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NOTES ON CERTAIN ASPECTS

of

RELATIONSHIP BETWEEN SOME INTRA-THORACIC AND

INTRA-CRANIAL DISEASES

by

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The writer is indebted, and wishes to express his grateful thanks, to the authorities of the Westminster, Brompton, Victoria Park, and Mount Vernon Hospitals for much of the Clinical and Pathological material upon which this paper is based.

Much of it has passed through his hands during his connection with one or more of these Hospitals.

There has been in recent years a good deal written in regard to the relationship which frequently exists between some of the morbid conditions of the abdomen and thorax. This is no doubt due, in a large measure, to the close anatomical connection between the two cavities.

The present treatise is an attempt to deal in some measure - by no means complete - with certain aspects of relationship which may exist between certain of the diseases of the lungs, pleurae and bronchi on the one hand, and of the

cranial cavity on the other. This relationship is necessarily almost entirely due to blood stream.

The subject will be divided into two sections:-

A. Pathology.

B. Diagnosis.

#### PATHOLOGY.

It may be as well to first of all briefly refer to the functional disturbances of the brain which may complicate pulmonary tuberculosis. First thoughts would incline to the opinion that, as pulmonary consumption is so essentially a disease of malnutrition and is so often associated, at any rate in its later stages, with pyrexia, and some degree of poverty of the blood, this disease would be by no means rarely complicated by insanity, since it may be assumed that an imperfectly nourished brain necessarily causes some instability of that organ, and therefore would be more liable to

disturbances of function, and the suspicion would be strengthened by remembering the fact of the toxaemic condition associated with so virulent an organism as the tubercle bacillus. The grey matter of the brain is a very vascular part of the body, and it would be thought that so sensitive an organ as the brain would not very uncommonly be influenced in its mental functions by so unfortunate a combination of untoward circumstances as general malnutrition, toxaemia, pyrexia, anaemia - all acting for a prolonged period - and the gloomy prognosis inseparable from most cases of this disease. Yet this is not so. My own observations of some thousands of cases, and a perusal of the records of others serve to illustrate the fact that a surprisingly small proportion of patients develop any of the forms of insanity, even when there is a decided hereditary tendency. It must not be supposed that insanity is not relatively more frequent

where there is a hereditary taint. It certainly is. But the point which the writer wishes to emphasise is that taking cases of pulmonary consumption as a whole, both where there is a history of insanity in the family and when there is not, the proportion who become insane is almost incredibly small.

This is in striking contrast with the reverse of the picture, namely that phthisis is a common complication of, sequel to, and fatal termination of insanity, as the records of a large number of asylums prove, especially in regard to cases of idiocy and congenital imbecility. This is no doubt due to the devitalizing influence which an impairment of the mental functions has upon the tissues of the body, rendering it more prone to the pathological effects of the tubercle bacillus. The great improvement which has in recent years taken place in the hygienic conditions of institutions for the insane has no doubt

largely led to a diminution of the prevalence of pulmonary tuberculosis in them. But the disease is still at least twice as common in the insane as in the sane.

It may be asked whether the evidence quoted by the writer in regard to the extreme infrequency of insanity in pulmonary tuberculosis may not possibly be not absolutely conclusive. It may be questioned whether the insanity may not occasionally be so pronounced in the subjects of early phthisis that the slight pulmonary lesion is missed, and consequently that some cases which are regarded as pulmonary tuberculosis complicating insanity are in reality cases of insanity complicating tuberculosis. For it is undoubtedly true that early pulmonary tuberculosis is frequently missed by non-proficient or careless examination; (it does not require a long experience at a special hospital to observe this); and further-

more, it is readily understood that the pulmonary condition may easily be overlooked because of the more unusual and important condition of the mental state. But if such were the explanation, it would mean that insanity occurs mostly in early phthisis, and that once the patient has got over this he is relatively likely to escape. This view cannot be seriously entertained. On the other hand, it is well known that phthisis among the insane is frequently latent, and haemoptysis is rare, even after the lungs have become markedly affected.

The present writer believes that what is called spes phthisica is a possible factor in the matter of the relative infrequency of insanity in phthisical subjects, by acting as a conservative agent in the mental equilibrium, and thereby diminishing

the degree of what may be called mental wear-and-tear which is so commonly present in prolonged and serious illnesses. Of course this theory cannot, in the nature of things, be proved. It is merely put forward as a plausible hypothesis.

Whatever may be the cause or causes of mental affections occurring in pulmonary consumption it is probable that they act by giving rise to some impairment of nutrition of the brain cells, whether that impairment is due to what may be described as circulatory changes or to the direct action of toxines.

The observations of the writer have led him to the conclusion that *spes phthisica* is present in a larger degree in those cases in which there is considerable or severe pyrexia. Indeed as far as his experience goes this peculiar mental optimism is re-

latively more frequent, and pronounced, in acute than in chronic, or latent pulmonary tuberculosis. It has been frequently noticed to increase with the height of the temperature curve and as the disease advances.

Now, it would be thought that the relative frequency of mental disturbance in pulmonary tuberculosis would have a fairly constant relationship to the presence or absence of fever, - since it may be assumed that pyrexia would be associated with some deleterious effect upon the cerebral functions, whether because merely of circulatory disturbances of the cerebrum or on account of the toxaemia which so frequently accompanies it. It is possible that the spes phthisica which so often becomes more pronounced with a higher tempera-

ture curve counter-balances the deleterious influences associated with such pyrexia. In chronic cases there is often not only an absence of *spes phthisica*, but actually a depression of spirits; this is usually associated with some constitutional depression.

Many alienists, especially those in France, believe that there is a special form of insanity in pulmonary tuberculosis. In this country Clouston has been pre-eminent in putting forward this view. He called attention to it as far back as 1863, and designated the disease "phthisical insanity". At the same time he admitted that anaemia of the brain, whatever its cause, was apt to produce a mental state similar to, and occasionally indistinguishable from phthisical insanity. Clouston maintains that phthisical insanity, broadly speaking, is characterized by a lack of vigour in regard to the symptoms, and that there is an abnormal mental suspicion

throughout. He was one of the first to show that the condition is frequently associated post-mortem with atrophy, anaemia, and oedema of the brain. It must not be supposed, however, that this pathological condition is only found in cases of definite insanity, because certainly anaemia and oedema were by no means uncommonly found by the present writer, while pathologist at the Victoria Park Hospital, in cases of mental disturbance which stopped short of insanity.

The mental phenomenon called *spes phthisica*, and insanity are not the only peculiar mental conditions which patients suffering from pulmonary tuberculosis may exhibit. There are other departures from normal mentality which may be present. It has for a long time been known that there is occasionally an abnormal brilliancy of mental function, not usually embracing the whole mental character however,

and often fitful. This mental state is often accompanied by pyrexia. It may be partly due to the fact that pulmonary tuberculosis often attacks persons of this kind of mental temperament. In chronic or latent pulmonary tuberculosis there may be a depression of spirits. This is as a rule associated with constitutional depression, such as languor. There may be all the symptoms of neuraesthesia. The patient may complain of this before or more than the pulmonary symptoms, as the neuraesthesia may be out of all proportion to the latter. The severe forms are the cases which are apt to end in true insanity, the first thing often being a tendency to be suspicious. Morel long ago pointed out that occasionally patients suffering from pulmonary tuberculosis may develop transient attacks of delirium. The present writer however, has observed very few of these cases. Lastly, patients suffering from pulmonary tuberculosis occasionally exhibit the

various forms of hysteria, and for this reason the lungs of hysterical patients should always be carefully examined, particularly if there is a family history of tuberculosis. Hysteria may be severe when the lung involvement is only slight.

Pathogenesis of mental affections during pulmonary tuberculosis.

There are at least three possible factors in the pathogenesis of mental affections occurring during pulmonary tuberculosis. They are:-

1. The rise in the temperature of the blood which accompanies practically all cases during some part of their career.
2. The presence of toxins in the blood.
3. Individual pre-disposition.

There may also be some unaccountable factor.

