manufacturing area would present its own problems of organization, but in a congested area such as Birmingham a considerable proportion of the factory population could be included.

The prevention of deafness is an important factor in the nation's health. An ear-treatment service based on the factory is a feasible method, causing the minimum interference with the productive capacity, of arranging treatment for a part of that section of the community of great importance to the economic wealth of the country.

Summary

Chronic ear diseases, in particular chronic suppurative otitis media, are potent causes of inefficiency, invalidism, or early death. Experience during the 1939–45 war showed that disease of the ear was a serious cause of wastage of man-power. The high incidence of this disease is largely due to inefficient treatment resulting from the absence of an ear-treatment service adapted to the economic needs of the population.

Before and during the last war many industrial concerns set up medical departments to safeguard the health of the employees and to treat minor injuries sustained at work. This report gives an account of otological work carried out in seven factory medical departments over a period of eighteen months, with the object of ascertaining (*a*) the incidence of suppurative otitis media in factory workers and (*b*) the results of treatment of ear disease in the factory medical department.

To determine the incidence of ear disease in the factory population 1,902 employees, selected at random, were examined. Of these, 3.3% were found to be suffering from suppuration in the middle ear and 17.8% had active or healed middle-ear disease.

A total of 1,711 patients complaining of ear, nose, or throat symptoms were examined at clinics set up in the factory medical department: 389 were found to be suffering from disease of the pinna and external auditory meatus, and 274 from chronic suppurative otitis media. The effect of otitis media in the causation of deafness and the results of treatment are considered in detail.

From the results of treatment it is deduced that, if 100 patients with unilateral chronic suppurative otitis media receive a full course of conservative treatment in a factory medical department for an average period of 5.2 weeks, 38 will have a dry ear at the end of treatment and will keep dry for at least six months after its termination, 45 will have a dry ear at the end of treatment but will relapse in less than six months (although standing a good chance of cure with subsequent treatment), 6 will be rendered quiescent, and 11 will need a surgical operation. The results show that conservative treatment will result in cessation of infection in a high proportion of cases, but the prospects of obtaining a lifelong cure are poor. It is concluded that a surgical operation does not offer an effective alternative method of treatment in all cases.

The effects of deafness and pain on the working capacity of the factory employees are discussed. It was found that in manual workers productive efficiency was affected more by pain than by deafness but that the latter may be a handicap to promotion.

The future expansion of otological treatment in factory medical departments on a permanent basis is discussed, and it is concluded that such a scheme is feasible, is adapted to the needs of the working population, and would reduce the present overloading of the hospital services.

I am indebted to Mr. Terence Cawthorne for his advice throughout the investigation; to Dr. Donald Stewart for advice on industrial medicine and for providing the link with industry; to Mr. C. S. Hallpike for help in the preparation of this paper; to the following industrial medical officers—Dr. J. G. Billington, Dr. E. H. Capel, Dr. J. G. Lawson, Dr. W. Jeaffreson Lloyd, Dr. W. A. McClennan, Dr. N. G. Marr, and Dr. A. White—for their help in the organization of an ear-treatment service; to the directors of the following organizations—Austin Motor Co., Ltd., James Booth & Co., Ltd., Birmingham Small Arms Co., Ltd., General Electric Co., Ltd., Guest, Keen, and Nettlefolds, Ltd., Imperial Chemical Industries, Ltd., and Joseph Lucas, Ltd.—for their co-operation in the investigation; and to the nursing staffs of the above-mentioned organizations for undertaking the treatment of patients.

VITAMIN D IN TREATMENT OF BOECK'S SARCOIDOSIS

BY

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Besnier–Boeck–Schaumann's disease, commonly known as Boeck's sarcoidosis, is now recognized as a diffuse reticulo-endotheliosis with the formation of a folliculoid tissue affecting particularly the lymphoid and haemopoietic tissues. The organs most commonly involved are the lymph nodes, spleen, lung, bone marrow, liver, eyes, and, in 50% of cases, the skin.

The skin lesions, when present, tend to cause considerable disfigurement, and hence from the patient's point of view constitute the main problem of the disease, which in other respects tends to be a benign condition without pain and systemic upset, and which progresses very slowly over a number of years. The skin lesions are of two types: (1) A symmetrical granulomatous condition affecting chiefly the nose, cheeks, ears, and fingers, described by Besnier in 1889 under the name lupus pernio. (2) Multiple granulomatous swellings of varying size affecting chiefly the face and upper limbs and having a translucent appearance. To these lesions Boeck in 1897 gave the name of cutaneous sarcoids.

It is clear that the skin lesions closely resemble tuberculous lupus vulgaris. Indeed, without a skin biopsy it is often difficult or impossible to separate the two conditions.

