it, may be taken without producing any glycosuria. The temperature tends to be subnormal and the pulse to be slow and of low tension. The metabolic rate was frequently found by Plummer to be as much as 25 per cent. below normal. The sexual power is diminished and there may be impotence in the male and sterility in the female, with atrophic changes in the external genital organs. The skin is soft, cool, and smooth. Polyuria occurs in some cases and so diabetes insipidus has been attributed to a deficiency of the posterior lobe, but recent investigations by Houssay and Leschke indicate that this malady is due to a lesion of the tuber cinereum rather than of the hypophysis itself. It is, however, to be remembered that the hypodermic injection of 1 c.cm. pituitrin every day or two often controls the polyuria for the time being, as a single dose has reduced the amount of urine passed in twenty-four hours from 13,000 c.cm. to 1,800 c.cm. the next day. It was naturally hoped that pituitary extract would be able to supply the missing hormones and remove the symptoms in these cases just as thyroid extract does so promptly in myxoedema. Some improvement does follow the administration of two or three grains of the whole dried gland several times a day. Cushing has found 12 grains three times a day necessary in one case to produce an improvement. The results have so far been disappointing, and clearly indicate that we are still unable either by oral or subcutaneous administration of pituitary extract to make good the loss of the special hormones secreted by this gland. Apart from these cases pituitrin has proved to be of service in raising blood pressure in cases of shock or heart failure and in stimulating peristalsis in inertia of the bowel. In obstetric practice also, as a uterine stimulant it is a powerful though sometimes dangerous therapeutic agent. It may be given subcutaneously in doses of 10 to 30 minims, or in the treatment of shock it may be added to an intravenous saline injection.

SUPRARENAL GLAND.

The normal suprarenal gland cannot be detected by physical methods of examination or by x-ray examination, and only tumours of these glands may be large enough to be palpable during life. Disease of the gland can therefore only be detected by a consideration of the symptoms which occur when the normal functions are changed by alterations in their structure or functional activity. The cortex and medulla have different functions. The medulla produces adrenalin, which has been shown by Langley and Elliott to be a powerful stimulant of the sympathetic system. The cortex is probably concerned with the development of the genital system. These glands, like those we have already considered, may undergo changes which lead either to excessive activity, on the one hand, or to loss of function on the other. We know very little of the results of overaction of the chromaffin tissue of the medulla with excess of adrenalin in the blood, though it has been suggested that it may be a factor in the production of the high blood pressure associated with granular kidney and other conditions. The overactivity of the suprarenal cortex which occurs in certain cases of hypernephroma in early life leads to a rare and interesting condition of precocious sexual development associated with somnolence. Destructive lesions of the suprarenal glands, most commonly due to tuberculous infection, cause the symptoms of Addison's disease, which are characteristic in the fully developed malady, but difficult to recognize in its incipient stages. The progressive asthenia, gradual fall of blood pressure, and pigmentation of the skin, and especially of the mucous membrane of the mouth, are the most helpful early signs of suprarenal failure. The treatment of suprarenal insufficiency is unsatisfactory, as we cannot as yet replace the lost function by the use of suprarenal extract in any known form, administered either by ingestion or injection, and I have not seen any definite improvement following this treatment in Addison's disease. Cases of recovery have been recorded, but it is possible that the symptoms have been due to loss of one suprarenal gland and have disappeared owing to compensation by the other gland. In a recently recorded case of recovery it was ultimately found that the symptoms had been due to a destructive lesion of one suprarenal gland. The value of adrenalin as a therapeutic agent is so well known that it is only necessary to mention its powerful local action in

