part of the body could be detected. It is therefore necessary to consider other possible causes of fat embolism.

Apart from fractures, widely recognized causes of fat embolism are severe contusion, deep laceration of skin, severe burns, operations on adipose persons, and forceful orthopaedic manipulations (Strauss, 1933). Concussion as a causative factor has been recognized for 70 years (Robb-Smith, 1941a), and its significance has been stressed also by Silverstein and Konzelman (1940), but it should be remembered that most of the evidence is of an experimental nature (Strauss, 1933). The claim made by Robb-Smith (1941a) that blast alone may cause fat embolism has not been confirmed by subsequent authors (Zuckerman, 1941), but, if found, it should be regarded as a complication.

Convulsions and violent exertion during certain types of psychoses such as delirium tremens are occasionally mentioned as a possible cause of fat embolism (MacCallum, 1936), but the fact that fractures are more often produced by epileptic convulsions than was known in the past tends to qualify the significance of these older views. We were unable to trace any reference to this point in modern neurological treatises. One of us (A. M.) has investigated five brains from epileptics dying suddenly during or after convulsions. In four of these he failed to find fat emboli in the bodily organs, including the brain. Occasionally intravascular substances staining light pink with Sudan and usually not occupying the whole lumen of the vessels were encountered. They were also found, however, in other conditions, including carbon monoxide poisoning and tuberculous meningitis. These lipoidal substances, whatever their significance may be, are not likely to be of an embolic nature. It is possible, however, that they may have been confused with fat emboli by earlier investigators. Only in one case of death after epileptic convulsions was true fat embolism of the lung and, to a lesser degree, of the systemic circulation found. This was in a patient suffering from lipoidosis of the Hurler type (gargoylism)*. The liver and spleen were enormously enlarged, and contained an abundance of fatty substances, which may have been an important facilitating factor, just as the danger of fat embolism is increased in operations performed on adipose persons.

Opinion is still divided on the role of the blood lipoids in the formation of fat emboli. The most fully substantiated instance of haemic origin appears to be alkali poisoning (Robb-Smith, 1941b), followed by either hyperlipaemia or lipoproteolysis. Macfarlane, Oakley, and Anderson (1941) were able to produce *in vitro* free fat from blood to which *Cl. welchii* toxins had been added. Winkelman (1942), surveying previous experimental evidence, seems to favour the haemic hypothesis in view of the presence of large amounts of fat in the lungs and brain following mild injury or fracture of the smaller bones of the body, which are not likely to release a supply of free fat sufficient to cause widespread embolism. It is interesting that hypercholesterolaemia occurs in a large proportion of cases submitted to electrical convulsion treatment as well as after spontaneous convulsions (Katzenelbogen, Baur, and Coyne, 1944).

At the present stage of our knowledge it is impossible to say which of the factors surveyed above has been operative in our case. Although there was no evidence of a fracture of bone or contusion or laceration of other fat deposits of the body, it must be admitted that an unobtrusive mild fracture or any other of the common sources of fat embolism might have been overlooked. So far, this case should be regarded as an exceptional complication of electrical convulsion therapy.

In reporting the above case it is not our intention to point out any increased risk associated with this form of shock treatment. It is well, however, in future post-mortem investigations of sudden and unexplained death after electrical convulsion therapy, to keep the possibility of fat embolism in mind, particularly if a fracture has been produced. One of us (D. T.) has made a previous observation of death produced by electric shock treatment: the patient was a female schizophrenic aged 42. During the first treatment a current of 130 volts, lasting 0.3 second, was given after lesser applications had failed to produce a convulsion. The fit lasted 58 seconds. After 3

hours the patient was still unconscious. At intervals until she died, 19½ hours after the fit, she almost regained consciousness. At the necropsy no injuries, burns, or fractures were found. There was acute pulmonary oedema throughout the lungs. The liver was slightly fatty, the uterus was absent, the meninges were congested, and the brain was macroscopically normal. No histological investigation was carried out.

The absence of a free interval before the onset of the terminal symptoms militates against the diagnosis of fat embolism in this case, although atypical cases have been recorded. Excessive vago-vasomotor stimulation (the second group of Alexander and Löwenbach, 1944) might be an alternative explanation.

