purgatives. The patient should be kept under strict medical supervision with attention to possible blood changes.

After the drug course has been completed all the above-mentioned procedures should be repeated; then any difference between the condition before and after treatment may be noted. Mere naked-eye observation before and after treatment is not of much value. It may be advisable to repeat the drug course after an interval of ten days, the examinations before and after treatment being again carried out.

In my latest case, that of a young English lady infected with trachoma, the bacteriological cultures before treatment showed a heavy growth of pneumococci and haemolytic streptococci, while after treatment by sulphapyridine there were only a few sparse colonies of non-pathogenic staphylococci and diphtheroids. There had been some blepharitis, which was cured by the treatment, but I had not suspected a bacterial infection of this severity. The phenomena of trachoma remained unaltered. That the gelatinous matter contained in the bleb-like excrescences or follicles of Stage IIa of trachoma—which was the clinical state of the conjunctiva—would be absorbed would have been too much to expect from any drug, whether ingested, injected, or applied to the surface of the membrane.

Discussion

Up to the present the drugs of the sulphonamide group have been found to be without effect on any virus disease, and most of us believe that it is to this class that trachoma belongs. In my opinion the good results which have been reported in the treatment of trachoma by these drugs have been procured by the elimination of superimposed bacterial infections. Remarkable results may be expected from this form of treatment in many cases of bacterial conjunctivitis and blepharitis.

It has been suggested that trachoma is becoming a rare disease in England, but between December 5, 1939, and January 12, 1940, I examined fifteen persons with the disease in an active and contagious stage, seven being of British birth and eight being Jewish refugees from Germany. Perhaps the most important of these was a private soldier from his regimental barracks.

The John Burford Carllill Laboratory,
Westminster Hospital Medical School.
January 13, 1940.

Professor Giuseppe Bastianelli, director of the Istituto di Malariologia "Ettore Marchiafava," Policlinico Umberto I, Rome, has sent the prospectus of an international course in malariology, to be held in Rome from July 15 to September 10. There will be lectures and demonstrations in haematology, protozoology, malaria parasites, and microscopical diagnosis, pathology of malaria, clinical study and treatment in the wards, entomology in relation to mosquitos, and the epidemiology and prophylaxis of malaria. The programme also includes practical work and laboratory demonstrations, instruction in the survey of a malarious area, and residence in experimental stations and in a centre of induced malaria. Several excursions have been arranged, some obligatory and others optional. The course is open to post-graduate physicians only. It will be held in French if required and if ten students at least are attending; but in any case interpreters will be available. The fee amounts to 400 lire, of which 300 will cover all practical demonstrations and free travel in connexion with obligatory excursions. Extra fees are charged for the optional excursions to Sardinia and to Northern Italy. Applications must reach the director before June 20.

EPILEPSY TREATED WITH EPANUTIN

BY

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During the past year forty-three sane male epileptics at St. David's Hospital have been treated with epanutin (sodium diphenyl hydantoinate). In the majority of cases the drug was given in place of phenobarbitone or prominal or rutonal. Several patients had also been having, in addition, mixtures containing bromides, belladonna, borax, chloral hydrate, or pilocarpine nitrate, etc. In such cases the mixture was continued, so that the present investigation indicates the results only of the substitution of epanutin for the barbiturates.

The date was noted when each patient appeared to be receiving his optimum dose of epanutin, and the subsequent period of months was compared with a corresponding length of time before starting treatment. None of the patients concerned had shown a marked seasonal incidence in fits during past years, and therefore the comparison of the two periods was considered to be fair. In regard to incidence of fits the following results were obtained:

Great improvement	..	..	..	20 cases (46.51%)
Improvement	..	..	..	7 „ (16.28%)
No change	..	..	..	6 „ (13.96%)
Worse	..	..	..	1 case (2.32%)
Treatment discontinued	..	..	..	9 cases (20.93%)

Total 43 cases

Effects of the Treatment

It will be seen that twenty-seven patients, or approximately 63 per cent. of the cases, have derived benefit from treatment. Among those cases regarded as showing great improvement one man who had had twenty-six major fits in the four months before treatment has had *none* in the four months following optimum-dose treatment. He has had, however, rather more observed attacks of petit mal. On the other hand, practically all cases showing great improvement have had fewer observed attacks of petit mal as well as grand mal, but several of the men have stated that they experience more "sensations." In addition, they all, with one exception, have appeared to improve psychologically, being brighter, more intelligent, and less introspective and hypochondriacal. Some of the men say that they feel better than they have done for years, one in particular mentioning that he felt as if he had "begun a new life." Even in those cases in which no improvement in the incidence of fits has been recorded the patients say that they are happier and more alert.

In the nine cases in which treatment was discontinued various toxic symptoms and signs had been manifested. In two cases there were pyrexia and skin rashes resembling respectively rubella and urticaria. In one case there was hypertrophic gingivitis, with nausea and vomiting. The other six cases showed some or all of the following symptoms and signs: tremulousness, intention tremor, ataxic gait, nystagmus, ptosis, slurring speech, insomnia, and mental confusion. Most of these toxic effects disappeared within a few days after cessation of treatment.

The patients' ages range from 17 to 58. Successful treatment has not been more marked at one age than at

another. From the experience gained so far one has the impression that patients of low-grade mentality are less likely to derive benefit and are more likely to exhibit toxicity than those nearer average intelligence.

