

than we have to the cause of that most baffling of all blood diseases, Addison's anaemia. The progress and the blood picture suggest the haemolytic type, which can be produced experimentally and which is caused by the poisons of the *Bothriocephalus*. In the profoundly changed metabolism of pregnancy and in the intensely katabolic metabolism of the *post-partum* states we assume the production of haemolytic agents—toxins—but, as French remarks, "the use of the word toxin almost connotes ignorance." Though progressive and often pernicious, the anaemia is caused by an agent which differs in one important particular from that which causes the anaemia of Addison. When recovery takes place it is permanent, and the woman may escape in subsequent pregnancies. The second patient in my series (whom I knew well) had an attack of extreme gravity, recovered, bore two children subsequently and was alive thirty years after the attack. Recovery from the Addisonian form may last ten, fifteen, or even seventeen (McPhedran) years, but such instances are exceptional, and in the cases of reported permanent recovery there is always the question of mistaken diagnosis.

The blood picture may be of value in estimating the outlook. Signs of active regeneration may be present, as in Mrs. A.'s case, indicated by blood crises and a large proportion of red cells with signs of recent formation, and the basophilic granulation described by Boggs and Morris and by Milne, the mitochondria (Sappington) and the reticulation described by Robertson and Bock.¹² The number may rise from 1 per cent., the normal, to 20 or 25 per cent. with marked bone-marrow stimulation. A high colour index is the rule in the pregnancy and *post-partum* cases. The blood condition is uncertain, however, as well shown in two exceptionally well studied cases in Meyer's clinic, reported by Jungermann,¹³ in which the contrast was striking, the one with low colour index and features of an aplastic anaemia, the other the characteristic Addisonian picture. Both were pregnancy cases, and both had normal deliveries and recovered completely. The absence of platelets is a feature of the common idiopathic anaemia, contrasting, in this respect, with the post-haemorrhagic and septic forms. In the hands of skilful students the criteria offered by the blood examination should, as a rule, be of great value in the prognosis.

My individual experience is exceptional and much more hopeful than indicated in the literature, and particularly in works on obstetrics. The seven cases seen in Montreal and Philadelphia recovered. I have not at hand our large material from the Johns Hopkins Hospital; but I do not remember a fatal pregnancy or *post-partum* case. The later appear to be the more fatal, and the cases reported by Elder and Mathews¹⁴ show that a fatal termination may follow in spite of the most careful treatment.

Acute haemorrhage *post partum* may be rapidly fatal from reduction in blood volume; very large amounts may be lost extending over several days, and yet recovery takes place.

The report of Robertson and Bock, just mentioned, contains much information of value in estimating the blood loss in haemorrhage and the means of treatment. From what is recorded, and from personal experience, I should say the danger of a grave anaemia progressive in character is not great after a fairly profuse haemorrhage. Once the bleeding stops, recovery is progressive and often surprisingly rapid. On the other hand, repeated small losses of blood after abortion or a normal delivery may be followed by an anaemia out of all proportion to the quantity of blood lost. The starting point, indeed, of a few cases of Addison's anaemia appears to be repeated epistaxis or bleeding piles.

The treatment of the cases is that of the severer forms—fresh air, rest, food, iron, and arsenic (in which I still have faith); and if the blood count is very low, 20 per cent. of corpuscles and haemoglobin, transfusion may be employed. The newer technique has many advantages, but the results do not, in Addison's anaemia at any rate, appear to be more favourable than those we had with the old Aveling or Roussel apparatus.

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Observations

ON

INFLUENZA AND ITS COMPLICATIONS.

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THE following observations were made during a severe epidemic of influenza amongst patients of the 3rd and 4th Scottish General Hospitals a few weeks ago. The majority of cases were amongst American troops, and most of the patients were ill on arrival at Glasgow by transport. Others were amongst British troops, and there was no essential difference between the two groups of cases except that pneumonia was more frequent amongst the former. At the outset we were struck by the prevalence of mixed infections, as has been found by various observers elsewhere, and we have endeavoured to trace the part played by the various organisms concerned, as regards both the complications which occurred and the manner in which a fatal result took place. The facts recorded refer chiefly to the results of *post-mortem* examinations, and we bring them forward, as it is desirable to have as many records as possible of the features of the epidemic in different localities. To speak generally, we may say that the symptoms were essentially those of severe influenza, with a preponderance of pulmonary affections, which may be roughly classified under the headings of bronchitis attended with marked irritation, bronchopneumonia, and lobar pneumonia. Amongst the pneumonia cases the mortality was very high.

