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THE GENERAL PRACTITIONER AND THE INFLUENZA PROBLEM

BY

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The general medical practitioner undoubtedly is closely concerned with the problem of human sickness attributable directly or indirectly to the operation of the influenza viruses. Long before the statistician has decided that an influenza epidemic has begun in the population, the practitioners in at least some parts of the country have begun to experience the well-recognized phenomena of crowded surgeries and long lists of sick people who require to be visited. There is no doubt that, if a solution of the problem of influenza could have been reached by mere clinical observation alone, someone concerned in actual general practice would have been the most likely person to suggest the remedy. As it is, however, mere clinical observation failed to distinguish any clear light in the darkness which enveloped the whole subject of influenza prior to the nineteen-thirties, when the first clues of the influenza viruses of animals and of man were picked up in the laboratory.

Now, laboratory workers concerned with the influenza viruses have always recognized the fact that influenza is a disease which lies peculiarly within the province of the general practitioner. Whenever opportunity has presented, the laboratory findings and problems, both solved and unsolved, have been laid before practitioners in the traditional manner. If it had not been for the great practical difficulties connected with the laboratory technique needed to prove the existence of human influenza virus infection, patients under the care of general practitioners would have been chosen for investigation instead of individuals in the Services, school-children, and others who were in fact investi-

gated. Nevertheless, though few direct tests have ever been made on subjects from a general practice, as knowledge has grown it has become clear that information furnished by the practitioners of this country has an important part to play in the general study of the epidemiology of influenza. The information referred to is that supplied in the form of notifications of deaths from influenza in the great towns of England and Wales. The manner in which this information has been correlated with the isolation of influenza virus from actual outbreaks of influenza or with serological tests has been referred to in detail on several occasions (Stuart-Harris, 1945, 1947). Briefly, the facts are that in the last ten years, whenever practitioners have notified 100 or more deaths from influenza in one week, laboratory workers have been able to obtain evidence that one or other of the influenza viruses is concerned in the causation of outbreaks of the disease in what are usually termed semi-isolated communities—i.e., schools, hospitals, or Service establishments. The years when the deaths never rose above 100 a week have also failed to supply the laboratory with evidence of virus infection. Furthermore, the laboratory worker has been able to correlate the type of curve obtained from plotting the figures of deaths from influenza with the type of virus concerned in the outbreak. Thus the sharp peaks reaching 1,000 or more in a week

have been associated with influenza virus 'A'. The lesser peaks between 100 and 500 have been associated with either or both of the two viruses A and B. These facts are shown in graphic manner in the accompanying chart.

Such facts would at once suggest that influenza virus infection in man is clinically recognizable. At the same time it has become clear to some of us who have studied patients from actual outbreaks that influenza virus infection in the individual is not recognizably different clinically from

Chart showing number of influenza deaths in the great towns from 1933 to 1947, together with the causative virus.

other acute infections of the respiratory tract. Furthermore, the cases which are notified as deaths from influenza are fatalities, whereas influenza is in the vast majority of instances a benign disease. Thus it has come about that those of us who have been concerned with research on the problem of influenza in this country are continually puzzled, first of all, why fatal cases of the human disease should be correlated with influenza virus infection, and, secondly, to know what sort of disease is constituted by this notification of a "death from influenza." The puzzle has not been merely that of the armchair speculative type but has concerned us because of the imperfection of our knowledge of the extent of the damage caused by the influenza viruses. We know that the virus is causative of that type of clinical picture commonly

termed uncomplicated influenza and probably of the complication of basar bronchiolitis. We also know that the rare case of acute rapidly spreading pneumonia with heliotrope cyanosis is associated with a staphylococcal infection of the lung combined with an influenza virus infection. Yet the relationship between influenza virus infection and the ordinary case of pneumococcal pneumonia seen during outbreaks is obscure. Indeed, the actual patient has usually given negative results when tested for evidence of influenza virus infection at the time of admission for treatment of the pneumonia. If we knew whether such cases were in fact initiated by influenza virus infection, even if the subsequent pneumonia was due to a pneumococcal infection permitted by the weakened defence of the respiratory tract, we should also know whether to expect that control measures such as immunization with influenza virus vaccines would prevent "deaths from influenza."

It seems, therefore, that more knowledge concerning the complications of influenza, and particularly of fatal cases, is needed. Such knowledge is not likely to be gained by investigation of the localized outbreaks of the disease such as those studied thus far, for complications of any character in the populations ordinarily affected are uncommon. Probably this is due to the type of subject affected, who is usually a previously healthy young adult or child. When the full-time department of medicine of the University of Sheffield came into being in 1946 we decided to attempt to study this problem from a different angle. In view of the fact that deaths from influenza must often occur in hospital, it seemed to us probable that a cross-section of the ordinary hospital cases of pneumonia admitted during an outbreak of influenza would be likely to include cases of a type familiar to practitioners and attributed by them to influenza. The department has clinical facilities in both the voluntary and the municipal hospitals of Sheffield, and thus is in a position to study such cases.

