medical attendants during the intensely distressing period of maximal disability is invaluable. Once deterioration appears to be checked a reasonably confident prognosis can be given—though a warning should be issued of the possibility of personality changes during the convalescence and the rather more remote danger of permanent impairment of intellectual capacity.

Summary

A description is given of eight examples of a clinical syndrome of gradual onset in which develops almost total paralysis of all motor function, originating first in the mid-brain and later in the whole brain-stem, accompanied by only mild pyramidal or long-tract sensory disturbance, and no cardiac or respiratory abnormality.

From a stationary stage of extreme gravity, dramatic total recovery has occurred in seven cases, with no neurological sequelae.

The pathology of the fatal case is described, and a state of transient cerebral oedema, possibly related to a systemic virus infection, is suggested as the basic cause.

I wish to express my thanks to Dr. William Gooddy and Dr. J. Hamilton Paterson for allowing me to refer to Case 4; to Drs. Hugh Fisher, J. Macaulay, and A. C. Kendall, consultant paediatricians, for referring to me Cases 5–8; and to Dr. A. L. Woolf and Dr. E. W. N. Trounson for the pathological studies on Case 8.

REFERENCES

Bickerstaff, E. R., and Cloake, P. C. P. (1951). *British Medical Journal*, 2, 77.
Espir, M. L. E., and Spalding, J. M. K. (1956). Ibid., 1, 1141.
Paterson, J. H. (1953). *Proc. roy. Soc. Med.*, 46, 726.

RETICULOHISTIOCYTOSIS (LIPOID DERMATO-ARTHRITIS)

BY

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[WITH SPECIAL PLATE]

This paper describes four patients with a similar and unusual syndrome of a widespread papular and nodular eruption and multiple arthritis. Circumscribed areas of destruction in bone were present, and in two cases this progressed to a "concertina" deformity of the fingers. Tendon-sheath swellings and patches of xanthelasma palpebrarum occurred in two of the cases. Histological examination of all involved tissue in every case showed the same type of giant cells, the cytoplasm of which appeared granular and in places finely "foamy." An unusual type of lipoid has been demonstrated in these cells. Two patients died, and in both, apart from widespread infiltration of tissues by the giant cells, a fibrinous pericarditis was present.

Twelve cases showing a similar clinical picture and histology have been described in the literature under various headings, and are summarized in the Table.

Personal Cases

Case I

Mrs. E. P., a housewife. Apart from a hysterectomy for fibroids when aged 40 she had not had any previous illnesses of note. No relevant condition had occurred in the family, and her only brother and sister were alive and well. The patient had been married for 25 years, but was childless. In December, 1949, at the age of 49, she developed painful swelling of the finger, shoulder, and knee joints. At the same time an eruption appeared on the fingers, elbows, both pinnae, the radial aspects of both forearms, and over the manubrium sterni. She came under our observation in July, 1950, and was seen at regular intervals until she died in 1952. When she was first seen there was a widespread papulo-nodular eruption, sheets of yellow-brown papules 0.2–2 cm. in diameter and associated with erythema being present over the forehead, ears, neck, naso-labial furrows, outer aspects of forearms and upper arms, the nail folds, the sacral region, and the anterior aspects of the thighs and lower legs. At the periphery of the involved patch of skin they were occasionally in linear distribution. The larger nodules were present on the scalp, both pinnae, bridge of nose, chin, elbows, dorsum of most fingers, sacral area, and knees. These tended to be purplish in colour. They were well raised from the skin surface and some were confluent (Fig. A). Local heat and pressure did not increase or decrease the number or size of the nodules. The teeth were healthy, but a few papules were present on the lips and gingival margins (Fig. B), the fraenum and posterior part of the tongue, and extending into the tonsillar recesses. There was widespread involvement of the joints associated with moderate pain and often considerable swelling and limitation of movement. Shoulders, elbows, wrists, finger-joints, knees, and ankles were involved. The axillary and inguinal lymph nodes were slightly enlarged. Blood pressure 180/100 mm. Hg.

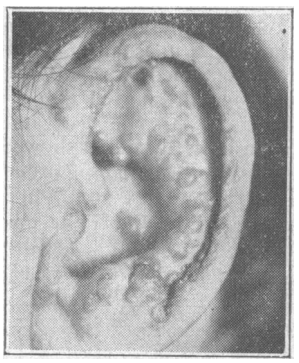

FIG. A.—Case I. Nodules and papules on ear.

