ance of hearing, and sometimes of taste and smell, none of which were present.

(b) The cortex. This would of necessity be an extensive lesion, and would involve the motor areas, causing considerable paralysis and probably twitchings.

(c) The subcortical area. That is somewhere in the white matter which lies between the cortex and the internal capsule (corona radiata), and this I consider the most likely position. C. L. Dana in his study of sensory localization found that total anaesthesia was either of functional or subcortical origin.¹

Applying the same tests to the other prominent symptom, the motor aphasia, I come to the same conclusion; for if the lesion had been in (a) the internal capsule, it must have been at the anterior end of the hind limb, at the genu, since it is here that the fibres to the tongue and those concerned in motor aphasia pass through. (b) The cortical centre concerned in motor aphasia is at the posterior end of the third left frontal convolution, but this is unlikely from the absence of paralysis or twitchings.

We are thus again compelled to fall back upon the subcortical area as the most likely position for the lesion; and this would also account for the very slight weakness down the right side. I do not attempt to explain the inequality of the pupils, which often occurs in perfectly healthy individuals.

I am, therefore, of opinion that the lesion in this case was a softening in the subcortical area of the brain.

This case was shown at the Liverpool Institution, in March 1900.

REFERENCE.

¹ Osler, *Principles and Practice of Medicine*, 4th ed., p. 1025.

The Croonian Lectures

ON THE

NATURAL HISTORY AND PATHOLOGY OF PNEUMONIA.

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Delivered at the Royal College of Physicians, London, by
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J. W. H. EYRE, M.D., etc.

LECTURE II.—[ABSTRACT.]

ALMOST all observers state that the virulence of pneumococci derived from different sources, when tested upon animals, is found to vary within great limits; and although Foulerton states that out of 19 cases he found the virulence practically the same in all, I think this can be accounted for by the fact that he did not use very accurate methods of measuring the virulence.

Eyre and I¹ have made a number of observations upon the virulence of pneumococci derived from various sources by inoculation of the rabbit. The virulence of each strain was then tested by injecting measured quantities of the cultivations into other rabbits. The following is the result:

Pneumococcus No. 1.—Derived from the sputum of a case of pneumonia; initial virulence corresponded to a minimal fatal dose of two loops.

Pneumococcus No. 2.—Derived from the sputum of a case of pneumonia; initial virulence corresponded to a minimal fatal dose of one loop.

Pneumococcus No. 3.—Derived from the pus in a case of meningitis complicating pneumonia; initial virulence corresponded to a minimal fatal dose of the whole of a blood-agar cultivation.

Pneumococcus No. 4.—Derived from the saliva of a healthy individual; initial virulence corresponded to a minimal fatal dose of one loop.

Pneumococcus No. 5.—Derived from the lung juice of a case of lobar pneumonia in an infant; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 6.—Derived from the rusty sputum from an atypical case of pneumonia; initial virulence corresponded to 0.01 of a loop.

Pneumococcus No. 7.—Derived from the saliva from a case of carcinoma recti; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 8.—Derived from a case of broncho-pneumonia in an infant; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 9.—Derived from the lung in a case of broncho-pneumonia in an infant; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 10.—Derived from a case of broncho-pneumonia in a child aged $\frac{1}{2}$ year; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 11.—Derived from a case of broncho-pneumonia in an infant; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 12.—Derived from the saliva in a case of interstitial nephritis; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 13.—Derived from the saliva in a case of occupation paralysis; initial virulence corresponded to 0.000001 of a loop.

Eyre, at the annual meeting of the British Medical Association, 1901, recorded five more cases.

Pneumococcus No. 14.—Derived from a case of pericarditis and pleurisy complicating pneumonia in a child aged 8; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 15.—Derived from the pus in the peritoneum of a child aged 3, suffering from pericarditis, peritonitis, meningitis, pleurisy, and fibrosis of the lung; initial virulence corresponded to 0.000001 of a loop.

Pneumococcus No. 16.—Derived from a case of pericarditis in a child aged 15 months; initial virulence corresponded to 0.1 loop.

Pneumococcus No. 17.—Derived from a case of cerebro-spinal meningitis in an infant; initial virulence corresponded to 0.1 loop.

