man (1950) of three cases of mycotic endocarditis, two of which were due to aspergillus infection, following antibiotic therapy.

We would suggest that in this case, also, the use of penicillin and chloramphenicol predisposed the damaged lung to infection with *Aspergillus fumigatus*, and that the terminal condition was due to the fungus rather than to any pathogenic bacteria. The case has been presented, therefore, to illustrate one of the dangers of antibiotic therapy—a subject of considerable interest at the present time. With the increasing use of antibiotics, similar cases may be seen more often in the future.

Summary

A middle-aged woman was treated with penicillin, streptomycin, and chloramphenicol for post-influenzal bronchopneumonia. At post-mortem examination the presence of *Aspergillus fumigatus* infection of the lungs was discovered. The relation of the infection to antibiotic therapy is discussed.

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PERIPHERAL NEURITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

BY

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Peripheral neuritis has not been described as a feature of systemic lupus erythematosus, although it is well known in the closely related condition of polyarteritis nodosa.

The course of systemic lupus erythematosus has been fully described by many authors, notably Libman and Sacks (1924), Keil (1933), Baehr, Klemperer, and Schiffrin (1935), Klemperer, Pollack, and Baehr (1941), and Cluxton and Krause (1943), but none of these makes reference to peripheral neuritis, nor do the case reports of Kaposi (1872), Goeckerman (1923), Keefer and Felty (1924), Jarcho (1936), Fergusson, Milne, and Shand (1949), Beare (1949), or Gold (1951). Ginzler and Fox (1940) report bilateral wrist-drop in their patient twenty-four hours before death, but without investigation into its cause, clinical or pathological.

No mention of systemic lupus erythematosus is made by Richards (1951) in a comprehensive review of ischaemic lesions of peripheral nerves.

The following case is therefore put on record.

Case Report

A housewife aged 34 was originally admitted to the Maida Vale Hospital for Nervous Diseases on June 23, 1949, with a five-weeks history of weakness of the legs and paraesthesiae in her hands and feet. In March she had had a febrile illness, associated with a rash, mainly on the face, that had been diagnosed as rubella. A right-sided pleurisy in 1947 was the only past medical history of note, and she had no recollection of having taken any drugs. There was no significant family history of illness.

Examination revealed a persistent pyrexia of 102 to 103° F. (38.9 to 39.4° C.), with a tachycardia of 100 to 120 a minute associated with marked malaise and wasting. An erythematous maculo-papular eruption was seen on the cheeks, bridge of the nose, angles of the jaw, and wrists. The mucous membranes were generally pale, but there was inflammation of the mouth, tongue, and pharynx. The lymph nodes were not enlarged and neither the liver nor the spleen was palpable. No abnormality was found in the respiratory system, abdomen, or cardiovascular system, and the blood pressure was 135/85 mm. Hg.

In the nervous system, the upper limbs showed a bilateral motor weakness, most marked peripherally, and all the tendon reflexes were absent. Sensation was normal apart from slight loss of two-point discrimination in each hand. A generalized flaccid weakness of the lower limbs was again most noticeable in the periphery, knee-jerk and ankle-jerks were absent, and there was a bilateral flexor plantar response. Light-touch sensation was absent in both legs up to the knees, and vibration sense, while impaired up to the knee on the right side, was completely absent on the left. Pin-prick sensation was unaffected. Calf tenderness was marked in both legs.

The urine showed a heavy cloud of albumin, a large number of erythrocytes, and a few pus cells but no casts. Numerous investigations were negative, including agglutination reactions, the blood W.R. and Kahn test, and an x-ray film of the chest. A blood examination revealed: haemoglobin, 73% (Haldane) (10.8 g. per 100 ml.); red cells, 4,300,000 per c.mm.; white cells, 4,420 per c.mm. (neutrophil polymorphs 2,800, eosinophils 360, lymphocytes 1,260 per c.mm.). Lumbar puncture showed a pressure of 170 mm., with no block, 120 mg. of protein and 695 mg. of chlorides per 100 ml., and 5 lymphocytes per c.mm.

Owing to the development of occasional pulmonary crepitations, a course of penicillin and "sulphatriad" was given, but there was no clinical improvement. Vitamin B was administered by injection and later by mouth with nicotinamide and ascorbic acid, but, beyond relieving the stomatitis to some extent, did not appear to have any effect.

Blood culture was negative on admission, but on three subsequent occasions *Bact. faecalis alkaligenes* was grown, sensitive to streptomycin *in vitro*. A week's treatment with this antibiotic (0.5 g. six-hourly) and a further course in August brought no improvement.

A slight generalized lymph-node enlargement developed at this time, but the spleen remained impalpable throughout. Lymph-node biopsy from the left axilla and a sternal marrow examination by direct smear showed no significant abnormality.