Clinical Course.—Many of the larger nodules remained unchanged, but a few new ones appeared. At times the sheets of papules became less prominent and the erythema faded, but for periods of a few weeks they were more marked and itching occurred. Seven months after the onset four or five large, typical xanthelasma palpebrarum patches were observed. In 1951 an irregular swelling developed in front of the wrists and appeared to be arising from the tendon

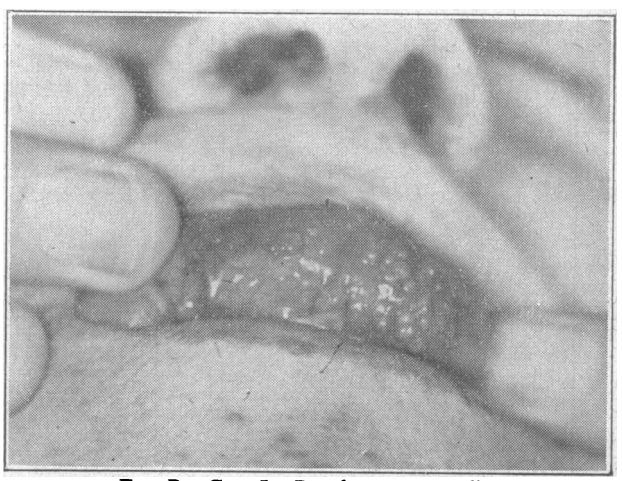

FIG. B.—Case I. Papules on upper lip.

sheaths; it remained for six months. The joints became worse and new ones were involved, including the hip, shoulder, sacro-iliac, vertebral, and temporo-mandibular joints. The finger and toe joints became unstable and the fingers shorter, causing wrinkling of the skin. A general kyphosis developed. The patient lost 3 stones (19.1 kg.) in weight, chiefly during the first year of the illness. There were long periods of intermittent moderate pyrexia usually coinciding with the exacerbations of the joint and skin lesions. The general condition steadily deteriorated, and in December, 1952, she developed fever and a cough and died after a few days.

Treatment did not appear to have any effect, and included A.C.T.H. (12.5 mg. twice daily for three weeks) and a low-fat diet over a period of two months. *X*-ray treatment (a single dose of 400 r at 85 kV) had no effect on the cutaneous nodules.

Investigations.—Blood Wassermann and Kahn reactions negative. Erythrocyte sedimentation rate (Westergren) varied from 5 to 41 mm. in one hour. Blood cholesterol 125–180 mg. per 100 ml. Serum calcium and plasma protein levels, blood counts, glucose tolerance curve, and liver function tests were within normal limits. The bone marrow showed an unusually high number of monocytes, of which a few contained a slightly foamy cytoplasm. The electrocardiograph showed a low T_2 and inverted T_3. Mantoux reaction: 1 in 1,000 negative; 1 in 100 positive. Analysis of an excised nodule showed 8% total ether-soluble lipoids.

X-ray Examination.—On chest radiography calcified lesions were present in the right apex and some pleural adhesions in the right costophrenic angle. At the first examination of the bones (August, 1950) a generalized osteoporosis was apparent, with numerous small marginal zones of subcortical destruction of bone adjoining the interphalangeal and midcarpal joints. These small zones of bone destruction gradually increased in size; new ones appeared, and by December, 1950, the hands, wrists, shoulders (Special Plate, Fig. 1), knees, and hips were extensively involved. Zones of bone destruction were also present in the posterior articular facets of the spine, the costo-transverse joints, the greater and lesser trochanters of the femora, the ischial tuberosities, and by May, 1951, in the anterior angles of the vertebral bodies. The skull showed no change.

Post-mortem Findings and Histology.—The body fat in general was reduced in amount and deep yellow-brown in colour. Submucous nodules were present on the posterior third of the tongue and in the larynx. The thyroid appeared normal. There were recent small bilateral pleural effusions. The lungs were congested, with collapse of the left lower lobe. A fibrinous pericarditis was present with an accumulation of some 300 ml. of heavily blood-stained exudate. The heart was enlarged, with dilated chambers and a soft, flabby myocardium. Valves and coronary arteries showed only moderate atheroma. Scattered peritoneal adhesions were present, including some recent ones over the anterior surface of the liver and enveloping the spleen. The liver, of normal size, showed on section a typical "nutmeg" appearance. The gall-bladder, kidneys, suprarenals, stomach, intestines, and right ovary were normal; the uterus and left ovary had been previously removed. There was widespread destruction of the articular cartilages; areas of firm granulation tissue extended into the underlying cancellous bone.