Pneumococcus No. 18.—Derived from a case of empyema following pneumonia; initial virulence corresponded to 2 loops.

The virulence is very easily lost on artificial cultivation; but on blood agar is retained for a much longer period. Eyre and I² found that some strains of the pneumococcus would retain their virulence for 66 days on blood agar, when the tubes were prevented from drying, and were kept at 37.5° C. The virulence can easily be increased by passages through the bodies of rabbits, for example:

Experiment.—A pneumococcus with the initial virulence corresponding to 2 loops has its virulence increased to 0.000001 of a loop after 8 passages through rabbits.

Monti increased the virulence by injecting the products of the bacillus proteus together with the pneumococcus; Pane by simultaneously injecting pneumococci and anthrax bacilli. The diminution of virulence on artificial cultivation can be shown by the following experiment:

A pneumococcus was isolated from the sputum of an atypical case of pneumonia. Its initial virulence was found to be such that an entire blood-agar cultivation injected into the subcutaneous tissue of a rabbit produced fatal septicaemia in two days, whilst one loopful of a cultivation caused a fatal septicaemia in 6 days. After 17 days on ordinary nutrient agar this pneumococcus was transferred to blood agar, when it was found that 6 entire cultivations required 16 days before causing the death of the inoculated animal.

Fraenkel found that one or two days' growth at 42° C. quite removed the virulence. A number of observations have been made upon the virulence of pneumococci at different stages of pneumonia. Patella³ removed pneumococci daily from the blood of the lung, and found a diminution in virulence; and Banti⁴ made similar observations. Weichselbaum⁵ found the cocci taken directly from the lung to be of different virulence when taken at different stages. Welch⁶ found that the most virulent cocci were present in the freshly hepatized lung. Fraenkel also found the cocci most virulent at an early stage.

VARIETIES OF PNEUMOCOCCI

We now have to inquire whether distinct varieties of the pneumococcus exist. Foá⁷ described two distinct varieties of the pneumococcus: the one he named the pneumococcus, producing a serous exudation in the subcutaneous tissue, a moderate number of cocci being found in the blood *post mortem*, and a small and soft spleen. The other variety—the meningococcus—produced no local reaction; the animal died with a large number of cocci in the blood and a hard spleen. He stated that rabbits immunized against the pneumococcus were not immunized against the meningococcus, and vice versa. He was unable to obtain a protective serum from the meningococcus.

Kruse and Pansini⁸ studied a large number of pneumococci obtained from different sources, and they found that strains, when first isolated, differ from one another to a remarkable extent, especially in respect to virulence; that the most virulent strains were most delicate and sensitive in artificial cultivations; and that the less virulent ones were able to grow under conditions in which the virulent ones were unable to flourish. Finally, they came to the conclusion that the one variety could be converted into the other. For instance, the slightly virulent pneumococcus, which would grow in artificial media at a temperature as low as 20° C., could, by passages through animals, be converted into a highly virulent type which would only grow on artificial media at 37° C. On the other hand, a highly virulent variety which would only grow at a temperature of 37° C., could be converted by cultivation into a variety which would grow at 20° C., and during this process the virulence was distinctly lowered.

Eyre and I have made similar observations, and I have generally noted that the pneumococcus which would grow at

20° C. was only of slight virulence. In one set of experiments we found⁹ that a highly virulent pneumococcus could be converted into an absolutely avirulent type, which was then capable of growing luxuriantly on all kinds of artificial media, whether acid or alkaline, and on gelatine at 20° C. It slowly liquefied the gelatine, retained its vitality for many months, and its microscopical appearances became altered from diplococci and streptococci to large masses of cocci and diplococci, and also cocci dividing into forms like the gonococcus. We were able to reconvert this strain back into the typical virulent form by means of inoculation.

Further, Eyre has found that with different strains of pneumococci apparently similar to one another there is a difference in the optimum reaction of the medium. We also observed that the virulence of some strains was very easily increased by passage through animals, but with some strains this was much more difficult. We further found that the former maintained their virulence on blood agar for a fairly long period, while the latter quickly lost their virulence on artificial cultivation.