In regard to the first, it is the opinion of the writer that it is not an important factor per se. It may possibly be so in those diseases, such as heat-stroke and pneumonia, where there is commonly more or less sudden elevation of temperature and the degree of pyrexia severe. The researches of Loewy have shown that the destruction of albumin is invariably increased in fever, while the destruction of fat is diminished. When the supply of unoxidised albumin in the brain is exhausted the mental faculties become impaired. Furthermore, the acceleration of the heart's action which usually co-exists with fever and which causes of itself an active hyperaemia and consequently results in an unduly large amount of over-heated blood being supplied to the brain within a given period, must cause an irritation of that organ. Later on, it acts in another way by causing a failure of the heart's power and as

a necessary consequence a passive congestion in the cerebral and a meningeal veins, with resulting anaemia and impaired function of the cerebral substance and in severe cases even leading to oedema. The reason the writer thinks that pyrexia is not per se an important or frequent factor in the causation of the mental affections occurring during pul. tub. is that such affections show by no means anything approaching a consistent relationship to the presence or the degree of fever. But on the other hand it is at least possible that pyrexia may act indirectly by giving rise to oedema and other circulatory changes as described, because he found the former present in by no means a small proportion of cases post-mortemed at the City of London Hospital for Diseases of the Chest in which during life there has been mental symptoms. A very diligent search was made in these cases for any signs of tuberculosis of the meninges

with a negative result; but for the sake of completeness it must be stated that inoculation to guinea-pigs was not resorted to.

In regard to toxæmia, this is much more likely to be a greater factor than pyrexia. It is well known that delirium may be the first symptom of an illness, before the temperature of the blood has risen or the cardiac action has become accelerated. Influenza may be taken as an example of this. Also fever in this disease is generally short in duration, and sometimes insignificant in degree compared with the prostration of mental strength which not uncommonly accompanies or follows the malady. Furthermore, it is at least probable that the histological cell-changes which are developed during the course of bacterial action are due not to the action of the bacteria but to their toxins, since it has been shown by Welsh that these changes may occur in a typical form

in diphtheria where only sterilised and filtered cultures were used. Enriquez and Hallion found that toxins of diphtheria injected under the skin of dogs resulted in great congestion, with haemorrhages, of the grey matter of the spinal cord, together with destruction of the nerve elements. Modern investigators are coming more and more to the conclusion that toxins are able to exert a most powerful deleterious influence on the nutrition of nerve cells. Still it must be remembered that these histological cell-changes may possibly be the result of some circulatory derangement of the cerebrum, and particularly of the oedema already referred to.

Individual predisposition is certainly a factor of some degree, since mental affections during the course of pulmonary consumption are certainly relatively more frequent in persons who have a hereditary taint than in

those who have not. But it cannot for a moment be seriously entertained that it is a factor of great importance, because it has been proved that these mental disturbances frequently occur in persons who have a perfect family history in this respect and are by no means infrequently absent in those with an extremely bad family history.

In conclusion it may be that the insanity of pulmonary tuberculosis is due to a combination of the three factors, that is there may be a toxaemic condition acting on an ill-nourished brain having a hereditary tendency. It is also of course possible, as in all other questions of this sort, that there is some unaccountable factor at work of which we have no knowledge at present.

We will now consider certain points of relationship between some organic lesions of the intra-cranial and intra-thoracic cavities.

### Tuberculosis.

That there should be a very intimate connection between tubercular meningitis and pulmonary tuberculosis is not surprising.

Tubercular meningitis is one of the principal complications of phthisis. It does not, however, occur in a large percentage of cases.

The present writer has analysed the post-mortem records of 378 cases of pulmonary consumption, who died in the Brompton Hospital. Tubercular meningitis was a complication in 14 of these cases, that is in 3.7%.

Of the 378 cases 276 were males and 102 were females. Of the males, tubercular meningitis was present in 10 instances, that is in 3.6%; and of the females in 4 instances, that is in 3.9%.

Of the 378 cases, 353 were cases of the fibro-

caseous, that is, the common variety of pulmonary tuberculosis; 22 of the caseous broncho-pneumonic variety; and 3 of the fibroid variety. (Of course, the first and third varieties usually terminate in an acute invasion of the lungs, either in the form of a broncho-pneumonic (through the air channels), or of a miliary (through the blood or lymph streams, mainly the former), or, what is commonest, a mixed broncho-pneumonic and miliary invasion; also what is primarily a broncho-pneumonic form is often associated with a miliary spread towards the end).

Of the fibro-caseous variety 262 were males; in 10 of which tubercular meningitis was present; that is 3.8%; and 91 were females, in 3 of which tubercular meningitis was present, that is, in 3.3%.

Of the caseous broncho-pneumonic variety 11 were males, in all of whom the cerebral meninges were spared, and 11 were females, in one of whom

they were affected.

The three cases of the fibroid variety were males, and tubercular meningitis was absent in each.

Analysing the fibro-caseous variety in regard to age at death, and as to whether tubercular meningitis occurs more frequently in certain decades than in others, we find in the case of the males that the highest death rate is between the ages of 20 and 30, where it is 38.2%, and tubercular meningitis a complication in 2.07%; the next highest death rate is between 30 and 40, where it is 28.2%, and tubercular meningitis a complication in 1.66%; the next is between 40 and 50, where it is 14.9%, and tubercular meningitis a complication in 0.4%; the next is between 10 and 20, where it is 12.4%, the next is between 50 and 60, where it is 5.4%, and the lowest between 60 and 70, when it is 0.8%, tubercular meningitis being absent in all of these cases.

In the case of the females the highest death rate is between the ages of 20 and 30, where it is 34.6%, and tubercular meningitis a complication in 0.4%; the next highest death rate is between 30 and 40, where it is 30.9% and tubercular meningitis a complication in 9%; the next is between 10 and 20, when it is 18.5%; the next is between 40 and 50, where it is 13.6%; and the lowest between 50 and 60, where it is 2.4%, tubercular meningitis being absent in all of these cases.

Analysing the caseous broncho-pneumonic variety, we find in the case of males that the highest death rate is between the ages of 20 and 30, where it is 54.54%; the next highest is between 10 and 20, where it is 27.7%; the next highest between 30 and 40: where it is 18.2%; tubercular meningitis was absent in all of these cases.

In the case of the females the highest death rate is between 10 and 20, where it is 88.9%,

and tubercular meningitis a complication in 12.5%; the next highest death rate is between 20 and 30, where it is 11.1%, tubercular meningitis being absent in these cases.

The present writer has also analysed the records of 100 cases of tubercular meningitis post-mortemed at the Brompton and Westminster Hospitals, 50 at each hospital, with a view to studying the pathological findings.

The great majority of the cases at the former hospital were adults, and at the latter were children.

The first obvious fact which stands out in a perusal of the pathological records of these cases is that tubercular meningitis in the adult is generally a terminal infection of pulmonary tuberculosis, whereas in the child it is usually a part of a generalized acute miliary tuberculosis.

If we enquire into the sources of infection in the body of tubercular meningitis we find that either the lungs or the mediastinal, cervical, or mesenteric glands are affected practically in all cases. The only possible exception is that of a male, aged  $5\frac{9}{12}$ , in whom, apart from the intracranial condition, the only abnormalities found

were a small yellow nodule in the mucosa of the bladder and hyperaemia of the mesenteric glands. It was not stated whether the latter were examined microscopically for evidences of tuberculosis, and therefore it is by no means certain that they were non-tubercular, because of the fact that the present writer, while at the Brompton Hospital, examined the mesenteric glands in a large number of cases, and it was proved that microscopic examination revealed the presence of tuberculosis in a large proportion of those in which there were no macroscopical evidences.

Although this treatise is only meant to deal with some intra-cranial and intra-thoracic morbid conditions, for the sake of completeness, it will refer also to the presence of tubercular lesions in other parts of the body in tubercular meningitis.

Of the 100 cases the lungs were found to be affected in all except 3, namely, the following:-

1. Female, aged 3<sup>10</sup>/12. Well-marked tuber-

cular meningitis: no naked eye evidences of tuberculosis of spinal cord, but turbid fluid at posterior end: lungs and pleurae quite normal: well-marked tubercular ulcers in peyer's patches of lower end of ileum: numerous flat yellow tubercles on convex surface of spleen.

2. Male, aged 9 months. Typical tubercular meningitis: muco-purulent fluid in both middle ears: well-marked tuberculosis of cord: numerous tubercles on parietal and visceral pleurae over against right lower lobe: lymphatic glands of lower cervical region and of mediastinum large, caseous and tubercular: mesenteric glands tubercular to a less marked degree: typical tubercular ulcers of intestines: a few tubercles on capsule of spleen.

3. Male, aged 5<sup>9</sup>/12. Well-marked tubercular meningitis: no obvious tuberculosis of lungs or pleurae: mesenteric glands hyperaemic; otherwise nil: one yellow small nodule in mucosa of bladder.

