undetected carcinoma of the cervix will lead to certain death.

The task is very difficult. Even Victor Bonney states: "Nor have I observed that patients in more recent years present themselves earlier in spite of modern propaganda." Lastly, the work of cancer investigation cannot be complete unless substantial help and co-operation come from the corporation and the Government.

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HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY AS THE FIRST SYMPTOM OF PULMONARY NEOPLASM

BY

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Hypertrophic changes in the fingers have often been described in diseases of the lung. The following case reports are published because in each patient changes in the limbs formed the earliest symptom of a pulmonary neoplasm. Three cases were diagnosed and treated as rheumatoid arthritis; the fourth was sent to the National Hospital, Queen Square, as suffering from acromegaly. Had the true significance of the changes in the limbs been realized the growth in the lungs might have been treated several months earlier.

Case Reports

Case 1.—In April, 1933, a man aged 56 began to notice that his feet and ankles were becoming larger; he could not get his boots on, and his knees felt stiff and uncomfortable. In October, 1933, his hands began to feel large and lumpy; they gradually became weak and stiff, and he had to give up his work. By November, 1933, in spite of rest, his elbow-joints and shoulders had become stiff; he developed a very slight cough, but had no sputum. In December, 1933, he was sent by his doctor, as suffering from acromegaly, to the National Hospital, Queen Square, where hypertrophic pulmonary osteo-arthropathy was suspected. His chest was radiographed, and a provisional diagnosis of pulmonary neoplasm made. In January, 1934, he was admitted to Brompton Hospital. The only abnormality discovered in the chest was impaired resonance at the right apex. His teeth were in good condition, his blood pressure was 140/30, and the heart sounds were normal. He had marked and painful hypertrophic pulmonary osteo-arthropathy of the hands and feet. Bronchoscopic examination failed to reveal any abnormality, although radiography had shown a rounded shadow in the right upper lobe suggesting the presence of a neoplasm. Radiography of the limbs showed new periosteal bone round the metacarpals, phalanges, radius, and ulna. In view of the increasing severity of the symptoms it was felt that surgical removal of the primary cause offered the only hope for the patient. Pneumonectomy was performed, but owing to his low condition the patient survived the operation only a short time. Examination of the removed lung showed a large columnar-celled carcinoma growing from the right main descending bronchus.

Case 2.—In December, 1933, a married woman aged 58, who had previously felt very well, began to have rheumatic pains, first in the feet, then spreading to the hands and left shoulder. In May, 1934, she noticed that her hands were larger and that the tips of her fingers were getting broader. In July, 1934, she went to a clinic and was treated for rheumatism, but did not improve. In the following August she developed a slight cough and a feeling of lassitude, and in November she was admitted to the Brompton Hospital complaining of lassitude and pains in the joints, especially those of the fingers and left shoulder. On examination the left apex was dull to percussion and the breath sounds were poor. One small gland was found in the left axilla. The hands were broad and the fingers "drumstick," while the bases of the nail beds were red and swollen. The interphalangeal joints were stiff and painful to move, and there were similar changes in the feet. Radiography of the chest showed a dense opacity in the upper and middle zones, suggesting atelectasis and the presence of a neoplasm. The left hand and foot showed the typical changes of hypertrophic pulmonary osteo-arthropathy. The ungual phalanges and the radius and ulna had burr-like expansions at the distal ends. In the tibia and fibula new periosteal bone was laid down in the form of an irregular capsule. The patient was given deep *x*-ray therapy, but a radiograph one month later revealed no change in her condition.

