The evidence cited cannot be regarded as conclusive, as the cases were all seen after recovery from deafness, but it is highly suggestive of a close relationship between reversible deafness, aphonia, muscular weakness, increased nerve accommodation, and hypercalcaemia. It is perhaps relevant to note that other causes of "chemical deafness" are quinine, which is well known to block nerve conduction (Cooper, 1924), and analgesics such as salicylates and acetanilid (Macht, Greenberg, and Isaacs, 1919). The latter drug at least has been shown to depress muscle-nerve excitability (Macht, 1919). Hyperparathyroidism is rare and is usually diagnosed at orthopaedic clinics. It is hoped that this paper will stimulate interest so that the occurrence of deafness can be fully investigated before and after operation.

Summary

Disturbances of hearing are reported in five cases of hyperparathyroidism, and aphonia in one case.

In three cases these symptoms disappeared after removal of a parathyroid adenoma, and examination showed no defect of hearing.

Increased nerve accommodation, demonstrated in one case, is suggested as a possible cause of these symptoms.

The cases are reported so as to draw attention to an unusual cause of nerve deafness.

I wish to thank Professor Sir John McNee, Mr. Roland Barnes, and Mr. J. Hinton Robertson for permission to study their cases; Mr. A. M. Andrew, of the department of physiology, for the use of his stimulator; and Dr. J. C. McKinley for the audiogram in Case 1.

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The National Multiple Sclerosis Society has published a 32-page booklet on *Psychological Factors in the Care of Patients with Multiple Sclerosis*, written by M. P. Harrower and R. Herrmann. A brief summary of facts on the nature of the disease and its management in the U.S.A. is followed by a discussion on the personality of the patient, the psychological aspects of his relations with the doctor, and the psychological difficulties peculiar to those with disseminated sclerosis. The use of psychological testing in diagnosis and as an adjunct to therapy is described. Group therapy for patients and relatives is advocated; occupational therapy in the home is important, and rehabilitation centres are also of value. The booklet may be had free of charge from the Society at 270, Park Avenue, New York, 17, U.S.A.

SKIN LESIONS AND DEAFNESS IN DISSEMINATED TUBERCULOSIS

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Skin lesions which form part of a clinical complex produced by the dissemination of active foci of tuberculosis in various organs of the body are comparatively infrequent, so that when they are encountered their significance may be overlooked. Early recognition of these lesions is desirable when the tuberculous disease is chronic. When it is acute, skin involvement may provide the earliest means of identifying the nature of a disease in which prompt administration of appropriate treatment is of vital importance.

In the first four cases of disseminated tuberculosis reported below cutaneous lesions were either prominent presenting features of the disease or were or might have been of diagnostic assistance; and it is interesting that deafness was recorded in two of them. In Cases 5-8 abnormalities of the skin produced by subcutaneous tuberculous lesions were important clinical features, and increasing deafness was a presenting symptom in the only one in which the disease was of an overwhelming nature.

Case 1

A man aged 50 was admitted to Ruchill Hospital on March 21, 1951, with a diagnosis of erysipelas. He had been in another hospital from December 15, 1950, to January 29, 1951, with a left lower lobe pneumonia which had failed to respond to penicillin, but showed complete resolution clinically and radiologically after treatment with aureomycin. Subsequently he remained well until March 18, when he developed what he thought was a stye on the left upper eyelid; on the 19th the inflammation involved the peri-orbital skin, and later other cutaneous lesions developed on the back of the neck.

On admission to Ruchill Hospital he was moderately ill. His pulse was 80 and respirations 16. His temperature was normal on admission but rose a few hours later to 103° F. (39.4° C.) and continued swinging to 103-104° F. (39.4-40° C.) until death. He had a purplish swelling round the left eye, with numerous small papules and pustules in the affected skin. On the back and right side of the neck were several infiltrated bluish plaques with surrounding erythema and scaling and also numerous small papules and pustules. A linear, infiltrated purplish lesion on the right malar region and several small crusted papules on the front and back of the chest were seen. The tip of the spleen was just palpable. The urine contained a trace of albumin. Blood examination showed: leucocytes, 6,000 per c.mm. (polymorphs 44%, lymphocytes 46%). A chest x-ray film on March 28 showed marked right hilar enlargement; the lung fields were clear except for a calcified primary focus in the right upper lobe with associated calcification in the right paratracheal glands. Sputum examinations were negative for *Mycobacterium tuberculosis*. Penicillin was given on admission, followed by aureomycin, and, from April 4, streptomycin, 1 g. daily, but there was no response.