Details of Twelve Similar Cases Recorded in the Literature

Serial No.	Authors	Title Given	Sex and Age	Joints Affected	Skin Lesions	Other Clinical Findings	Course	Comments
1	Targett (1897) ..	—	F 65	"Rheumatic and gouty habit"	Small tumours on fingers	—	—	—
2	Parkes Weber and Freudenthal (1937); Parkes Weber (1943, 1944, 1948, 1955)	Non-diabetic cutaneous xanthomatosis with hypercholesterolaemia and atypical histological features	M 35	Knees and other joints	Widespread, chiefly on hands, face, elbows, and buttocks	Loss of weight and intermittent fever. Tendon-sheath tumours on back of wrists	Gradual improvement over period of 10 years; many nodules disappeared	Blood cholesterol 350 mg.% (one occasion). Improvement followed fat-poor diet
3	Portugal *et al.* (1944)	Histiocitomatosis gigantocitaria generalizada	M 44	Widespread joint involvement	Widespread papules and nodules	Tendon-sheath tumours	Some papules and nodules disappeared	—
4	Graham and Stansfield (1946)	A case of hitherto undescribed lipoidosis simulating rheumatoid arthritis	M 20	Widespread joint involvement of rheumatoid arthritis pattern	Nodules and papules on scalp, face, elbows, wrists, fingers, and back	Kyphosis and depression of sternum	A sarcoma developed in the axilla, from which the patient died	At necropsy giant-cell infiltration found in muscle, periosteum, synovial membrane, and bone
5	Caro and Senear (1952)	Reticulohistiocytoma	M 50	Hands, feet, spine, and jaws	Papules and nodules on hands, elbows, face, and ears	—	Some papules and nodules disappeared, but new ones developed	—
6	Caro and Senear (1952)	Reticulohistiocytoma; but prefer the term "reticuloendothelial granuloma"	F 56	Hands, wrists, and knees	Papules and nodules on face, ears, neck, forearms, and fingers	—	After 4 years skin lesions were smaller	—
7	Montgomery (1952; in discussion following presentation of Cases 5 and 6)	Reticulohistiocytoma	M 30	Nil	Papules on face, arms, and trunk	—	Papules later disappeared	—
8	Montgomery (1952; in discussion following presentation of Cases 5 and 6)	Reticulohistiocytoma	F 24	Fingers and other joints swollen	Papules on scalp, forehead, nose, neck, and arms	—	—	—
9	Allington (1950; and in discussion following presentation of Cases 5 and 6)	Reticulohistiocytoma	F 66	Chronic rheumatoid arthritis	Nodules on face, ears, forearms, elbows, and ankles	Thyroid adenoma	After 4 years most nodules had disappeared and joints had improved	Improvement followed thyroidectomy
10	Laymon (1952); also Goltz and Laymon (1954)	Reticulohistiocytoma and multicentric reticulohistiocytosis of skin and synovia	M 52	Back, fingers, knees, and shoulders	Papules over fingers, hands, ears; nodules over knuckles	Tendon-sheath tumours of wrists	Skin cleared after 6 months; died one month later of carcinomatosis	Condition began 4 months after resection of adenocarcinoma of colon
11	Goltz and Laymon (1954)	Multicentric reticulohistiocytosis of skin and synovia	F 40	Neck and limb joints	Papules over forehead, scalp, shoulders, chest, and on fingers	Tuberculous lymph node in axilla	—	—
12	Davies and Wood (1955)	Reticulohistiocytoma	F 47	Rheumatoid type of arthritis affecting hands, knees, and other joints	Papules over fingers, neck, ears, and scalp	—	In 3½ years joints became worse, but papules retrogressed and became minimal	This is Case 1 of these authors; their Case 2 is of a solitary nodule and not included here

The changes were most prominent in the knee and shoulder joints.

Histologically, the epidermis was normal. The nodules situated in the upper half of the dermis consisted of an aggregation of large rounded or oval multinucleate cells enveloped in a scanty fibrillary stroma. The cells varied in size up to 50 μ in diameter, and contained from one to twenty or more nuclei, small, compact, and irregularly disposed within the cell. The abundant cytoplasm was eosinophilic, and in most of the cells of homogeneous texture; a faint granularity was discerned in some, and in a few there was a very fine foamy appearance. The submucous laryngeal nodule showed the same appearance. In contrast with the nodules, the xanthelasma palpebrarum lesions showed typical lipoid cells, coarsely vacuolated and staining readily with Scharlach R. The granulation tissue from the eroded areas of bone consisted of large, sometimes multinucleate, cells with abundant eosinophilic slightly granular cytoplasm, closely packed in a scanty stroma which was free from inflammatory cells (Special Plate, Fig. 2). The cells were essentially similar to those found in the skin lesions. In some areas distant from the giant-cell accumulation, connective-tissue cells were swollen and interspersed with larger rounded cells similar to those constituting the main bulk of the "tumour." Transitional forms were seen, suggesting that the giant-cell aggregations were derivatives of the synovial fibrocyte. Apart from the skin nodules and joints, the same large cells were found scattered through the dermis and subcutaneous tissues, in bronchial lymph nodes and endocardium. No similar change was demonstrated in kidney, ovary, or spleen.

Histochemical Investigations.—Examination of frozen sections of skin and a subcutaneous nodule with the usual series of Sudan stains failed to demonstrate any lipoid except for a faintly positive result with the periodic-acid–Schiff (P.A.S.) technique. The Sudan dyes (chiefly Sudan IV) were orginally used, either as a saturated solution in 70% ethanol or in Herxheimer's fluid. Later it was found that a more complete dye transfer from solvent to lipoid phase of the section was obtained by the use of the dye as a saturated solution in pyridine (50%) solvent. With this technique, sudanophilic material (S.M.) was found in considerable quantities, mainly in regions of compact collagen fibres, either related to groups of the giant cells or lying free between the fibres. In addition it was present in fibrocytes deeply placed in sheets of apparently normal capsular collagen fibres and in certain chondrocytes. The intracellular and extracellular globules of S.M. were of fairly uniform size (0.7–1.6 μ); they showed birefringency of a low order, and notably in synovial cells and chondrocytes were circumferential.