arresting haemorrhage from the skin and mucous membrane by causing constriction of the blood vessels, and its useful action in stimulating the heart and raising blood pressure when given intravenously in shock or in the collapse of toxic conditions. Liq. adrenalini hydrochlor. may be given subcutaneously in doses from $\text{m} \frac{1}{2}$ up to $\text{m} \times$ for the relief of spasmodic asthma with marked benefit. Professor J. N. Langley has found that adrenalin also relaxes the oesophagus, and suggested to me several years ago that it would be well to try it in cases of spasmodic stricture. In adopting this suggestion the adrenalin has been given by the mouth, in the hope that its local action on the oesophagus would relax the spasm, so as to avoid the frequent repetition of hypodermic injections. In two recent cases of oesophageal spasm under my care at the Manchester Royal Infirmary the administration of $\text{m} \times \text{v}$ of adrenalin solution in half an ounce of water five or ten minutes before each meal has had a striking effect in relaxing or preventing the spasm, so that the patients were able to take their food without difficulty.

REFERENCES.

- ¹ *Lancet*, May 4th, 1912, p. 1188. ² *Endocrinology*, vol. iv, No. 1, p. 7. ³ *BRITISH MEDICAL JOURNAL*, March 13th, 1920. ⁴ *Acromegaly*, by Leonard Mark. ⁵ *Arch. Radiol. and Electrotherap.*, 1920, 24, 261.

A FATAL CASE OF MALIGNANT TERTIAN MALARIA CONTRACTED IN THE NORTH OF ENGLAND.

BY

ERNEST E. GLYNN, M.D., F.R.C.P.,

PATHOLOGIST, ROYAL INFIRMARY, LIVERPOOL; PROFESSOR OF PATHOLOGY, UNIVERSITY OF LIVERPOOL;

AND

J. C. MATTHEWS, M.B. CANTAB., M.R.C.P.,

ASSISTANT PHYSICIAN, ROYAL INFIRMARY, LIVERPOOL.

(From the Thompson-Yates Laboratory, University of Liverpool.)

The following preliminary note of a fatal case of malignant tertian malaria contracted in the North of England is recorded:

M. B., a girl typist, aged 18, a resident in Liverpool, was admitted in a moribund condition to the Royal Infirmary, Liverpool, at 4.30 p.m., October 12th, 1920, under the care of Dr. J. C. Matthews. The only history obtainable at the time was the following: The patient had been seriously ill for a few days; on account of delirium her doctors thought she might have meningitis. After a slight haemorrhage, apparently from the vagina, she was also seen by a gynaecologist, who diagnosed metrorrhagia, and, finding her profoundly anaemic and unconscious, sent her to hospital.

On admission the patient, a poorly developed girl, was in *extremis*, unconscious, blanched but not jaundiced, and pulseless. The temperature was 102.6°. There was no evidence of meningitis, nor of the exanthemata. She died two hours later.

The *post-mortem* examination was made twenty hours after death. Blood anaemic. Brain: apparently normal, no meningitis. Lungs: a moderate amount of oedema and mucopurulent bronchitis. Heart: weight 8 oz., normal, no fatty degeneration. Mouth: healthy, no trace of pyorrhoea. Oesophagus, stomach, and intestines opened from end to end—normal, no evidence of blood. Some of the lumbar lymphatic glands slightly enlarged, and red like haemolymph glands. Liver: weight 3 lb., slightly browner than normal, no haemosiderin reaction. Spleen: 1 lb. 7 oz., retains its shape, of normal consistency, but dark, rather like malaria. Pancreas, suprarenals, kidneys and bladder normal. Uterus: normal size, but menstruating; one haemorrhagic corpus luteum. Bone marrow of the shaft of the femur a uniform terra-cotta red,* that of the sternum redder and more succulent than normal.