Repeated blood examinations during the illness showed a steady decline in the leucocyte count from 6,000 on admission to 1,000 per c.mm. a few days before death; the erythrocytes declined in that period from 3,200,000 to 2,100,000 per c.mm. The patient died on April 11.

Post-mortem examination revealed grossly enlarged, caseous, and necrotic right paratracheal glands. The adjacent right main bronchus was the site of extensive tuberculous caseation in which many tubercle bacilli were demonstrated. The left lower lobe showed only some post-pneumonic fibrosis. Sections of the liver, spleen, and sternal bone marrow showed numerous miliary necrotic foci, round a proportion of which was a feeble cellular response. The kidneys were apparently healthy. By mischance the affected skin of the neck was not histologically examined.

Case 2

A man aged 20 was admitted to Ruchill Hospital on April 13, 1952. About a month previously he had begun to feel lethargic, and for the past five days he had suffered from rigors, headaches, pains in the limbs, and nausea. Three days before admission a rash appeared. On examination he appeared seriously ill. His temperature was 101° F. (38.3° C.), pulse 100, respirations 20, and B.P. 120/75. Scattered over the distal parts of the upper limbs, buttocks, trunk, and back of the left ear were little papules about 10–20 mm. in diameter, surrounded by an area of erythema and topped by a crust. There were also a few bright-red petechiae on the forehead and behind the ears. The urine contained a trace of albumin. A blood count showed: erythrocytes, 4,300,000 per c.mm.; Hb, 12.6 g. per 100 ml.; leucocytes 8,400 per c.mm. (polymorphs 53%, lymphocytes 35%).

On April 14 penicillin treatment was begun, but the patient's condition began to deteriorate, and next day he became moderately deaf and little areas of faucial ulceration were noted; there was also a post-nasal discharge tinged with blood. He became irrational and incontinent on the 16th, and next day a fresh crop of petechiae appeared on the distal part of the limbs and a few on the trunk and face. It was observed that in a day or two the "petechiae" developed into little crusted papules of the type noted on admission. His temperature swung between 104 and 105° F. (40 and 40.6° C.). Streptomycin, 1.5 g. daily, plus P.A.S. was begun on April 17.

Histological examination of a skin-biopsy specimen taken on April 19 showed necrosis of surface epithelium and the upper part of the corium in ulcerated areas, but staining with Ziehl-Neelsen's method did not demonstrate acid-fast bacilli. The patient continued to improve somewhat, although the pyrexia continued, and by April 22 he was rational and no longer incontinent, and no more skin lesions had developed.

On April 17 a chest radiograph showed a circular lesion about 1.5 cm. in diameter in the right upper lobe and a similar lesion in the left upper lobe; the appearances suggested fibro-calcific quiescent pulmonary tuberculosis. Liver-function tests showed no abnormality, and the liver was not enlarged, but the biopsy of this organ on May 19 showed several granulomatous follicles with giant-cell systems, the appearances corresponding with tuberculosis. Pyrexia continued, the patient's condition deteriorated, and by June 2 he was semi-moribund; isoniazid, 8 mg. per kg. was then substituted for streptomycin. The improvement was dramatic: his temperature finally settled on July 16, he made a steady recovery, and has remained well.

During his stay in hospital attempts to culture *M. tuberculosis* from sputum, gastric washings, urine, and faeces were unsuccessful.