The resemblance to tuberculosis is not confined to the skin lesions, and in recent years many writers have speculated on the possibility of sarcoidosis and tuberculosis being variants of the same disease. The following points provide good reason for such speculation: (1) The basic pathological lesion in sarcoidosis, the sarcoid follicle, consists of endothelioid cells and a zone of lymphocytes just as in the tubercle follicle. There is, however, no caseation, and the presence of tubercle bacilli cannot be demonstrated. (2) The distribution of the disease process in sarcoidosis—i.e., in the reticulo-endothelial system—is essentially the same as in tuberculosis. (3) The development of active tuberculosis is the commonest cause of death in sarcoidosis, but whether this is *post hoc* or *propter hoc* it is not possible to say.

The position has been adequately summarized by Cameron and Dawson (1946), who state that "while there is much against the idea of a tuberculous basis, notably the frequent absence of a positive Mantoux reaction, there are sufficient resemblances, clinical, radiological, and histological, to suggest a probable causal relationship." It may be that sarcoidosis is a low-grade tuberculosis of non-caseating type.

In view of the recent successful treatment of lupus vulgaris with calciferol it seemed possible that the skin lesions in sarcoidosis might react favourably to similar treatment and thus alleviate considerable aesthetic embarrassment in patients so afflicted. Care, however, was required in selecting suitable cases, since spontaneous improvement is a common phenomenon in sarcoidosis and this might be erroneously attributed to the administration of calciferol. Eventually one case was selected in which the lesions had been slowly progressing for a period of nine years and in which spontaneous improvement was not expected.

Report of Case

The patient, a single woman, came to the Royal Infirmary, Edinburgh, for the first time as an out-patient in 1938, when she was aged 43. Her past history was negative apart from a tendency to bronchitis. At that time she had a well-marked lupus pernio causing an erythematous induration of the nose,

cheeks, the forehead above the bridge of the nose, and a small area under the chin. There was considerable disfigurement. The process had started six years previously with nasal obstruction and discharge and a red patch on the left side of the nose which had gradually extended.

The "cutaneous sarcoid" element was also present in the form of raised indurated areas on the dorsal aspects of both arms above the wrists. In addition the fingers were markedly swollen and distorted and purple in colour, with breaking down of the nails of the most affected fingers. The toes showed similar but less severe changes. The rest of the skin surface was normal.

There was no clinical evidence of the other common manifestations of sarcoidosis, such as enlarged spleen, enlarged lymph glands, and uveoparotitis, but skiagrams of the hands and feet revealed the classical osteitis cystica changes. A skiagram of the chest showed prominence of the hilar shadows, which is typical of sarcoidosis, but there was no evidence of the more classical multiple nodular opacities in the lungs; there was also calcification of glands in the left hilum, indicating a previous tuberculous infection. The Mantoux test was negative, as would be expected in sarcoidosis. A skin biopsy was not done, since the diagnosis was not in doubt.

Between 1938 and 1947 the patient reported many times at the Royal Infirmary. Her general state of health remained excellent and she had no complaints apart from the disfigurement. Ultra-violet therapy and deep *x*-ray therapy did not improve the skin lesions. A photograph taken in 1943 is reproduced to indicate the appearance at that time (Fig. 1). In June, 1947, she was admitted with a view to instituting calciferol therapy. Fig. 2 demonstrates the state of the skin lesions before the administration of calciferol. The lupus pernio had become slightly worse since 1943, and a new patch had appeared on the upper lip. The fingers were also more involved, with ulceration of the skin in several areas. It is clear that the condition had been slowly progressing since the time of her first visit in 1938.

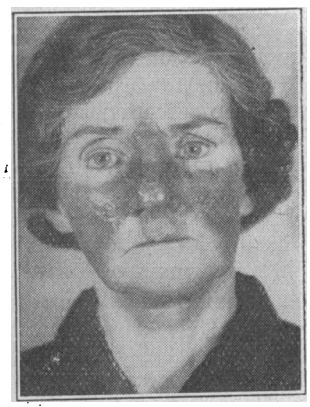

FIG. 1.—Showing the erythematous induration of the lupus pernio in 1943. The appearance was similar but less marked in 1938.

FIG. 2.—June, 1947, before calciferol therapy. The lupus pernio is more extensive and an additional patch has appeared on the upper lip.

Calcium metabolism was investigated for the first time, with the following results: serum calcium, 10.6 mg. per 100 ml.; serum phosphorus, 3.9 mg. per 100 ml.; alkaline phosphatase, 5 units (King); acid phosphatase, 3 units (King); calcium balance, normal. Hence, despite the radiological changes in the bones, there was no disturbance of calcium metabolism.

The B.S.R. was 3 mm. in 1 hour (Westergren), indicating the absence of rapid tissue destruction. Haemoglobin, red blood cell count, white blood cell count, and differential count were essentially normal. The blood urea was 47 mg. per 100 ml.