Importance of Correct Dosage

As has already been noted by all investigators, the dosage of epanutin is very important, and the drug should be introduced gradually, without sudden withdrawal of previous medication. Two capsules (each containing one and a half grains) daily may be useless; three daily may prove to be the perfect therapeutic dose; and four daily may produce pronounced toxic symptoms and signs in the same patient. There is evidently a very small margin between the therapeutic and the toxic dose. Of the thirty-four patients at present continuing with this treatment, nine require four capsules daily, nineteen have three capsules daily, and the remaining six men only two capsules daily.

So far no diminution in the efficacy of the treatment has been observed. Even in those patients who have been taking the drug for eleven and twelve months no increase of dose has been required and no signs of mental deterioration have been observed. There appears to be no doubt that epanutin is less hypnotic than the barbiturates and in suitable cases is a more powerful anti-convulsant. Further prolonged trial in large numbers of cases is necessary, however, before a satisfactory estimate of the real value of this drug can be attained.

Summary

Epanutin has been administered to forty-three epileptics during the past year, and twenty-seven (63 per cent.) have derived benefit in regard to both incidence of fits and psychological outlook.

The drug appears to be much less hypnotic than phenobarbitone, etc.

The margin between the therapeutic and the toxic dose is very small.

Various toxic reactions are mentioned.

Clinical Memoranda

Heparin in Subacute Bacterial Endocarditis

A recent experience of the treatment of subacute bacterial endocarditis with heparin and sulphapyridine¹ suggests the following practical points. Our patient, who was already in an advanced state of the disease, grew steadily worse under the treatment and died. It seems essential to give the treatment as early as possible owing to the development of a haemorrhagic tendency and renal insufficiency in the later stages. The former obviously increases the risk, while the latter makes it difficult for the patient to deal with a large amount of fluid or salt given parenterally. The cannula should be tied in with a thread, as catgut loosens after a week or ten days. The volume of injection cannot well be kept below a litre a day if it is to flow regularly, but it should not greatly exceed this, and certainly not more than a litre of normal saline should be given in the twenty-four hours, any further heparin required being dissolved in a 5 per cent. solution of glucose in water. We also gave our patient on separate occasions a litre of blood and sodium sulphapyridine along with the heparin. We found she required about 15 mg. heparin (Roche) an hour to keep her venous coagulation time longer than one hour; at the beginning

of treatment this was too little and at the end too much. In another case I should start off with a priming injection of the order of 0.5 to 1 mg. heparin per kilo. The cost of treatment, buying heparin by the gramme, works out at about 30s. a day, or about twenty guineas for a fortnight's course, which, as one of my assistants remarked, is no more than the fee for a visit by a consultant. Finally, I should emphasize that it is desirable to estimate the coagulation time on the venous blood by the method of Lee and White, using four tubes, for the following table suggests that blood obtained by skin puncture (Dale and Laidlaw method) reflects the state of coagulability very poorly.

	Coagulation Time	
	Dale and Laidlaw	Lee and White (average of four tubes)
13.2.40	1 min. 45 sec. Infusion of heparin begun	6 min. 30 sec.
15.2.40	10.30 a.m. 16 min. 4.30 p.m. 9 min.	— —
16.2.40	7 min. 30 sec.	15 min.
17.2.40	8 min.	90 min.
18.2.40	10.0 a.m. — 6.0 p.m. —	75 min. 15 min.
19.2.40	7 min.	8 min. 30 sec.
20.2.40	7 min.	2 hrs.
21.2.40	11 min.	Over 2 hrs.
22.2.40	20 min.	Over 24 hrs.
	Died	

Treatment was practically suspended for twelve hours on February 18 owing to smart haemorrhage from the kidney; the coagulation rapidly returned towards normal and the amount of bleeding diminished. Death occurred on February 22, and at necropsy we saw the usual features of subacute bacterial endocarditis plus a subarachnoid haemorrhage.

One question in conclusion: Has anyone observed either rheumatic or bacterial endocarditis in a haemophilic?

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A Ministry of Health circular to all local authorities states that arrangements should be made in the evacuating areas for the immediate examination of all children registered by their parents for evacuation when air attacks develop, and for the remedial treatment of any condition which would render the children unsuitable for billeting on private householders. The initial examination should be finished within three weeks of the close of registration on March 30. Children whose condition is not satisfactory should be re-examined at intervals of not more than one month, while those known to have suffered from scabies or from severe pediculosis should be examined at more frequent intervals. Reasonable expenditure on extra staff for the examination and treatment of children may be charged to the evacuation account. Plans should also provide for examination of the children immediately before evacuation—that is, either on the day on which they travel or the preceding day. The names and addresses of the medical officers in charge of arrangements in the receiving areas should be made known to the authorities of the evacuating areas as soon as possible. In the receiving areas the local education authority should be responsible for the medical examination arrangements. Special centres should be available, and the children should be examined at a rate of not less than 400 an hour. A similar circular has been issued by the Department of Health for Scotland.

¹ Kelson, S. R., and White, P. D. (1939). *J. Amer. med. Ass.*, 113, 1700; Friedman, M., Hamburger, W. W., and Katz, L. N. (1939). *Ibid.*, 113, 1702.