Case 3

A man aged 69 was admitted to Ruchill Hospital on April 19, 1951. For some time before admission he had lost weight and more recently had complained of anorexia. Three weeks before admission a slightly productive cough had developed, together with pain under the sternum. On admission his temperature was 101° F. (38.3° C.), pulse 80, and respirations 20. On the front and back of the chest

were a few dark-red macules and nine dull-red papules, some of which were surmounted by a crust. The lesions closely resembled acne vulgaris, but had appeared only about six weeks before admission. Physical examination was otherwise negative. Blood examinations showed: erythrocytes, 4,000,000 per c.mm.; Hb, 11 g. per 100 ml.; leucocytes, 4,600 per c.mm. (polymorphs 55%, lymphocytes 42%). Pyrexia continued, the temperature swinging between 101 and 102° F. (38.3 and 38.9° C.). A chest-film report on April 24 stated: "The right root is enlarged, but there is no intrapulmonary lesion. There is a healed primary focus at the right apex."

On April 27 a right pleural effusion developed. A chest-film report on May 4 stated: "There is now considerable thickening of the right pleura and some loss of volume of the right lower lobe. The right root remains enlarged. The appearance is now strongly suggestive of bronchial carcinoma." A biopsy of a skin lesion taken on May 4 showed giant-cell systems suggestive of tuberculosis. Streptomycin, 1 g. daily, and P.A.S., 20 g. daily, were started on May 13. On May 29 it was reported that *M. tuberculosis* had been cultured from pleural fluid received on April 27. Direct examinations and culture of sputum, bone marrow, urine, gastric washings, bronchial secretions, and materials from a skin lesion were negative for *M. tuberculosis*. The temperature settled on May 29, and no further skin lesions appeared. Streptomycin and P.A.S. therapy was stopped on July 13 after 67 g. of streptomycin had been given.

The patient left hospital against advice on August 11 and was readmitted in poor general condition on September 21. Apart from slow deterioration in his general condition, and extension of the disease in the right lung in spite of further streptomycin and P.A.S. therapy, there were no additional significant clinical features. He died on March 15, 1952.

Post-mortem examination revealed bronchopneumonic tuberculosis in the right lower lobe with a few areas of more chronic disease here and at the right apex. Areas of recent tuberculous caseation were scattered in the left lung. The right paratracheal glands were enlarged and caseous. Tuberculous pericarditis was noted, and the peritoneum was studded with numerous tuberculous foci. The liver was of normal size, but was riddled with large and small tuberculous abscesses; the spleen was similarly affected. The mesenteric glands were caseous. The kidneys were apparently healthy. Section of the bone marrow showed no abnormality.

Case 4

A woman aged 71 was admitted to Ruchill Hospital on December 21, 1952. She had been in excellent health until five months before that date, when dysphagia had occurred. Examination of the throat and a barium swallow in a general hospital had revealed no abnormality. Subsequently she complained of weakness, loss of weight, hoarseness, pain in the throat, and slight productive cough. About two months before admission her hearing, which had previously been good, steadily deteriorated until she became almost totally deaf. Dusky-red papules appeared in the skin and continued to do so in spite of penicillin.

On admission her temperature was 98.4° F. (36.9° C.), pulse 78, respirations 18, and B.P. 110/70. She was well built but had obviously lost a good deal of weight. She was intelligent, and, apart from almost total deafness, no abnormality was detected in the nervous system. The tongue, uvula, and pharynx were inflamed and ulcerated; the larynx could not be properly examined. The right cervical glands were enlarged. Nine dull-red papulo-necrotic lesions about 0.5–1 cm. in diameter were noted on the forearms, chest, and face. The tip of the spleen was palpable. Physical examination of the chest was negative, but radiography showed small areas of consolidation scattered in both lung fields. Blood examination showed: erythrocytes, 4,600,000 per c.mm.; Hb, 9.8 g. per 100 ml.; leucocytes, 7,600 per c.mm. *M. tuberculosis* was not detected on repeated direct microscopical examination of the sputum.

Biopsy of a skin lesion on December 22 was reported on as follows: "The ulcer base is composed of tuberculous granulation tissue with giant-cell systems, early caseation, and superadded acute pyogenic inflammatory change. Acid-fast bacilli are present." The patient died suddenly on January 4, 1953.

Post-mortem examination revealed numerous small areas of tuberculous disease in both lungs, especially numerous in the upper lobes and left lower lobe. The tracheo-bronchial glands were enlarged, but not caseous. No disease was apparent in the stomach, intestines, or liver, but the mesenteric glands were caseous. The spleen was studded with caseous foci, and miliary lesions were present in the left kidney. The right kidney was healthy.