An interesting phenomenon was observed on performing a 1 in 1,000 Mantoux test. No reaction was visible after the customary 48 hours, but a definite strong positive was present after 72 hours. The same delay was found with 1 in 100 tuberculin. The previous Mantoux test, in 1938, was given as negative, but it might not have been observed for more than 48 hours. There is no mention in the literature of a delayed positive in sarcoidosis. It may be that this phenomenon has resulted in some cases being given as Mantoux-negative when in actual fact they are delayed positive.

Calciferol therapy was started with 100,000 units daily by mouth in the form of high-potency "ostelin" tablets. This was continued for 15 days (total, 1,500,000 units), when the appearance of violent toxic effects compelled stoppage of the drug. The toxic effects were similar to those reported by Dowling, Gauvain, and Macrae (1948)—namely, thirst and polyuria, constipation, headache, tiredness, loss of appetite, and sickness. There was no rise in the serum calcium, indicating once more that toxicity is not directly related to biochemical changes. The blood urea, however, rose to 60 mg. per 100 ml.

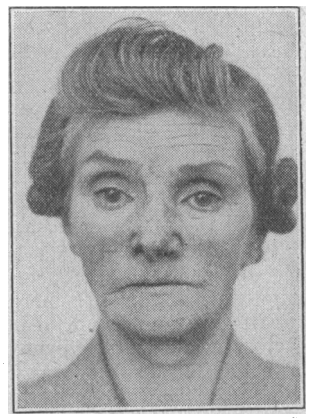

FIG. 3.—September, 1947, two months after cessation of calciferol therapy. Apart from residual deformity of the nose, the face is almost normal in appearance.

During the period of the toxic effects—three weeks—dramatic improvement occurred in the skin lesions. The erythematous induration of the lupus pernio largely disappeared and the patient no longer felt diffident about appearing in public. The gross lesions in the fingers did not improve to such an extent, but the swelling was reduced and the ulceration which had appeared in the last year cleared up. The slighter lesions of the toes also showed some improvement. It is interesting to note that the main clinical improvement occurred during the period of alarming toxic effects. When these had settled down calciferol was administered again in reduced dosage (50,000 units every second day), but the patient was still intolerant, and treatment was suspended after two weeks. Nevertheless the clinical improvement has been maintained (see Fig. 3).

Comment

It has been pointed out that, in the treatment of lupus vulgaris, calciferol may "flare up" a tuberculous lesion elsewhere (Dowling and Prosser Thomas, 1946; Dowling, Macrae, and Jones, 1946; Powell, Pearsall, and Wigley, 1948). This may also apply in sarcoidosis, since a radiological follow-up in the present case shows slight progression of the osteitis cystica changes during the period of improvement of the skin lesions. The radiological appearances in the chest have not altered, but the patient's bronchitic symptoms have become worse. In view of this unfortunate tendency calciferol should not be used in the treatment of sarcoidosis unless the skin lesions are of sufficient degree to justify the risk.

Peterkin (1947—personal communication) has found that, apart from "flaring up" a distant lesion, calciferol may cause extension and ulceration of the lupus pernio. It is interesting that in the present case during the first week of therapy the patient complained of tingling in the facial lesion and the erythema became more pronounced, thus giving rise to considerable anxiety. This is another risk which should be kept in mind when calciferol therapy is contemplated.

Summary

A case of Boeck's sarcoidosis is presented in which the skin lesions had been slowly progressing for nine years and in which, therefore, sudden spontaneous improvement was not expected.

The administration of calciferol in the form of high-potency ostelin tablets resulted in dramatic improvement of the skin lesions. The main improvement occurred during a three-weeks period of severe toxic effects unrelated to the level of serum calcium.

The relationship of sarcoidosis to tuberculosis is discussed. It may be that they are the same disease. The response of the skin lesions of sarcoidosis to treatment with calciferol resembles that of lupus vulgaris, this being another point in favour of a close relationship.

In view of the risks of "flaring up" a sarcoid lesion elsewhere and of causing sudden extension and ulceration of the skin lesions, calciferol should not be used in the treatment of sarcoidosis unless the skin lesions are extensive and disfiguring.

A delayed positive tuberculin reaction is described in sarcoidosis.

I am greatly indebted to Professor Charles Cameron for his advice and criticism and for the photographs taken in 1947. I am also indebted to the Department of Radiotherapy, Edinburgh Royal Infirmary, for the photograph taken in 1943. I wish to thank Dr. W. D. D. Small for permission to publish the case.

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ARSENICAL ENCEPHALOPATHY DURING TREATMENT OF TROPICAL EOSINOPHILIA

BY

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Prebble (1946) made an extensive survey of the literature on arsenical encephalopathy during treatment of syphilis and reported 187 cases of encephalopathy among Indian troops treated for syphilis as in-patients. He concluded that Indians are particularly susceptible to the condition.