Last winter a number of explosive outbreaks of influenza occurred during January in Army camps housing German prisoners-of-war in the Midlands. From each of three outbreaks Dr. Margaret H. Miller was able to recover strains of an influenza virus and identified the serological response in cases of the disease as that found in influenza A. The general public at this time was largely unaffected, though the deaths from influenza rose and reached a peak of 211 in the first week of February and workers at the National Institute for Medical Research (Dudgeon *et al.*, 1947) identified influenza A outbreaks in the South of England.

Though the weather was very severe in the Sheffield region fewer cases of pneumonia than the average were admitted to hospital during the winter. An analysis of the week's work of several general practitioners in the Sheffield area was carried out by Dr. J. Pemberton; this showed, however, that 30 to 50% of their work during the first week of February was concerned with diseases of the respiratory tract. Dr. A. Dick studied the clinical features and bacteriology of some 40 cases diagnosed as pneumonia and admitted under my care during January, February, and March. The patients were often only mildly ill, their illnesses responded in the usual way to chemotherapy, and none died. Pneumococci were, however, usually identified in the sputum, including pathogenic organisms such as Types I, II, VII, and VIII. A few tests of sputa from such patients were made by Dr. Miller with the technique which was successful in the case of the influenza patients, but virus strains were not obtained. Yet the serological tests on the cases of pneumonia suggested that many of the patients admitted in January and February had in fact suffered from

an infection with influenza virus A at some time shortly before or during the pneumonic episode. The results surprised us and, largely because of their unexpected character, we failed to establish by adequate control studies the crucial point of whether, so far as the virus was concerned, the patients with pneumonia were in any way different from Tom, Dick, or Harry of the general population. In other words, the influenza A of last winter might have affected a similar proportion of individuals in the general public as in the cases of pneumonia by an unusually widespread subclinical infection, even though the "epidemic" seemed to be restricted clinically to certain community groups. It thus remains for us to repeat the study during future outbreaks in order to determine whether cases of ordinary pneumococcal pneumonia at the time of influenza outbreaks are or are not related to the virus infection. Because of the periodic character of influenza outbreaks, this work will probably take some years to complete.

Meanwhile, however, it seemed to us possible to collect together useful information concerning the cases which are actually notified by practitioners as "deaths from influenza." Only in this way will it be possible to decide whether mortality from influenza is particularly liable to occur in any one section of the population. It may be worth while pointing out in this connexion the probability that heart failure may be precipitated by influenza virus infection. An example of such a case is given below; this would have been regarded as that of ordinary bronchopneumonia and congestive heart failure had it not been for the serological results, which clearly implicated influenza virus A. It is possible, therefore, that this investigation may reveal information of value in connexion with a variety of topics, and may supplement the observations made on our own patients. It will be particularly important, for instance, to ascertain whether there are any clinical differences between deaths from influenza notified in years when influenza virus infection is not identified and those occurring in years when the viruses are active.

In order to provide sufficient material for statistical analysis within a reasonable period of time it will clearly be necessary to collect data from many sources. The more detailed clinical and laboratory observations possible on patients in hospital will then furnish a useful collateral study to the wider investigation which is proposed.

Case Report

A man aged 52 was admitted on Jan. 24, 1947, in a condition of great restlessness, with a history of cough and dyspnoea for about four weeks, increasing greatly in the four days before admission. He presented signs of hypertensive heart disease with congestive failure, though there was as yet no oedema. Rhonchi were heard in the lungs and over the left base, which was slightly impaired to percussion; there were numerous rales. There was a low irregular fever (98–100° F. (36.7–37.8° C.)) for three days, accompanied by tachycardia (100–110) and a slightly increased respiratory rate (20–26). After four days the restlessness had if anything increased, the signs in the lungs persisted unchanged, and orthopnoea was present. Skiagrams by portable apparatus showed congestion at both lung bases and considerable cardiac enlargement. Inoculation of the sputum into mice yielded a pneumococcus which could not be typed. Treatment with penicillin was begun, and continued for nine days. A week later the general condition had improved, but venous congestion had increased, sacral oedema had appeared, and the heart sounds showed a triple rhythm. The blood pressure had risen from 160/85 on admission to 185/120. There was no further deterioration, but the heart failure was slow to respond to therapy by digoxin and venesection, and basal rales persisted at both lung bases. Further treatment with diuretics was followed by slow improvement and the patient was

discharged on March 28 in reasonable health though still with cardiac enlargement and hypertension. The serum antibodies to the PR8 strain of influenza virus A and the Lee strain of virus B were estimated in samples collected on admission (Jan. 25) and on Feb. 15 by the agglutination-inhibition test (Hirst). The results showed that the antibody level against influenza virus A had increased 64 times during the progress of the patient's illness, whereas that against influenza virus B had remained unchanged.

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AMOEBIC ABSCESS OF THE LEFT BUTTOCK IN A SYMPTOMLESS CYST CARRIER

BY

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Cutaneous amoebiasis has been reported from many parts of the world. The cases fall into five groups according to their connexion with other primary conditions: (1) those following the drainage of an amoebic abscess of the liver (Heimbürger, 1925); (2) those following the drainage of a lesion of the appendix (Cole and Heideman, 1929); (3) those following a colostomy for a rectal obstruction (Smyth, 1946); (4) those about the anus associated with amoebic colitis (Van Hoof, 1926); and (5) those without any direct connexion with the viscera.