Case 5

A man aged 57 was admitted to Ruchill Hospital on February 20, 1951. He had been in good health until about three weeks before admission, when he began to suffer from weakness, loss of appetite, and a cough which later produced a little sputum. About a week before admission he became deaf.

On admission he was seriously ill. The pulse was 80, and the respirations 20. His temperature was 98.4° F. (36.9° C.), rising in the evening to 102° F. (38.9° C.), and continued to swing until his death. Examination of the chest revealed slight impairment of the percussion note and fine crepitations over the right lower lobe. The liver edge was palpable two fingerbreadths below the costal margin. The patient was moderately deaf. Physical examination was otherwise negative. The urine contained some albumin and a few leucocytes; Fouchet's test for bile pigments was positive. A blood count showed: erythrocytes, 4,500,000 per c.mm.; Hb., 11.8 g. per 100 ml.; leucocytes, 4,000 per c.mm. (polymorphs 87%, lymphocytes 7%). Blood urea was 85 mg. per 100 ml., and a van den Bergh test gave a delayed direct reaction. X-ray examination on February 22 showed extensive consolidation throughout the right lung and in the left upper and mid-zones; the affected areas had a hazy rather than a solid appearance. Repeated sputum examinations were negative for *M. tuberculosis*.

On February 27 10 painless nodules about 20 mm. in diameter were felt in the subcutaneous tissues of the anterior abdominal wall, and two were noted on the anterior chest wall. A nodule was excised and sent for pathological examination; the report was as follows: "Histological examination shows skin in which there is much congestion of the arterioles in all layers, but no other abnormality."

Slight jaundice was noted on March 1. On March 6 the leucocytes numbered 7,000 per c.mm. (polymorphs 82%, lymphocytes 13%). The patient died on March 7.

Only a limited post-mortem examination was allowed. A nodule on the abdomen was opened; pus flowed out and many acid-fast bacilli were demonstrated on direct microscopical examination; *M. tuberculosis* was grown on culture of the pus. A portion of liver was removed; histological examination showed lesions which were mainly necrotic, though some showed a slight surrounding cellular reaction; numerous acid-fast bacilli were noted in the lesions.

Case 6

A boy aged 16 was admitted to Ruchill Hospital on March 27, 1950. Eight weeks before admission two swellings had appeared—simultaneously—one over the dorsum of the right foot and one in the left mastoid region. He was admitted to a surgical ward in a general hospital. The swellings became fluctuant; penicillin was given, and both abscesses were incised. Bacteriological examination of pus revealed *M. tuberculosis*, and a subsequent chest radiograph showed mottling of a coarse miliary character in the right upper lobe.

On admission to Ruchill Hospital his temperature was normal, and subsequently remained normal except for an

occasional rise to 99° F. (37.2° C.). Pus was draining from the wounds in the abscesses, and *M. tuberculosis* was grown on culture. Chest radiography showed the features previously described, and a radiograph of the mastoid processes showed no evidence of bone involvement. Culture and guinea-pig inoculation of gastric washings, and a 24-hour specimen of urine did not reveal the presence of *M. tuberculosis*. Treatment with streptomycin and P.A.S. was instituted on April 3, and the patient was discharged well on September 27.

Case 7

A youth aged 18 was admitted to Ruchill Hospital on August 10, 1950. About two years before admission a swelling had developed on the dorsum of his right hand. Two months before admission a subcutaneous nodule had appeared under the nail of his third right finger, another on his left wrist, and several on the right forearm; some of these nodules subsequently became fluctuant. A chest film at that time showed an enlarged left root with infiltration into the lung field.

On admission his general condition was good, his temperature was normal, and he felt well. X-ray examination of the chest now showed miliary opacities throughout both lungs. Treatment with streptomycin and P.A.S. was begun on August 17 with a dosage of 1 g. of streptomycin and 20 g. of P.A.S. daily; a total of 100 g. of streptomycin was given. The lung fields cleared by January 18, 1951, and, although several further abscesses appeared on the left forearm soon after admission, most had resolved in a further month; one or two continued to discharge pus from time to time, but all had healed by June, 1951. Several samples of pus aspirated from different abscesses were cultured, but *M. tuberculosis* was grown on only one occasion.