Summary

A case has been described in which sudden death after electrical convulsion therapy was caused by cerebral fat embolism.

Neither a fracture nor any of the other recognized causes of fat embolism were found post mortem. Other possible causes of fat embolism have been considered, but no final decision is justified at the present moment. The problem calls for special clinical and pathological attention in similar cases.

We wish to thank Mr. J. W. Hulme, Assistant Deputy Coroner, Southern District, County of London, and Mr. H. G. Broadbridge, Coroner for the Western District of Middlesex, for permission to publish the case. We are also indebted to Dr. J. H. Ewen, medical superintendent, Springfield Hospital, and Dr. C. Friedman for additional clinical data. The histological slides and photomicrographs have been prepared by Mrs. E. Beck.

REFERENCES

- Alexander, L., and Löwenbach, H. (1944). *J. Neuropathol. exp. Neurol.*, **3**, 139.
 Alpers, B. J., and Hughes, J. (1942). *Ibid.*, **1**, 173.
 Ebaugh, F. G., Barnacle, C. H., and Neuburger, K. T. (1943). *Arch. Neurol. Psychiat.*, Chicago, **49**, 107.
 Katzenelbogen, S., Baur, A. K., and Coyne, A. R. M. (1944). *Ibid.*, **52**, 323.
 MacCallum, W. G. (1936). *Textbook of Pathology*, Philadelphia and London.
 Macfarlane, R. G., Oakley, C. L., and Anderson, C. G. (1941). *J. Path. Bact.*, **52**, 99.
 Napier, F. J. (1944). *J. ment. Sci.*, **90**, 875.
 Nielsen, J. M., and Ingham, S. D. (1940). *Bull. Los Angeles neurol. Soc.*, **5**, 130.
 Nightingale, G. S., and Meyer, A. (1940). *J. ment. Sci.*, **86**, 819.
 Robb-Smith, A. H. T. (1941a). *Lancet*, **1**, 135.
 — (1941b). *Proc. roy. Soc. Med.*, **34**, 639.
 Silverstein, A., and Konzelman, F. (1940). *Confin. Neurol.*, **3**, 129.
 Strauss, H. (1933). *Zbl. ges. Neurol.*, **66**, 385.
 Winkelman, N. W. (1942). *Arch. Neurol. Psychiat.*, Chicago, **47**, 57.
 Zuckerman, S. (1941). *Proc. roy. Soc. Med.*, **34**, 171.

PELLAGRA IN A MORPHINE ADDICT

BY

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Quite apart from those areas where it is endemic and due to inadequacy of the local diet, or where it is associated with alcoholism (Deeny, 1942), pellagra has been recorded in a variety of conditions interfering with digestion and absorption. It is not uncommon in chronic psychotics and in cases with peptic ulcer—classes of patient who may limit their diet voluntarily. Cases in which morphine appears to have been the chief factor are rare (Bean, Spies, and Blankenhorn, 1944). We therefore record the following instance.

Case History

The patient, the widow of a medical practitioner, was said to have been a morphine addict for 12 years. She took the drug in the form of 1/3-gr. tablets hypodermically—at one time as many as 20 a day. Latterly she had taken only 12 a day. In one particular week she had taken 200 tablets. The usual amount was about 100 a week. She also took large quantities of aspirin. There was a history of dyspepsia but no radiological evidence of peptic ulcer, and it is certain, in view of her behaviour, that her frequent complaints of pain were efforts to obtain morphine.

Since the addiction developed she had taken little food. She ate no vegetables and little fruit. Occasionally she ate a lamb chop, but no other meat, no milk (except in coffee), and no eggs. Her diet consisted almost exclusively of white bread and butter, a little cheese, a little bacon, tea, and marmalade. She became very thin, in contrast to her former plumpness.