The salient features of the *post-mortem* examination were therefore the anaemia, the greatly enlarged spleen, and the marked erythroblastic reaction of the bone marrow. The patient's friends, who had very reluctantly granted the necropsy, demanded the death certificate before it was finished so as to obtain an order for burial before the registrar's office closed. A provisional diagnosis was therefore considered. There was no evidence of leucocythaemia—the spleen in particular was too small for the

* The colour closely resembled that shown by Carnegie Dickson in the transverse section of the bone marrow of the femur from a case of pernicious anaemia (Plate XI, Fig. 2). It was not so dark as the marrow from a case of acute streptococcal septicaemia (Plate XI, Fig. 1, W. E. C. Dickson, *The Bone Marrow*, Longmans Green and Co., London, 1908).

myeloid variety,* and the absence of greatly enlarged lymphatic glands negatived the lymphatic variety. The spleen was too small and not tough enough for splenic anaemia; besides, in our experience fatal cases of this disease are so rare, that there have only been three *post-mortem* examinations upon it in the Royal Infirmary during the last twenty years; all were adults and all were associated with cirrhosis of the liver.†

Therefore, to suit the convenience of the relatives, the death certificate was signed as "pernicious anaemia," but it was definitely stated in the *post-mortem* room that the macroscopic absence of fatty degeneration of the heart and of free iron in the liver, also the presence of a greatly enlarged spleen, made this diagnosis very unsatisfactory.‡ Though the spleen was noted to be "dark rather like malaria," the possibility of this disease was dismissed.

Films were next made of the blood; the spleen, portions of liver, and bone marrow were removed for further examination. The bone marrow was first investigated; a smear treated with alcohol and ether and stained by the Leishman method was found to contain pigmented parasite-like bodies. This was immediately shown to Dr. Blacklock and Professor Stephens of the Tropical School, who made a provisional diagnosis of malaria from the presence of pigment and of organisms resembling crescents. The blood films and smears of the spleen were next examined, and Professor Stephens found numerous segmenting malignant tertian parasites. An attempt was at once made to obtain portions of the brain,§ but the body had already been removed for burial.

At subsequent examinations of additional material numerous crescents were found in the bone marrow and a moderate number in the spleen and blood smears. Sections of the liver and spleen showed a moderate amount of melanin and numerous malaria parasites. The liver contained a minute trace of haemosiderin. The spleen was absolutely engorged with blood; there was no fibrosis. A differential count of a *post-mortem* blood film showed 10 per cent. polymorphs, 28.2 per cent. lymphocytes, 61.4 per cent. mononuclears, 0.4 per cent. eosinophiles—500 white cells examined. During this count 19 normoblasts but no megaloblasts were seen. The erythrocytes were deficient in haemoglobin; there was slight poikilocytosis, but no anisocytosis, and no polychromatophilia, nor punctate basophilia (J. C. M.).

Clinical History.

An investigation of the patient's past history was then undertaken by Drs. Blacklock and Matthews, and the following facts elicited:

The patient was born in Liverpool, and lived in the same house in the town for ten years. She was rather anaemic and liable to headache. She had not worked for about eight weeks—there was no necessity for her to work, and she was not very strong. On September 14th five or six teeth were removed under ether; there was little haemorrhage. On September 25th she went with her brother to a North of England health resort; though pale she was apparently active and well. On September 27th she spent part of the day in a valley which was subsequently found by Dr. Blacklock to harbour large numbers of hibernating larval and adult anopheles mosquitoes. On September 29th she vomited once, but next day was apparently well, and went for a long walk. On October 1st she arrived home flushed and ill. For the next two days she remained in

* The average weight of the spleen in five consecutive necropsies at the Royal Infirmary on adults with myelogenous leukaemia was 92 oz., the minimum being 48 oz.

† The average weight of the spleen in these three cases of splenic anaemia (Banti's disease) was 73 oz., the minimum being 35 oz.

‡ The average weight of the spleen in ten consecutive necropsies upon adults with "pernicious" anaemia was 7½ oz.; the two maxima being 14½ and 13½ oz., and the minima 4 and 3 oz.; in every case there was a marked haemosiderin reaction in the liver and extensive fatty degeneration of the left ventricle, and the bone marrow of the shaft of the femur showed, when examined, an erythroblastic reaction.