Further histochemical investigations were made on serial frozen sections to detect any sudanophilic lipoid which might be "masked" by virtue of chemical combination with proteins, polypeptides, or mucopolysaccharides. No proteolytic dissociation was demonstrated after incubating sections in a solution of papain for one hour at 37° C. No change was noted after alkaline hydrolysis, but acid hydrolysis with 10% acetic acid for one hour at 37° C. or N/1 hydrochloric acid for eight minutes at 56° C. gave a moderate increase in the amount of both intra- and extracellular S.M. There was no increase in S.M. after incubating sections in hyaluronidase solution for 19 hours at 37° C., although certain structures formerly P.A.S.-positive became P.A.S.-negative. Prolonged attempts at defatting sections (ether, chloroform, xylol, di- and tri-chlorethylene) for periods up to five days reduced only slightly the fine diffuse pinkish sudanophilia of the cytoplasm of the aggregated giant cells, but completely eliminated the larger intra- and extracellular globules of S.M. and the neutral fat of tissue lipocytes.

The results of these investigations did not reveal the presence of lipoid in combination with either protein or mucopolysaccharide. The moderate increase in S.M. after weak acid hydrolysis may indicate the presence of some polypeptide–lipoid complex which was mainly intracellular in site. Furthermore, the results obtained would suggest that the intra- and extracellular S.M. was probably chemically similar.

Case II

Mrs. F. M. G., a housewife. There had been no previous significant illness and there was nothing relevant in the family history. In September, 1947, when aged 50, the patient noticed some yellowish marks on the left upper eyelid, and in March, 1949, slightly itching papules appeared on the face, ears, and arms. She came under our observation in September, 1949, when examination revealed sheets of closely set, shiny reddish-brown papules, varying in diameter from 1 to 3 mm., over the pinnae, behind the ears, in the eyebrows, on both cheeks, the sides and bridge of the nose, the extensor

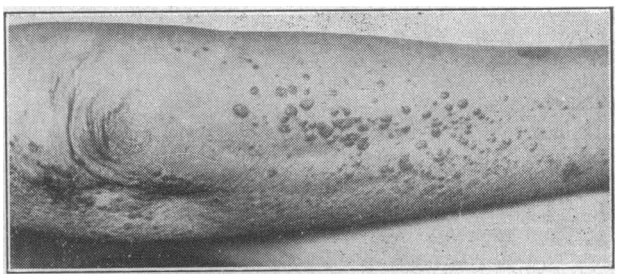

FIG. C.—Case II. Papular eruption on forearms.

surfaces of both arms (Fig. C), and over both shins. The areas so affected were slightly erythematous. Five or six xanthelasma palpebrarum lesions of 0.5–1 cm. diameter were present on both upper eyelids. No lesions were apparent on the buccal mucous membrane.

Clinical Course.—By March, 1950, the papules round the ears and on the cheeks had almost disappeared and those on the forearms had become flatter; the xanthomatous plaques on the upper eyelids were less noticeable. However, by September, 1951, the nodules had again become more prominent and then involved the V of the neck. Only one of the xanthelasma palpebrarum lesions remained. In October, 1952, she complained of pain in both knees, and later in the shoulders and ankle-joints. From 1952 to 1954 the sheets of papules cleared in some areas, but fresh lesions appeared, usually at the edge of the fading patches.

When seen again in 1956 the eruption was widespread, with clear areas of skin on the points of the elbows and knees, in the axillae, behind the knees, and on thighs and buttocks. In many places these clear areas were ringed by a continuous edge of fused papules. Papules were also present on the lips. Certain areas where nodules had been noted previously were now clear, but had an atrophic wrinkled appearance. There was no sign of the xanthelasma palpebrarum patches. A tendon-sheath swelling was present on the front of the left wrist. She complained that the joints had gradually become stiffer, being worse in the hot weather. The spleen and liver were easily palpable. Enlarged lymph nodes were present in the right axilla.

Investigations.—Wassermann and Kahn reactions negative. Blood cholesterol 130–250 mg. per 100 ml. Plasma protein level, blood count, glucose tolerance curve and liver function tests within normal limits.

X-ray Examination.—A progressive change was noted starting in June, 1952, with small areas of decalcification in one phalanx, the left os magnum and scaphoid. Further erosions developed on the phalangeal margins in both hands and feet, and on the right scapula at the site of insertion of the supraspinatus tendon. By January, 1956, new areas of bone destruction were demonstrated in the right scaphoid and os magnum.

Histology.—Sections from a skin nodule showed essentially the same picture as in Case I. In addition some smaller elongated cells with similar cytoplasm appeared to represent transitional forms between the stroma fibrocytes and the fully developed giant cells.

Case III

Mrs. J. L., a housewife. In 1950, when aged 48, she had complained of itching, followed three months later by pain in the joints and shining brown papules on the hands. Papules then gradually developed on nail folds, backs of fingers, hands, arms, face, neck, trunk, buttocks, thighs, and lower legs. Larger nodules appeared over elbows and knees. Papules were present on the tongue and mucous membranes of the mouth and pharynx down to the level of the thyroid cartilage. The joints became more swollen and stiffer until the patient was almost immobile. Her general condition gradually deteriorated; she lost weight, and finally died in April, 1954.