The epidemic was essentially associated with the presence of the *Bacillus influenzae* (Pfeiffer). Owing to lack of sufficient time at our disposal we were unable to undertake so extensive an examination of sputa as we would have wished, but the organism could usually be found without difficulty, and was often present in enormous numbers. In a small proportion of cases it could not be found, but with regard to these latter it must be recognized that, whilst the microscopic picture is often characteristic, the identification of the organism by microscopic means, when it is scanty, is impossible; and, of course, it is in such cases that the isolation by culture is attended by special difficulty. In over a dozen cases where the organism was present in considerable numbers it was cultivated from the sputum without difficulty, and in many instances the number of colonies obtained exceeded those of other organisms. Cultures were obtained also at *post-mortem* examinations from the bronchial mucosa, the pneumonic patches, abscesses, etc.; in fact, from all the lesions with which it was found associated. The characters of the bacilli isolated agreed in all essentials with those described by Pfeiffer and recently by C. J. Martin, and it is accordingly unnecessary to say anything under this heading. Blood cultures were made in fifteen severe cases, but with negative result in all as regards the influenza bacillus. In five of these cases pure cultures of the pneumococcus were obtained, to which further reference is made below.

The medium which we used throughout was a mixture of defibrinated human blood and tryptic agar, in the proportion of about one to eight; and we have not yet made any systematic examination of other media recommended. The agar being melted, and its temperature being brought to 55°C., the blood is added and mixed, and the mixture is poured into small Petri dishes. For inoculation, a drop or two of bouillon or sterile saline solution is placed on the surface of the medium. This is inoculated from the sputum or other material, and then spread over the surface in the usual way with a bent glass rod. Colonies on this medium remain small, but appear to come up in large numbers; they are practically invisible by transmitted light, there being no alteration of the medium around, but are readily distinguished on examination with a lens by obliquely reflected light. On this medium, however, the bacilli undergo involution at an early stage, and we do not regard the medium as an optimum one. For staining the bacilli in sections we found Giemsa's stain most suitable. The ordinary solution is diluted with fifteen parts of water, and the sections are stained overnight. The process of dehydration with alcohol gives the necessary differentiation.

Post-mortem examinations were performed in 26 cases, and in all a pneumonic lesion was present. In 17 the

lesion was bronchopneumonia, in 4 bronchopneumonia with lobar pneumonia, and in 5 lobar pneumonia alone. Of the 5 cases of lobar pneumonia both lungs were affected in 4, an unusually high proportion.

Micro-organisms Present.

In relation to the cause of death, we may mention that in four other cases in which a *post-mortem* examination was not made, the pneumococcus was cultivated from the blood before death. In addition to the ordinary blood cultures in bouillon, growth was obtained also from a drop or two of blood on the surface of agar tubes, and sometimes more than fifty pneumococcus colonies developed in a tube. Apparently the organism was present in unusually large numbers. These septicaemic cases occurred at the early period of the epidemic, before we had permission to perform *post-mortem* examinations on U.S.A. cases, and at this time the proportion of cases of lobar pneumonia was greater than at a later period.

Taking these 30 cases in all, we find that in 13 the cause of death was pneumococcus infection, in 6 streptococcus infection (5 cases of septicaemia and 1 of large empyema), in 4 cases staphylococcus septicaemia, in 1 case meningococcus septicaemia, in 1 case tetragenus septicaemia, and in 1 case septicaemia due to staphylococcus and pneumococcus. Thus, in 4 cases only can death fairly be ascribed to the intensity of the influenza infection.