It will be seen that these 3 cases were children under 6 years of age. In two of them the source of infection was certainly in the abdomen, and the only serous membranes involved were the cerebral meninges.

In the other case the pleurae was apparently affected, without the lungs, the lymphatic glands were extensively involved, and the intestines and spleen were also affected.

In regard to the variety of tubercular lesions found in the lungs, the following were the results of an analysis, the different ages also being considered.

Under 1 year of age - 11 cases.

In 4 - caseous nodule or nodules, with miliary  
tubercles also.

" 4 - miliary tubercles alone.

" 1 - caseous broncho-pneumonic tuberculosis,  
with miliary tubercles also.

" 1 - caseous broncho-pneumonic tuberculosis,  
without miliary tubercles.

" 1 - no evidences of tuberculosis of lungs.

Therefore miliary tubercles present in 8  
of 10 cases in which lungs involved.

Between 1 and 2 years of age - 10 cases.

In 6 - miliary tubercles alone.

" 2 - caseous nodule or nodules, without  
miliary tubercles.

" 1 - caseous nodule or nodules, with  
miliary tubercles also.

" 1 - fibro-caseous, without miliary  
tubercles.

Therefore miliary tubercles present in 7 of  
10 cases.

Between 2 and 3 years of age - 4 cases.

In 2 - miliary tubercles alone.

" 1 - caseous broncho-pneumonic tuberculosis,  
without miliary tubercles.

" 1 - caseous nodule or nodules, with  
miliary tubercles also.

Therefore miliary tubercles present in 3 of  
4 cases.

Between 3 and 4 years of age - 6 cases.

In 5 - miliary tubercles alone.

" 1 - no evidence of tuberculosis of lungs.

Therefore miliary tubercles present in all  
cases involved.

Between 4 and 5 years of age - 4 cases.

In all miliary tubercles alone.

Between 5 and 6 years of age - 6 cases.

In 4 - miliary tubercles alone.

" 1 - caseous tubercle or tubercles, with  
miliary tubercles also.

" 1 - no evidences of tuberculosis of the  
lungs.

Therefore miliary tubercles in all cases in which lungs involved.

Between 6 and 7 years of age - 1 case.

Miliary tubercles alone.

Between 7 and 8 years of age - 3 cases.

In all miliary tubercles alone.

Between 8 and 9 years of age - 1 case.

Caseous nodule or nodules, without miliary tubercles.

Between 9 and 10 years of age - 1 case.

Miliary tubercles alone.

Between 10 and 15 years of age - 1 case.

Fibro-caseous, with miliary tubercles also.

Between 15 and 20 years of age - 4 cases.

In all, fibro-caseous, with miliary tubercles also.

Between 20 and 30 years of age - 23 cases.

In 20 - fibro-caseous, with miliary tubercles also.

In 2 - fibro-caseous, without miliary  
tubercles.

" 1 - fibroid, with miliary tubercles  
also.

Therefore miliary tubercles present in 21  
of 23 cases.

Between 30 and 40 years of age - 16 cases.

In 11 - fibro-caseous, with miliary  
tubercles also.

" 3 - fibro-caseous, without miliary  
tubercles.

" 2 - miliary tubercles alone.

Therefore miliary tubercles present in  
13 of 16 cases.

Between 40 and 50 years of age - 8 cases.

In 7 - fibro-caseous, with miliary  
tubercles also.

" 1 - miliary tubercles alone.

Therefore miliary tubercles present in all  
of 8 cases.

Between 50 and 60 years of age - 1 case.

Fibro-caseous, without miliary tubercles.

It will be seen that of the 97 cases in which the lungs were affected:-

In 49 - fibro-caseous variety, 43 with military tubercles and 6 without.

" 4 - caseous broncho-pneumonic variety, 2 with military tubercles and 2 without.

" 9 - caseous nodule or nodules, 6 with military tubercles and 3 without.

" 2 - fibroid variety, 1 with military tubercles and 1 without.

" 33 - military tubercles alone.

Thus military tubercles were present in 85 and absent in 12 cases.

Analysing the 33 cases in which military tubercles alone were present in regard to age, we find the following:-

Under 1 year of age	- 40%
Between 1 and 2 years of age	- 60%
Between 2 and 3 years of age	- 50%
Between 3 and 4 years of age	- 100%

Between 4 and 5 years of age	-	100%
Between 5 and 6 years of age	-	80%
Between 6 and 7 years of age	-	100%
Between 7 and 8 years of age	-	100%
Between 8 and 9 years of age	-	none
Between 9 and 10 years of age	-	100%
Between 10 and 15 years of age	-	none
Between 15 and 20 years of age	-	none
Between 20 and 30 years of age	-	none
Between 30 and 40 years of age	-	12.5%
Between 40 and 50 years of age	-	12.5%
Between 50 and 60 years of age	-	none

In regard to the frequency with which parts of the body other than the lungs were affected in 100 cases of tubercular meningitis, the following facts were found.

Bronchial glands in 32 cases: 20 of these were 10 years of age or under, that is 62.5%.

Other intra-thoracic glands in 29 cases:

21 of these were 10 years of age or under, that is 72.4%.

Cervical glands in 5 cases: 4 of these were 10 years of age or under, that is 80%.

Mesenteric glands in 25 cases: 21 of these were 10 years of age or under, that is 84%.

Larynx - in 19 cases: none of these was 10 years of age or under.

Trachea - in 7 cases: none of these was 10 years of age or under.

Bronchi - in 2 cases: neither of these was 10 years of age or under.

Pericardium - in 4 cases: none of these was 10 years of age or under.

Spleen - in 36 cases: 34 of these were 10 years of age or under, that is 94.4%.

Liver - in 32 cases: all of these were 10 years of age or under, that is 100%.

Kidneys - in 45 cases: 27 of these were 10 years of age or under, that is 60%.

Intestines - in 57 cases: 23 of these were 10 years of age or under, that is 40.4%.

Generative organs - in 11 cases (9 were males): 1 of these (male) was 10 years of age, that is 9.09%.

Bladder - in 2 cases : neither of these was 10 years of age or under.

Peritoneum - in 17 cases: 10 of these were 10 years of age or under, that is 58.8%.

Brain-tuberculoma - in 6 cases: 3 of these were 10 years of age or under, that is 50%.

It will be observed that the larynx, trachea, bronchi and pericardium escaped in all cases of 10 years of age and under.

A striking fact is that although the liver was affected in 32 cases they were all 10 years of age or under. (Of course it must be borne in mind that the organ was not examined microscopically in all cases; and the writer, while at the Brompton Hospital, proved that tuberculosis could

not be excluded unless such an examination were made. Still the fact remains that, as far as macroscopic evidences were concerned, those patients above 10 years of age escaped).

Intra-cranial complications other than tubercular meningitis occurring in pulmonary tuberculosis -

The present writer has studied the record of over 2500 cases of pulmonary tuberculosis post-mortemed at the Brompton Hospital. He has found that apart from those cases in which there was an intra-thoracic complication of the tubercular condition of the lung - such as pulmonary abscess, gangrene empyema, pyo pneumothorax - an intra-cranial complication other than tuberculosis (tubercular meningitis and tuberculoma of the brain) was found in only one instance. The case was that of a male in whom there was a healed tubercular lesion at the apex of the right lung; the rest of the lungs was merely emphysematous: there was a small cyst in the cortex of the left kidney: the brain contained multiple abscesses, filled with greenish pus, and varying from the size of a pea to a walnut, in all the lobes of the cerebrum, in the right crus, and the right lobe of the

cerebellum, No primary focus was detected. It is probable that the source of the septic condition was other than the tubercular lesion of the lung. This is rendered practically certain by the fact that the lung lesion was found to have been healed. It may therefore be confidently stated that tuberculosis is practically the only intra-cranial lesion which occurs as a complication of pure cases of pulmonary tuberculosis.

#### Bronchiectasis:

The writer has examined the post-mortem records of 63 cases of bronchiectasis, apart from those cases in which there was a certain amount of bronchiectatic dilatation concomitant with pulmonary tuberculosis.

In sixteen of these 63 cases intra-cranial abscess or abscesses were present, that is in a percentage of 25.4, or rather over 1 in 4. No other intra-cranial complication was found in

these cases except where acute suppurative meningitis was a concomitant of some of the cases of intra-cranial abscess, and in one case of purulent meningitis complicating bronchiectasis was found, but here there was an empyema as well.