X-ray Examination.—Sharply defined and rounded areas of osteoporosis without evidence of bone reaction were present in outer ends of clavicles, bones of hands and fingers, and to a less extent in legs, feet, and upper part of right radius.

Post-mortem Findings and Histology.—Dr. R. B. T. Baldwin has kindly furnished us with the necropsy report and material for histological examination.

A diffuse thickening was present round the vocal cords, with pea-sized nodules on the right side. The lungs showed a purulent bronchitis and a small infarct at the right base. There was an acute fibrino-purulent pericarditis. The heart chambers were dilated and the muscle was soft and pale. The bronchial and hilar lymph nodes were enlarged; there was a severe cardiac cirrhosis of the liver and the spleen was moderately enlarged.

Histologically, the skin nodules showed essentially the same appearances as in Case I. The giant cells were particularly large, being up to 100 μ in diameter (Special Plate, Fig. 3). The bronchial lymph nodes showed large aggregations of the same type of giant cell as seen in the skin nodules. An incidental and unexpected finding was infiltration of the hilar lymph nodes by carcinoma suggestive of a bronchial origin, although no primary growth was discovered in the lungs or elsewhere.

Case IV

Mrs. E. H., a housewife. In October, 1944, when aged 25, she complained of itching over the abdomen, and a month later had pain, swelling, and stiffness in the wrists, fingers, ankles, and shoulders. She was given a course of intramuscular injections of gold in January, 1945, and during this treatment papules developed on the ankles, face, eyelids, external auditory meati, and central upper back. The condition gradually progressed, and in May, 1945, she was admitted to the Radcliffe Infirmary, Oxford, under the care of Dr. A. B. Carleton; and in 1947 to the Leeds General Infirmary under Dr. J. T. Ingram, where she was seen by one of us (R. P. W.). At this time the eruption was chiefly present over the outer upper arms, front and outer aspects of the thighs, lower abdomen, ears, neck, cheeks, and forehead. It consisted of dusky browny-red shining papules, often follicular and in some areas linear in distribution. The mouth and tongue were clear. She was unable to walk, and the fingers showed concertina type of deformity.

Investigations.—Blood total cholesterol 98–190 mg., free cholesterol 63 mg., and cholesterol esters 127 mg. per 100 ml. Serum calcium plasma protein, blood Wassermann and Kahn reactions, and E.S.R. all normal; Mantoux reaction positive to 1 in 10,000.

X-ray Examination.—Punched-out defects involving carpal bones and terminal phalanges of both thumbs and fingers were reported in 1945. By April, 1948 (Dr. G. H. Illingworth), there was extensive destruction of the proximal and distal interphalangeal and metacarpo-phalangeal joints, and of the wrist joints, leading to telescoping of the fingers (Special Plate, Fig. 4). There were similar changes in the metatarso-phalangeal, tarsal, ankle, and elbow joints. Areas of decalcification were also present in the shafts of the radius and ulna on both sides. A chest skiagram in April, 1957, showed diffuse mottling throughout both lungs.

Histology (Professor D. H. Collins).—In the corium were ill-defined cell groups containing giant cells with up to a score of nuclei and an abundant slightly "foamy" cytoplasm. A few histiocytes, lymphocytes, neutrophils, and eosinophils were also present. Scharlach R stained a small amount of lipoid in the giant cells a rusty colour. The appearances were essentially similar to those of the section from Case I.

Discussion

Clinical Features

The average age of onset was 42, with extremes of 20 and 66 years. There were ten females and six males. One patient had a sister with widespread joint disease, but apart from this there was no family history of similar complaints, nor was there any significant past history. In eight cases the onset of the eruption and the joint symptoms coincided. In five cases the joint symptoms preceded the eruption, respectively by two months, six months, one year, four years, and several years. In Case II the rash developed two years before the involvement of joints. The papules and nodules were from 0.2 to 2 cm. in size. The smaller ones, shining and yellow-brown in colour, were chiefly in patches associated with erythema. In most cases they were confined to one or two areas, but in some became widespread. The commonest areas involved were the backs of the hands and fingers, outer aspect of the forearms and upper arms, forehead, margin of the nose, ears, and on the fronts and sides of the neck, including the V. The larger nodules were more purple and present over bony prominences, including the elbows, knees, scalp, bridge of nose, chin, sacral area, and dorsum of fingers. At times the eruption became less prominent and occasionally disappeared. Papules were present on mucous membrane in four cases. All cases except No. 7 (see Table), about which very few clinical details are available, had pain and often swelling of numerous joints, usually affected symmetrically. The hands and fingers were often involved, and the clinical picture was that of rheumatoid arthritis with in some cases severe crippling. Tendon-sheath swellings were present in five cases. Cases I and II developed plaques of xanthelasma palpebrarum, which after a period of one to two years gradually faded. Two cases had enlarged lymph nodes, and in one of these the spleen and liver became palpable. Bouts of pyrexia occurred and there was considerable loss of weight in Case I.

