

weight. The following figures are remarkable but illustrate the point. The titre of this serum was high and never varied, i.e., 1 in 800.

| Date :                   | Jan. 19 | Jan. 20 | Jan. 21 | Jan. 22 | Jan. 23             |
|--------------------------|---------|---------|---------|---------|---------------------|
| Weight in grammes ..     | 1,550   | 1,580   | 1,600   | 1,610   | 1,600               |
| Amount of blood taken .. | 15 c.c. | 12 c.c. | 12 c.c. | 21 c.c. | 14 c.c.             |
|                          |         |         |         |         | rabbit still lives. |

We have ventured to publish this method which is both rapid and effective as the scarcity of animals renders the productivity of serum of real importance. In any serum in which the question of group agglutinin is not of paramount consideration, quantities much in excess of those mentioned may be obtained. With us a 1,500 gramme rabbit gave 125 cubic centimetres of highly specific serum of a titre of 1 in 200 and this could probably be exceeded. We may state that although we supply large quantities of normal serum per month no animal has been killed in the laboratory in the last ten weeks for this purpose, it having been procured by this method of bleeding.

#### NOTES ON THE SYMPTOMATOLOGY AND MORBID ANATOMY OF SO-CALLED "SPANISH INFLUENZA," WITH SPECIAL REFERENCE TO ITS DIAGNOSIS FROM OTHER FORMS OF "P.U.O."

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THE recent outbreak of a number of cases of what appears to be a new form of so-called "influenza" has greatly added to the number of cases admitted to the base hospitals with the provisional diagnosis of "P.U.O." and some months' experience in the medical wards of a large base hospital in France has suggested to me that it would be useful to attempt to classify the chief diagnostic features of some of the principal conditions which are admitted to hospital with this diagnosis.

The term "P.U.O." although useful, and in some cases necessary, is at the same time too loose, and too much lacking in scientific exactness, to be wholly satisfactory. Moreover a more exact diagnosis is desirable, both from the point of view of prophylaxis, and if necessary isolation, and also for the purpose of prognosis as to the probable duration of the patient's unfitness for military service.

Certain of the conditions liable to be included under this heading have but to be remembered to be excluded in the majority of cases, by appropriate clinical or bacteriological examination. Among these may be mentioned: (1) Malaria; (2) *Bacillus coli* infections, particularly *coli bacilluria*; (3) malignant endocarditis. But a smaller group remains, comprising (4) the trench fevers; (5) the enteric group, including typhoid and paratyphoid fevers, which for my purpose may be considered together; and (6) the influenzal group, including true influenza and the recent epidemic, which in the present condition of uncertainty as to its bacteriological causation, may be provisionally termed "Spanish" influenza; and (7) certain aberrant cases of cerebrospinal meningitis.

The symptomatology of "Spanish" influenza is characteristic and in view of the extreme prevalence of this disease at present, it will be useful to first consider

in some detail the principal features of this complaint as seen in France, considering *en passant* the various points which serve to distinguish it from other diseases closely resembling it.

The incubation period appears to be short, about three to four days. The mode of onset is characteristically sudden. A patient may be at work in his usual health in the morning and in the evening he may be in hospital with a temperature of 102° to 104° F. and presenting the appearance of acute illness. The earliest symptoms are usually shivering, pains in the limbs and back and very severe headache, generally but not invariably frontal in situation, sore throat, and in almost all cases an irritating severe cough is also complained of.

The appearance in most cases is quite characteristic. The patient lies curled up in bed in a drowsy condition, with flushed face and injected conjunctiva, but there is little coryza, and physical signs in the early stages at any rate, are remarkable by their absence. The facies apart from the absence of coryza, remarkably resembles that of a measles patient a day or so before the appearance of the rash.

Although severe sore throat may be complained of, little can be seen in the throat beyond some general injection of the fauces, although in some cases œdema of the uvula, or slight degree of tonsillitis is present.

Severe and irritating dry cough is usually present, but there may be no discoverable physical signs in the lungs at first. On the other hand some coarse rhonchi may be heard over the larger bronchial tubes, or a few crepitations may be heard at one or both bases.

In other cases there is an early generalized bronchitis, and in some few instances, a dry pleurisy, particularly in the left axilla, may make its appearance almost at the onset.

A small percentage of patients develop serious pulmonary complications, and the pneumonia arising in these cases presents several distinctive features. It is of a mixed lobar and broncho-pneumonic type. Several large patches of consolidation may be found, but not as a rule at the extreme base of the lung. Favourite situations appear to be in the axilla, or in the middle third of the lower lobe. A remarkable feature is the not infrequent presence of well-marked ægophony without other signs of fluid, over the consolidated area. The very loud tubular breathing and crepitations together with the increased vocal resonance, and the presence of the signs of more normal lung tissue below the patch, suggest that this ægophony is due to a very thin layer of purulent exudation over the pneumonic patch, shut off by pleural adhesions, and thus prevented from gravitating to the lower part of the pleural sac. This is confirmed by the post-mortem findings.

