at an earlier date, and it does not therefore appear that a high degree of immunity exists between the two diseases. (*b*) The experiments of Lauda and Stöhr (1926) did not support those of Lipschütz and Kundratitz. They inoculated 55 children with herpes zoster vesicle fluid, but failed to obtain a positive local reaction in a single case. Nevertheless, three of the children developed varicella 14 days after the inoculation. (*c*) Zoster has been described in isolated communities where varicella is unknown, as in Cantor's (1921) report on Christmas Island and Woolley's (1946) report on three cases on Tristan da Cunha. The numbers involved in both these instances were very small, and so the reports should be treated with reserve.

It is still undecided whether the two conditions are due to the same virus, to distinct but antigenically similar viruses, or to a mutation of a reversible nature in the structure of the organism. Under the electron microscope the virus of herpes zoster is indistinguishable from that of varicella; from the clinical and pathological viewpoints this organism has an affinity for skin and nerve tissue. In children and in adults who have not previously had either disease or have not been exposed to subinfection of the virus, the tendency is for an infective dose of the virus to result in varicella, as a result of which a high degree of immunity to the organism is usually established. In the majority of adults repeated exposure to and subinfection by the virus seem to result in partial immunity of the individual. W. Russell Brain (1931) considered that the sensory neurone had a tissue immunity feebler than that of other parts of the body, or that its immunity might be temporarily diminished by a preceding lesion, so that an infective dose of the virus in adult life tended to produce herpes zoster.

Summary

Six cases of herpes zoster varicellosus are described. In one of these cases two contacts developed varicella within the incubation period of that disease, and during the incubation period one of these two varicella cases was responsible for conveying the infective agent of herpes zoster to another contact. The literature on the subject is briefly reviewed. It is concluded that herpes zoster and varicella are very closely allied; the definition of the exact relationship of the organisms must be left to the bacteriologist.

I wish to thank Professor G. H. Percival for helpful advice in preparing this paper. Thanks are also due to Dr. R. H. A. Siwain for the bacteriological investigations and to Mr. T. C. Dodds for the histological preparations and photographs.

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PULMONARY ASPERGILLOSIS FOLLOWING POST-INFLUENZAL BRONCHOPNEUMONIA TREATED WITH ANTIBIOTICS

BY

J. D. ABBOTT, M.D., Dip.Bact.

H. V. J. FERNANDO, M.B., B.S.

K. GURLING, M.D., M.R.C.P.

AND

B. W. MEADE, M.B., B.S.

(From King's College Hospital and Medical School, London)

The association of fungus infections with antibiotic therapy is now well recognized. Although many references are to be found in the American literature, few examples have been recorded in this country. We therefore think the following case of pulmonary aspergillosis is of interest.

Case Report

A housewife aged 51 was admitted on February 9, 1951, during an influenza epidemic, with a diagnosis of post-influenzal bronchopneumonia and toxic purpura. Her symptoms, which began three weeks previously, were typical of the prevalent influenza. The cough became worse, though the sputum was scanty, mucopurulent, and never blood-stained. She remained febrile, and three days before admission developed a purpuric rash.

Clinical Examination.—The patient was slightly cyanosed, dyspnoeic, and febrile—temperature 99.5° F. (37.5° C.), with a dry mouth—and obviously very ill. There were petechiae and haemorrhagic bullae on her face, arms, and legs which were considered to be typical of a "sedormid" eruption. She had taken three tablets before this rash appeared. There was slight impairment of the percussion note at the right base, and diffuse moist sounds were heard over both lower lobes. She had a regular tachycardia of 120, slight venous engorgement, and a little oedema of the ankles suggesting mild congestive failure. The blood pressure was not recorded because of bullae on the arms. A radiograph of the chest on February 9 showed obliteration of the right costophrenic angle with heavy lung shadows and only slight mottled opacities in both lower zones.

Special Investigations.—A blood count showed: Hb, 94% (Haldane); white cells, 18,000 (neutrophils 95%, lymphocytes 1.5%, monocytes 3%, metamyelocytes 0.5%); platelets, 230,000 per c.mm.; clotting-time, 5 minutes (capillary tube); bleeding-time, 3½ minutes (Duke). The urine contained: albumin, a trace; sugar, a trace on occasions; pus cells, 1–4, and red cells, 0–3, per ⅙ field. Blister fluid was sterile. Direct examination of the sputum on February 12 showed numerous pus cells and a few yeast forms; no acid-fast bacilli were seen. Culture yielded a heavy growth of *Bact. coli* sensitive to streptomycin and chloramphenicol, and a heavy growth of *Candida albicans*.