He referred to a report by Glaser and Immermans on two non-fatal cases of encephalopathy which had received arsenic for conditions other than syphilis. Lees (1937) also observed this condition among cases of disseminated sclerosis and Hodgkin's disease after the administration of an arsphenamine product. Viswanathan (1947) reported the post-mortem appearances in a patient with tropical eosinophilia who developed encephalopathy after two 0.3-g. injections of neoarsphenamine. He, however, did not state whether syphilis was definitely excluded before treating the case as tropical eosinophilia. A further case of tropical eosinophilia in which encephalopathy developed after two 0.3-g. injections of neoarsphenamine and death occurred is described below.

Case Report

A Tamil mess cook aged 26 was admitted to 48 Indian General Hospital on Oct. 8, 1946, with a complaint of cough and breathlessness on exertion. The chest showed rhonchi all over it. A skiagram revealed changes associated with chronic bronchitis but no evidence of tuberculous infection. The total leucocytic count was 12,400 per c.mm., with 61% eosinophils—i.e., absolute eosinophilia of 7,564 per c.mm. The Wassermann reaction and Kahn test were negative. Tropical eosinophilia was diagnosed and 0.3 g. of neoarsphenamine was given on Oct. 24 and on Oct. 27. He complained of fever and shivering after the second injection, and became dull and apathetic on Oct. 30. The temperature rose to 103.8° F. (39.9° C.); a blood film showed no malaria parasites. He suddenly became restless and began to have convulsions on Oct. 31; later he became delirious and finally coma supervened. His respirations were stertorous, eyes fixed, pupils dilated, and the reaction to light was sluggish. There was no neck rigidity. Abdominal reflexes were absent, deep reflexes were exaggerated, and plantar response was flexor. Blood pressure was 150/85, blood urea 60 mg. per 100 ml. Blood films showed no malaria parasites and urine contained no sugar or acetone. Coma deepened, and he died within eight hours of the onset of acute symptoms. Necropsy was performed ten hours after death. All organs, except the central nervous system, lungs, and liver, were within normal limits.

Macroscopic Appearances.—The pia-arachnoid all over the brain was congested and meningeal vessels were full. Cerebral grey matter was hyperaemic, and small blood vessels in the white matter of both hemispheres were congested. The choroid plexus was very engorged. No haemorrhages were detected on the surface of the brain or on section. The pleural cavity contained no free fluid or adhesions. The lining membrane of the right and left bronchi was congested. Bronchioles were slightly dilated; their mucous membrane was congested, and they contained mucopurulent secretion. The lungs showed no evidence of bronchopneumonia on palpation or on section. The liver was normal in size, and the cut surface revealed no change.

Microscopical Appearances.—Brain:—Examination revealed lymphocytic infiltration of the perivascular spaces and of the substance of the brain tissue in the vicinity of the capillaries. The capillary endothelium was swollen. Liver cells showed fatty change and foci of necrosis infiltrated by lymphocytes. I have no record of the histopathology of the lung. Cerebrospinal fluid taken during necropsy showed the following findings: total cell count, 280 cells per c.mm.; type of cells, 95% mononuclears, consisting of lymphocytes, plasma cells, and endothelial cells; stained deposit, no organisms; protein, 180 mg. per 100 ml.; Nonne–Apelt reaction, positive 1; Wassermann reaction, one volume of a 1 in 5 dilution showed partial inhibition of lysis; with one volume of a 1 in 2.5 dilution, one volume of undiluted fluid, and two volumes of undiluted fluid lysis of cells was inhibited. The Wassermann test was carried out by Wyler's modification.

Comment

This case was diagnosed clinically as arsenical encephalopathy. Post-mortem findings did not show haemorrhages or demyelination — important characteristic features of arsenical encephalopathy according to earlier writers. Prebble (1946), however, reported that these features were observed in only one out of 40 patients whose brains were closely studied by Krainer at the Central Military Pathological Laboratory, Poona. Microscopical appearances of the brain tissue in my case were similar to those described by him in some of his cases. The disease process in the liver was not so advanced that it could have caused death, but it was very probable that the damaged liver cells delayed the metabolism of arsenic as suggested by Friedman and Shinefeld (1941).

During life the patient gave no history of syphilis or of lapsed treatment. He had been attached to the hospital as a mess cook for three years and had not sought admission to a special treatment centre for venereal diseases during that time; nor did he show any signs or symptoms of meningeal, cardiovascular, or parenchymatous syphilis during life. Microscopy of the brain tissue also did not reveal any evidence of syphilis. Lymphocytic infiltration of the perivascular spaces has been regarded as a general form of central nervous system reaction and is not indicative of any one pathological condition. The blood Wassermann reaction and Kahn test were negative four days before he was put on neoarsphenamine. Cerebrospinal fluid collected during necropsy, however, gave a positive