I have already mentioned Foà's observation that animals immunized against one strain of pneumococcus were not necessarily immunized against another. Eyre and I made similar observations.¹⁰ We found that Pane's serum protected against 4 out of 5 strains of pneumococci examined, but that against another typical pneumococcus (variant), which was obtained from a fatal case of pneumonia, it had no protective power.

LOCAL LESIONS.

Recently Eyre and I have observed the local lesions produced by different strains of pneumococci when injected into the subcutaneous tissue of rabbits; we found that in some cases the exudation is of a cellular type, while in other cases it is of a fibrinous type, and we have gone still further and found that in most cases the strains derived from lobular pneumonia produced a cellular type of inflammation, while, when derived from cases of lobar pneumonia, the inflammation was of a fibrinous type.

The method we adopted in these experiments was to introduce a definite known quantity of a twenty-four-hour old blood-agar cultivation of the selected strain of pneumococcus into the subcutaneous tissue of the abdomen of a full-grown rabbit, having previously shaved the hair from a large area in order that the local reaction might be the more easily observed. In our earlier experiments the bulk of the injection amounted to about 1 c.cm., which was injected by means of a hypodermic needle. In our later experiments, however, we reduced the bulk of the inoculum by suspending the required dose of cultivation in about 1/2 c.cm. of fluid to avoid mechanical disturbance of the subcutaneous cellular tissue; to the same end we used a very fine hypodermic needle.

We investigated in this way ten different strains of pneumococci, namely, pneumococcus 2, 3, 5, 6, 7, 8, 9, 10, 11, and 12, and found that these various pneumococci could be arranged in two groups, the one group comprising 2, 3, 5, 6, and 7, and producing local lesions characterized macroscopically by the moist semi-gelatinous appearance of the exudation separating the skin from the abdominal muscles by about the third or fourth day, and microscopically by the quantity of fibrin filaments observed in this situation. The members of the second group (comprising 8, 9, 10, 11, and 12) at a similar interval after inoculation showed, on the other hand, a firm opaque yellow exudation which microscopically consisted almost entirely of small round cells. Those strains of pneumococci which were the vigorous fibrin formers were derived from cases of lobar pneumonia, whilst those responsible for the cellular type of inflammation were for the most part derived from cases of lobular pneumonia.

The question, then, whether different types of pneumococci are obtained from different affections in the human body we can definitely answer in the affirmative. One point, moreover, seems to be fairly clear, and that is, that when the pneumococci are obtained from the mouths of healthy individuals the virulence is not so high, nor can it so easily be increased as in the cases which are derived from pathological lesions.

We must also attempt to answer the question as to how far these varieties are permanent. Some are certainly not, as will appear from the observations of Kruse and Pansini, as well as from my own observations. Apparently certain characters are more strongly impressed upon some types of pneumococci than upon others (for example, some varieties

very easily acquire and maintain virulence), but these characters can be altered by appropriate means; we thus see how certain lesions will occur with some varieties of pneumococci and not with others; with some varieties bronchopneumonia is produced, while with others it is lobar pneumonia. The sudden transference of one type into a different type was observed by us in the case of the saprophytic type which we have already mentioned; in this instance a single passage through a rabbit converted it at once into a typical parasitic type.

IMMUNITY.

Rabbits can be immunized in various ways, the best being that advocated by the Klemperer brothers, by the intravenous injection of about 12 c.cm. of a broth cultivation which has been destroyed by exposure to a temperature of 60° C. for one or two hours, and subsequently inoculating the animals with living cultivations. During this process many animals die, but those which recover are rendered immune to subsequent inoculation. There are other methods; for instance, inoculation with attenuated cultivations, the injection of filtered cultivations, and the injection of the glycerine extract of infective blood. G. and F. Klemperer, Foà, and Carboné were the first to show that the blood serum of immunized animals protected other animals when injected either at the same time or subsequent to inoculation. Arkharow and Issaef obtained similar results, and in this country I was the first to confirm these results.¹¹ Foà also made the observation that the blood serum of animals which die of marasmus during the process of immunization is capable of producing marasmus in other animals.