Progress and Treatment.—Treatment was begun at once with crystalline penicillin, 500,000 units eight-hourly. Two days later the patient was afebrile, the pulse rate had fallen, and she was much improved. On the fifth day, however, despite the absence of fresh physical signs in her chest, the temperature rose, penicillin was discontinued, and chloramphenicol was given, 3 g. initially and 0.5 g. six-hourly. By the tenth day her temperature was 100° F. (37.8° C.); she had a pleuritic pain in the right chest, auricular fibrillation had developed, and the sputum, still scanty, became purulent and streaked with blood.

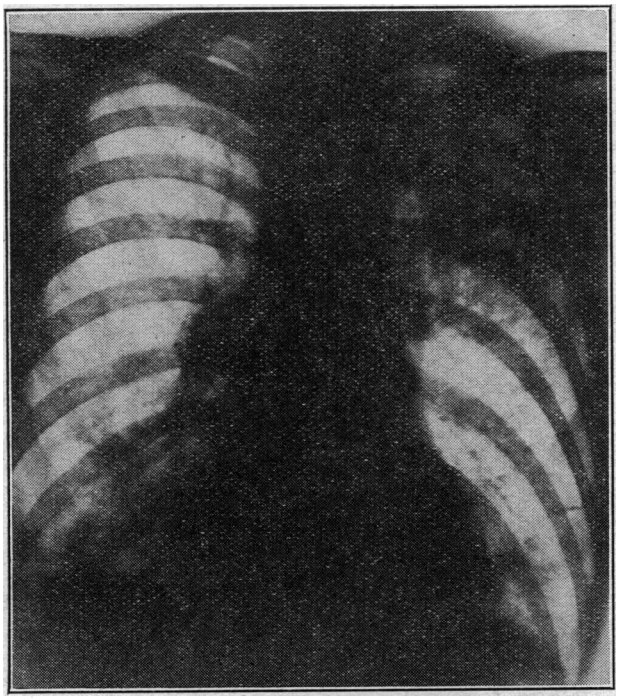

FIG. 1.—Radiograph of chest (February 19) showing opacities in left upper and mid-zones.

A chest radiograph on the eleventh day (February 19) showed extensive mottled opacities in the left upper and mid-zones containing what appeared to be irregular thin-walled cavities. Streptomycin, 0.5 g. twice daily, was now given in addition to chloramphenicol. On February 20 the sputum contained numerous pus cells, with occasional yeast forms and filaments suggestive of *C. albicans*; no acid-fast bacilli were seen. Culture yielded a predominant growth of *C. albicans*. From that time the patient's condition deteriorated, and she died in coma 16 days after admission.

Post-mortem Findings

The body was that of a thin elderly woman. There were several bullae on the arms, face, and feet which did not appear infected. Both lungs were emphysematous and oedematous. The left upper lobe contained a thin-walled cavity 5 cm. in diameter which had a trabeculated lining dusted with fine white and grey particles. The rest of this lobe showed bronchopneumonic consolidation, as did the right lower lobe to a lesser extent. The pancreas showed a haemorrhagic area in the tail, with several areas of softening elsewhere. The kidneys were pale and their capsules stripped easily. On the right side there were two large recent infarcts, and on the left several smaller less recent areas of infarction.

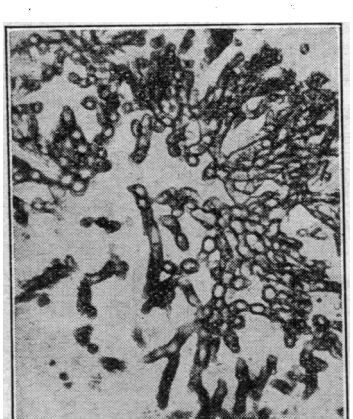

FIG. 2.—Section through lining of cavity in left upper lobe, showing fungal mycelium typical of aspergillus. H. & E. (×320.)