§ In view of the importance of this case it seems advisable to state that I have only made one other examination upon a fatal case of malaria—namely, the following: On October 23rd, 1915, a sailor, aged 35, from an unknown port, with no clinical history, was brought into the hospital moribund and died immediately. At the *post-mortem* examination the cerebro-spinal fluid was pale yellow. There were small brownish-red subpial haemorrhages, one in particular about three-quarters of an inch in diameter on the superior surface of each cerebral hemisphere; small punctiform haemorrhages were also present on the dura mater of the anterior fossa. Sections of the brain showed that the capillaries were loaded with malaria parasites. Professor Stephens confirmed the diagnosis of cerebral malaria. The spleen was 11b. 9 oz., firm and dark chocolate colour. The liver 3½ lb. very dark brown. A microscopic section of both organs showed considerably more melanin pigment than was present in the girl. The bone marrow of the femur was yellow, slightly tinged with red. If there had been any obvious macroscopic changes in the brain of the girl they would have been noticed. (E. E. G.)

bed, vomiting occasionally. On October 4th she went to see a doctor. During the ensuing three days she was apparently better. On the 7th she felt faint. On the 8th, while walking in the street, sudden faintness came on; she asked a passer-by to take her home, and the doctor was sent for. She went to bed feeling very thirsty, but her head was clear. On the 9th she vomited; she became slightly delirious, got up, fell on the floor, and had to be carried back to bed; she said she could not move her legs. On the 10th she complained of very severe headache with photophobia, and was unconscious at intervals. On the 11th she was worse, and the haemorrhage occurred from the uterus. Her temperature, taken for the first time, was found to be 100°. On the 12th she was removed to hospital. At no time during the illness did she complain of shivering or sweating; there was apparently no diarrhoea, but there is some evidence that no urine was passed during the last two days of life.

This clinical history is consistent with a first attack of malignant tertian malaria of the pernicious type and algid variety.

The illness apparently lasted thirteen days. The absence of cellular hyperplasia and of fibrosis of the spleen and the comparatively small amount of melanin pigment in it, suggest an infection of recent origin; the absence of any obvious macroscopic lesion in the brain confirms this conclusion. On the other hand, the size of the spleen—namely, 23 oz., or 644 grams—suggests a subacute infection. Ross quotes Kelsch and Kiener, who "state that in eighty autopsies they found the weight to vary from 400 to 1,500 grams, and to average 914 grams (chronic malaria)." James, however, points out "that great splenic enlargement is a feature of many of the cases which occur in children of simple tertian malaria in England"; though our patient was not a child, she was only 18.

The development of the erythroblastic reaction of the bone marrow is remarkably rapid, but Carnegie Dickson shows a coloured drawing of the femur from a case of pneumonia of five days' duration in which nearly all the yellow marrow has been replaced by red marrow (Plate IX, Fig. 1.)

The Place of Infection.

Dr. Blacklock found no mosquitos in the house where the patient lived. She was, however, accustomed to walk in one of the parks and country round Liverpool, in which district anopheles mosquitos occur. A full account of the parasites, of the histology and of the mosquito survey, together with a discussion of certain problems connected with this case, will be published subsequently by Dr. Blacklock in the *Annals of Tropical Medicine and Parasitology*.

Malaria in England.

James (1920) refers to the special inquiry into indigenous malaria. He states that 330 cases occurred "from September, 1917, to the end of 1918—38 in the navy, 224 in the army, and 68 in civilians." The most northerly case occurred in Grimsby. "In 1918 about 85 per cent. of the cases were detected during August and September." He further "states that all the locally contracted cases of malaria so far reported in this country have been infections with the benign tertian parasite," also that "no death occurred." A few cases of malignant tertian have been noted in France. Lastly, he states that "among the civilians who contracted malaria in England between 1917 and 1919 no fewer than 75 per cent. were children." It appears, therefore, first, that the patient contracted the disease either about or beyond the reported northern limit of indigenous malaria in England; second, that it is the first case recorded in recent years in England of indigenous *malignant tertian* malaria, and of *fatal* indigenous malaria. It is very probably not the only case of malignant tertian malaria which has recently occurred in England.

