rest, physiotherapy, balneotherapy, and myocrisin. Ten injections of myocrisin were given whilst he was an in-patient, and the course was to be completed by his private doctor after discharge. Immediately after the twelfth injection, in February, 1947, he developed a massive generalized exfoliative dermatitis involving almost the whole of his skin surface. The total dosage of myocrisin given by then was 0.86 g. He was readmitted to hospital on June 3, when it was found that there had been a dramatic improvement in his arthritis; he now had no obvious manifestations of the disease, and the corrected suspension stability had improved from 58% in the first hour on the previous admission to 92%. However, a generalized exfoliative dermatitis involved the whole of his body, including scalp and face, associated with severe itching.

He was admitted for the third time on Oct. 21, when his general condition was found to be unchanged. His dermatitis had become more chronic: very little skin surface was not involved, and there were large areas of induration, especially over parts subject to pressure and where he had scratched himself. BAL therapy was started on Oct. 24 and concluded on Nov. 21, a total of 56 ml. having been given. There was no marked improvement until Oct. 30, when the itching ceased completely and the exfoliation was noticed to be less severe. The condition steadily improved, the rash gradually disappearing and the areas of induration becoming softer. On Dec. 1 only pinkish discoloured patches remained, and these were confined to those parts where the dermatitis had been most severe and the induration maximal. There were no complications during the treatment. Corrected suspension stability in the first hour was 83% at the beginning of treatment and 88% on Nov. 28.

Discussion

In these two cases the effect of BAL on gold dermatitis was dramatic. This was particularly so in Case 2, in which the condition was very severe and had existed for nine months before treatment was started. No other case of over three months' standing relieved by BAL can be found in the literature, and in one case of three months' standing the dermatitis proved resistant to BAL (Ragan and Boots, 1947).

The occurrence of inflammation at the site of injection is of interest. Similar complications have been reported (Lockie, Norcross, and George, 1947), but in view of the striking relief of symptoms it is not felt that this is an indication for stopping treatment.

An interesting point emerging from both these cases is the time interval of six days after institution of treatment before improvement began. No such regular period has been noted in other reports.

Frequent blood counts, corrected suspension stability estimations, and urine examinations were done, but no significant change was noticed during the course of treatment. There were no complications except the inflammatory reaction in the buttock already described.

Ragan and Boots (1947) suggest that after relief of dermatitis by BAL, symptoms of rheumatoid arthritis previously improved by aurotherapy might recur within a month. No such change has yet been noted in these two cases. Both have now been under review for four weeks. In Case 1 the fall in corrected suspension stability after treatment was stopped was not considered significant from this point of view, because of the associated inflammatory complication.

Summary

Two cases of dermatitis due to aurotherapy treated by BAL are described, one of a more chronic type than any so far described in the literature.

The type of preparation of BAL and its method of administration are detailed.

The complications are discussed.

The return of symptoms of rheumatoid arthritis after therapy has not been noted in these cases.

The same time interval of six days between institution of treatment and relief of symptoms occurred in both cases.

I should like to express my thanks to Dr. J. B. Bennett for kindly allowing me to treat these cases, and to Dr. G. D. Kersley and Dr. H. J. Gibson for their encouragement and help in preparing this paper.

REFERENCES

- Cohen, A., Goldman, J., and Dubbs, A. W. (1947). *J. Amer. med. Ass.*, **133**, 749.
Collins, D. H., Gibson, H. J., Race, J., and Salt, H. B. (1939). *Ann. rheum. Dis.*, **1**, 333.
Lockie, L. M., Norcross, B. M., and George, C. W. (1947). *J. Amer. med. Ass.*, **133**, 754.
Peters, R. A., et al. (1947). *British Medical Journal*, **2**, 520.
Ragan, C., and Boots, R. H. (1947). *J. Amer. med. Ass.*, **133**, 752.
Slot, G., and McDonald, A. D. (1947). *British Medical Journal*, **2**, 773.

"AMELLIN" FOR DIABETES

BY

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"Amellin," an extract of *Scoparia dulcis* (broom), has been claimed by Nath¹⁻⁷ to have an important therapeutic action in diabetes. A critical study of his papers gives no clear evidence of this; indeed, the reasoning is so widely divergent from current views on carbohydrate metabolism as to be an argument against his thesis. However, since amellin appears to have inspired some credence in India it seemed desirable to give it a trial.

In two cases this was done, and the results, after careful investigation, show no effect of this substance on diabetes. Some details are here recorded of one case without and another with insulin. Both patients were supplied with a mixture of amellin, calcium gluconate, and lactose, and were instructed to take a measured 5-gr. (0.32-g.) dose by mouth thrice daily for three months.