Case 3.—In November, 1931, a man aged 53 first noticed pain and swelling in the knee-joints. This was treated as "housemaid's knee," but did not improve. The pain and swelling then spread to the ankles, wrists, elbows, and shoulders (in that order), and a diagnosis of rheumatoid arthritis was made. In February, 1932, he noticed that his fingertips were becoming larger; at this time he was being treated at Bath. His medical attendant found suspicious signs in his lungs, although the patient had not complained of any pulmonary symptoms. A radiograph of the chest was taken, and he was then sent to the Brompton Hospital out-patient department, where a radiograph (August, 1932) revealed a large mass at the base of the right lung. A few rhonchi and weak breath sounds were heard at this base. Shotty glands were found on both sides of the neck, and a large smooth gland was palpable in the right axilla. Nothing else abnormal was discovered. The knees, ankles, and wrists were generally enlarged, but there was no limitation of movement. The fingers were "drumstick" in shape, and the small joints of the fingers and toes were thickened. The bones showed typical periosteal thickening. On bronchoscopic examination a small nodule was detected projecting from the posterior wall and partially occluding the lumen of the right main descending bronchus. A portion of this was removed and was found to be a squamous-celled carcinoma. Radon seeds were inserted through a bronchoscope. In November, 1932, radiography showed no change in the opacity, but the condition of the joints was less painful. In July, 1933, the patient was keeping well and working; he had neither cough nor pain. The fingers were unchanged. In January, 1934, another radiograph showed no change in the opacity, and the patient was still well and working.

Case 4.—In April, 1932, a man aged 45 found that his knees were swollen; they were painful while walking, but were relieved by rest. He was told by a medical practitioner that he had rheumatoid arthritis, and was given an ointment to rub into them. In May the patient first noticed that his fingers were swollen; this swelling steadily progressed. In June he underwent an operation for appendicitis. In August a pain in the right scapular region began. He continued with his work until November, when cough developed with dyspnoea on exertion. He was admitted to Brompton Hospital in February, 1933. There were a few discrete glands in the groin, and the breath sounds at the right base were weak. Well-marked "drumstick" clubbing was present in both hands. Radiography showed an opacity at the base of the right lung, and a bronchogram indicated that the lipiodol had failed to fill the right descending bronchus at the site of the opacity. Bronchoscopic examination revealed a red granular area in the lateral secondary division of the right descending bronchus. A portion of this was removed and proved to be carcinomatous. Thoracotomy was performed in the hope of removing this growth, but a firm mass—the size of a cricket ball—was found in the right lower lobe, invading the middle lobe and extending into the hilar region.

Since this was considered irremovable radon seeds were inserted and the patient was discharged in a somewhat improved condition.

Clinical Signs

Clubbed fingers were mentioned as a symptom of tuberculosis by Hippocrates, and French writers of the present time call them *doigts hippocratiques*. Hypertrophic pulmonary osteo-arthropathy, however, was not described until P. Marie (1890) published his account. Bamberger (1891) drew attention to the disease independently almost at the same time.

The actual deformity in clubbed fingers is as follows. The fingers of both hands are thickened and bulbous and the terminal phalanges are enlarged. The nail beds may be red and swollen and the nails are curved longitudinally and laterally. The bones and joints are not affected, nor is the skin itself changed in any way. Troussean likened the change to the head of a serpent.

In hypertrophic pulmonary osteo-arthropathy the changes may not affect the tips of the fingers first; in fact the metacarpo-phalangeal region may remain normal. Marie described the disease as follows. "Symmetrical osteitis of the four limbs, chiefly localized to the phalanges and terminal epiphyses of the long bones of the forearm and leg, sometimes extending to the roots of the limb and flat bones, and accompanied by a dorsal and lumbar kyphosis and some affection of the joints."

Radiography may reveal proliferative changes in the ungual phalanges. New subperiosteal bone is laid down and sharply marked off, and sometimes there are irregular burr-like expansions in the distal half. More rarely small osteophytes are present at the proximal end, near the line of joint cartilage. Changes in the joints may affect the peri-articular tissues early. Later, erosion of the cartilage may take place, with lipping.

Kessel (1917), Montgomery (1916), Locke (1915), and others have observed many cases, and believe that clubbing represents the early stage of hypertrophic pulmonary osteo-arthropathy. They found that when there was simple clubbing clinically bony changes were present on *x*-ray examination. Lasserre (1932) considered that vasomotor and venous stasis formed a favourable soil, and that there might be a deformity of the soft parts only, the presence of toxins being necessary for new bone formation.

Aetiological Classification

The underlying causes seem to divide the patients into two main groups:

1. Patients in whom there is some element of toxic absorption, such as (*a*) pulmonary suppuration, as in lung abscess, bronchiectasis, and empyema, or (*b*) chronic intestinal infection and toxaemia, as in biliary cirrhosis, chronic diarrhoea, rectal polypus, and sprue.

