

(alkylamino-6-methoxyquinoline), which is receiving at the present time an extensive trial in the treatment of malaria in South America, India, and other endemic centres of the disease.

Unfortunately, toxic manifestations are all too commonly seen in patients undergoing treatment with plasmoquine, by far the commonest of which are cyanosis and abdominal pain; in fact, a certain degree of cyanosis, most marked in the lips, is almost the rule in patients under treatment with plasmoquine, and, although *per se* unassociated with any particular discomfort or immediate danger, constitutes a most valuable danger signal of intolerance to the drug, which should, in the opinion of most clinicians, immediately on its appearance, be withheld for a few days. This cyanosis has been shown by numerous observers to be due to partial conversion of the oxyhaemoglobin of the blood into methaemoglobin.

Thus Fischer and Weise (1927) found that methaemoglobinaemia could always be detected in 25 out of 26 patients a few days after the commencement of treatment, and they found, further, that the degree of methaemoglobin in the blood depended more on the degree of anaemia of the patient than the dosage of plasmoquine. (With this latter conclusion we cannot agree, for in our small series it was found that toxic symptoms—amongst others, cyanosis—were much more common in the case of patients under treatment with comparatively large daily doses of the drug (0.1 gram) than when a smaller daily dose (0.04 gram) was used.) The above two observers also concluded that it was the alkylamino group which was the cause of the methaemoglobinaemia, as in the case of acetanilid and phenacetin poisoning.

In our series the above two toxic symptoms of cyanosis and abdominal pain appeared with some regularity between the sixth and the tenth day of treatment, and, whilst comparatively common, as stated above, in patients receiving 0.1 gram daily (10 out of 17 cases), were also met with, although in a smaller proportion (7 out of 36), in those who received the much smaller dose of 0.04 gram daily; this suggests that personal idiosyncrasy to the drug is marked in certain cases, and it has even been suggested (Sinton and others) that racial susceptibility may play a part, the Northern European being apparently specially intolerant to any but the smallest doses.

That even susceptible individuals, if not too thoroughly poisoned by plasmoquine, may develop tolerance to its toxic manifestations is suggested by the following striking fact. If the drug be stopped directly cyanosis is noted or abdominal pain complained of, for one to three days, its readministration to complete the full course of twenty-one days, after this short break, has, in our series, been unattended, in all but a minority of cases, by any recurrence of toxic symptoms.

Unfortunately, cyanosis, at least in its early stages, is almost impossible to detect clinically in dark-skinned races, and in these we must be guided either by daily spectroscopic tests of the blood—a somewhat laborious proceeding and usually impossible in the field—or by the onset of the equally common and important early manifestation of abdominal pain, a symptom which must *never* be disregarded in patients undergoing plasmoquine medication.

A further interesting point arises. It is reasonable to predict that the fatal complication of heliotrope cyanosis will occur in future pandemics of influenza under similar conditions of "mass exhaustion" as it has occurred in the past, and is even now probably seen in isolated cases. If Professor Haldane's theory as to its causation, in spite of evidence to the contrary, be correct, we must be very wary in treating so-called "clinical malaria," which may turn out to be influenza, with a drug like plasmoquine, thus possibly adding an exogenous to an already developing endogenous methaemoglobinaemia. In any case I consider it safer, in view of the toxic nature of the drug, to reserve plasmoquine for the treatment of cases in which malarial parasites have actually been demonstrated in the blood, and in which other factors than malaria, either causative or contributory, can be reasonably excluded, reserving our old ally, quinine, for the treatment of "clinical" malaria and other cases of doubtful etiology.—I am, etc.,

S. SMITH,
Major, R.A.M.C.

Murree, India, July 17th

TREATMENT OF PLACENTA PRAEVIA.

SIR.—The letter from Dr. D. C. Macdonald in your issue of August 10th (p. 278) requires an answer.

I have been to many discussions in different parts of the world, and I do not think I have ever been to one of greater value to the profession at large than that on placenta praevia, on July 25th, at the British Medical Association Meeting in Manchester. The number of speakers was great, and every aspect of the subject was amicably discussed. The meeting was ably conducted by an excellent chairman, who requested repeatedly that those who wished to speak should hand in their names. Why did not Dr. Macdonald do so? There was no "wrangle" about the pros and cons of Caesarean section, but obviously it was necessary to discuss them pretty fully at the present juncture.

While the *absolute* diagnosis of placenta praevia can only be made on vaginal examination, I always advise that, once ante-partum haemorrhage occurs, the case should be sent into hospital *without* vaginal examination being made. If the case is being treated at home, it is conducted as if it were in hospital.

Dr. Macdonald seems to have been particularly fortunate with ovarian residue. After a prolonged trial in a large number of cases, we were forced to discard it because of the absence of results.

