

SOME OBSERVATIONS ON THE RECENT INFLUENZA EPIDEMIC

AT A BASE HOSPITAL IN FRANCE.

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I.—An "Intensive" Culture Medium for the Isolation and Growth of Pfeiffer's Bacillus.

As the growth of *B. influenza* is better in association with staphylococcus than in pure culture, it appeared that possibly the basis of the symbiosis was a pabulum created by a proteolytic ferment generated by the latter organism, containing all the split-products of protein in all stages of cleavage. If this were true, then *B. influenza* would be expected to grow abundantly in the presence of an active tryptic ferment in the medium. The simple method of trypsinising whole blood and adding it to ordinary nutrient agar yielded a prolific growth of the organism. Strict asepsis must be observed in the technique, as subsequent sterilisation is inadmissible, the whole point of the method being to avoid the inactivation of the ferment.

A simple method adopted was the following:—

Into a 10 c.cm. syringe containing 3 c.cm. of citrated (1 per cent.) physiological saline, 5 c.cm. of rabbit's blood is drawn; this is quickly added to a mixture of 5 c.cm. citrated saline with 2 c.cm. liq. trypsinæ co. contained in a test-tube. The whole is mixed and placed in the incubator for one hour to start the proteolysis of the serum-albumin and globulin. Meanwhile, 100 c.cm. of nutrient agar (acidity + 10) in a 200 c.cm. flask is cooled down to 46° C. in a water-bath. The trypsin-blood, previously placed for a minute or two in the bath, is added to the agar at 46° C. Ten plates are quickly poured, and afterwards stored in the ice-chest until required.

The red blood cells are not too far altered by this treatment to preclude facility in making observations on the hæmolytic power of organisms, provided that growth has not exceeded 24 hours in the incubator, for in the latter case the red cells would be completely digested by the ferment.

This medium may be used with advantage for the growth of other delicate organisms—e.g., the gonococcus.

Note on oxygen supply.—For the growth of obligatory aerobes it has been shown that the essential constituent in blood media is the hæmoglobin. Is the function of the Hb to provide a readily available supply of oxygen? To determine this point, an agar medium was made in which neutralisation was effected by the chemical equivalent of sodium peroxide in place of caustic soda. The employment of this peroxide is confronted with technical difficulties. Since prolific growth on potato may be due to the presence of oxidases and peroxidases, one may possibly find that the addition of minute quantities of certain colloidal metals will be easier to incorporate in media for the same purpose. The call for oxygen by these obligatory aerobes is probably due to the necessity for the rapid oxidation of products like lactic acid, which inhibit growth.

II.—The Extreme Prostration and the Involvement of the Suprarenal Capsule.

Perhaps the most striking feature of the present influenza epidemic is the extreme prostration. Suddenly the patient appears to lose his physiological resistance completely, and in 24 hours the pulse becomes almost imperceptible. This atonia drew attention to the condition of the suprarenal body. In the first autopsy (in which the heart, spleen, liver, and kidneys were normal) the left adrenal was soft, diffident and congested. On examining histologically it revealed multiple hæmorrhages in the medulla extending into the zona reticulata of the cortex and œdema of the cells of medulla and cortex. (Further examinations were held up by routine work.)

It is possible that adrenalin in small doses, repeated four-hourly, might prove useful during this period of marked asthenia, to be followed in convalescence by the administration of suprarenal capsules until repair is complete. The arterial tension might be used as an index for the control of treatment.

III.—An Organism Resembling *B. pestis* in Appearance.

Introduction.—Cultural examination of the aseptically obtained lung-juice from a case of "influenza" eight hours after death gave an organism resembling *B. pestis* in appear-

ance. To eliminate the possibility of it being one of the many types of organism found post mortem the lung-juice was aspirated immediately after death (within a quarter of an hour) in the second case. From these two cases—both German prisoners of war—similar colonies grew out.

It was not until a fortnight later that the same organism was isolated from the throats of "carriers"; these were again two German prisoners of war, who had been sent in for bacteriological diagnosis of diphtheria and were found to be negative. [It may be of interest to record here that in two cases of death from this "influenza" the Klebs-Löffler bacillus was recovered from the lung. Aphonia had been a symptom in one of these cases.] The characters of the plague-like organism will now be given:—

Morphology.—The organism is remarkably pleomorphic. The type found in parent culture is a short plump bacillus. Its breadth ranges 1–2 μ ; its length varies, mostly 2–3 μ ; here and there longer forms may be met with up to 4 or 5 μ .

Staining characters.—The most striking characteristic is the marked polar staining. The organism stains well with aniline dyes. It does not retain the stain in Gram's method.