Of these 16 cases 15 were true abscesses and 1 multiple pyaemic. Of the former, 8, were in the left hemisphere only, 4 in the right, 1 was bilateral (2 abscesses on the right side and 1 on the left), 1 in the middle lobe of the cerebellum, and in regard to 1 the position was not mentioned. It will be seen therefore that the left hemisphere is distinctly more frequently involved than the right, the proportion being 2 to 1 when cerebral. Of the 15 true abscesses, 12 were cerebral, 2 were cerebellar, and in 1 case the position was not mentioned. This shews that the proportion of cerebral to cerebellar is 6 to 1, or a percentage of 85.5. Of the cerebral cases, 7 were in the left hemisphere, 4 in the right, and 1 case was

bi-lateral. Therefore it will be seen that the proportion of uni-lateral to bi-lateral is 11 to 1, or a percentage of 91.6: and that 7 were in the left hemisphere as compared to 4 in the right, that is a proportion of 63.6% were on the left side. Of the cerebellar cases, one was in the left lateral lobe, whilst the other was in the central lobe.

Position of the true abscesses in the aforementioned 11 cerebral cases.

The abscesses were found in the following positions -

1. Left side; ascending parietal, supra-marginal, angular convolutions, all close to the cortex.
2. Left side: ascending parietal convolution, superficial 1 inch from surface, (purulent meningitis over left frontal lobe).
3. Right side: in optic thalamus, posterior limb of internal capsule.
4. Right side: inferior frontal convolution (absence of localising symptoms).

5. Left side: anterior part of parietal lobe (at one part it had burst below and opened into the lateral ventricle).
6. Three abscesses:
  - A. Left side: upper portion of motor area extending on either side of the Fissure of Rolando.
  - B. Right side: over facial area.
  - C. Right side: occipital lobe, superficial.
7. Right side: about midway between the Fissure of Rolando and the Fissure of Sylvius, but mostly posteriorly, superficial.
8. Right side: almost completely limited to the occipital lobe, encroaching slightly on the neighbouring part of the temporo-sphenoidal lobe, (ruptured into the posterior cornu of the lateral ventricle, pus found in this, and some in the left ventricle).
9. Left side: centrum ovale (size of a millet seed).
10. Two abscesses:
  - A. Left side: temporo-sphenoidal lobe, communicating with the posterior horn of the left lateral ventricle: pus seemed to have found its way to the base in the region of the anterior commissure.

B. Left side: an abscess the size of a filbert, situated slightly above the position of A. (Purulent meningitis of the base in this case).

11. Two abscesses:

A. Left side: ascending frontal about two inches external to the great median fissure, encroaching on the posterior extremity of the middle frontal.

B. Left side: a second abscess the size of a large bean just above position of A.

It will be seen, in regard to these cerebral abscesses, that 6 were in very close relationship with the Fissure of Rolando, that is in 46.1%. (Of these 6, 3 were rather more behind, one rather more in front and two neutral); 1 was below the Fissure of Rolando; 1 in the inferior frontal convolution; 1 in the temporo-sphenoidal lobe; 2 were in the occipital lobe; 1 was in the optic thalamus; and 1 was in the centrum ovale.

Of the two cerebellar cases, one was in the left lateral, and the other in the middle lobe.

In regard to the number of the abscesses there was really only one abscess present in all excepting one case, because in two of each of the other cases the second abscess was so near to and smaller in size than the first that it was pretty certain that it was secondary to it.

In regard to the size of these 18 intracranial abscesses, (including the one where the position was not known), 9 were large - the size of a tangerine orange or hen's egg - , one was medium in size, - pigeon's egg - , 6 were small - size of a hazel nut or almond - (two of these were secondary, as previously noted)- , and one the size of a millet seed. Of those abscesses near the surface of the brain only one was small, and one medium in size; the others were large. Of the 6 small abscesses two were cerebellar, one was situated in the optic thalamus, two were secondary, and only one was near the surface of the brain.

As to the contents of the abscesses, there was nothing peculiar to note, only pus being present

in every case. In 8 cases purulent meningitis complicated the presence of abscess. It will therefore be seen that lumbar puncture - to be afterwards described - would have been of inestimable diagnostic value in these cases at least.

Pyo-pneumothorax.

Of 78 cases there was no intra-cranial complication in any.

Actinomycoses.

Of 3 cases there was no intra-cranial complication in any.

Abscess of the Lung.

Of 6 cases cerebral abscess was present in one: It was the size of a hen's egg, situated in the right frontal lobe reaching up to the surface at the extreme apex and so superficial that the abscess broke at the highest point. Posteriorly it extended back to the anterior horn of the lateral ventricle which it had invaded. It was lined by a thick pyogenic membrane. It contained thick

greenish foetid pus. (In this case pulmonary tuberculosis was present).

Gangrene of lung.

Of 15 cases cerebral abscess was present in 2.

In both these there was empyema as well.

Empyema.

Of 43 cases, cerebral abscess was present in 5. (Of these, however, pulmonary tuberculosis was present in one, and pulmonary gangrene in 3), and purulent meningitis was present in one; (here there was also bronchiectasis however).

## DIAGNOSIS.

It is not the intention of the writer to make an ordinary clinical study of the differential diagnosis between any intra-thoracic and intracranial diseases, or their complications. Such will be found in the various text-books of medicine. But he thinks that a definite purpose will be served if he enters into a consideration of some specific points in this relation.

The points he has chosen are those either not touched upon, or very briefly or inadequately referred to in text-books.

- They are -
1. Kernig's Sign.
  2. Lumbar puncture.
  3. An examination of the blood.

### KERNIG'S SIGN.

Sixteen years ago, Kernig discovered a sign in meningitis which has been called after his name, Kernig's sign.

The present writer ventures to think that the discovery has not attracted the studious attention which it deserves. In his opinion the phenomenon which Kernig was the first to point out is in the front rank of the means at our disposal in the differential diagnosis of meningitis. The accounts of it in the text-books of medicine are so meagre that he has thought it advisable to review the literature of the subject. The latter is by no means large.

The sign as noted by Kernig consists in the inability to extend the leg fully when the thigh is at a right angle with the trunk, owing to marked flexor contracture. The discoverer was in the habit of eliciting it by getting the patient to sit up on the edge of the bed with the legs over-hanging - thus bringing the thigh at a right angle with the body - and then the operator attempted to fully extend the legs, one at a time.

In the normal individual the leg can be almost completely extended when the patient is in this

position. Kernig believed that an angle of 135 degrees or less is a positive sign, though it may be as low as 90 degrees. He pointed out that in a patient in whom the sign is present, the leg could be completely extended as long as the thigh was not placed at approximately a right angle with the trunk.

Kernig arrived at his conclusions after an examination of fifteen cases of acute meningitis. The diagnosis was confirmed in eight by autopsy. Thirteen were of the cerebro-spinal form; one tubercular; and one suppurative. He believed that the sign was constant, that it appeared as early as did the rigidity of the neck, and that it was late to disappear, often persisting until the patient was well on in convalescence. He believed that it was present in all affections of the pia, whether acute inflammatory or not, and he noted its presence in some other conditions as well. Thus, for example, he found it in a case of oedema of the pia, in a case of hyperaemia of the meninges which he thought was

possibly a commencing tubercular meningitis, in a case of localised meningitis from otitis media, in a case of pachymeningitis haemorrhagica, in a case of chronic leptomeningitis, and a case of spinal caries.

It was Friis, who, in 1887, first published confirmation of Kernig's discovery.

Osler, in 1897, was the first to point out that it was possible to elicit the sign by the patient being on his back, and then after flexing the thigh on the trunk to a right angle, an attempt was made to extend the leg on the thigh. This has the advantage of greater convenience. The only requirement is that the leg should be placed at a right angle with the body before attempting to extend the leg.

Friis, in 1887, examined sixty cases of cerebro-spinal meningitis. The sign was present in fifty-three, that is, in 88%. In two of the remaining cases it was doubtful; in three the examination was quite unsatisfactory; and in two the sign was absent.

The same writer, in 1892, during another epidemic of cerebro-spinal fever, found it present in twenty-one of twenty-six cases, that is, in 80%. He considered that there was no relation between the sign and the rigidity of the neck.