Of 11 cases where the clinical course is known, the eruption retrogressed in seven and completely disappeared in two of these. The joint condition gradually progressed in three of these cases, but in one it improved and in one other, after a period of seven years, the active process appeared quiescent. Four patients died 4 years, 11 months, $3\frac{1}{2}$ years, and 3 years after the onset, the cause of death being malignant neoplasm in the first three and undetermined in Case I. Case II improved following a fat-poor diet. Other cases improved after a similar period without such a diet, and in Case I two months on a low-fat diet while in hospital had no apparent effect.

Pathological Features

Case II had a raised blood cholesterol level (350 mg. per 100 ml.) and Cases II and III each on one occasion had readings of 250 to 235 mg. per 100 ml. respectively. The histological picture of all the material examined was dominated by the presence of a varying number of the same type of unusual large cell. Apart from the aggregations in the skin and synovia, similar isolated cells were demonstrated in the marrow, lymph nodes, endocardium, voluntary muscle, periosteum, and scattered through the subcutaneous tissues. On morphological grounds it seems likely that these abnormal cells were neoplastic. Transitional cells between fibrocytes and the giant cells suggest that the latter were derived from the fibrocytes of the skin, synovial membrane, and elsewhere. The cytoplasm of the giant cells did not show the usual staining reactions of lipoid, and it is suggested that the material may be a polypeptide–lipoid complex. The fact that this material was shown to be present in small

E. R. BICKERSTAFF: BRAIN-STEM ENCEPHALITIS

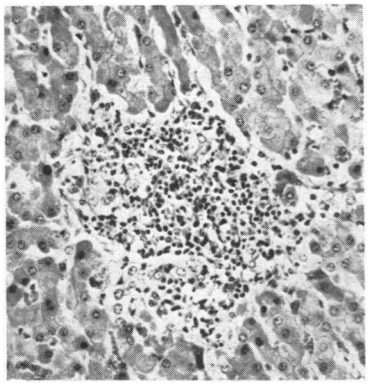

FIG. 1.—Case 8. Section of liver, showing marked round-cell infiltration of portal tract with commencing pyknosis of adjacent liver cells. (Stained haematoxylin and eosin. ×158.)

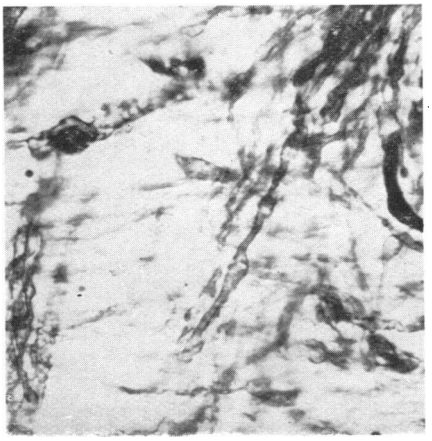

FIG. 2.—Case 8. Section from mid-brain, showing swelling and beading of myelin sheaths. (Woelcker stain. ×565.)

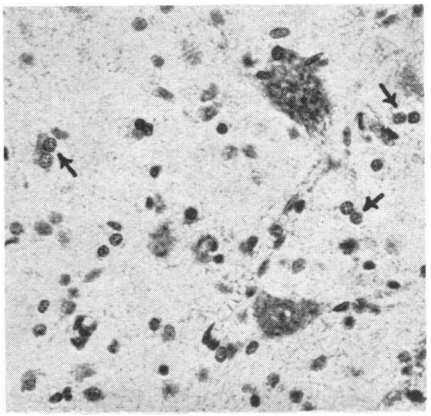

FIG. 3.—Case 8. Section from region of third-nerve nucleus, showing swelling and "twinning" of astrocytes (arrowed). (Nissl stain. ×264.)

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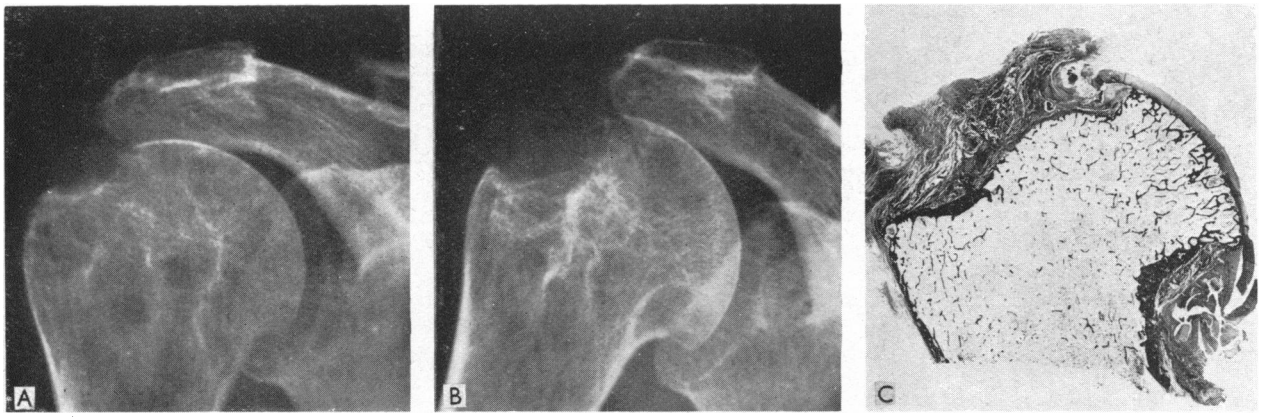