Other "Foreign" Diseases Contracted at Home.

It is interesting to observe that other infective diseases besides malaria* are now recognized to develop not infrequently at home, which were formerly thought to be practically confined to foreign, particularly tropical, countries. Perhaps we may be allowed to refer to our own recent experience, which doubtless agrees with that of others.

1. *Paratyphoid Infections*.—The agglutinative capacity of the blood of 40 uninoculated civilian hospital patients

* Malaria, of course, was once endemic in England; and there has been a recrudescence of it owing to the war.

suffering from "enteric" (?) was recently tested. In 15 there was no agglutination; 20 gave evidence of a pure typhoid infection, but 5 gave evidence of a pure paratyphoid B infection. Further, in two other cases of acute pleural effusion in civilians, paratyphoid B bacillus was isolated from the exudate.¹

2. *Bacillary Dysentery*.—This was formerly thought to be confined to asylums, yet Flexner Y bacillus was isolated from a boy with acute diarrhoea, and from two out of 504 healthy recruits in a training camp; Shiga's bacillus was isolated from the spleen of a woman who had always lived in Liverpool, and who died of puerperal sepsis, but was found *post mortem* to have chronic ulcerative colitis.²

3. *Amoebic Dysentery*.—Fifty-nine patients in an English asylum suffering from acute dysentery were examined for protozoa, "in 3 cases vegetative *Entamoeba histolytica* were found in the stools."³

REFERENCES.

¹ J. H. Abram and E. E. Glynn: *Lancet*, 1919, vol. ii, p. 283. ² E. E. Glynn, Vera Foley, Mary Price, A. L. Robinson, E. M. Berridge: Special Report Series, No. 7, Med. Res. Com., 1918, pp. 57, 103. ³ S. P. James: *Malaria at Home and Abroad*, Bale, Sons and Danielsson, London, 1920. ⁴ R. Ross: *The Prevention of Malaria*, Murray, London, 1910, p. 128. ⁵ A. Malins Smith: *Ann. Trop. Med. and Parasitol.*, 1919, July, vol. xiii, No. 2, p. 177.

MINER'S NYSTAGMUS: SUGGESTIONS FOR ITS PREVENTION.

BY

D. LECHMERE ANDERSON, L.R.C.P. AND S. EDIN.,
D.P.H.,

MEDICAL OFFICER OF HEALTH, DONCASTER.

SOME suggestions I made to Mr. T. H. Mottram, C.B.E., Divisional Inspector of Mines for the York and Midland Division, with the object of reducing the amount of miner's nystagmus in our coalfields, were embodied by him in his annual report for 1919. Further inquiry has strengthened my opinion that the only way to eliminate the "grave," or what might be termed "compensation," cases of miner's nystagmus is by some such method as therein outlined, and, as the outcome of an informal conversation with Dr. J. S. Haldane, I have endeavoured to state the case somewhat more fully in the following article.

The importance of removing the personal factor in the causation of the disease has been somewhat overshadowed by concentration of thought and effort on removal of the external exciting factors. Inquirers have centred their researches on questions of posture and illumination; that is, attempts have been made to eliminate nystagmus by improving the conditions in the mine instead of preventing the man who is predisposed to the disease from entering the mine.

No man the refractive condition of whose eye is normal will develop miner's nystagmus to such an extent as to incapacitate him from following his employment as a miner. Of this I am persuaded from investigations among men suffering from miner's nystagmus in the Doncaster area.

Astigmatism is by far the most frequent predisposing cause of miner's nystagmus, and the greater the degree or the more marked the abnormality, the more susceptible will the subject be when exposed to the exciting factors of this disease. A subject with mixed astigmatism in oblique meridians will almost certainly develop the disease when exposed to the conditions of a collier's life. Simple refractive errors, myopia and hypermetropia, also act as predisposing causes, though to a much less degree.

