at least in part, by the methods of urine collection employed. Mustafa and Pinkerton used midstream specimens, as did Donald et al.[4] who found a similar incidence of postoperative infection in patients who had not been catheterised. We diagnosed infection only from specimens obtained by catheter or suprapubic aspiration.

In the days immediately after major vaginal surgery there is a copious vaginal discharge and the patient's painful perineum (and sometimes her age) militates against the production of uncontaminated urine. We surveyed 75 patients for bacteriuria on the seventh day after major vaginal surgery by collecting a midstream urine from each, followed two hours later by a catheter specimen. All of these were interpreted by the same bacteriologist (T. A. M.). Comparison by qualitative methods showed that 26/75 (35%) gave false positive information. Quantitative methods reduced this to 9/75 (12%). As these specimens were taken by nursing staff who were aware that an investigation was in progress, we feel that these are minimum figures for misleading contamination. Our results agree with those of others [5–7]; so we stress the need for cautious interpretation of midstream specimens of urine after vaginal surgery.

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