She had had attacks of diarrhoea at intervals for three years. These were controlled "only by morphia." She had had brown patches on her skin off and on for years, and used to be distressed

* This case will be published in full, together with two other cases affected by the same condition.

about their unsightliness. They did not irritate, and they showed the usual seasonal variation. Since taking morphine she had been very moody—easily excited, then depressed. She rarely went out, and often made scenes—screaming, etc.—when the morphine allowance was finished. Her son dreaded coming home. She was admitted to the observation unit, St. Alfege's Hospital, on Aug. 7, 1941. She was pale, and the typical brownish branny patches on her skin stood out in contrast. In general the exposed areas were pigmented. There were particularly well marked pigmented patches over the manubrium sterni and nape of the neck, disposed "neck-lace" fashion, also on the backs of the fingers, wrists, and insteps. Her tongue was pale and very smooth. There was no fur, despite the poor appetite and the fact that she had taken so little food before admission. Her blood pressure was 110/70. There was gross oedema of the ankles.

All tendon-jerks were absent. The patient said that they had been absent for years. She did not display the classical pellagrous dementia. Cerebration was quick and fairly accurate. She was hypochondriacal, and would resort to any device, from violence to wheedling, to get morphine. She was very self-centred. The blood Wassermann reaction and Kahn test were negative. A barium meal showed evidence of "gastritis" (thickening of rugae), with poor gastric tone and some initial delay followed by rapid emptying. No ulcer was demonstrated.

Progress.—The patient remained at St. Alfege's Hospital for 11 days, improving considerably and putting on weight. She had been extremely emaciated, with deep-sunken eyes, but at the time of her transfer had filled out considerably. No morphine was given, and after the first day no sedatives, although her craving persisted and she became very depressed when refused the drug. However, she soon became more reasonable and co-operative, and was willing to discuss other subjects than sedatives. On Aug. 18 she was transferred to Bexley Hospital, where a blood count showed Hb 44%, R.B.C. 2,430,000, C.I. 0.9. The patient was given large doses of iron and liver extract. Subsequent blood counts were as follows: Sept. 23—Hb 48%, R.B.C. 3,390,000, C.I. 0.71; Dec. 3—Hb 88%, R.B.C. 5,000,000. She was given nicotinic acid in 50-mg. doses six times daily, and thiamine in 50-mg. doses twice daily subcutaneously to a total of 1.8 g. Shortly after transfer she collapsed and was very ill for a few days. On recovery from this attack her physical improvement was progressive. She developed a ravenous appetite. There was at first no mental improvement, but four months after the beginning of treatment the mental state also changed for the better, and by mid-January, 1942, she had improved strikingly. She was quick, lively, cheerful, and took an active interest in her surroundings and in plans for her future. She was much less pale and the branny patches had become less evident. She was able to get about well and had put on much weight. There was still some oedema of the ankles on exertion. She was discharged home on Feb. 7, 1942.

When visited 16 months later the patient was active, able to walk several miles, and could do her housework; but unfortunately she had not co-operated in out-patient treatment, and was receiving no vitamin concentrates. She had deliberately restricted her diet on account of dyspepsia, and was taking only the small priority ration of eggs and milk which she was allowed, together with a very little bread-and-butter. She again had slight oedema of the ankles and branny patches on face, neck, arms, wrists, and hands; and her memory, especially for names, was poor. She declared that she was not taking morphia or alcohol.

Discussion

It is clear that in this case, as in most cases of vitamin deficiency, there was evidence of shortage of more than one essential factor (Sebrell, 1940). The main pellagrous picture is attributable to a nicotinic acid deficiency, but the polyneuritis and the cardiovascular disturbance suggest a thiamine lack, and the anaemia may have been due to a shortage of iron or of pyridoxine (vitamin B₆; Unna, 1940). The exact mechanism of causation cannot be determined with certainty, but the principal factor was probably the apathy and loss of appetite induced by morphine addiction.

The effect of morphine on digestion and absorption is complex. The secretion of digestive juices is diminished (Douthwaite, 1932; Edwards and Gunn, 1941), but the effect of this reduction is counterbalanced by a subsequent increase in the gastric secretion and by the fact that the food remains longer in the stomach and intestine. Thus there is no reduction in absorption attributable to the direct action of morphine. It does not therefore appear that direct disturbance of digestive function by the drug can have been a prominent factor in the production of pellagra.