I was the first to immunize a horse, and thus to obtain sufficient serum for the treatment of cases of pneumonia.¹² This serum was of a potency that 0.03 c.cm., when mixed with 10 lethal doses of living pneumococci, and the mixture injected into the peritoneal cavity of a rabbit, prevented death. Several cases of pneumonia were treated with this serum with satisfactory results, but subsequent observations have shown that the serum is not very efficacious. Mennes¹³ in the same year described some serum obtained from a horse. Pane¹⁴ described in March, 1897, a serum obtained from donkeys which, in doses of 1 c.cm. injected intravenously, protected rabbits against 3,000 fatal doses of pneumococci injected into the peritoneal cavity. Eyre and I¹⁵ tested this serum carefully upon rabbits. We found that it possessed the protective powers attributed to it by Pane; in all we examined five strains of pneumococci, and we found that the protection was absolute against four strains, but that against the fifth strain there was no protection whatever. During the progress of a case of pneumonia the serum acquires protective powers, as was shown by the brothers Klemperer. I have repeated some of these experiments, and have found that there is a certain amount of protective power, but that it is decidedly feeble.

THE MECHANISM OF THE ACTION OF THE SERUM.

Eyre and I made a series of experiments with reference to the action of serum.¹⁶ We first tested a number of serums obtained from normal animals; and found that the normal serum of the rabbit, the guinea-pig, and the fowl, when mixed with a minimal fatal dose, possessed slight protective powers. The rabbit and the fowl serum in doses of 0.5 c.cm., thus protected against a minimal fatal dose, as did the guinea-pig's serum in doses of 0.03 c.cm.; but when we used a tenfold fatal dose none of these serums protected. The serum of a horse which had been immunized against the streptococcus possessed no protective powers, even against a minimal dose. Mennes also found that the antistreptococcus serum of a horse had no protective power. The serum of an immunized rabbit and the serum of immunized horse protected against ten lethal doses in doses of 0.03 c.cm. and 0.015 c.cm. respectively. It is thus clear that during the process of immunization specific protective substances are produced in the serum.

SEAT OF FORMATION OF PROTECTIVE SUBSTANCES.

In my early experiments I found that the removal of blood from an immunized animal rendered it for a time susceptible to inoculation, and that after bleeding an immunized animal it could easily be infected within the next few days, but that if the inoculation were postponed for four or five days the

animal was not infected.¹⁷ It would appear from this that the protective substances continue to be manufactured in some organ, and are thrown into the blood. Wassermann,¹⁸ however, found that the blood serum of an immunized animal protected a guinea-pig against 400 lethal doses in quantities of 0.8 gram, while the bone marrow protected in as small a quantity as 0.2 gram.

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MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

URTICARIA ACUTA.

IN the *BRITISH MEDICAL JOURNAL* of April 12th, 1902, Dr. F. S. Palmer gave an interesting account of two cases of urticaria acuta which he believed to be due to the ingestion of spring rhubarb. A case which tallied, with his in almost every particular was under my care in the early part of the year. The patient was a little girl, aged 7, who suddenly developed feverish symptoms, and complained of great cutaneous irritation.

I was called on the morning after the first restless night, by which time urticarious patches had broken out all over the body, but were most marked on the chest and lower limbs. Here and there the rash had assumed a bullous form, there being small spherical elevations filled with a clear yellow fluid, reminding one of pemphigus. These were surrounded in each case with an areola of angry redness. There was marked fever, the temperature on the first day being 103.5°, gradually falling to normal, which was reached on the third day. As in Dr. Palmer's cases, there was considerable facial erythema, and in addition a blueness under the eyes deeper in colour than I have seen in any case of sickness. Before the end of the third day the vesicles had become purulent, and some had assumed an oval outline with a slightly depressed centre, looking suspiciously like small-pox pustules in the stage of umbilication, but when opened they were unilocular, showing a bright-red base lying immediately beneath the cuticle. The little patient, in spite of her condition, was bright and cheerful, complaining of nothing but the irritation which, as she said, had kept her awake at nights although she was so sleepy. On inquiry into her diet her relatives said that she had eaten very freely of some stewed rhubarb, and that they had purposely allowed her to do so thinking it would act like spring medicine. A specimen of urine was not obtained until after the severe symptoms had subsided. This was free from albumen but deposited an abundance of urates, but whether or not it contained an excess of oxalates was not ascertained.

Liverpool.