Case 1.—A factory worker aged 57 was found to have diabetes in May, 1946, but before this trial had received no treatment other than restriction of his daily carbohydrate to 180 g. The blood sugar had gradually fallen from 348 mg. per 100 ml. at the onset to 144 mg. per 100 ml. in November, 1946. Thereafter his diabetes became progressively worse, so that heavy glycosuria and hyperglycaemia (blood sugar, 252 mg.) were constant by July 2, 1947. Insulin was obviously necessary at this stage, but was withheld in order to test amellin. After three months of treatment with this drug his weight had fallen by 1½ lb. (680 g.), traces of ketone bodies accompanied his glycosuria, and the blood sugar was 348 mg. per 100 ml. His general health had declined to a state comparable to that at the onset of his disease. When protamine-zinc-insulin, only 16 units daily, replaced amellin, his weight rose by 3½ lb. (1.59 kg.), the urine became sugar-free, and the blood sugar four hours after breakfast was 206 mg. per 100 ml., while his general health showed the usual improvement.

Case 2.—A Civil Servant aged 47, who in the course of a routine medical examination in 1938 was found to have diabetes, had since the inception of treatment kept detailed records of his tests and progress. When amellin was begun on June 2, 1947, his urine contained large amounts of sugar by reason of his low renal threshold, but ketones were absent and the blood sugar five hours after his single mixed daily dose of 24 units of protamine-zinc with 12 units of soluble insulin was only 46 mg. per 100 ml. The soluble insulin was reduced by 4 units and amellin started with no alteration in his daily carbohydrate. On Sept. 3, 1947, after three months of amellin, the urine showed traces of ketone bodies with heavy glycosuria, the blood sugar four hours after insulin was 125 mg. per 100 ml., and his weight had fallen by 7 lb. (3.18 kg.). His previous records

showed comparable variations, and it was obvious that amellin had not made the slightest difference to the closely studied pattern of his progress.

This test was undertaken on the suggestion of Dr. R. D. Lawrence and Prof. F. G. Young at the request of the Medical Research Council and the (then) India Office. Acknowledgment is due to Prof. M. C. Nath for his kindness in supplying a sample of amellin for the test.

REFERENCES

- ¹Nath, M. C. (1941-2). *Sci. and Cult.*, 7, 572.
- ²— (1943). *Ann. Biochem. exp. Med.*, 3, 55.
- ³— and Banerjee, S. R. (1943). *Ibid.*, 3, 63.
- ⁴— and Chowdhury, N. K. (1943). *Ibid.*, 3, 121, 147.
- ⁵— (1944). *Ibid.*, 5, 11.
- ⁶— Chakrovorty, M. K., and Banerjee, S. R. (1943). *Ibid.*, 3, 107.
- ⁷— — and Brahmachari, H. D. (1945). *Ibid.*, 5, 102.

THE PRE-ERYTHROCYTIC STAGE OF HUMAN MALARIA, *PLASMODIUM* *VIVAX*

BY

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In the issue of *Nature* dated Jan. 24, 1948, Shortt and Garnham reported the finding of pre-erythrocytic forms of *Plasmodium cynomolgi* in the liver of *Macaca mulatta*. A more detailed description of the appearance of these parasites, as seen on the sixth and seventh days of the incubation period, was given later by Shortt, Garnham, and Malamos (1948). *P. cynomolgi* being so closely similar in its morphology and life-cycle to *P. vivax* of man, it was reasonable to infer that, at a corresponding stage of the incubation period of an infection the pre-erythrocytic stage would also closely resemble that of *P. cynomolgi*.

The affiliation to the London School of Hygiene and Tropical Medicine of the Ministry of Health's Malaria Laboratory at the Horton Hospital for Mental Diseases, Epsom, where malarial treatment of general paralysis is carried out as a routine, supplied the means of verifying this supposition, and suitable arrangements were made through Dr. G. Macdonald, Chairman of the Tropical Course Subcommittee of the Council of the London School of Hygiene and Tropical Medicine. As there was at the time no suitable patient about to undergo this treatment at Horton Hospital, we applied to the Bucks County Mental Hospital, Aylesbury. The superintendent, Dr. J. S. I. Skottowe, who had a patient requiring malarial infection by mosquito-bites, was glad to co-operate with us, and transferred the patient to Horton for treatment, at the same time obtaining his consent and that of his wife to the performance of a biopsy on the liver during the incubation period of the infection.