A further possibility is suggested by the work of Shideman and SeEVERS (1941), which indicates that chronic morphine addic-

tion and thiamine deficiency both produce the same sort of metabolic defect (characterized by a reduction of the normal increase in oxygen output from muscle following addition of pyruvate and co-carboxylase *in vitro*). Ellinger, Hassan, and Taha (1937) noted that dehydrogenases are inhibited by narcotics. This would not account for the pellagrous features of the above case, but might be partially responsible for the development of polyneuritis and oedema. The tendency, after cessation of therapy, to relapse without a return of the morphine addiction does not eliminate any of these possibilities, since, on the one hand, permanent metabolic changes may have been caused by the prolonged habituation to morphine, and, on the other, her diet after discharge was probably inadequate.

Summary

A case of pellagra in a long-standing morphine addict is discussed. There were also polyneuritis and anaemia. Great improvement occurred with treatment, followed by relapse on cessation of therapy. Loss of appetite due to morphine was thought to be the cause of the pellagra. (The possibility that morphine may disturb metabolism more directly is considered.)

Our thanks are due to Dr. Eli Davis, deputy medical superintendent, St. Andrew's Hospital, Bow, for his help in diagnosis and treatment of the patient and for his assistance in the compilation of this report.

REFERENCES

- Bean, W. B., Spies, T. D., and Blankenhorn, M. A. (1944). *Medicine*, Baltimore, 23, 1.
Deeny, J. (1942). *British Medical Journal*, 1, 157.
Douthwaite, A. H. (1932). *Hale-White's Materia Medica*, p. 295, London.
Edwards, C. W., and Gunn, J. A. (1941). *Cushny's Pharmacology and Therapeutics*, p. 384, London.
Ellinger, P., Hassan, A., and Taha, M. M. (1937). *Lancet*, 2, 755.
Sebrell, W. H. (1940). *J. Amer. med. Ass.*, 115, 851.
Shideman, F. E., and SeEVERS, M. H. (1941). *J. Pharmacol.*, 71, 390.
Unna, K. (1940). *Ibid.*, 70, 400.

MALARIA EPIDEMICS AT EXCEPTIONALLY HIGH ALTITUDES IN KENYA

BY

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Malaria in tropical and subtropical countries is usually thought to disappear once a certain altitude is reached, though the accepted "safe" height varies from place to place. Six thousand feet is usually regarded as the upper limit. Manson-Bahr (1941) quotes figures for Abyssinia which indicate that the transmission of malaria in that country ceases at 6,600 feet, though doubtful records exist of cases of benign tertian malaria at Addis Ababa at 8,175 feet. Schwetz (1942) in a review of the African literature gives limits up to 5,000–6,500 feet.

Hitherto in Kenya Colony malaria was thought to be absent from places above 7,000 feet. In June, 1941, a small farming community at Londiani (7,500–7,800 feet) was suddenly stricken by a severe epidemic of the disease. On 12 of the 14 farms at least one European became infected between June and August, and on every farm cases of malaria were numerous among the African labourers. Blood slides taken from 35 ill Africans (of non-immune tribes, and long resident in the district) were examined, and 27 showed malaria parasites. Twenty-six of these infections were *Plasmodium falciparum*, and one was *P. vivax*. This represented only a small sample of the total number of cases. The European infections were malignant tertian with the exception of a single case of benign tertian.

The Londiani district (75 miles from the provincial centre, Kisumu) comprises a small township with an Indian bazaar and native location surrounded by European farms extending for a radius of about 12 miles. There was also at the time of the outbreak a large military camp sited at Londiani. Bordering the farms there are extensive areas of forest reserve in which live African squatters numbering several thousands. The epidemic particularly affected the farms and the military camp, though in the latter many of the cases may have been relapses from infections contracted elsewhere. It is interesting to note that little malaria occurred in the isolated huts of the forest squatters.

The epidemic came to an abrupt end in August, 1941. Smaller outbreaks occurred in 1942, 1943, and 1944, at the same season.