

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.

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THE PRE-ERYTHROCYTIC STAGE OF HUMAN MALARIA, PLASMODIUM VIVAX

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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.

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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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