Bull found the sign present in a case of tubercular meningitis; in a case in which there was a solitary tubercle of the cerebellum, with a few miliary tubercles in the over-lying pia, with tuberculosis of the lungs, lymphatic glands, kidneys and intestines; and in a case of otitis media with caries of the petrous portion of the temporal bone, thrombosis of the transverse sinus and common jugular vein, and ecchymoses in the basal pia and especially over the frontal lobe and a small quantity of serum in the posterior fossa. It will be seen that there was some affection of the pia mater in all. Bull did not consider the sign was pathognomonic of meningitis or even of pial trouble, but was merely indicative of an increase of intra-cranial pressure. From an examination of cases, Hensch came to the

conclusion that the sign was not pathognomonic of meningitis, but that it may exist without that lesion. Blumm found it present in seven out of nine cases of cerebro-spinal meningitis.

Netter published two series of cases of meningitis. In the first series, the sign was present in twenty-three out of twenty-five cases, that is, 92%, twelve being cases of cerebro-spinal meningitis, eight of tubercular, and three a mixture of both; and a second series of forty-seven cases in which the sign was present in 90%. Thus there was a combined percentage of 91. With its occurrence in so high a percentage of cases, and together with the fact that in one of the negative cases the child had very advanced tuberculosis, while in another the test was made only once, he came to the conclusion that its presence warrants a positive diagnosis of meningitis.

Herrick reported his observations on nineteen cases of meningitis, eight of which were post-mortemed, nine being cerebro-spinal (epidemic), seven

tubercular, two pneumococcal, and one syphilitic with an acute process superadded. In seventeen of these cases, that is in 89.4%, the sign was present. The other two cases were children aged 3 and 4 years respectively, in whom there was only a single examination made shortly before death, when there was an absence of rigidity of all the muscles, including the neck. It has often been noted that the rigidity and retraction of the neck muscles may vary in their intensity, and even completely disappear just before death. In twenty-five healthy individuals selected at random there was an absence of Kernig's sign in all. In 100 cases of diseases other than meningitis the sign was only present in two, one being a case of subdural haemorrhage, and the other that of a woman suffering from gonorrhoeal rheumatism of the knee who had been in bed for several weeks with the legs flexed. Those cases in which the sign was absent included pneumonia; delirium tremens, both with

and without pneumonia; tetanus; uraemia; typhoid fever; cerebral haemorrhage; cerebral thrombosis; cerebral syphilis; tumour of the brain; multiple sclerosis; ataxic paraplegia; general paralysis of the insane; tabes dorsalis; hysteria; acute endocarditis; erysipelas of the face, in which there was high pyrexia, rigidity of the neck, delirium, and other cerebral symptoms. The case of subdural haemorrhage was a man, and there were among other symptoms unconsciousness, and rigidity, and retraction of the neck. On the other hand, Magri found the sign present in cases of typhoid, and pneumonia. Packard has reported three cases in which the sign was absent where it may be expected. One was a case of leptomeningitis, following pneumonia; another was a case of general military tuberculosis, in which the cerebral & spinal membranes were involved; and the third was a case in which there were military tubercles over the motor area of the cortex. These three cases were infants.

Thyne found the sign present in a case of haemorrhage into the right lobe of the cerebellum and the fourth ventricle.

In a hundred non-meningitis cases Shields found an angle of 120 degrees or less in five cases, viz., in one case of typhoid, the angle being 110 degrees on one side (in this case, however, it did not disappear during convalescence); in another case of typhoid the angle being 110 degrees on both sides; in one case of uraemia, the angle being 110 degrees; and in two cases of hemiplegia, the angle in one being 115 degrees and in the other 120 degrees.

It should be particularly noted that in none of these cases was the angle below 100 degrees. Kernig took 135 degrees or less as his standard. But many observers since have taken an angle of 115 degrees or less, and this certainly excludes very few cases of meningitis. When it is remembered that the angle obtained in any individual case depends partly on the force used in extending the leg;

how impossible it is to obtain very accurate measurements, even with the aid of an instrument, on account of the irregular contour of the parts; and how it varies within certain limits, according to the personal equation of the observer, it may with tolerable certainty be asserted that its presence in these cases is not absolutely conclusive.

The mass of evidence appears to show that Kernig's sign is present, at one time or another, in the large majority of cases of acute meningitis - certainly at least 80%, and probably in more. A proper technique is desirable; the sign should be searched for daily; it may be transitory; it may appear late; occasionally it is unilateral. Its absence, especially in the early stage, apparently does not absolutely exclude meningitis: we should then enquire for other evidences of the disease, and these will almost certainly be forthcoming. We should invariably be satisfied that local causes do not interfere with the proper extension of the lower limbs, such, for example, as sciatica, myositis, old

contractures from nervous diseases, and arthritis of the hip or knee. The sign can be exceedingly well simulated in sciatica, as everyone who has made specific enquiries in regard to this point knows. On the other hand in some cases of spasticity and delirium patience will serve to overcome the resistance of the muscles. To sum up, therefore, it may with confidence be asserted that in the presence or absence of Kernig's sign we have a means at our disposal which is of the greatest value in the differential diagnosis of acute meningitis, whether tubercular, or due to any of the other well-known causes, & when present with other signs of meningitis it is confirmatory in the highest degree. In the opinion of the writer it deserves to rank next in importance to the information gained by the examination of the cerebro-spinal fluid, or the finding of miliary tubercles in the choroid. It is of greatest service in distinguishing acute inflammation of the cerebral-meninges from diseases other than meningitis in which head symptoms are present.

Of course, the sign is not absolutely pathognomonic. How many such are there in medicine? Exceedingly few.

### LUMBAR PUNCTURE.

During the last sixteen years lumbar puncture has increasingly become one of the most important means of differential diagnosis of certain diseases of the nervous system.

Providing it is carried out with proper precautions, there is no risk attending it. At Westminster Hospital, it is done as a matter of routine in all cases where it is likely to be of diagnostic value. The precautions we are in the habit of adopting are that the operation should be performed with strict regard to what may be called surgical cleanliness; that whenever possible the patient should rest for some time after the operation, preferably for from twenty-four to forty-eight hours, because otherwise it may cause severe headache: and that only a small quantity - from 3 to

5 C.C. - of cerebro-spinal fluid should be withdrawn at one sitting. It is an undoubted fact that in all the recorded cases in which unwelcome results have followed the operation, there has been a neglect of one or more of these simple precautions. These facts being so, we may say that lumbar puncture should be employed as an aid to differential diagnosis in all cases in which head symptoms complicate any disease of the bronchi, lungs, or pleurae.

It may be true that some writers have exaggerated the diagnostic value of lumbar puncture; and it is furthermore true that up to the present time many problems in relation to it are unsolved, as, for example, the proper significance of the presence of cholin. Yet it is none the less indisputable that lumbar puncture is of great value in differential diagnosis, particularly in cases of meningitis.

Normal cerebro-spinal fluid is colourless, like water. In most cases of meningitis it is found to be more or less turbid, and may even be purulent.

Osler has pointed out that the fluid may be alternately turbid and clear according to the exacerbations and remissions of the disease. In severe, fatal, meningococcal meningitis, and also in the acute stage of that disease, the fluid is practically always turbid; in chronic cases and those which ultimately either completely recover, or terminate in hydrocephalus, it is usually clear. The degree of turbidity in tubercular meningitis may be very slight. It may unhesitatingly be said that the presence of clear cerebro-spinal fluid coincident with what may be called acute head symptoms is strong evidence of the absence of meningitis. Blood-stained fluid may be indicative of several things. First of all it may be accidental, due to the wounding of an arachnoid vessel at the time of operation. In these cases generally the bleeding ceases in a few moments, and consequently the fluid becomes increasingly clearer. Blood-stained fluid may also be found in cases of severe meningitis and of pre-existent cerebral or spinal sub-arachnoid haemorrhage, whether traumatic or non-traumatic.

Normally the cerebro-spinal fluid contains a trace of serum-globulin and of albumose. When an excess of albumin is present it may be inferred that we are dealing either with acute meningitis, or general paralysis of the insane. In tubercular meningitis the coagulum usually floats in the middle of the liquid, is translucent or grey, with perhaps a few white flakes: whereas in general paralysis it generally sticks to the sides of the vessel and is often yellow. In the Rev. Neurol., Paris, of April 30th., 1903, Guillam and Paraut describe a further means of distinguishing cases of general paralysis. In sixteen cases whose cerebro-spinal fluid they examined, they found that after precipitating the globulin with a saturated solution of magnesium sulphate, filtering the fluid and boiling the clear filtrate, a characteristic precipitate was invariably obtained with the second boiling. In chronic cases of pneumococcal meningitis and those which ultimately either completely recover or

result in hydrocephalus there may be no excess of albumin present. Albumin is also sometimes found in uraemia. The differential diagnosis is here easily made on clinical grounds. One of my colleagues at Westminster Hospital, Dr. Hebb, as well as others, has made investigations as to the presence of cholin in the cerebro-spinal fluid. Normally it is present only in minute quantity. But it is easily demonstrable in the blood and cerebro-spinal fluid in organic degenerative diseases of the nervous system. It can be crystallised as a combined platinum salt according to the method of Halliburton and Mott. These crystals have been obtained in cases of cerebral haemorrhage, multiple sclerosis, and syringomyelia; in other words, in katabolic organic processes of the central nervous system.