Case 8

A man aged 21 was admitted to Ruchill Hospital on December 4, 1949. He complained that for some months he had not felt well, had developed a productive cough, and had lost weight. Six weeks before admission he noted the appearance of a lump on the left foot, another on the right forearm, and one month before admission a painful swelling of the right testicle.

On examination his temperature was 99° F. (37.2° C.). Fluctuant, tender subcutaneous swellings were present on the dorsum of the left foot, the right forearm, and the anterior surface and left side of the neck; there were more fluctuant, tender subcutaneous swellings on the left forearm, left wrist, dorsum of the left hand, left knee, and right and left thighs; the lower pole of the right testicle was painful, tender, and swollen.

The liver was palpable two fingerbreadths below the costal margin, and examination of the chest revealed rales and diminished air entry in the left lower lobe. *M. tuberculosis* was cultured from sputum and from pus aspirated from a fluctuant swelling. A chest radiograph showed fibro-caseous tuberculosis in the left upper lobe and also miliary opacities, apparently of more recent origin, in the same area. The left lower lobe was emphysematous. Blood examination showed: erythrocytes, 4,400,000 per c.mm.; Hb., 14.4 g. per 100 ml.; leucocytes, 17,200 per c.mm. (polymorphs 53%, lymphocytes 33%).

With streptomycin and P.A.S. therapy the miliary opacities in the left upper lobe cleared, but fresh subcutaneous lesions continued to appear every few weeks despite repeated courses of these drugs until isoniazid therapy (8 mg. per kg. daily) was instituted on April 24, 1952. After left pneumonectomy and thoracoplasty on December 1, 1952, the patient improved and is now well.

Discussion

These case reports indicate that early recognition of the nature of skin lesions appearing in the course of the graver forms of disseminated tuberculosis may be of great value,

because there may be no other definite lead to the correct diagnosis, and appropriate treatment must be prompt to have a chance of achieving success.

Some of the lesions described as involving the skin were really subcutaneous, consisting of nodules which in some instances developed into abscesses of various dimensions. When the lesions arose in the dermis itself they varied greatly in appearance: in Case 1 they were multiform, consisting of papules and pustules in purplish-red skin, and violaceous infiltrated lesions; in Case 2 "petechiae" developed into tiny papules surmounted by a vesicle and later crust; in Case 3 innocuous-looking papules resembled the lesions of acne vulgaris; and in Case 4 the lesions looked like small indolent furuncles.

Biopsy specimens were histologically examined in Cases 2, 3, 4, and 5. The one from Case 2 showed only areas of necrosis, but giant-cell systems and areas of caseation were noted in those from Cases 3 and 4, and acid-fast bacilli were also demonstrated in that from Case 4. The specimen from Case 5 was of a small subcutaneous nodule, and the only abnormality noted was dilatation of capillaries and arterioles; when another nodule was examined *post mortem* eight days later its centre contained pus in which there were many tubercle bacilli.

In fulminating cases of disseminated tuberculosis histological examination of affected tissue may show areas of necrosis swarming with tubercle bacilli rather than characteristic tubercle formation. Necrosis was the prominent histological feature in Cases 1 and 5. In such instances involvement of the bone marrow may give rise to abnormalities of the peripheral blood: Ball *et al.* (1951) reported three cases with leucopenia and reviewed similar cases; Leibowitz (1938) recorded a case with a leukaemoid blood picture and reviewed similar cases; and Rennen (1922) reported a case with polycythaemia. Leucopenia, amounting by the time of death to a virtual agranulocytosis, was noted in Case 1. Histological examination of the bone marrow supported the suggestion of Ball *et al.* that sternal marrow examination may be diagnostically helpful in cases of disseminated tuberculosis, especially when there is an abnormal blood picture; and Horowitz and Gorelick (1951) have described a suitable technique for culture.