FIG. 1.—Case I. Head of right humerus, showing progressive destruction: (A) January, 1951; (B) August, 1951. (C) Post-mortem section showing replacement of spongiosa by swollen synovial tissue.

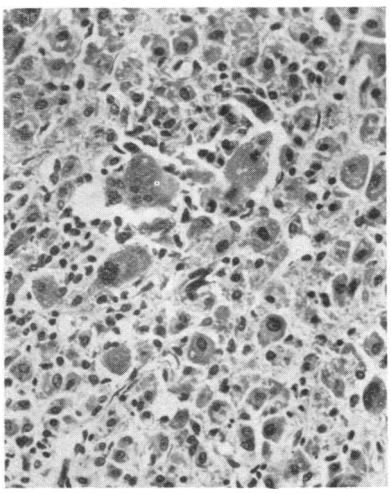

FIG. 2.—Case II. Photomicrograph taken from the edge of an eroded area in the head of the humerus, showing replacement by synovial granulation tissue packed with giant cells similar in morphology to those of the skin lesions. (×200.)

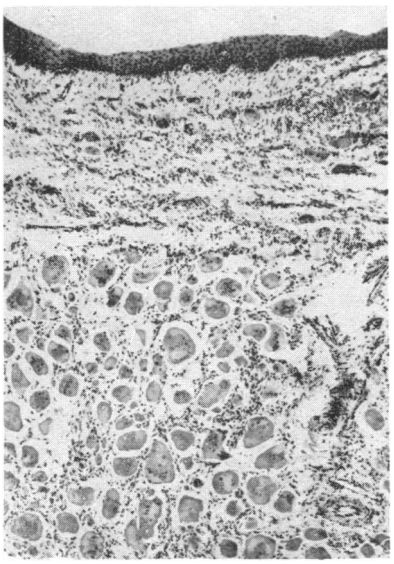

FIG. 3.—Case III. Photomicrograph of skin nodule, showing abundant multinucleate giant cells. (×40.)

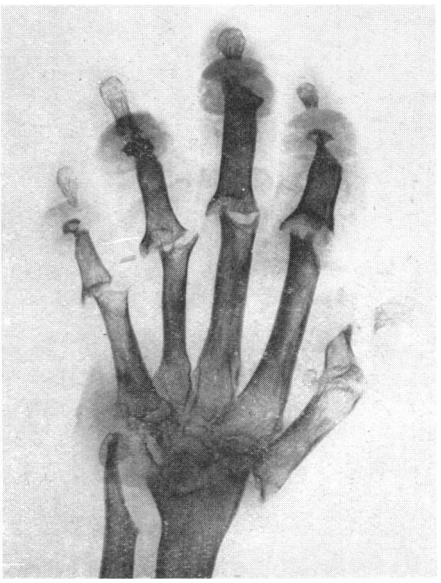

FIG. 4.—Case IV. Radiograph of hand, showing gross bony destruction.

amounts in cells in a relatively isolated position argues strongly in favour of an intracellular origin rather than histiocytic phagocytosis.

Radiological Features

The radiological appearances show many features resembling rheumatoid arthritis, but differ in a number of ways: the bone is destroyed rapidly, whereas the destruction of articular cartilage proceeds more slowly; involvement of the terminal interphalangeal joints is extensive; some unusual joints, such as the posterior articulations of the lumbar spine and the costotransverse joints, are affected; some bony sites other than joints are involved—for example, the connective-tissue attachments on the femoral trochanters, ischial tuberosities, anterior angles of vertebral bodies, and the shafts of long bones such as the radius and ulna.

Relationship to Allied Conditions

Although cases similar to those here presented cannot be found in the literature of the xanthomatous disorders, certain features, notably the multiple xanthelasma palpebrarum and presence of giant cells laden with sudanophilic material, indicate a connexion. There is a histological resemblance to the giant-cell synovioma of tendons and joints, and, although clinically the conditions are not clearly related, it is to be noted that five of the cases in the series developed tendon sheath tumours. Granular-cell myoblastoma also has a similar histological appearance. Such tumours are usually solitary, although a few cases of multiple myoblastomata have been described (Bloom and Ginzler, 1947; Powell, 1946). None of these has a close clinical resemblance to the cases included here, and no similar bone and joint changes are described. It is interesting that Pearse (1950) has shown that the cytoplasm of the granular-cell myoblastoma contains a lipoid probably in combination with protein and sugars or amino-alcohols. Subcutaneous nodules in rheumatoid arthritis may be widespread, but never approach the dissemination and the papular appearance of the cases described here, nor is the histology similar. Fletcher (1946) reported a case of severe rheumatoid arthritis in which after 4½ years extensive subcutaneous nodules developed. These showed an appearance more like the necrobiotic nodule of rheumatoid arthritis, but numerous "foam cells" and many multinucleated giant cells were present. Presumably this case is closely related to the series under discussion.