Finally, Sir, I cannot end this letter without warning Dr. Macdonald to avoid applying forceps through an os "three parts dilated," especially in placenta praevia: he is courting disaster.—I am, etc.,

BETHEL SOLOMONS,
Master, Rotunda Hospital.

Dublin, Aug. 13th.

PREVENTION OF TUBERCULOSIS OF BOVINE ORIGIN.

SIR.—Some important conclusions emerge from the discussions reported from the Sections of Diseases of Children, Tuberculosis, and Public Health, at the recent Annual Meeting of the British Medical Association.

1. That the elimination of tuberculous animals from dairy herds is impracticable. (Savage, *Journal*, August 3rd, p. 203.)
2. That in spite of recent preventive measures (13,800 cows were slaughtered in 1928), there is still a widespread infection of the milk supply with tubercle bacilli in some areas. (McNeil, *Journal*, August 3rd, p. 194.)
3. That such infection, rather than decreasing, is slightly increasing. (McNeil, Kay Menzies.)

Answers to questions in Parliament have indicated:

4. That probably nearly 2,000 infants die of bovine tuberculosis each year, and that several millions sterling are expended annually in the treatment, convalescence, and after-care of the survivors.

It would appear that the strictly logical method of stamping out the source of bovine tuberculosis in cattle is likely to prove economically impossible, involving as it does frequent inspections and the slaughter of many animals. Moreover, the grade A and certified milks are priced far beyond the pockets of the poorer classes, who suffer from the maximum incidence of the disease.

The practical deduction must be that the problem of prevention must be approached from a different angle. All milk supplied to infants and young children should be sterilized. At present this is accomplished by two methods: pasteurization; and drying. One process exposes the milk to heat for at least thirty minutes; the other, at any rate the roller process of drying milk, takes only three seconds. The advantages of the short exposure are that very little damage, if any, is done to the vitamin C or to the soluble calcium, both of which have been shown to suffer from the prolonged method of pasteurization (Daniels and Stearn).

If a national policy is to be adopted for the prophylaxis of bovine tuberculosis, it is time that the expensive and unpractical method of attempting to eliminate tuberculosis in cattle was shelved. But before adopting the measure of employing sterilized milks, care should be taken to select a process of sterilization which involves the least damage to the essential elements of the foodstuff. It

would be disastrous if, in avoiding the Scylla of bovine tuberculosis, shipwreck should happen after all on the Charybdis of scurvy and rickets.—I am, etc.,

Bristol, Aug. 11th.

FRANK BODMAN, M.B., M.R.C.S.

ULCER-CANCER OF THE STOMACH.

SIR,—In a leading article in the *Journal* of August 3rd (p. 209) there is a reference to my observations on the frequency of ulcer-cancer of the stomach, but the figure quoted, 6 per cent. of cases of cancer showing microscopic evidence of previous ulceration, is incorrect. My most conservative estimate in this connexion was between 15 and 16 per cent. (vide the *Proceedings* of the Cancer Congress, London, 1928). It was approximately 6 per cent. of excised ulcers which showed evidence of commencing malignancy—a very different matter.—I am, etc.,

Sligachan, Skye, Aug. 10th.

M. J. STEWART.

"ACTIVATED" FLUORESCIN IN THE TREATMENT OF CANCER.

SIR,—Much more evidence—theoretical, experimental, and clinical—seems to me to be needed before a new "cure for cancer" can be accepted in "activated" fluorescein. All substances "fluoresce" or give off "characteristic" radiations when bombarded with x or gamma rays, in a series corresponding with their atomic numbers; these rays are very "soft"—that is, they penetrate only a millimetre or so of water or tissue. That any substance has yet been found to be useful in "intensifying" treatment (as an "intensifying" screen intensifies diagnostic rays) remains to be proved, though many substances have been tested with this aim (copper, silver, arsenic, iodine, lead, potassium, etc.).

There are so many points open to question in the article published in the *British Medical Journal* of August 10th (p. 233) that I for one remain sceptical as to sodium fluorescein being to any practical degree the much-hoped-for treatment "intensifier." Dr. Mottram's experiments *in vitro* with sarcoma tissue are of interest, but his results, so far as they go, cannot be carried over to tumours in the patient with rapidly changing body fluids.

One surely might have expected some more definite physical, experimental, and clinical proofs that "these rays . . . exhibit a potent lethal action on malignant cells"—more, that is, than any other ionizing rays produced in the tissues—and that "the actual rays which are employed to kill the cancer cells are neither x rays nor radium rays, but a totally different ray, the nature of which is not quite certain, but is most probably a ray near the ultra-violet line of the spectrum" (Dr. Claude Goulesbrough, *Daily Mail*, August 15th). But we have no such proofs afforded us. On the contrary, we have a number of confused and apparently erroneous statements. May I refer to a few?