Anaemia and leucopenia developed slowly, and by July 27 the haemoglobin was 45% (Haldane) (6.6 g. per 100 ml.), and there were 2,400 white cells per c.mm. (neutrophil polymorphs 1,600, lymphocytes 600, monocytes 200 per c.mm.). On this day 3 pints (1.7 litres) of Group A Rh-negative blood was given, raising the haemoglobin to 70% and improving the general condition, but not reducing the temperature.

By now some improvement in the peripheral neuritis was apparent, although the tendon reflexes were still absent and

the wasting was no less obvious. A further blood transfusion of 3 pints (1.7 litres) was given on August 19, when the haemoglobin had fallen to 60%.

On the following day five epileptiform seizures occurred with loss of consciousness and movements of the head and eyes to the left. For the remainder of the illness bilateral extensor plantar responses were present and bilateral retinal exudates were also noted. Lumbar puncture on August 22 showed 90 mg. of protein per 100 ml. and 12 lymphocytes per c.mm.

The skin lesions had gradually disappeared and by August 25 there was only a slight scaling in the affected areas. The blood pressure now was 120/90 and the urine showed a heavy precipitate of albumin. The heart was not enlarged and there were no significant murmurs and no pericardial rub. Her general condition remained grave, with a pyrexia of 100 to 102° F. (37.8 to 38.9° C.) and a tachycardia of 110 to 130 a minute. On August 25 she was transferred to St. Mary's Hospital.

The relevant investigations thereafter included: Plasma proteins 4.8 g. per 100 ml. (albumin 2.1 g., globulin 2.7 g.); E.C.G., low voltage in all leads with flat or absent T waves. Muscle biopsy showed no evidence of polyarteritis nodosa.

A course of chloramphenicol was given (0.25 g. six-hourly for six days), and a further course of penicillin (500,000 units twice daily), but with no effect. Late in November the temperature fell to normal, but the tachycardia persisted and her general condition deteriorated. Oedema developed, with a large ascites and a right pleural effusion, and the blood pressure rose steadily to 170/120. Severe abdominal pain occurred on December 16, and on the 18th there was evidence of acute generalized peritonitis. A laparotomy was undertaken, but the patient died on December 18 while on the operating table.

Necropsy Report

Necropsy was performed on December 19. *Cardiovascular system*: The visceral pericardium had a patchy gelatinous appearance and the myocardium was pale brown in colour with scattered paler areas throughout its substance. The endocardium, valves, and coronary arteries appeared normal. The heart weighed 375 g. *Respiratory system*: There was a small right hydrothorax and both lungs were very oedematous. *Digestive system*: The peritoneal cavity contained a large amount of turbid fluid. *Haemopoietic system*: The spleen was of normal size, firm, and congested, and had a small infarct. The Malpighian bodies and trabeculae were prominent. *Genito-urinary system*: The kidneys, each weighing 220 g., were pale in colour, and prominent glomeruli and small scattered haemorrhages were visible in the cortex, which was of normal width. *Nervous system*: No macroscopic changes were noted.

Microscopical Examination

Cardiovascular System.—The pericardium was thickened and showed a diffuse cellular infiltration, the main components of which were lymphocytes and plasma cells. Organization was occurring and capillary loops and fibroblasts were conspicuous. In the adipose layer of the epicardium there were granular eosinophilic areas, probably representing changes in the ground substance. The myocardium showed scattered areas where muscle fibres had disappeared. There were no distinctive connective-tissue changes. The endocardium and valves showed no abnormalities.

Respiratory System.—There was a generalized oedema, but neither vascular nor connective-tissue changes were observed.

Digestive System.—The small intestine showed several small vessels with eccentric intimal thickening; similar changes were seen in the mesenteric vessels.

Haemopoietic System.—The spleen showed the typical concentric periarterial fibrosis found in systemic lupus erythematosus (Fig. 1).

Genito-urinary System.—In the kidneys, the glomeruli showed both "wire loop" lesions and patchy necrotic areas, often associated with crescents. The interstitial tissue was diffusely infiltrated with lymphocytes and plasma cells. Fibrinoid necrosis was present in afferent arterioles and interlobular arteries. Cellular reaction in relation to these was minimal.

Central Nervous System.—No vascular changes were found in the brain, although numerous sections were examined.