The presence of a reducing substance, now definitely proved to be sugar, is as yet of no

diagnostic value. It is quite absent in all the forms of acute meningitis. In four cases at Westminster Hospital, proved by postmortem examination to be tubercular meningitis, it was found in three.

It is when we come to study the results of the microscopic examination for cellular elements in the cerebro-spinal fluid that we see the great diagnostic value of lumbar puncture. This, the so-called cyto-diagnosis, is the most important method of examination. The fluid should be centrifuged, and after thorough centrifugalisation the sediment, if any be present, or in its absence the last few drops of fluid in the tube, are transferred to a slide, fixed by heat, and stained by methyl blue or by Jenner's stain, mounted in Canada balsam and examined with a microscope.

In order to diminish the degree of possible error, which is inevitable in this rough process, Fuchs and Rosenthal have devised an ingenious method. Instead of centrifugalization they add to the cerebro-spinal fluid a fixed proportion of a staining agent, and then count the number of cells in a modified Thoma-Zeiss chamber.

Normally the cerebro-spinal fluid contains very few cells. The French authors were in the habit of examining a large number of fields with a 400 - 450 power, and they considered that an average of over 3-4 lymphocytes to a field is abnormal. Merzbacher gives six to eight as the upper normal limit. Normal fluid may contain a few endothelial plates; it never contains polymorpho-nuclear leucocytes; their presence is always pathological and indicates some acute process within the meninges.

The all important point , put briefly, is that in acute meningitis there is leucocytosis, and that the leucocytosis is chiefly in the tubercular form lymphocytic, whereas in meningitis due to other bacteria, and especially in the acute suppurative form of inflammation the prevailing cell is the polymorpho-nuclear.,

This bare statement needs elaboration, for investigations have elucidated many facts.

First of all can we say that a lymphocytic leucocytosis is invariably present in cases of tubercular meningitis? The answer is in the negative. Marcon-Mutzner has recorded the case of a man, aged 40, in whom there were physical signs of a tubercular consolidation of the apex of the right lung, and who developed signs of acute meningitis, including Kernig's sign. Lumbar puncture was performed, and the prevailing cell of

the fluid withdrawn was found to be the polymorpho-nuclear leucocyte. The patient died three days later, and on post-mortem examination the typical appearances of tubercular meningitis were present.

F.E. Batten has mentioned a case in which there was an excess of the polymorpho-nuclear variety of leucocyte.

Graham Forbes collected the results of fifty cases of tubercular meningitis. He found an excess of lymphocytes in twenty-five, and of polymorphs in two cases; there were scanty lymphocytes and degenerate cells in eleven, and no cells in two cases. In the former two cases, however, clinical and post-mortem evidence revealed the fact that polymorpho-nuclear excess was associated with a chronic condition terminating acutely.

Purves Stewart has found in a rapidly advancing tubercular meningitis as many as 30%

of polymorphs.

The writer of this thesis suggests that a possible explanation of at least some of these exceptional cases may lie in the fact that they may have been cases of mixed infection. It is believed by many that in pulmonary tuberculosis a secondary infection by streptococci, staphylococci, pneumococci and other organisms is a common occurrence. (This will be referred to later). In each of these the prevailing cell is usually the polymorpho-nuclear..

The writer has collected a series of cases from the clinical and pathological records of Westminster Hospital. The following are the results: In fourteen cases of tubercular meningitis the cerebro-spinal fluid was examined, and the diagnosis confirmed by the autopsy. In all these was there a leucocytosis. In nine of them the records stated that there was a lymphocytic excess. Of the remaining five - in three

the fact of leucocytosis was merely mentioned, without stating whether the lymphocytes or polymorphs were in the majority: in one it was merely stated that there were numerous leucocytes of both varieties; (pyelitis was present in this case): and in one it was stated that the polymorphs and monomorphs were in about equal number; (in this case a pre-vertebral abscess was found post-mortem; no micro-organisms were discovered in the cerebro-spinal fluid during life). Of the nine cases in which there was lymphocytosis the fluid certainly contained some polymorpho-nuclear cells in four; one case was doubtful. Of the total number of fourteen cases there were some polymorphs in at least six, and possibly in seven. In regard to the age, in no case was it stated that the lymphocytic cell was in excess above the age of eight: of the other cases one patient was twenty-five, one was ten, and one was sixteen

years of age.

Lymphocytosis may be present in diseases other than tubercular meningitis. It is therefore important, for the purpose of differential diagnosis, to exclude these affections. In acute meningitis, due to other bacteria than to the tubercle bacillus, that is, in acute infective meningitis, such as, for example, the streptococcal, the meningococcal, and the posterior-basilar, when recovery sets in, that is in the sub-acute or chronic stages, - and indeed during their convalescence, - if on the way to recovery the polymorpho-nuclear cells diminish in number and the lymphocytes increase; the latter, however, are not permanent, as they disappear as convalescence becomes fully established.

Farquhar Buzzard has suggested that lymphocytosis may even occur in the initial stages of cerebro-spinal fever and meningitis due to some of the common pyogenic organisms. But no proof

has been put forward on behalf of this suggestion.

Lymphocytosis is more marked in general paralysis of the insane, and tabes dorsalis, than in any other diseases. Although Siermerling has reported a case of apparent general paralysis in which three successive punctures failed to reveal a lymphocytosis, and Nieder and Mamlock have recorded a case in which lymphocytes were absent at one examination and present later on, most observers believe that it is always present in the former. Purves Stewart has cited eleven cases of this disease in which the average number of lymphocytes per field was 127.5, the lowest count in one case being 26.6, and 22 tabetic cases in which the average count was 131.4, and the lowest 36. We must be very searching in our clinical examinations for the presence of tabes dorsalis, because the indications may be very slight.

Lymphocytosis is present in syphilitic meningitis, in sub-acute and chronic affections of the meninges due to other causes but not caused by acute microbial infection, in cerebro-spinal syphilis of adults, and in congenital syphilis in which there is obvious affection of the nervous system. Therefore in a given case in which we suspect tubercular meningitis we must be sure that the patient was not previously the subject of one of these diseases. It has rarely been met with in herpes zoster, sciatica, mumps, gliomatous tumour of the brain in which there was no involvement of the meninges, tubercular tumour of the surface of the brain, acute anterior polio-myelitis, and in syphilis even in the absence of any nervous lesion. Also Rendu published an account of a patient admitted comatose and aphasic. On examination of the cerebro-spinal fluid the lymphocytes predominated; yet at the autopsy fracture of the skull was found.

Lymphocytosis was found in a case of chloroma, with associated chronic meningitis, at the Westminster Hospital.

But these are exceptions, and therefore it may be said that providing pre-existing cerebro-spinal syphilis, tabes dorsalis, and general paralysis of the insane can be excluded, the presence of lymphocytosis in cases of acute forms of meningitis is strong positive evidence that the inflammation of the meninges is of a tubercular origin, and this is especially the case in children, where the presence of lymphocytosis is almost without exception indicative of tubercular meningitis. Furthermore, it must be remembered that we have at our disposal the bacteriological examination of the cerebro-spinal fluid as a supplementary and confirmatory method of diagnosis. This will be referred to later.

A polymorpho-nuclear excess is met with in severe, fatal, meningococcal meningitis, and also

in the acute stage of that disease; in posterior-basilar meningitis & meningitis due to pneumococci, staphylococci, streptococci and other bacteria, excepting the tubercle bacillus.

Exceptions must be mentioned.

F.E. Batten has quoted a case in which perfectly normal cerebro-spinal fluid was obtained within a week of death from widespread cerebro-spinal meningitis.

It has already been noted that in the sub-acute or chronic stages there may be a lymphocytic instead of a polymorpho-nuclear preponderance: indeed, in chronic cases it may be that the only cells found are a few lymphocytes which are often degenerated.