In some of these influenzal pneumonias the toxæmia is severe and death rapidly ensues from acute heart failure. These cases frequently present an appearance very similar to that of a patient suffering from purulent bronchitis. The colour is a curious bluish tint, suggesting at first sight that he is suffering from extreme right heart failure, but physical examination of the heart and pulse do not confirm this, and the condition appears to be due to extreme toxæmia rather than to any mechanical embarrassment of the right heart.

In other cases not quite so acute, œdema of the lungs supervenes, large quantities of semipurulent sputa are expectorated, but the patient dies from heart failure secondary to asphyxia.

The heart conditions of a very large proportion of these cases of Spanish influenza is interesting. Without any marked alteration in the size of the heart as discovered by physical examination, and with the apex beat little if at all displaced, there is a well-marked reduplication of the first sound at the apex or of the pulmonary second sound, which is also frequently accentuated; not infrequently both sounds are reduplicated. In many cases this probably indicates the presence of some degree of myocarditis. It is noteworthy that in a large proportion of cases examined post mortem here, myocarditis was found, and more or less dilatation of the heart was constant. In cases in which a murmur develops and becomes increasingly musical with displacement of the apex beat, the question of an early ulcerative endocarditis must be considered, and a blood culture and leucocyte count should be made with a view of excluding this condition.

In at least four instances I have seen a scarlatiniform rash so closely resembling the rash of scarlet fever that very careful examination was required to decide that we were not dealing with a case of the latter disease. The rash, however, was more markedly patchy in distribution, evanescent and recurrent, in some cases irritating, and the appearance of the patient's face and throat, together with the absence of the rapid pulse and strawberry tongue of scarlet fever, and also the comparatively low temperature at the time of appearance of the rash enabled us to exclude the existence of this disease.

One patient, however, who gave a history of another man in his hut having had a rash, was transferred to an isolation hospital, but at a post-mortem examination made after his death from broncho-pneumonia a few days later, the appearances presented were precisely those found in other cases of deaths from this influenzal form of pneumonia.

The tongue of these influenzal cases is almost invariably dirty and furred, and in some cases there is an offensive almost pathognomonic odour of the breath.

The onset of pyrexia is very sudden, the temperature rapidly rising to 103° F. or higher. The duration of pyrexia is generally short, and under appropriate treatment and rest in bed the temperature rapidly falls about the third to fifth day to normal, thereafter probably rising to about 99° F. on the following evening, a week from the date of onset, remaining below normal. If the pyrexia persists after the first week, it is probable that either some pulmonary complication is present, or that the diagnosis of influenza must be reconsidered, special attention being given to the possibility of the case being one of the enteric group.

The pains of this type of influenza are very characteristic, they are referred almost invariably to the muscles and soft tissues, and to a less extent to the joints rather than to the bones themselves.

The most common sites of pain are in the muscles of the thighs and calves, the lumbar muscles and muscles of the back of the neck, and to a less extent the knees and ankle-joints. The headache of influenza has already been referred to. In a very large proportion of cases it is frontal, in some cases occipital, and in a few referred to the vertex. The headache is in some cases very persistent, continuing for some days after the patient's temperature has fallen to normal, and is almost invariably extremely severe at first. The pains differ considerably from those of trench fever. In the latter the pains are most frequently referred

to the bones themselves, particularly to the inner and outer edge of the tibiae, and the bones are often very tender to palpation. The acute nocturnal exacerbations of the pains are more marked in trench fever than in influenza.

The pains of the abdominal group of influenza cases may arouse the suspicion of appendicitis. They are however more general, although frequently referred to the lower part of the abdomen. There is, however, little or no muscular rigidity, and the tenderness to deep palpation is not more marked in the right iliac region than in the left. The pain does not tend to become localized and the fever and pulse-rate do not indicate progressive lesion.

There is a group of cases admitted with occipital headache and pain in the neck, closely resembling cases of cerebrospinal meningitis, but as a rule the rigidity of the neck is much less marked. In some of these cases the diagnosis is rendered more puzzling by the presence of what I may describe as a "spurious" Kernig's sign, i.e., it is impossible to say that Kernig's sign is absent, although it is more of the nature of a "clasp knife rigidity" than a true Kernig's sign. Lumbar puncture may however be necessary to exclude cerebrospinal meningitis, when although the fluid may escape under high pressure, it is clear, and does not present the characteristic cytological features of the latter disease.