WM. BRAMWELL, M.A., M.D., B.Ch.Dubl.

A CASE OF HARD CHANCRE OF UPPER LIP; SUPPOSED SOURCE OF INOCULATION.

RECENTLY, while acting as Senior Assistant Surgeon to the Nottingham General Dispensary, I was consulted by a female patient, aged 20, who suffered from a sore in the centre of the upper lip. She saw me on March 5th, 1902, and said she had first noticed it about a week previously. Its appearance at once suggested a specific nature, and the submaxillary glands were enlarged and shotty.

The girl was to all appearances a virgin, and denied having kissed anybody, except a girl friend some months before. Her occupation was to attach labels to parcels in a warehouse;

this she did by first licking the labels. Supposing it to be syphilitic, I prescribed the solution of mercury perchloride 20 minims, and potassium iodide 5 gr., three times daily. After about two weeks treatment the hair fell out and a rash with a sore throat and mucous patches developed. The amount of the liq. hydrarg. perchlor. was increased to 60 minims thrice daily, and the iodide to 10 gr. doses. The sore was treated from the first with a local application of lotio nigra in weak solution, and a powder containing calomel and bismuth was dusted on. About April 7th the sore had healed, leaving a cicatrix. After another month of this treatment the "secondaries" had pretty well disappeared, when smaller doses were again substituted.

The main interest of this case is the source of inoculation. Did she get syphilis from licking the labels? I remember listening to a well-known surgeon one day giving a clinical lecture on a patient who had an ulcer on the tongue. The patient indignantly denied that he ever had venereal disease, whereupon the surgeon replied, "Gentlemen, we must take all these statements *cum grano salis*, and the best salt is K.I." There can be no doubt, however, that the system of fixing labels adopted by some firms—as in this case—is highly dangerous and ought to be abandoned.

Lybster, N.B.

J. NOONAN MEADE, L.R.C.P. & S.E.

TREATMENT OF RHEUMATOID ARTHRITIS.

THE following case of so-called rheumatoid arthritis is of interest inasmuch as it was treated by a method recommended by Dr. P. W. Latham, of Cambridge. This is based on what I firmly believe to be the true pathology of this disease—the neural theory, others urging strongly the infective theory. I see no reason why the two should not go hand in hand; given that it is infective, one can easily believe that the particular poison exerts its chief influence on the spinal cord. I think the name should be changed; if this disease were called poliomyelitis many misconceptions of the true nature of this distressing and intractable malady would be to a large extent removed. As long as the disease is considered a kind of rheumatism, the joints will receive attention and the spinal cord be neglected.

Mrs. W., married, aged 43; had had much illness and worry. On January 10th, 1901, she was found to be much wasted, with much pain, and practically every joint in the body stiff and swollen. She had glossy finger tips, and was bedridden. She was treated for a time on ordinary lines.

On March 18th two freshly prepared blisters were applied, one on each side of the tenth dorsal vertebra, and were kept open with savin ointment about twelve days.

On April 16th similar blisters were applied, one on each side of the lower cervical and upper dorsal vertebrae.

On April 19th the patient had more feeling in her feet.

On May 28th raw meat juice ordered, a teaspoonful four times a day.

On June 10th the patient felt stronger and better, and spent some hours in the open air on fine days. The blisters were repeated in the lower dorsal region.

On July 18th she could use her knees better.

On August 6th there was considerable increase in weight.

On February 5th, 1902, she could walk with crutches.

In April she could walk without crutches, and did housework. In addition to blistering the patient had massage at home and at Buxton. The contrast between this woman's present condition and her former almost hopeless state is very marked.

Bournemouth.

W. J. MIDELTON, L.R.C.P., M.R.C.S.

PSORIASIS INHERITED (?) FROM MYXOEDEMATOUS PARENT.

THE following case seems worthy of record as affording some evidence of a possible inheritance of thyroid deficiency. I was recently consulted by a young woman, aged 27, who had been suffering from a persistent attack of psoriasis for the last four years. She had undergone a lengthy treatment with various remedies, but without any benefit. At that time thyroid extract had not been administered.

I subjected her to a course of vapour baths with some improvement, but having elicited a history of myxoedema in her mother, I thought it well to order the extract. Recovery