In practically all of these cases motile entamoebae were found in fresh preparations from the lesions of the skin. The case described below falls into the last category. The only references we can find in the literature that are at all analogous to our case differ from it in some respects; these will be discussed later. Van Hoof (1926) reported the case of a negro woman who suffered from dysentery in 1915 for which she received injections, probably emetine, but was not cured. In July, 1925, multiple ulcerations appeared on the skin of the buttock and around the anus, some of the ulcers communicating with the bowel. In the pus of both the fistulous ulcers and those not communicating with the rectum active entamoebae containing red blood cells were found; after specific treatment with emetine the amoebae could no longer be demonstrated and the lesion healed rapidly. In our case there was no history of previous dysentery, and the most careful search failed to reveal any direct communication with the rectum.

Ngai and Frazier (1933) described a case in which a papilloma of the anal region was invaded secondarily by *Entamoeba histolytica*. We believe that a secondary invasion of a staphylococcal abscess occurred in our case. This is reported, as, apart from the rarity of the condition, it is felt that similar cases may arise during the next few years in Service personnel, and unless the condition is recognized at an early stage gross destruction of the tissue will occur as in the case reported by Norwich and Muskat (1946). Their case occurred in a negro, who gave a history of a small blind boil appearing near the anus which eventually burst and instead of resolving was followed by a rapidly spreading ulceration. There was a previous history

of colicky lower abdominal pain and diarrhoeal stools with occasional blood. On his admission to hospital an ulcer measuring 5 in. by 2 in. (12.5 cm. by 5 cm.) was present on the left buttock, extending obliquely across the sacrum to the opposite buttock. Sigmoidoscopy revealed a large necrotic ulcerating area covering the posterior wall, while a biopsy from the edge of the ulcer of the skin revealed the presence of numerous *E. histolytica*. A colostomy had to be carried out to prevent soiling of the ulcerated area, but eventually, after specific anti-amoebic therapy followed by a skin graft, complete healing occurred.

This case differs from ours in that there was gross ulceration of the rectal mucosa. An extensive search through the literature has failed to reveal an exactly parallel case to the one here recorded.

Case Report

A warrant officer aged 27, of excellent physique, was admitted to an R.A.F. station sick quarters on Jan. 4, 1947, with a painful swelling on the left buttock which had been discharging pus for five days. He stated that he had had some pain in the left buttock about four months previously and that there was a swelling in this region. Apart from pain on sitting this gave no trouble and did not interfere with his normal activities. On Dec. 29, 1946, the swelling burst and discharged pus, and after this the pain increased in severity and he reported sick.

Previous History.—In September, 1945, he was kicked in this area while playing football in Bombay, where he had served for two years. He returned to the United Kingdom in October, 1946, and three weeks later he first noticed the pain in his buttock. He had never had dysentery, and remembered only one mild attack of diarrhoea, lasting one day, during his tour abroad.

Present Illness.—He was transferred to an R.A.F. station hospital on Jan. 4. On examination a slight bilateral inguinal adenitis and a swelling of the left buttock some 4 in. by 4 in. (10 cm. by 10 cm.) were found. This swelling was hard centrally but soft and fluctuating peripherally; pus was escaping from a small opening, and probing of this opening revealed a short sinus some 3/4 in. (1.9 cm.) long. Pus from the sinus grew *Staphylococcus aureus* and *albus*. His B.S.R. was 40 mm. in one hour. A skiagram of the lumbar spine and pelvis revealed no abnormality. The skin showed dark purplish discoloration. The W.R. and Kahn test were negative. The abscess was incised on Jan. 8, and two main cavities were found communicating with each other and lying subcutaneously; there was no sign of any communication with the rectum. Histological examination of the curettings revealed granulation tissue with aggregations of plasma cells scattered among the polymorphonuclears; there was no specific evidence of tubercle or actinomycosis. After the operation short-wave therapy and the instillation of 100,000 units of penicillin on alternate days led to considerable local improvement, and the abscess cavity appeared to be granulating satisfactorily. On Jan. 18 further undermining of the skin laterally led to pocketing of pus and the appearance of fresh sinuses.

Local treatment having failed it was decided to try the effect of systemic penicillin, and a million units were given over five days without any response. The failure of any form of treatment and the unusual features of the ulcer then suggested that it was a fungous infection (? sporotrichosis), and iodides were given for several days, again without any noticeable improvement.

By Feb. 19 the ulceration had spread both medially and laterally, and fresh sinuses had appeared near the medial edge. The abscess had to be reincised on Feb. 21, and gelatinous material was curetted from the sinuses, but the cultures were sterile. Histological examination of the material from the curettings revealed an oedematous granulation tissue infiltrated with plasma cells and macrophages and scanty cells which resembled *E. histolytica*. The patient was transferred to Princess Mary's Royal Air Force Hospital for further investigation. Examination showed a granulating ulcer measuring