In addition to the conditions mentioned, various complications produced by organisms other than the *B. influenzae* were of common occurrence—for example, pneumococcal pleurisy, apart from lobar pneumonia (7), pneumococcal meningitis (1), streptococcal pleurisy and empyema (3), ulcerative endocarditis due to *Staphylococcus aureus* (1), streptococcal pericarditis (1), streptococcal peritonitis secondary to empyema (1), and pulmonary abscesses due to various organisms (5). It seems unnecessary to give details with regard to individual cases, as the important points are the cause of death and the secondary complications met with.

Of the 26 cases, bacilli of influenza type were found at the *post-mortem* examination in 22, including all those in which bronchopneumonia was present. In 4 of the 5 cases of pure lobar pneumonia no influenza bacilli could be detected. Cultures were made from 11 cases, and in 10 of these Pfeiffer's organism was isolated without difficulty. Failure in this one case is difficult to explain, as the bacilli present were in fair numbers and had the characteristic features; the picture on microscopical examination of sections also was typical. In the other 11 cases inference as to the presence of the organism was made from microscopical examination alone, but, from our experience, we are confident that in practically all it was really Pfeiffer's bacillus; in many of them its features and its occurrence in characteristic clumps, or within leucocytes, made doubt hardly possible.

Pneumococci undoubtedly played a very important part in the cases observed. Our experience is that they are practically always present within the bronchi, and they are often found along with influenza bacilli in the terminal bronchioles. Croupous pneumonia due to the pneumococcus may be superadded to the bronchopneumonia, or may occur apart from it. Of 5 cases of pure croupous pneumonia we failed to detect influenza bacilli in 4. A purely pneumococcal infection may, however, be regarded in a sense as an integral part of the epidemic. The association of pneumococci with the lesions of influenza will probably be attended by an increase in their virulence; thus there will be a greater tendency for pneumococcus infections to spread from patient to patient. The conditions obtaining on board a transport, for example, are specially favourable to such an occurrence.

Streptococci, though less frequent than pneumococci, were also often met with. We refer below to a particularly virulent form of bronchopneumonia produced by this organism in association with the *B. influenzae*. Staphylococci and Gram-negative diplococci were comparatively frequent, whilst tetrads and various other organisms were not uncommon.

In addition to the case of meningococcus septicaemia mentioned above, there occurred seven other cases of cerebro-spinal fever amongst patients suffering from, or convalescent after influenza, making eight in all. The disease was specially severe, and death occurred in every case. A

special feature was the unusually high proportion of three cases of meningococcus septicaemia without meningitis. The marked virulence of the infection may be explained, in part at least, as due to diminished resistance following on influenza. (In two of these cases *post-mortem* examinations were made, but in neither was any influenza lesion found, the patients apparently having recovered from the latter disease. The other five cases were removed to a civil isolation hospital and *post-mortem* examinations were not performed by us; these seven cases are accordingly not included in our series.)

The Bronchopneumonic Lesion.

From the point of view of morbid anatomy the outstanding feature is the bronchopneumonic lesion. This is of great importance, as, apart from influenza, it is rarely met with in the adult, and never in epidemic form. Both lungs may be studded throughout with patches of consolidation showing the typical grouping, at first pinkish and ill defined, later paler and more distinct. Haemorrhage and oedema are present to a varying extent, and are sometimes extreme when the patches are still of small size. Larger patches may be formed by confluence, but, even in cases of considerable standing, the discrete character may be well maintained, while not infrequently the patches are comparatively firm to the touch, owing to the presence of secondary interstitial change, as will be described. Acute vesicular emphysema is usually a prominent feature, and even interstitial emphysema may be met with. The mucous membrane of the bronchi is swollen and shows intense congestion and haemorrhage, the colour being frequently of a deep dull red. The larger tubes contain a varying amount of secretion, often blood-stained, and purulent plugs can usually be expressed from the terminal bronchioles. The microscopical picture corresponds, and has a general similarity to that met with in the bronchopneumonia of children. The bronchioles and alveolar passages are tightly plugged, chiefly with leucocytes along with a varying amount of desquamated epithelium, though the latter is sometimes little in evidence. In the acute stage the epithelium may be entirely lost, and a condition of actual erosion of the bronchioles may be present; but in the cases of less intense nature there may be hyperplasia of the epithelium, which may form a thick layer in which mitotic figures are to be found. The consolidated air vesicles are filled chiefly with polymorphs, but fibrin may be present in varying degree; and a common feature is the presence, immediately around the wall of the bronchus, of a ring of air vesicles containing fibrinous plugs. This fibrin is usually dense, and very few leucocytes are present with it. It appears to be practically free from organisms, and apparently represents an exudation in an outward direction from the blood vessels of the inflamed bronchial walls. The importance of this is that such fibrin is difficult of absorption, and in the later stages active organization of it has been found. Thus there results a chronic interstitial pneumonia with complete obliteration of the vesicles involved; in one or two instances this was of extensive nature. Both from clinical facts and from what we have found at *post-mortem* examinations, it is evident that influenzal bronchopneumonia is often difficult of resolution. The patient may suffer from marked cyanosis and dyspnoea for a considerable time, whilst influenza bacilli may be present in the purulent sputum in enormous numbers. Such patients often make an apparently complete recovery, but it is likely that a certain amount of interstitial pneumonia is a common sequela.