Rich and McCordock (1929) found that miliary tuberculosis occurred four times as often in white persons over the age of 60 as it did in those aged between 20 and 60, and Spain (1947) noted a similar age distribution in adults with haematogenous tuberculosis.

The relatively high proportion of older persons among those suffering from disseminated tuberculosis suggests that in later years there is a waning of immunity in some people, so that tuberculous disease takes in them the form it is apt to assume in children.

Ball *et al.* considered that in their three cases the source of the bacilli was either a recent primary complex or a lesion of the same nature as a primary complex which had occurred because previous tuberculous infection had completely healed. In our Case 1, however, there was a calcified primary complex in the right upper lobe, and it seems possible that products of the initial pyogenic infection of the left lower lobe, which would drain to the calcified right paratracheal glands (Rouvière, 1932), activated a latent focus there.

The deafness which occurred in three out of the five more acutely ill patients is worthy of attention, because further experience may prove it to be of some diagnostic importance in certain cases of acute tuberculosis. Interest in this symptom was aroused by the study of two patients encountered in the hospital. One was a woman of 20 who presented with a pyrexial illness, increasing and eventually severe deafness, and consolidation of the right lower lobe; after some weeks without antituberculous drugs the temperature settled, the general condition improved, the deafness gradually disappeared, and when the right lung was later removed the right lower lobe was found to be almost replaced by tuberculous caseation. The other patient was a woman of

20 who became deaf soon after the onset of very acute, widespread bilateral pulmonary tuberculosis; the temperature eventually settled and the deafness actually disappeared during the period of administration of streptomycin and P.A.S.

By the time the last patient was encountered, an alert old lady of 71, the recent onset of severe deafness did not appear to be contrary to but rather consistent with a clinical diagnosis of disseminated tuberculosis based on loss of weight, painful throat, and the appearance of suspicious skin lesions.

Deafness cannot be common in cases of acute tuberculosis; or the fact of its occurrence would be better known, though at the same time it is obvious that its presence could easily be ignored in seriously ill patients. It is interesting, however, that Pagel and Woolf (1949) record the symptom of increasing deafness in a case of fulminating tuberculous septicaemia. In the five cases of deafness seen by us there was no evidence of tuberculous meningitis or of middle-ear disease, and it seems likely that the deafness was the result of toxæmia. Deafness occurs in the course of other communicable diseases, presumably for the same reason; it is common in rickettsial diseases such as typhus, and in the later stages of typhoid fever.

In conclusion, the cases described above illustrate the variety of clinical features which may be present in disseminated tuberculosis—pyrexia, skin lesions, deafness, mental confusion, leucopenia, buccal ulceration, laryngitis, respiratory symptoms and signs, splenic enlargement, and jaundice. It may be difficult to make an early diagnosis, but if suspicion is aroused confirmatory evidence may be obtained from biopsy of any skin lesions which may be present, biopsy of sternal marrow, or aspiration biopsy of the liver.

Summary

Attention is drawn to the diagnostic importance of skin involvement in disseminated tuberculosis. Eight cases of the latter condition, four with cutaneous and four with subcutaneous lesions, are described. The occurrence of deafness was recorded in three of five cases in which toxæmia was severe. The clinical features of disseminated tuberculosis are discussed.

Our thanks are due to Dr. T. Anderson, reader in infectious diseases, University of Glasgow, for his helpful criticism and advice in the preparation of this paper, and to Dr. J. H. Lawson, physician-superintendent, Ruchill Hospital, for his interest and his kindness in allowing us access to case records of patients who were under his care.

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The only population group whose diets in 1951 gave some cause for concern was large families with several children or adolescents, according to the National Food Survey Committee's second annual report on "Domestic Food Consumption and Expenditure." The report gives estimates of household expenditure on all kinds of foods and of the quantities of these foods consumed by families of different social class and different composition. Analyses of the energy value and nutrient content of the diets of the various groups are also given. During the period under review, food prices bore the full impact of the inflation caused by the Korean war; but, in general, food expenditure and consumption kept pace with rising prices, and the level of the diet was maintained. There was some further narrowing of the dietary gap between social classes, but the diets of large families revealed certain inadequacies, notably in protein and calcium.