TABLE I.

| Disease                | Mode of onset     | Fever                                      | Pains: characteristics of   | Bacteriological examination     | Blood count           |
|------------------------|-------------------|--|---|---------------------------------|-----------------------|
| Malaria                | Sudden            | Intermittent as a rule                     |   | Parasites in blood,             | ..                    |
| <i>Coli</i> bacilluria | Gradual           | Prolonged and irregular                    | Renal, vesical or ureteric tenderness   | <i>B. coli</i> in urine         | ..                    |
| Malignant endocarditis | Gradual or sudden | Constant, prolonged and irregular          |   | Blood culture may be positive   | High leucocytosis     |
| Trench fevers          | Sudden            | Frequent relapses                          | Pains in bones, especially shins, worse at night, shins tender  |                                 | Moderate leucocytosis |
| Spanish influenza      | Very sudden       | Short, rarely relapses, subsides by crisis | Pain in head, usually frontal and back; pains in legs, usually muscular; in calves and thighs, continuous all day |                                 | Moderate leucopenia   |
| Influenza              | Very sudden       | Short, subsides by crisis; less acute      | Pain, especially in head and back   | Influenza bacilli in sputum     | Leucopenia            |
| Enteric group          | Gradual           | Prolonged; gradual onset subsides by lysis | Vague; general  | Widal's reaction                | Leucopenia            |
| Cerebrospinal fever    | Sudden            | High and irregular                         | Headache, usually occipital   | Cerebrospinal fluid cloudy, &c. | Leucocytosis          |

A blood count is of great value in helping to discriminate between the various causes of P.U.O. The trench fevers are usually accompanied by a moderate leucocytosis. Malignant endocarditis, scarlet fever, and cerebrospinal fever as a rule show a marked leucocytosis. The enteric group is more usually characterized by a leucopenia. In "Spanish influenza" the leucocyte count usually varies between 5,000 and 9,000 per centimetre.

Very few cases of influenza show a true relapse, and the occurrence of a pyrexia relapsing within a few days in a supposed case of influenza suggests the probability of the case being one of trench fever.

I regret that the few cases in which the urine has been examined prevent me from making any observation on this point. I have not touched on the bacteriology of these cases, for at present this aspect of the disease is *sub judice*.

Tables I is a summary of the principal diagnostic points of the commoner causes of P.U.O. Table II gives an analysis of the post-mortem findings in thirty cases diagnosed as "influenza" at a hospital base in France during June and July, 1918. For these tables, and for other valuable suggestions, I am much indebted to Captain T. W. G. Shore, R.A.M.C., Pathologist to ——— Administrative District, France.

TABLE II.—SUMMARY OF POST-MORTEM FINDINGS IN THIRTY CASES DIAGNOSED "INFLUENZA."  
MORE OR LESS DILATATION OF HEART CONSTANT.

|  |                |    |                                |  |
|--|----------------|----|--------------------------------|--|
| Myocarditis  | .. ..          | .. | In 20 out of 30                |  |
| Endocarditis of mitral valve   | .. ..          | .. | " 2 " 30                       |  |
| Pleurisy   | .. ..          | .. | " 26 " 30                      |  |
| Pleural effusion   | .. ..          | .. | " 8 " 30                       | .. (Generally purulent).   |
| Broncho-pneumonia  | .. ..          | .. | " 27 " 30                      | } Broncho-pneumonia the rule. Often confluent, less so in later cases. |
| Lobar pneumonia  | .. ..          | .. | " 1 " 30                       |  |
| Confluent broncho-pneumonia  | .. ..          | .. | " 11 " 30                      | } Miliary or shotty broncho-pneumonia in later cases.                  |
| Miliary pneumonia  | .. ..          | .. | " 4 " 30                       |  |
| Pus in bronchioles   | .. ..          | .. | " 12 " 30                      | .. Resembling purulent bronchitis cases. Commoner in later cases.      |
| Collapse when present along vertebral border of lung. Emphysema common anteriorly. |                |    |                                |  |
| Nephritis  | { Acute in 7   | }  | Kidney as a rule pale—"toxic." | Suppression of urine in one case.                                      |
|  | { Chronic in 2 |    |                                |  |
| Jaundice in 2.   |                |    |                                |  |
| Spleen generally enlarged.   |                |    |                                |  |
| Pulmonary glands always enlarged.  |                |    |                                |  |
| Liver generally shows some fat.  |                |    |                                |  |
| Pulmonary abscess in 3.  |                |    |                                |  |
| Abscess in brain in 1.   |                |    |                                |  |
| Old tubercle in 7. (Much higher than average in B.E.F.)                            |                |    |                                |  |