Examination of peripheral nerves in the leg showed that some fibres had disappeared but most of them remained, showing no abnormality with a myelin stain. The endoneurium was increased in amount, varying from bundle to bundle. Abnormalities of the blood vessels in the epineurium were noticed. There were no active lesions such as were seen in the kidney, but numerous vessels showed evidence of previous damage. The arteriole in Fig. 2 shows evidence of old obliteration of the lumen with recanalization, and in relation to it is a group of chronic inflammatory cells. The small artery seen in Fig. 3 shows an eccentric fibrotic thickening in the intimal zone with thinning of the muscular wall over it. The internal elastic lamina is intact and new elastic is present in the fibrous tissue. This vessel has been followed in serial sections, but there was no evidence of previous complete rupture of the wall with loss of elastica and fibrous replacement of the media such as one normally sees in healed periarteritis nodosa. In discussing peripheral neuritis in polyarteritis nodosa, Kernohan and Wolman (1938) described healed vessels in which regeneration of the internal elastica had taken place, and the vessel in Fig. 3 may represent either an organized thrombus or a healed necrotizing lesion with regrowth of the internal elastica lamina. The distribution of the vascular lesions was patchy. Sections taken at certain levels showed completely normal vessels, while those taken at others showed lesions such as have been described.

FIG. 1.—Spleen. Concentric layers of collagen surrounding small artery. Haematoxylin and van Gieson. ($\times 110$.)

FIG. 2.—Peripheral nerve. Arteriole has been obliterated and recanalized. Chronic inflammatory cells in relation to it. Haematoxylin and eosin. ($\times 180$.)

Discussion

The combination of a prolonged pyrexial illness, renal dysfunction, serous effusions, and central nervous involvement of sudden onset suggested the diagnosis of either systemic lupus erythematosus or polyarteritis nodosa. The skin lesions and the progressive neutropenia were in favour

FIG. 3.—Peripheral nerve. Artery with gross intimal thickening and thinning of muscularis over it. New elastic-tissue formation. Hart-Sheridan method for elastic. ($\times 420$.)

of the former diagnosis, as was the female sex of the patient. On the other hand, the peripheral neuritis which gave rise to the presenting symptoms suggested polyarteritis nodosa, particularly when no previous account of this lesion in systemic lupus erythematosus could be found.

That this was a case of systemic lupus erythematosus could not be doubted after the post-mortem examination, although there is no satisfactory explanation for the repeatedly positive blood cultures.

The diagnosis of peripheral neuritis is established by the combination of a lower motor-neurone lesion, paraesthesiae, and sensory loss in all four limbs, together with bilateral calf tenderness.

From the histological evidence already given, it is postulated that the neuritis was of a similar nature to that described in polyarteritis nodosa by Wohlwill (1923), due to ischaemic changes in the nerves produced by an obliterative arteritis of the arteria nervorum. In view of the now generally accepted belief that systemic lupus erythematosus is a widespread disease of collagen it is not surprising to find these vessels involved. Indeed, rather is it to be wondered why polyneuritis is not a more frequent manifestation of this disease process.

Summary

A case of systemic lupus erythematosus in a woman aged 34 is described in which the presenting picture was one of peripheral neuritis.

It is considered that the peripheral neuritis was due to ischaemia consequent on vascular lesions in the vessels supplying the nerves.

We wish to record our indebtedness to Dr. J. W. Litchfield and Dr. P. H. Sandifer, the physicians in attendance on the patient, for their permission to report this case and for the interest they have shown in this paper; to Dr. J. F. Taylor, who carried out the necropsy; and to Mr. A. Beasley for the preparation of countless serial sections. We are most grateful to Professor W. D. Newcomb and Professor G. W. Pickering for their help and advice.

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A FOLLOW-UP STUDY OF 238 LEUCOTOMIZED PATIENTS*

BY

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This follow-up study was undertaken to assess the results of standard prefrontal leucotomy in 238 patients who underwent the operation at Crichton Royal between 1943 and 1948. Although it may be accepted that the value of the operation is established for chronic obsessional states and chronic affective psychoses, unexpected failures and unexpected successes are often met with. It was hoped that from a study of our own patients there would emerge criteria that would help us to select those individuals likely to respond to the operation. A special interest was taken in schizophrenics because they made up more than three-quarters of the series and because they form the great therapeutic problem. Partridge (1950) has published a valuable book on his personal follow-up of 300 patients over a period of one and a half to three years after operation; he was more interested in the clinical appearances than in the tabulation of results. We, on the other hand, to avoid being influenced by clinical impressionism have made a detailed examination of our material and results.

Material

TABLE I.—Composition of the Clinical Material

Diagnosis	No. of Cases	Percentage of Cases
Schizophrenia	194	81.1
Affective psychoses	21	8.9
Obsessional neurosis	14	6.3
Mainly organic psychoses	9	3.7
Total ..	238	100

Important features of our series were that all the patients were diagnosed and selected for operation according to the uniform standards of our hospital, while with the exception of the first 16 patients all operations were carried out by the same surgeon. The diagnosis in the 238 cases is shown in Table I. Most of the patients received the standard coronal cut of Freeman and Watts, but in 52 chronic cases

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