Histology.—Sections from the left lung showed the cavity to be lined with a densely felted layer of fungal mycelium and occasional conidia. The structure of the mycelium and conidia was typical of aspergillus (Fig. 2). Neither mycelium nor yeast forms of *C. albicans* were seen in the lung tissue. The adjacent lung showed consolidation, with a haemorrhagic fibrinous exudate. Fragments of mycelium were found in the lung tissue throughout the upper lobe and to a less extent in the lower lobe, where there was a less-pronounced exudate. Sections from the right lung showed some bronchopneumonic consolidation in the lower lobe, with fragments of mycelium in the exudate filling some bronchioles. In the pancreas there were irregular areas of haemorrhage and necrosis. One artery showed necrosis of all coats and scanty cellular infiltration with polymorphs, lymphocytes, plasma cells, and reticulo-endothelial cells, together with surrounding fibrosis. Several blocks from the kidneys showed a number of small arteries with areas of medial fibrosis. No fungal mycelium was seen in the sections from the pancreas or kidney.

Bacteriology.—Material from the lung cavity showed conidia typical of the *Aspergillus* genus. Cultures yielded a heavy growth of *Aspergillus fumigatus* Fresenius, together with a scanty growth of *C. albicans*, coagulase-negative staphylococci, and haemolytic streptococci, not of Lancefield groups A, C, or G.

In view of these findings the cause of death was considered to be toxaemia due to post-influenzal bronchopneumonia complicated latterly by aspergillus infection. Neither the purpura nor the presence of *C. albicans* seemed to contribute significantly.

Discussion

The occurrence of primary aspergillus infection of the lungs is well recognized, particularly in France and America. It occurs most often in patients who are in contact with fungus-contaminated grain, such as agricultural workers and pigeon-feeders. The clinical manifestations of this disease may briefly be said to fall into three groups: the bronchitic, the acute bronchopneumonic, and the chronic granulomatous types, the latter simulating tuberculosis (Virchow, 1856; Renon, 1897; Van Ordstrand, 1940; Cooper, 1946).

Secondary infection associated with other lung diseases is also described, and may occur in tuberculous cavities, bronchiectasis, and even bronchogenic carcinoma (Lapham, 1926; Kampmeier and Black, 1934; Donaldson *et al.*, 1942). Sometimes a blood-borne dissemination gives rise to endocarditis, granulomatous lesions in many organs, meningitis, and even brain abscess (Geiger *et al.*, 1945; Cawley, 1947; Grekin *et al.*, 1950).

The interest of our patient lies in the rapid development of a cavitating bronchopneumonia while massive doses of antibiotics were being administered. The extent of the lung disease shown radiologically was greater than expected from the physical signs, but was in keeping with her progressively deteriorating condition. The necropsy findings confirmed the presence of bronchopneumonic consolidation and of cavitation in the left upper lobe, the wall of which was lined with mycelium. Mycelium was also found in other parts of the lung.

Recent reports have shown the frequent association of fungus infection with antibiotic therapy. Thus Woods *et al.* (1951) describe a series of 25 cases of moniliasis apparently a direct sequel of the use of antibiotics. Of these, 20 had oro-pharyngeal, 3 intestinal, and 2 broncho-pulmonary moniliasis. They suggest that suppression of bacteria usually competing for food with the coexisting *C. albicans* is probably the most important factor in the development of these infections. The disturbance of vitamin synthesis due to alteration of bacterial flora in the gastro-intestinal tract may also be of importance. Harris (1950) reports some success with vitamin-B complex in the prevention and treatment of moniliasis following antibiotic therapy. Foley and Winter (1949) suggest that penicillin may actually enhance the growth and pathogenicity of *Candida* species.

Tomaszewski (1951) recently analysed the side-effects of 126 cases treated with chloramphenicol and "aureomycin"; he remarks on the frequency of a fungal flora in the oral cavity, with a disappearance of the normal bacterial flora. Of particular relevance to our case is the report by Zimmer-

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

R. H. HEPTINSTALL, M.D.

Senior Lecturer in Pathology

AND

G. S. C. SOWRY, M.D., M.R.C.P.

Assistant to the Medical Unit

St. Mary's Hospital, London, W.2

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 Schifrin (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