It is suggested that the condition is due to an abnormality in connective-tissue metabolism probably akin to that which occurs in rheumatoid arthritis. However, in the series of cases now described the histochemistry of this change and the resulting histology are different.

Recently cases of this condition have been reported under the heading of reticulohistiocytoma or reticulohistiocytosis. This title does not seem adequate to describe the clinical condition or the underlying disordered connective-tissue cell biochemistry. The term "lipoid dermato-arthritis" is preferred.

Summary

Four patients having an unusual eruption and arthritis are described. Twelve cases with a similar clinical and histological picture have been recorded in the literature under various titles. The eruption consists of sheets of yellow-brown papules over the backs of the hands and fingers, the face, forearms, and other areas, being widespread in some cases. Purple nodules are also present. Xanthelasma palpebrarum and tendon-sheath swellings may occur. The joint condition resembles a severe rheumatoid arthritis, with a number of minor differences and marked bone destruction. The histology of all involved tissue shows the same type of giant cell with an abundant granular cytoplasm which probably contains a lipoid-polypeptide complex.

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References

Allington, H. V. (1950). *Arch. Derm. Syph. (Chicago)*, **62**, 452.
Bloom, D., and Ginzler, A. M. (1947). Ibid., **56**, 648.
Caro, M. R., and Seneaf, F. E. (1952). *A.M.A. Arch. Derm. Syph.*, **65**, 701.
Davies, B. T., and Wood, S. R. (1955). *Brit. J. Derm.*, **67**, 205.
Fletcher, E. T. D. (1946). *Ann. rheum. Dis.*, **5**, 88.
Goltz, R. W., and Laymon, C. W. (1954). *A.M.A. Arch. Derm. Syph.*, **69**, 717.
Graham, G., and Stansfield, A. G. (1946). *J. Path. Bact.*, **58**, 545.
Laymon, C. W. (1952). *A.M.A. Arch. Derm. Syph.*, **66**, 647.
Montgomery, H. (1952). Ibid., **65**, 708.
Parkes Weber, F. (1943). *Brit. J. Derm.*, **55**, 1.
—— (1944). *Ann. rheum. Dis.*, **4**, 3.
—— (1948). In McKenna, R. M. B.: *Modern Trends in Dermatology*. Butterworth, London.
—— (1955). *Lancet*, **2**, 395.
—— and Freudenthal, W. (1937). *Proc. roy. Soc. Med.*, **30**, 522.
Pearse, A. G. E. (1950). *J. Path. Bact.*, **62**, 351.
Portugal, H., Fialho, F., and Miliano, A. (1944). *Rev. argent. Dermatosif.*, **28**, 121.
Powell, E. B. (1946). *Arch. Path. (Chicago)*, **42**, 517.
Targett, J. H. (1897). *Trans. path. Soc. Lond.*, **48**, 230.

EXFOLIATIVE CYTOLOGY OF THE COLON AND RECTUM

PRELIMINARY REPORT ON THE RECTAL WASHING TECHNIQUE

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[WITH SPECIAL PLATE]

Earlier reports on the cellular content of rectal discharges were made by those concerned with the diagnosis of specific inflammatory disease of the colon—that is, bacterial and amoebic dysentery (Dutcher, 1903; Jurgens, 1907; Anderson, 1921; Callender, 1925). Their interest was necessarily confined to the bacterial and parasitic content of the rectum and colon. In recent years there have been several papers in the American literature on the cytological content of the rectum and colon and the recognition of exfoliated malignant cells in cases of neoplastic disease of the large bowel. One of the problems for the cytologist working in this field is the difficulty of obtaining suitable specimens from such a large organ as the colon. A variety of techniques have been described, but none is entirely satisfactory, particularly where the lesion is situated in the proximal colon.

Previous Investigations

Bercovitz (1941) examined the cellular content of bowel discharges in a very large number of patients with normal and diseased large bowel and described the cellular flora, but did not report the presence of malignant cells in his cases of large-bowel tumour. In 1947 Wisseman *et al.* made a brief report on the diagnosis of carcinoma of the colon at various locations from the splenic flexure down to the rectum by the examination of smears prepared from the rectal contents obtained during proctoscopy. Wisseman *et al.* (1949) later reported their experiences with smears taken during sigmoidoscopy as well as proctoscopy with reference to the diagnosis of malignant epithelial tumours. The accuracy of cytological diagnosis of malignancy in the latter series was 76%, as compared with 79% by *x*-ray examination and 67% by sigmoidoscopic examination. Ayre (1950) described one case in which carcinoma of the rectum had been successfully diagnosed by cytology with a smear