In cases fatal at a later stage, some of the larger areas of consolidation are usually pale in colour and firm in consistency, or may show commencing softening; in fact, all stages to typical abscess formation may be met with. This lesion occurred in five of the cases, and in others small abscesses were found on microscopical examination. In one case a superficial group of abscesses had ruptured into the pleural cavity, giving rise to empyema, in which both influenza bacilli and streptococci were present.

In some cases of influenzal bronchopneumonia there is no pleurisy, though the pleural surface appears dull; and on microscopical examination we have found a hyaline swelling of the subendothelial connective tissue, without evidence of the presence of fibrin. A varying degree of fibrinous exudate, however, has been found present in

many cases, and where it was marked we have always found pneumococci, occasionally associated with streptococci. The latter organism, however, tends to produce exudation with more fluid, and all stages up to typical empyema may be met with. In our series of *post-mortem* examinations there were only 2 cases of empyema, but we have also examined the pus from 10 other influenza cases during life, making 12 cases in all. In 2 of these influenza bacilli and streptococci were present, in the other 10 streptococci were present alone. These were the only two instances in which we found infection of the pleural fluid with the bacillus of influenza. There is no doubt that empyema is a comparatively common complication, occurring usually somewhat late, and the possibility of its occurrence should always be kept in view.

Bacteriology.

Looking at the matter from the bacteriological side, we may say that there occurs a descending infection of the respiratory passages with Pfeiffer's bacillus and other organisms, of which pneumococci and streptococci are by far the commonest and most important. An infection of the terminal bronchioles and alveolar passages may follow, giving rise to bronchopneumonia; and when this happens the influenza bacillus appears to us to be the most important causal agent. In sections it can often be found in large numbers amongst the leucocytes in the lumen of the bronchioles, and a large proportion of the bacilli are usually contained within leucocytes. Our results in these respects agree generally with those of Pfeiffer, obtained in the last great epidemic. In some cases the organism appears to be present almost alone, especially in cases which run a less acute course. On the other hand, we have had examples of very acute bronchopneumonia where streptococci were associated in large numbers with Pfeiffer's organism. In these the patches of consolidation were of smaller size and less defined, as described above, and were associated with intense haemorrhage and oedema. There appears also to be a greater amount of loose fibrinous exudate in the adjacent air vesicles than is present in the uncomplicated cases. Actual necrosis of patches of lung tissue was met with in several instances. In one case where there was little consolidation, and where the lesion appeared of trifling nature, microscopical examination revealed the intensity of the infection, streptococci being present in enormous numbers; and there was general lysis of the red cells. In other cases, pneumococci, Gram-negative diplococci, staphylococci, and various bacilli may be present in association with the influenza bacilli. When pneumococci are abundant there tends to be, again, exudation of looser fibrin. At any stage there may be a diffuse infection of the lung with this organism, a croupous pneumonia resulting. We have noted above the frequent occurrence of fibrinous pleurisy due to the pneumococcus, without pneumonia; and this is another illustration of the readiness with which the organism invades the lung tissue in influenza. Septicaemia due to the pneumococcus was found in several cases, and in one case there was a pneumococcal meningitis. In the abscesses we found influenza bacilli along with various other organisms—pneumococci, streptococci, staphylococci, tetrads, etc. At this stage also septicaemia may occur and be the cause of death.