2. Patients in whom clubbing appears to be due to cyanosis and right-sided heart failure, as in chronic pulmonary tuberculosis, and in pulmonary fibrosis and heart disease, particularly the congenital disorders.

In the toxic group the changes may come on very rapidly, as in lung abscess, when the fingers are generally sausage-shaped, red, and swollen. In this type of patient the condition of the fingers tends to clear up after the source of the toxins has been removed. In several patients with bronchiectasis and marked clubbing the condition of the fingers almost vanished following the eradication of the diseased area by lobectomy.

Clubbing nearly always improves in lung abscesses treated adequately. Puig (1932) reported hypertrophic pulmonary osteo-arthropathy in a patient with an acute abscess of the lung, with rapid disappearance of the clubbing as the lung condition improved. The disappearance of the capsule was only comparable with that seen in syphilitic dactylitis energetically treated. The same has been found with clubbing in intestinal infections. Moulonquet and Salomon (1932) described the clubbing in two patients suffering from colitis and stricture of the rectum; in both the clubbing cleared up following colostomy and rectal lavage.

The second group appears to be associated with cyanosis and right-sided heart failure. It is well known that clubbing is common in, and is diagnostic of, those forms of congenital heart disease which produce cyanosis and dyspnoea. Fishberg (1932) found that whenever clubbed fingers occurred in phthisis the patient was also suffering from dyspnoea and dilatation of the right side of the heart. This would suggest that there was a mechanical disturbance of the circulation causing peripheral stasis, which is probably also the basis of the clubbing which develops in congenital heart disease.

Jones (1931) considered that when the soft tissues only were involved the cause was peripheral dilatation and slowing of circulation due to right-sided heart failure. He found clubbing present in 40 per cent. of congenital heart lesions and in 25 per cent. of cases of subacute endocarditis. He believed that in the latter the clubbing was due to a local disturbance, as opposed to the general cardiac back pressure in congenital heart lesions. Others have reported clubbing in subacute endocarditis, and Puig (1932) noted it as the first sign in one of his patients. Whether the clubbing is due to general toxaemia, to something akin to "Osler's nodes," or merely to cardiac failure is not known.

Conclusion

In spite of much discussion little is nevertheless known or understood of the true pathology or aetiology of the changes in the limbs described here. Why should hypertrophic pulmonary osteo-arthropathy appear in some patients with pulmonary neoplasm when there is no evidence of either obstruction to the flow of blood through the lungs or of absorption of toxins? None of the patients reported here showed any symptoms suggesting either factor.

Some writers suggest that these changes are due to metabolic toxins produced by the breaking down of body tissues, the toxins causing a vasomotor disturbance with peripheral dilatation of the capillaries. While the pathology of the disease remains so obscure the clinical connexion between the changes in the fingers and those in certain pulmonary diseases should not be overlooked. These changes, as we have seen, may appear before any other clinical sign. They will, if recognized, lead to an earlier diagnosis and treatment of the underlying condition.

Summary

1. Four cases with pulmonary neoplasm are reported in which the earliest symptom was hypertrophic pulmonary osteo-arthropathy.

2. The aetiology of this condition is briefly discussed and the relevant literature reviewed.

3. It is suggested that investigation of the lungs should not be overlooked in patients with "rheumatism" or with changes in the joints appearing without known cause, as well as in those with acromegaly.

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OCULAR PARALYSES FOLLOWING MUMPS

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The comparative rarity of the neurological complications of mumps and their unusual localization and termination in one of the two following cases have led us to put them on record.

Case I

A boy aged 9 came to the Coventry school clinic in December, 1929, because he had recently found that he could not see to read. While at the clinic he vomited, and it was noticed that a large quantity of the vomit came through the nose. He had had mumps three weeks previously, and a fortnight before admission he noted that he could not see to read. For the past fortnight food had regurgitated through his mouth.

There was complete paralysis of accommodation; the pupils were widely dilated and did not react to light. No external muscles were affected. The vision was as follows: right eye, 6/60, with + 2 = 6/9; and the left eye, 6/60, with + 2 = 6/9. There was slight blurring of the edges of both disks. The knee-jerk was absent on the right side, and its presence on the left was doubtful. The boy was admitted to the eye wards of the Coventry Hospital. A swab was returned as negative for the Klebs-Loeffler bacillus. He was transferred to the medical wards and lost sight of.