Infection of the patient was effected by feeding upon him, on two successive days, a large number of *Anopheles maculipennis atroparvus* mosquitoes infected with *P. vivax* and by the intravenous inoculation of isolated salivary glands of a certain number of the same mosquitoes. Seven days after the first feeding by mosquitoes a biopsy was performed on the liver under local analgesia by Mr. E. J. Radley Smith. The material, when examined in sections, revealed the presence of plasmodial masses studded with chromatin particles very similar in appearance to those previously seen in the case of infection of the monkey with *P. cynomolgi*. The forms seen measured up to 42 μ

in diameter and showed in some instances the vacuoles noted in the case of *P. cynomolgi*.

There seems no doubt that these bodies are the pre-erythrocytic forms of *P. vivax* in man. The material in our possession is being studied and further observations will be communicated when completed.

In recording this finding we wish to express our indebtedness to Dr. Skottowe for his help in obtaining a suitable patient requiring treatment by mosquito-induced malaria; to Dr. W. D. Nicol, superintendent, Horton Hospital, for admitting this patient and for making all the arrangements for our investigation; and to Mr. E. J. Radley Smith, who performed the biopsy of the liver. The technical operations connected with this investigation were most efficiently carried out by Messrs. W. Cooper and E. Blackie, and Misses Wall, Stedman, and Maryon.

REFERENCE

- Shortt, H. E., Garnham, P. C. C., and Malamos, B. (1948). *British Medical Journal*, 1, 192.

Medical Memoranda

Allergy to Penicillin

The personal experiences outlined in the following case report may be found of interest.

CASE HISTORY

The patient, a general practitioner aged 34, had a personal and family history of migraine, and a family but not personal history of hay-fever. On May 8, 1947, he fractured the neck of the femur. Open reduction was carried out under general anaesthesia on May 12, and reduction in imperfect position was maintained by a Smith-Petersen "pin." Convalescence was interrupted by 20 to 25 stitch abscesses between June 1 and Sept. 1. A keloid scar developed. He had a fixed flexion of 35-40 degrees and a nocturnal pyrexia of 99.8° F. (37.7° C.) throughout. There was a leucocytosis of only 10,650. On Oct. 10 radiographs gave no evidence of bony union, and the condition was unaltered. Comparative radiographs showed possible bone abscess in the great trochanter. The "pin" had not shifted. From Oct. 21 to 25 inclusive he was given 500,000 units of penicillin intramuscularly three times a day (total 7,500,000 units). There was no history of previous penicillin therapy.

The immediate results of penicillin therapy were: pyrexia abolished, fixed flexion reduced to 10 degrees, regression of keloid scar, great diminution of pain, and general condition much improved. There was no change in this encouraging state (except that a radiograph on Nov. 11 showed the first sign of callus) until Nov. 12 (17 days after cessation of penicillin therapy), when he was awakened at 4 a.m. by irritation of the left eyelid. During the day general simple urticaria developed, with lesions up to 4 cm. square. Next day the condition was the same. Very little of the body was unaffected. "Benadryl" in full dosage was given without benefit. The temperature was 99.6° F. (37.55° C.), and the pulse 100. On the 14th the swelling was less of the cutaneous and more of the subcutaneous tissues ("angioneurotic oedema" or Quincke's disease). Adrenaline hydrochloride in doses of 5, 5, 8, 10, 10, and 15 min. (0.3, 0.3, 0.5, 0.6, 0.6, and 0.9 ml.) was given at intervals, with no benefit. The temperature was 99.8° F. (37.7° C.), and the pulse 90-110. Two "antistin" tablets were given thrice daily on the 15th and 16th, with no benefit. Oliguria and dysuria were present.

On the 17th periarticular swelling of various joints (large and small) occurred. Each lesion lasted about 36 hours after a precipitate onset. No benefit was derived from 1/2 oz. (14 ml.) mist. sod. salicyl. two-hourly. The temperature was 99.2° F. (37.3° C.), and the pulse 90. He had epigastric discomfort and diarrhoea. "Anthisan" was tried without effect.

In addition intermittent oedema of fauces, glottis, and tongue occurred from Nov. 18 to 21, and from the 19th to the 24th asthma and paroxysmal rhinorrhoea occurred intermittently by day and night. This was relieved by ephedrine 1 gr. (65 mg.), by mouth. He had considerable pain in the hands and feet and severe pruritus all over the body, especially on a change of temperature. His temperature was still 99.2° F. The pulse was steady except during asthma.

In view of dermatographism and the obviously "vascular-permeability" nature of the residual symptoms a course of 20 mg. of vitamin K (synthetic) twice daily was started on Nov. 28. Whether by coincidence or not, the pruritus ceased immediately and there were no further joint lesions.

I would like to thank Sir Arnold Stott and Dr. P. J. W. Milligan for their care and sympathy during the above troubles.

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