General Considerations.

No one doubts that epidemic influenza is due to a specific organism, yet in hardly any other disease do we meet with such a variety of lesions and complications, produced by various organisms of common occurrence apart from influenza. Apparently the explanation is that the specific organism leads to a diminished resistance of the bronchial mucosa, and thus bacterial growth extends to the finest tubules, and bronchopneumonia frequently follows. The organisms most frequently associated with the *B. influenzae* in the bronchial tubes are pneumococci and streptococci, though staphylococci, tetrads, Gram-negative diplococci, and various bacilli are often present. These organisms play an all-important part in the production of the various lesions—pleurisy, empyema, pericarditis, endocarditis, meningitis, pulmonary abscesses, etc. Another feature, evidently related to diminished resistance, is the frequent occurrence of septicaemia, and this may happen at a comparatively late, as well as at an early stage. Lobar pneumonia also may be met with; it may occur before bronchio-

pneumonia has been established, or, on the other hand, may be superimposed on it. In our series, though not large, there was an unusually high proportion of cases of double pneumonia; in several of these the influenza bacillus could not be detected.

The question comes to be whether the *B. influenzae* (Pfeiffer) is the essential cause of the disease, or whether it is merely associated with an undiscovered virus, possibly ultra-microscopic, as some have supposed. Microscopic examination of sections shows that the influenza bacillus is specially related to the bronchopneumonia, a special feature of influenza; it is often the predominant organism, and may abound not only in the bronchioles but in the air vesicles beyond. In other words, a lesion common in influenza, and rare apart from it, is associated with the appearance of this delicate organism in large numbers; and, as this lesion represents the farthest extension of bacterial growth in a downward direction, it seems not unlikely that the *B. influenzae* is the agent which so markedly lowers the general resistance of the bronchial passages. Thus it may be the real cause of the disease. On the other hand, there is the possibility that the presence of an ultra-microscopic organism underlies all the phenomena; and the results of further investigation on this point must be awaited. But in any case it appears to us that Pfeiffer's bacillus plays a very important part in the production of the characteristic lesions.

THE AFTER-RESULTS OF GASTRIC OPERATIONS.*

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OPERATIONS are performed upon the stomach for various conditions. My own series of 175 operations include ulcers and perforations of the stomach and duodenum, carcinoma of the stomach or oesophagus, hour-glass contraction of the stomach, obstruction of the pylorus due to cicatrices of former ulcers and the pressure of a congenital cyst, haemorrhage, intussusception, and leather-bottle stomach.

There were twenty-one cases of perforation of the stomach or duodenum. Ten of these cases were saved from death, and only in one instance was there a recurrence. In all the eleven who died perforation had existed for more than twenty-four hours when I first saw them, and most of them were well under the influence of morphine. One case in which perforation had existed for forty-eight hours lived for five days, and would probably have recovered save for an attack of pneumonia. In one case which had been perforated for four hours I removed fifty gall stones from the gall bladder at the same operation. The patient made an uneventful recovery, and she has not suffered since. I do not favour these double operations. The performance of a gastro-enterostomy, which has been advocated in such cases, adds considerably to the risk. In my experience it is not advisable; if it were, I should prefer to perform it at a later period.

The prime factors in saving life are to operate upon these cases at the earliest possible moment, and to avoid the administration of morphine. Even if a journey has to be undertaken it would be safer to administer an anaesthetic than to give a dose of morphine, which may make the difference between success and failure.

The gastro-enterostomy operations number 116. Some were performed with the object of giving temporary relief in cases of malignant disease, but the majority were for the purpose of establishing a new route for the exit of food into the jejunum, because the pylorus was partially occluded. In two cases the operation was performed for the relief of symptoms due to hourglass constriction of the stomach. In another case I excised the hourglass constriction. The results in all three cases were equally satisfactory. Hence gastro-enterostomy would appear to be preferable, since it is a far less serious operation than excision.

The immediate mortality in my series of cases is 2 per cent. It is sufficiently small to be almost a negligible factor in deciding upon operation. The suffering due to

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