Most observers are agreed that ametropia is the rule in cases of miner's nystagmus. Various authors have published figures ranging from 90 per cent. downwards, but my experience has led me to believe that unless nystagmus is associated with ametropia it will not be so grave in type as to incapacitate a miner from following his occupation. Severe nystagmus may, of course, be due to the other known causes of the condition, such as affections of the cerebrum or cerebellum, diseases of the labyrinth, sclerosis cerebri, etc.

Age as a Factor in the Production of Miner's Nystagmus.

In my series of cases the highest age incidence was 40 to 44, as shown in Table I; the explanation is that physio-

logical changes are then occurring in the lens resulting in presbyopia. This imposes an additional strain upon the neuro-muscular mechanism concerned in accommodation and convergence. Given, then, that there exists an error of refraction as mentioned above, the disease will be particularly prone to manifest itself at the age of presbyopia. That this should be so lends support to the theory that an error of refraction is an essential factor in the production of the disease.

TABLE I.—Age Incidence of Miner's Nystagmus; showing Number affected in Five-yearly Age Groups.

Age 20-24	...	...	...	...	...	3
25-29	...	...	...	...	...	3
30-34	...	...	...	...	...	10
35-39	...	...	...	...	...	16
40-44	...	...	...	...	...	24
45-49	...	...	...	...	...	19
50-54	...	...	...	...	...	16
55-59	...	...	...	...	...	8
60-64	...	...	...	...	...	2

Length of Colliery Life as a Factor.

Length of life as a collier bears no direct relation to the incidence of miner's nystagmus. It is not a matter of surprise that miners who have a long record of life underground should have a high incidence of nystagmus, as shown in Table II. As presbyopia increases so does its influence as a factor in the production of nystagmus when the eye is ametropic; and the greater the abnormality of refraction the greater the influence.

TABLE II.—Showing duration of Work in Collieries in Five-yearly Groups and Number of Men with Nystagmus.

1 to 5 years	...	...	...	...	...	2
6 to 10	...	...	...	...	...	4
11 to 15	...	...	...	...	...	9
16 to 20	...	...	...	...	...	12
21 to 25	...	...	...	...	...	12
26 to 30	...	...	...	...	...	19
31 to 35	...	...	...	...	...	16
36 to 40	...	...	...	...	...	11
41 to 45	...	...	...	...	...	5
46 to 50	...	...	...	...	...	2
51 to 55	...	...	...	...	...	1

Heredity as a Factor.

Other observers have found a hereditary history of nystagmus in as many as 20 per cent. of their cases. In my opinion it is not nystagmus that is hereditary, but the refractive error. Similar errors of refraction are commonly found in parents and children. What more natural, then, than that with the transmission of an error of refraction there should be associated a tendency to miner's nystagmus? The latter disease is thus not in itself hereditary, but the refractive errors—the personal predisposing causes of miner's nystagmus—are markedly so.

Classification of Causes.

The chief factors which result in the production of miner's nystagmus are thus:

Predisposing.

1. *Errors of Refraction*.—These, when associated with the conditions of a collier's work, may result in miner's nystagmus at any age period. When this occurs in early life the astigmatism present is usually severe in type or abnormal in character.

Exciting.

(a) *Presbyopia*.—This has a marked influence upon ametropic eyes in the production of nystagmus when associated with the conditions peculiar to coal miners' work.

(b) *Defective Illumination, etc., in Coal-mining Work*.—This in itself cannot create "grave" miner's nystagmus in an emmetropic eye.

If we accept the theory that refractive errors are the main predisposing causes of the affection we should exclude men who have certain types of ametropia from following the occupation of a miner. In the great majority of employments the eyesight of young persons has to be tested before commencing work. This ensures correction of errors of refraction, whereas the eyesight of the collier is seldom if ever examined or corrected until the onset of disease renders it imperative. It is easy to understand how, in a man affected with uncorrected ametropia, the defective lighting of a coal mine and the posture at work would impose an additional strain upon the ocular muscles.