It is always advisable to make a bacteriological examination of the cerebro-spinal fluid withdrawn, in addition to the so-called cyto-diagnosis, because the result of such an examination often supplies conclusive evidence of the

nature of the lesion from which the patient is suffering. It confirms and frequently supplements the information which has already been obtained from examining the colour, chemical composition, and number and variety of the cellular elements. The fact is each acts as a control and adjunct to the other.

There are three methods of examination, each of which should be taken advantage of whenever convenient. They are -

- a) The preparation and examination of films.
- b) Cultural examination.
- c) Inoculation experiments on animals, especially guinea pigs and rabbits.

The last-named has the disadvantage that it takes some time, but it confirms the results obtained by the other two.

The organisms which may be found in the cerebro-spinal fluid are the following:-

1. Tubercle bacilli.

In the fourteen cases collected from the clinical

and post-mortem records of the Westminster Hospital already referred to, twelve were examined for organisms by the film method; cultures were made in three of these; animals were not employed in any. In the twelve cases of undoubted tubercular meningitis, tubercle bacilli were only found in three. Streptococci and staphylococci, together with tubercle bacilli, were found in one instance: (here polymorpho-nuclear cells were present as well as lymphocytes).

Graham Forbes was more fortunate. He stained films in 26 recent cases, and found tubercle bacilli in 21. He attributes his success to the fact that he was in the habit of staining the fine lymph-clot which usually forms on standing and in which the bacilli could easily be recognised without prolonged search.

Of course, the finding of tubercle bacilli in the cerebro-spinal fluid is positive proof that the patient is suffering from tuberculosis of the

cerebral or spinal meninges, or both.

It should, however, be remembered that failure to discover tubercle bacilli, even after inoculation into animals, by no means excludes tuberculosis. On the contrary such a negative result in acute meningitis is strong evidence that the inflammation is of tubercular origin, because in the other forms of acute meningitis the respective organisms (meningococcus, pneumococcus, streptococcus and staphylococcus, etc.) are practically always present. The relatively frequent non-success in demonstrating the tubercle bacillus in the cerebro-spinal fluid of patients suffering from tubercular meningitis corresponds with the same in regard to the fluid of undoubted tubercular pleurisy. Observations by J.J. Perkins, as well as by the present writer, at the Brompton Hospital proved the latter beyond all shadow of doubt.

## 2. Meningococcus.

This is always present both in the film preparations and cultures in the severe and fatal cases, and in the acute stage of cerebro-spinal fever; in less acute cases they may not be found in the cultures and only a few in the films; while in chronic cases there are usually only a few degenerated diplococci or no organisms at all.

## 3. Pneumococci.

This is an organism easily demonstrated in and cultivated from the cerebro-spinal fluid.

The investigations of A. Fraenkel, Foá and Uffreduzzi, Weichselbaum, Netter, and others, have shown that the diplococcus pneumoniae is a very frequent cause of purulent leptomeningitis. It is found as the only pathogenic micro-organism in 60% of such cases.

Pneumococcal meningitis may not only occur during the course of an acute lobar pneumonia - the physical signs of which may either be absent

or indefinite - but it may also occur without an attack of pneumonia. In fact it appears to have been fairly conclusively proved that in the majority of cases pneumococcic meningitis originates independently of any lung lesion. It may be a septicaemic infection due to disease in some other distant part of the body, e.g., endocarditis; or it may be a pneumococcic infection of the meninges occurring as part of a general septicaemia without an obvious primary lesion. Thus, Debove published a case of a man, aged 54, who developed symptoms of cerebral excitation similar to those of alcoholic delirium, and later symptoms of peritonitis. He died in a few days and at the post-mortem general purulent peritonitis with purulent infiltration of meninges were present; pneumococci were found in the pus. This was a case in which there was a general infection by pneumococci, which had spared the lungs, but had settled in the meninges and peritoneum: or it

may be secondary to a direct extension from middle ear disease, or from the nasal cavity and adjoining sinuses, as shewn by Weichselbaum, Zörkandörfer and others: (it may incidentally be remarked that no doubt the latter may account for some cases of so-called idiopathic meningitis). And lastly, since it is generally believed that the suppuration which occurs in a tubercular cavity of the lung may be due to the pneumococcus and not to the tubercle bacillus, we would expect, at least on theoretical grounds, that the organism would occasionally be found in the cerebrospinal fluid, as a terminal infection in pulmonary tuberculosis. But no such case was found in the Westminster Hospital series, nor has the writer been able to find one in the literature on the subject.

From what has been said, therefore, it is evident that the occurrence of the pneumococcic meningitis, as proved by the presence of pneumococci

in the cerebro-spinal fluid, and other signs, during the course of any disease of the lungs, bronchi, or pleurae is by no means proof positive that the meningitis is secondary to the intrathoracic condition. The diagnosis of the primary source may be made on ordinary clinical lines.

#### 4. Staphylococci and streptococci.

These organisms are found in the cerebro-spinal fluid in cases of acute suppurative meningitis. This is always secondary, either to direct extension from a local disease, e.g., of the middle ear, cranium, fossae, or spinal column; or secondary to a septicaemic infection due to disease in some distant part of the body, such as abscesses, and occurring as part of a general infection.

We have to note, however, one or two special points:

First of all, it must be borne in mind that unless the most stringent precautions are taken in regard to what may be called surgical cleanliness,

contamination may destroy the value of the examination. This applies more to staphylococci than to the streptococci variety. Even when the greatest care has been exercised it is necessary to say that, as a general rule, the discovery of a common pyogenic organism is of no reliable value if an examination of the films made from the centrifuged deposit reveals no increase of cells. And lastly, in this relation, it is possible that a terminal infection of the meninges by staphylococci and streptococci may occur in pulmonary tuberculosis, because the suppuration which occurs in a tubercular cavity is generally due, in large measure at least, to bacteria other than the tubercle bacillus, and especially by staphylococci and streptococci. Furthermore, these organisms are occasionally found in the cerebro-spinal fluid together with the other characteristics significant of tubercular meningitis. In these cases, however, there are usually also at least

some polymorpho-neuclear cells. Such an one was found in the Westminster Hospital series analysed by the writer and already referred to.

5. Miscellaneous, such as Friedländer's bacillus of pneumonia, Pfeiffer's bacillus, bacillus typhosus, bacillus anthracis, bacillus coli communis.

These are merely enumerated in order to shew that they are among the causes of meningitis. Their presence is practically pathognomonic that the meningitis is due to one or other of these organisms. It is true that the influenza bacillus, and also the bacillus of Friedländer are supposed to sometimes cause a secondary infection in pulmonary tuberculosis, but on looking through the literature of the subject the writer has been unable to trace any case in which any of these organisms have been found in the cerebro-spinal fluid as a complication of consumption.

Nauwerck published a case of influenza and

encephalitis in which Pfeiffer's bacillus was cultivated from the fluid in the ventricles. Apparently the point of entrance of the organism was by means of the nasal cavity.

Lastly, the presence of malignant disease of the central nervous system has been demonstrated by finding tumour cells in the cerebro-spinal fluid.

Let us now give some illustrations in which the results obtained by the careful and thorough examination of the cerebro-spinal fluid may prove of great value in the differential diagnosis of some intra-thoracic and intra-cranial diseases and their complications. Indeed, it frequently affords the best means we have at our disposal.

No better example could be taken than pneumonia. It is a matter of common experience that the differential diagnosis between the early stages of pneumonia and meningitis in children is often a matter of extreme difficulty;

for the former disease is frequently ushered in by head symptoms simulating the latter, and pulmonary physical signs may either be absent or indefinite. The prognosis and treatment of the two morbid conditions is sufficiently different as to render the matter important, and as has been stated, lumbar puncture performed under proper precautions is a harmless operation. In pneumonia uncomplicated by meningitis there is an absence of leucocytosis and of organisms in the cerebro-spinal fluid, in contrast with what is found in meningitis whatever its origin. We can further determine which form of acute meningitis is present. It may be confidently asserted that lumbar puncture gives results so near to being absolute that, in cases where any doubt exists as to the significance of cerebral symptoms, it is the best means of deciding the point with practical certainty. Furthermore, when, because of definite pulmonary physical signs, there is no doubt about the presence of pneumonia,

lumbar puncture is of value in deciding whether there be any intra-cranial complication present or not.