Cultural characters.—Isolation and growth are difficult in comparison with *B. pestis*. The organism was first isolated from the top, shallow, partially desiccated film of a serum slope. This suggested that it grew best on a hypertonic neutral medium; subcultures were therefore made on 2 per cent. salt neutral agar plates.

The parent growth on serum appears as a white colony about 1–2 mm. diameter in 24 hours. Subculture on gelatin proved a failure on two occasions. Subculture on salt-agar yields dense cream-coloured circumvallate colonies up to 3 mm. diameter in 24 hours; these show chains of bacilli and pear-shaped involution forms. (Hankin describes similar forms for *B. pestis* grown under the same conditions.)

Pathogenicity.—This has not been satisfactorily investigated. Only subcultures on salt-agar have been tested, and these were found to be avirulent; hypodermic injection of a rat caused 3 or 4 days' illness with subsequent recovery, whereas intraperitoneal inoculation of a guinea-pig only served to sharpen the appetite.

Further investigation with early cultures on a less attenuating medium is desirable.

Conclusion.—The organism thus agrees with *B. pestis* in morphology and staining characters, but isolation and growth are far more difficult than with *B. pestis*. Its virulence, if any, may depend on the concomitant action of some other organism—e.g., *Streptococcus brevis* or *viridans*—similar to what is suggested for Pfeiffer's bacillus.

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SOME CLINICAL ASPECTS OF LONG-STANDING PULMONARY TUBERCULOSIS.

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THE last decade has seen a wide dissemination of knowledge with regard to pulmonary tuberculosis among the medical profession. Thanks more to individual apostles than to the teaching of the medical schools, practitioners now think far more frequently of tubercle in patients showing pleurisy, hæmoptysis, or intractable cough, and realise that in the great majority of cases these events signify pulmonary invasion, and in most cases metastasis from a previous lymph-gland focus. Meanwhile the books and journals English and foreign, shower on their readers methods devised to facilitate a yet earlier diagnosis.

While, therefore, current medical literature abounds in appeals for the early diagnosis of *early* tubercle, it may seem odd that one should have to plead for the early diagnosis of *late* tubercle. But the fact remains that one sees case after case in sanatoria, in which pleurisy or hæmoptysis occurred seven or eight years ago, after which the patient was lost sight of from a medical point of view, and consequently was not thought of as a possible case of phthisis when he applied to a doctor after some years for the relief of further symptoms.

So benign is the course of phthisis, that many of these patients whose treatment only lasted a week or two at the time of the original manifestation, have maintained reasonable

health and working capacity over several years without attaining pathological healing. This was very obvious in the review of recruits for the Army, where in so many cases men were accepted not as cases of obsolescent tubercle fit for service, but simply without any recognition that they were in any way abnormal. Many have stood military life well; many, alas, have gone under.

Non-recognition of Cases and its Results.

That some of these cases should have escaped recognition need cause one no surprise; there are many conditions much more easily observed. In the absence of careful history-taking, and with a frequent absence or denial of sputum on the part of the patient, a cursory chest examination on the traditional lines may not rouse suspicion, since compensatory changes in the chest have a marvellous power of masking signs, especially in men, in whom the round, silent, emphysematous chest is commoner than in women.

The chest may be reasonably resonant, except perhaps at the extreme apices, and there may be no adventitious sounds of any kinds. The breath sounds may be weak or slightly harsh in quality, but more or less equally so all over. But while in some cases the physique may be good, careful inspection of the chest is generally enough to provide the necessary clue. Shelving apices and local rib deformities and asymmetries, supraclavicular hollows, muscular wasting about the shoulder-girdle, heart displacements, localised respiratory movements, and the use of extraordinary accessory muscles of respiration; some or all of these will help to indicate the damage that has been done.

The result of these cases being missed is that many patients who are really old chronic phthisical subjects, are not recognised as such when they first begin to feel run down, and too often it is only when they have gone on to breakdown, and their chests are a mass of squeaks and crackles that they are diagnosed at all. The fortunate few who find their way to a sanatorium when their initial manifestation of pulmonary invasion occurs, learn automatically that they have consumption. They are marked down as tuberculous; and that greatly to their advantage, since a subsequent toxæmic bout is less likely to be passed over as influenza, and the past history is much more likely to be brought to the notice of the medical attendant.

But even assuming that the old obscure fibroid cases are lucky, and previous to breakdown get swept into the net of the tuberculosis institutions, even so, they are not always recognised at once for what they are. Charts of their chest condition are handed about from one place to another, with perhaps a few strokes across the clavicles and "no adv. sounds," just as though they were cases of early pulmonary deposit. This is most unfortunate, because their difficulties and their treatment are not entirely the same as those of the early case. Most of the ordinary canons of sanatorium routine are common to both. Both must have rest until toxæmia has subsided. But the old fibroid cases have a disability which the early cases do not present, and I should prefer to call it their *mechanical disability*.