1. What proof is there that fluorescein gives off specially strong secondary radiations (as with light rays) with only medium treatment x rays and the very hard gamma radium rays—not fluorescing with soft or very hard x rays?

2. If the "fluorescein rays" were all-important, and the x rays and radium rays were comparatively inactive, why was such a large dose of x rays given as a three-pastille dose (half-distance scale)? The statements that a "mild dosage" was given, a "three-quarters pastille" dose (skin scale), must lead many to think that only small x -ray doses were needed, whereas full erythema doses were given, and repeated three times at weekly intervals—in all, very large x -ray doses.

3. How is this to be reconciled with statements that the use of the fluorescein reduces the quantity of radium required?

4. Details of the eight cases of "apparent recovery" would be interesting; the "clinical details" refer chiefly to the first case treated, for which I see two explanations alternative to that adopted: it is impossible to irradiate equally a convex area 7 by 5 inches from a tube in one position, and newer or more actively growing parts of a tumour often respond more quickly to irradiation than the older areas.

5. All the conclusions (a) to (e) follow equally well from adequate irradiation treatment apart from fluorescein.

The healing of ulcers may perhaps to a slight degree be accelerated by simultaneous treatment with fluorescein, brilliant green, or other substances; and any substance

so used may be heralded as a "new ray" used in cancer treatment. But to deny the efficacy of three full erythema x -ray doses within three weeks, and repeated, with "four to six months' continuous treatment," and then to claim that the results depend on a new "unknown ray" (and even when this ray is localized in the skin painted over a large tumour), seems to me to belong more to the realm of magic than to that of scientific treatment.—I am, etc.,

London, Aug. 17th.

J. H. DOUGLAS WEBSTER.

POST-VACCINAL ENCEPHALITIS.

SIR,—In the *British Medical Journal* for August 17th (p. 324), Dr. Poston raises the question of an epizootic encephalitis amongst rabbits. It is an interesting fact that in May, 1918—that is to say, when the epidemic encephalitis of that year was abating and the great influenza epidemic that commenced formally in the June was brewing up—an account was given in the *Globe*, by Mr. Edmund Hallett of Hendon, of an "epidemic amongst rabbits" which had cost him then recently the loss of many young rabbits. Mr. Hallett inclined to the "belief that some form of paralysis attacks the head of the animal."

It is to be hoped that the atmosphere of prejudice which in 1918 attended and surrounded the discussion of so many subjects may gradually become as much clearer in medicine as in other spheres, and that the relation between epidemics and epizootics of influenza and encephalitis will be seen sanely and whole.—I am, etc.,

London, W.1, Aug. 17th.

F. G. CROOKSHANK.

PHYSIOLOGICAL STUDY OF ASTHMA.

SIR,—It is a matter for regret that Dr. Eric Holmes, in his letter in your issue of August 18th (p. 324), does not mention what he considers is the true explanation of the asthmatic paroxysm instead of merely affirming that there were no grounds at present for the views I had advanced and explained in my letter of July 27th, as though my arguments were not worth answering.

But Dr. Holmes tells us that Drs. Brodie and Dixon "were dealing, not with clinical asthma, but with an experimental condition which resembled it very closely indeed. They would probably not deny, in theory, the possibility of rhythmical contraction and dilatation playing a part in the clinical condition . . . quite satisfactorily accounted for by other and directly observable factors." Now the essence of my one criticism is that the laboratory conditions were so different from the conditions of a patient in asthma that, however correct the interpretation of the experimental factors, as such, these factors do not apply to the clinical conditions, and do not satisfactorily account for the clinical conditions.

The view I hold is not "the possibility of rhythmical contraction and dilatation playing a part" only in the clinical condition, but that they alone quite satisfactorily account for the clinical condition, while continuous bronchial spasm cannot do so.

It is just thirty years since I put forward my clinical interpretation of the respiratory phenomena in an asthmatic paroxysm, and after Dr. Holmes's letter I was glad to read afresh the original contribution of Drs. Brodie and Dixon published four years later, but still find no sufficient grounds for altering my views after an inspection of the tracings. As Professor Dixon is still away from home in South Africa, I may be forgiven if I prefer to await his return to meet any argument he may do me the honour to advance against my interpretation of the clinical factors at issue.—I am, etc.,

Bristol, Aug. 19th.

PATRICK WATSON-WILLIAMS.

CARE OF THE UNMARRIED MOTHER.

SIR,—I was much interested in Dr. R. A. Gibbons's plea for the unmarried mother (August 10th, p. 276). In York there is a sheltering home run by the district branch of the Diocesan Association for Preventive and Rescue Work. There are many maternity cases among the women and girls admitted to this home. Each is given ante-natal care until the time for her confinement approaches. Meanwhile arrangements have been made for her admission