Again, in certain diseases of the lungs, bronchi, and pleurae, intra-cranial abscess is by no means uncommon. For example; it has already been shewn in this treatise that it usually occurs in nearly one in four cases of bronchiectasis. The question of operation may arise. The great value of an examination of the cerebro-spinal fluid is that it may enable the surgeon to determine whether there be a concomitant meningitis, which would contra-indicate operative interference. Again, it is well known that otitis media may be due to pneumococci, which may or may not be associated with pneumonia. It is an exceedingly difficult problem whether the presence of pyrexia after a mastoid operation is caused by a temporary intoxication, or a cerebral, or cerebellar abscess, or suppurative meningitis with or without an abscess.

Leucocytosis of the cerebro-spinal fluid would denote the presence of meningitis, and therefore veto an operation. We can make certain of this by an examination of the cerebro-spinal fluid.

Again, instead of tubercular meningitis the intra-cranial morbid conditions complicating consumption may be an abscess or suppurative meningitis, secondary to a concomitant bronchiectasis, abscess or other septic pulmonary lesion, or pus in the pleural cavity.

Again, influenzal meningitis complicating influenzal pneumonia may be differentially diagnosed by lumbar puncture - a by no means easy task apart from this method of examination, since similar head symptoms may occur in both.

And lastly, in regard to typhoid fever, lumbar puncture may be of great value in differentiating between it, typhoid meningitis, staphylococcal infection from the thoracic viscera, and acute generalised tuberculosis, in all of which

there may be cerebral symptoms.

Many more such illustrations could be given. But enough has been already said to shew that an examination of the cerebro-spinal fluid should never be omitted when there is any difficulty in regard to the differential diagnosis of intra-cranial diseases on the one hand, and diseases of the lungs, pleurae, or bronchi on the other, or of their complications.

#### EXAMINATION OF THE BLOOD.

##### Bacteraemia.

For some years now there has been much attention paid to the subject of bacteraemia, that is the presence of bacteria in the blood.

Great advance has been made in regard to the great importance of a thorough knowledge of proper technique. Formerly very varied results were obtained, and consequently dissimilar and sometimes contradictory conclusions drawn by different in-

investigators, and these were undoubtedly in large measure due to faulty technique.

It now seems generally agreed among competent authorities that, in order to get reliable information, it is advisable to use a considerably larger amount of blood than was the custom previously. It may confidently be stated that a minimum of 5 C.C. is absolutely necessary; and where it is possible it is better to try and secure as much as 20 C.C. As an example of this may be cited the fact that, speaking generally, pneumococci are found in the blood in cases of pneumonia in proportion as a larger or smaller quantity of blood is used. No doubt the increasing success in demonstrating their presence is partly the result of employing liquid media, especially bouillon, and a high concentration of blood instead of high dilutions so that the so-called bactericidal action of the blood - serum, may be overcome.

Another point of the utmost importance is

that, in order to avoid contamination, the most stringent antiseptic precautions should be taken. This was scarcely possible by the old methods of stabbing the skin. Coplin obtained very satisfactory results by introducing a sterile hypodermic needle of a large calibre, or a trocar and canula, or even an aspirating needle into the median vein.

Whenever possible, it is advisable to examine the blood at varying periods of the different diseases, and to have advantage of inoculation into guinea pigs, or rabbits, or both, as well as the routine film and cultural examination.

Verification of what was found during life by examination of the blood post-mortem is not reliable for the reason that, in certain diseases, organisms which were not present during life may be present just preceding death, as shewn by Longcope and others, probably because of a progressive decrease in the bacteriolytic blood-complement which permits the blood to become

invaded by bacteria, some of which may be harmless. saprophytes. For this reason positive results obtained by post-mortem examination of the blood should not be taken as conclusive evidence of an infection. In this connection, it may be worth while mentioning that experiments conducted with the most stringent precaution by Horton-Smith, Hartley and myself on a number of cases of advanced pulmonary tuberculosis at the Brompton Hospital, in which there were hectic fever and its accompaniments present during life, and vomicae containing much purulent material found in the lungs after death, revealed the presence of streptococci and staphylococci in the blood of the heart, spleen, liver, and other organs, or in the pericardial fluid in a much smaller percentage of cases than was expected. This is in striking contrast with the opinion of Schabad, who believes that these organisms are present in the blood in almost all the cases which reach the post-mortem

room.

Tuberculosis - Up to the present time tubercle bacilli have exceedingly rarely been demonstrated in the blood. This is in contrast with the fact that Curine, Fournier, and Beaume, found the organism <sup>in the urine</sup> in most of the cases of acute tuberculosis which they examined, and believed that the kidney need not be tubercular, providing the disease is rapidly progressing. Kronig discovered tubercle bacilli in the blood during life in a patient who afterwards died of acute miliary tuberculosis. The method employed was to thoroughly shake a few drops of blood in about 10 C.C. of distilled water until a brownish-red transparent liquid resulted, and after centrifugalisation, the sediment was examined for tubercle bacilli by the ordinary method.

The bacterial flora of the blood in tuberculosis are usually of secondary importance. They denote the presence of a mixed infection. Among

others who have worked at this subject are the following, together with the results obtained,

Hewelke discovered bacteria other than the tubercle bacillus in 14 out of 27 cases, staphylococci being present in 7, while in the remaining 7 unknown, or non-pathogenic organisms were found: Petrurschky-- staphylococci and streptococci in one of eight cases: Straus - in none of nineteen cases: Sittmann - staphylococci in one of five cases: Kraus - staphylococci in one of fourteen cases: Lasker - streptococci only in one, and staphylococci albi only in another of sixty-eight cases, though the blood examined was taken from a vein in the arm; Michaelis - cocci in eight of ten cases: Jakowski - staphylococci and streptococci in seven of nine advanced cases, staphylococci in five, streptococci in three, and both in one: Hirschloff - bacteria in four of thirty-five cases, in which remittent fever seemed to indicate a mixed infection; the staphylococci found were of

very low resistance in these cases; there were no metastatic abscesses; the blood was taken from the median vein, and various media were employed: Schabad - staphylococci in six of seven cases; the same writer has found pneumococci and the tetragenous cocci, but much more rarely: and lastly, the present writer - positive results in a very small proportion of cases.

Pneumonia - In studying the literature relating to the relative frequency of pneumococcic septicaemia in pneumonia, it becomes at once evident that the results of different investigators show the greatest possible variation.

The following are some of them. The Klemperer brothers failed to find pneumococci in the blood in any of the cases of pneumonia they examined: E.K. White demonstrated their presence in three of nineteen cases; no organisms save pneumococci were discovered in any: Stacey - in seven of seventeen cases; in only three of

of these cases, however, before death: Troussaint - in 53% of 58 cases: Silvestrini and Sertole - in five of sixteen cases: Rosenow - in 132 of 145 cases; in four of these the organism was demonstrated in the blood before a positive diagnosis of pneumonia could be made; (this may indicate that a lobar pneumonia may possibly be a secondary localisation of the primary blood invasion); and lastly, and most important, Powchaska - in all of fifty cases examined in recent years; twelve ended fatally; in each case nearly ten C.C. of blood were employed by means of a sterilized syringe.

Friedlander's bacillus has occasionally been found. E. Phillips cultivated it from the blood obtained during life, and demonstrated the organism in the pulmonary lesion at the autopsy, although the pneumococci were not obtained.

Influenzal Pneumonia - The bacillus is found in the blood with no degree of constancy.

From a study of what has been said it will be observed that bacteraemia is of comparatively little value in the differential diagnosis of diseases and complications of the lungs, pleurae and bronchi on the one hand and of the cranial cavity on the other. Tubercle bacilli are at the most so extremely rarely found in the blood that the demonstration or absence of such cannot be relied upon as indicative of the presence or absence of a tubercular septicaemia.

The finding of organisms other than the tubercle bacillus in the blood in cases of pulmonary tuberculosis may occasionally be of value.

The demonstration of the pneumococcus in the blood is not of value in the differential diagnosis of pneumococcal complications, since Powchaska found it present in that fluid in all cases of pneumonia.

It may serve to prove that the patient is suffering from a pneumococcal infection, as shown by Rosenow.

The demonstration of the influenza bacillus in the blood is so difficult that the success or failure in finding it is of no great significance in diagnosis.

#### Leucocytosis.

The present writer has reviewed the work done by Stein and Erbmann, Cabot, Maragliano, F.G. Burrows, Cazin & Gros, Heiman & Koplik and C. Langdon Gibson on this subject, and the result of his study is that the absence or presence or degree of leucocytosis are of no certain value in the differential diagnosis of diseases and complications of the lungs, pleurae and bronchi on the one hand and of the cranial cavity on the other.

The writer begs to offer this Thesis to the kind consideration of the Authorities.

Finis.