Oxygen-want.

Generally speaking, they have achieved all the compensation of which they are capable, and their response to exertion varies according to the extent of the damage to their respiratory apparatus. The early case has no marked difficulty in getting his blood oxygenated. If he is at all dyspnoeic it is generally a toxic manifestation which disappears with his toxæmia. But the old chronic remains dyspnoeic on exertion when quite free from toxæmia, and his disability is reflected in his colour oftener than the textbooks would lead one to suppose. Unfortunately, most doctors only recognise a person as "cyanotic" when he is (in the modern sense of the word) quite blue, as in congenital heart disease or some cases of "idiopathic" emphysema. But this intense blue appearance represents more than pure oxygen-want. It is oxygen-want plus venous congestion, and the cyanosis of old tubercle and other conditions is not always a striking blue, but more often an ashen, livid, or leaden tint. It may be that the blue colour occurs where there is some degree of right heart congestion; in many of these chronic cases we certainly get some objective evidence of the heart working under strain, but unfortunately little work has been done as yet, which enables one to estimate the amount of the mechanical disability directly attributable to the myocardium. The main thing to recognise is, that when a tuberculous

person is cyanosed or livid, his blood is not properly oxygenated for the degree of activity in which he has at that moment engaged. He may not complain of dyspnoea except on strenuous exertion, though his respiration may be increased both in rate and depth. The range of automatic compensation is wide. I have even seen patients engage in a short period of obvious forced breathing at the sight of a hill, thought quite unconscious of the fact!

But the question is, To what extent does this slight chronic oxygen-want matter? More, it may be, than is usually supposed. Apart from any theoretical disadvantage to viscera already past their prime, there is reason to think that it may be a direct cause of physical and mental ill-health. Many chronic tuberculous subjects who show none of the ordinary signs of tuberculous toxæmia, who keep an afebrile chart, and whose signs are quiet nevertheless complain of vague malaise, with many queer subjective symptoms, some of sympathetic type; sinking feelings, feelings of constriction, palpitation, insomnia, headache, nausea, depression, and nervousness, and other sensations reducing both their comfort and their working capacity. One cannot attribute all of these to the imagination or to indiscretions in diet. It is naturally most difficult to place them accurately, but perhaps it will be possible eventually to separate the syndrome of "anoxæmia" from that of tuberculous toxæmia, when the effects of slight oxygen-want over long periods are more definitely understood. This is certainly one of the directions in which increased coöperation is required between the physiologist and the clinician.

Relation to Classification and Treatment.

In handing on these cases to the care of another, it is plainly going to help him very little in assessing their capacity or recording their progress, to know that they are "ambulant afebrile," or that they come into Class 2 or 3 of Turban's grouping. Nor does Philip's valuable method enable one to record shortly *all* the essential factors. But with a small modification it would do so. In any case of pulmonary tuberculosis one wants to record shortly: (1) extent of lesions; (2) degree of toxæmia; and (3) mechanical disability; and this might well be done by the combination of the letters L T M, numbered from 0 to 3. Thus cases like those under consideration would often be L₃T₀M₁—extensive lesions, no toxæmia, slight mechanical disability. In so far as shorthand notes of cases are of value, such a method would cover the essential factors of pulmonary tuberculosis in all its stages. And in actual practice such a note certainly makes for careful observation of patients, by continually drawing one's attention to fundamentals. It is especially in institutions that patients are so liable to go automatically through a routine, unless anything gross happens to call attention to their particular needs.

Again, in special treatments, like artificial pneumothorax, it is most essential to consider all the factors involved. It is of doubtful advantage to an old fibroid case (except as a life-saving operation) to flatten out his foci by collapse therapy, and at the same time to leave him with too little lung to carry on his occupation with comfort, and with an overworked heart handicapped by the embarrassment of a displaced mediastinum. And the same care is wanted in fixing the limits of activity for these chronic cases where surgical treatment is not undertaken. They will not generally benefit by being taken past the stage of exercise represented by light gardening, nor is there any justification for making them short of breath.

The country is alive with schemes, some in an early stage, some already in working, for dealing with the tuberculous patients discharged improved from sanatoria. How are these old chronic fibroid cases going to fare? Their working capacity is often great, and their expectation of life indefinite. They can do a relatively large quantity of work, assuming it is work of the right kind and within their respiratory capacity, but they are not capable of sudden great exertion, and are most comfortable on a fairly sedentary job. It follows that in the laudable desire to get them open-air conditions we must not overlook their limitations. If we are going to send them to open-air colonies we must make provision for sedentary occupations, many of which are compatible with open-air conditions. They will certainly live longer and do more useful work under the light physical strain of sedentary employment than they would by going blue in the effort to get through the average day on a farm.