He was written for and examined on July 4, 1934, when he was aged 14. The disk edges were still somewhat blurred, but the eyes were apparently quite normal, and there was no evidence of any paresis of any extrinsic or intrinsic muscles. At the time of the first visit we found that Osler in his *Textbook of Medicine* had mentioned that mumps was occasionally followed by peripheral neuritis.

The case may be summed up as an example of the picture presented by post-diphtherial paralysis of the intrinsic muscles of the eye, but caused by the virus of mumps. It is probable that the slightly blurred disks were physiological and had nothing to do with the infection.

Case II

Another boy, aged 12, came to the Eye Department of Coventry Hospital on March 15, 1933, complaining of blurred vision in the left eye and inability to see things on the right side without turning the head in their direction. The symptoms had come on gradually a few days previously. One month before this date he had developed mumps. The attack was of ordinary severity, and he did not stay in bed. A sister had suffered at the same time. There had been no headache, fits, or any cerebral symptoms. His previous health had been very good. One brother had died recently from pulmonary tuberculosis and a sister from meningitis, probably tuberculous.

We found that the vision in the right eye was 6/24, and with glasses 6/4.5. In the left eye it was 6/24, and with glasses 6/18. Both fundi were normal. All the intrinsic and extrinsic muscles supplied by the third nerve were paralysed on the left side. The pupil was widely dilated and inactive. There was incomplete left ptosis, with compensatory overaction of the left half of the frontalis. Food regurgitated through the nose. The general nervous system was normal. The Mantoux and Wassermann tests were negative. No Klebs-Loeffler bacilli were found. There was a history that twelve months previously the left eye had been struck by a golf ball and that two stitches had been put into the lids, one into each. The eye was not damaged, and there was no diplopia after the blow.

On March 17 paresis of the left external rectus appeared; the superior oblique remained active. On May 23 the paralysis of the eye muscles was reported to be improving, and on June 19 the eye movements were almost normal. On July 17 all the eye movements were normal except deorsum vergens. The pupil was still dilated. On August 21 the left pupil was still dilated and inactive, and upward movement of the eye was defective. No change was noted on October 2, December 11, or December 18. The vision of the right eye was 6/4.5 and of the left 6/18 partly (with glasses).

On January 15, 1934, there was slight defect of convergence and abduction. The pupil was still dilated and inactive on March 5. Deorsum vergens was still defective. There was no change on April 9. On May 14 there was still third nerve paralysis; the left pupil was fully dilated and inactive. The fundi were normal. The condition was not so good as previously. In November there was still no change or improvement.

Comment

Numerous investigations of cases of uncomplicated mumps have shown that a meningeal reaction, as indicated by a lymphocytic pleocytosis, is present in most cases of this disease, even in the absence of any symptoms or signs indicative of cerebral involvement. It seems probable that the virus of mumps is itself potentially neurotropic, since several cases are on record in which clinical meningitis and encephalitis have preceded the onset of the glandular swelling. The pathology would therefore seem to be distinct from that of the cerebral complications of the other virus diseases (such as vaccination, varicella, and encephalitis), in which it is generally held that the neurological complication is caused by a dormant virus which has been awakened to activity by the attack of the exanthem.

The peripheral nerve palsies accompanying mumps are often considered to be of the same nature as those associated with various toxins and infections, and to be a lesion of the peripheral nerve endings; but in view of the frequent meningeal reaction of parotitis it would seem equally likely that in some cases the lesion is one of the nerve trunk near its root (a meningo-radiculitis). This would bring the pathology into line with that of the peripheral (cranial and spinal) nerve palsies associated with the various forms of meningitis, acute and chronic.

The time of onset of the neurological complications is usually at the height of the parotitis, while it is subsiding, or in the early period of convalescence (third to fourteenth day). Periods of three weeks have been recorded. The longer interval of six weeks in Case II is unusual.

It appears certain that in some cases cranial nerve palsy due to the mumps virus may occur in patients in whom there has been no apparent parotitis and no orchitis, as is shown by the occurrence of such palsies in contacts in barracks during epidemics, and in a member of the family of a definite parotitic patient. The possibility of such an