appeared to come from the middle meatus, and by means of the probe bare bone could be detected in the region of the anterior ethmoidal cells. This may possibly require further treatment; but the notable feature was the disappearance of the gastric symptoms and the general improvement alongside the diminution of the nasal discharge.

In considering the general results of excessive or purulent discharge from the nose, we cannot, of course, leave out of count the nervous or mental element. It can easily be understood that in people of neurotic temperament, the sensation of secretion passing over the pharyngeal wall and the constant hawking to rid themselves of it may give rise to effects on the general health. Add to this the troublesome pharyngitis and laryngitis which is so frequently got as a result of nasal affections, with, in many cases, a certain degree of dysphagia, and we have a local condition which is calculated to set up a state of mind favouring abnormal introspection, giving rise to depression of spirits, loss of appetite, insomnia, and the general ill-health caused thereby.

It would appear, therefore, advisable in cases of chronic ill-health, associated or not with gastric derangement, to include among the possible causes certain affections of the nose and naso-pharynx, and especially those giving rise to a discharge of a muco-purulent or purulent character. The patient himself may make no complaint of this—indeed, he may be unaware of the existence of anything wrong with his nose, and the condition may only be revealed by careful rhinoscopic examination. As I have already stated, it is probable it will be found in most cases that the nasal affection is of the nature of a contributory cause, and that there has previously existed some digestive weakness which makes the patient more liable to the evil effects of the entrance of purulent material into the stomach; and that, while treatment directed to the nose is necessary to enable a cure of the more general state of health to be brought about, it must be looked upon rather as a reinforcement of, than as an alternative to, the more usual methods.

NOTE ON HAEMOSOZIC SERA.

BY

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In a preceding note,¹ we gave an account of experiments made to produce an antihæmolytic (haemosozic) serum by injections of ox bile into rabbits. We were only moderately successful, for unless added to bile in very large doses the serum delayed, but did not prevent, hæmolysis. In our opinion this result was due partly to the fact that it was impossible to produce a high degree of immunization owing to the cachexia caused in rabbits by repeated injections of bile, and partly to the great variety of substances which the serum of animals injected with bile might contain.

Preliminary experiments² having shown us that the bile contained not only two hæmolytic substances at least, but also one haemosozic substance, it seemed probable that on the introduction into the animal organism of such a complex fluid, reactions similarly complex might follow. We therefore endeavoured, in the first instance, to separate roughly the different substances present in bile, and to prepare sera by injecting each substance separately into different animals.

Our *modus operandi* was as follows: Ox bile taken aseptically shortly after slaughtering the animals was dried in vacuo over sulphuric acid. When completely dried it was finely powdered and repeatedly extracted with ether. This was decanted off, and the dried residue left after evaporation was suspended in physiological salt solution. This emulsion we call the ethereal extract. The same powdered bile was now extracted for 24 hours with absolute alcohol in the cold, the precipitate collected on a filter, washed with absolute alcohol and dried in vacuo. This precipitate when suspended in water we call the aqueous extract. The residue left after evaporation of the alcohol was dissolved in water and formed the alcoholic extract.

We had therefore: First, the substances soluble in ether (ethereal extract); secondly, the substances soluble in alcohol (alcoholic extract); and, thirdly, the substances insoluble in or precipitated by these two reagents (aqueous extract).

1. The ethereal extract is insoluble in water, and contains cholesterin, lecithin, and the fatty substances which are

soluble in ether. The extract can be suspended in water only with difficulty, and though not toxic in itself when injected intravenously, it proves fatal by causing emboli. The subcutaneous injection of the extract of 300 c.cm of bile is followed by no particular symptoms, even when such large doses were repeatedly injected. Temperature and weight remained normal, or the animals increased in weight even, and no inflammatory symptoms were noticed at the point of inoculation. This extract is undoubtedly haemosozic when added to bile, for it diminishes though it never completely neutralizes the hæmolytic properties of bile. The serum of animals repeatedly injected with this extract has no special hæmolytic or haemosozic properties and indeed does not differ in its action on bile or blood from normal serum.

2. The alcoholic extract is very soluble in water; 0.20 gram injected intravenously kills a rabbit weighing 1,000 to 1,200 grams; death supervening in the majority of cases only after a few days. The temperature rises two or three hours after the injection, but the fever is of short duration. In one of our rabbits 0.10 gram gave rise to a profuse hæmorrhage of the ear on the injected side lasting two days. Subcutaneous injection was followed by intense inflammation ending in necrosis of the skin at the point of inoculation. When injected under the skin of the ear, dry gangrene was the result. The part in contact with the liquid became parchment-like and thin, and finally fell off.

Phlebitis was the rule after intravenous injection. In short, the alcoholic extract produced all the lesions of the skin generally following on the injection of bile. Repeated injections, even of small doses, produced cachexia. The animals lost their appetite, diminished in weight, suffered from diarrhoea, and died, the temperature falling for some time before death. The necropsy showed no macroscopic lesions. A 2 per cent. solution was slightly, and a 5 per cent. solution very, hæmolytic; but if heated to 100° C. for thirty minutes such solutions lost their hæmolytic properties. The serum of animals repeatedly injected with small doses of this extract was haemosozic, that is, it prevented the hæmolytic action of the alcoholic extract and of bile, but had no action on the ethereal or watery extracts. The serum of animals which had received three or four injections was more haemosozic than the serum of animals which received larger doses. Some of these sera when mixed with bile in equal proportions altogether prevented hæmolysis, a result which we had seldom been able to obtain with the sera of animals injected with bile. The serum when mixed with bile in a test tube gave rise to a very fine precipitate, which did not settle down altogether at the bottom of the tube, but which did not pass through a paper filter. When heated to 56° C. for thirty minutes the serum completely lost its hæmosozic properties.

3. The aqueous extract was not wholly soluble in water. A filtered solution of 0.10 gram injected intravenously caused death in 8 to 10 hours. The same dose injected subcutaneously without previous filtration produced a hard tumour surrounded for some days by an inflamed area. This tumour was sometimes as large as a walnut, and enclosed an encysted abscess, containing very thick, cheesy, but aseptic pus composed almost exclusively of more or less degenerated mononuclear wandering cells. The poisonous properties of this extract were marked therefore, and one had necessarily to proceed very slowly when injecting animals with it.

Moreover immunization was rendered very difficult by the fact that the animals appeared to become more susceptible to the poison. Very small doses of the extract were borne well as a rule at first, but when such doses were repeated, the fever not only increased, but lasted longer after each injection. The animal's weight diminished and cachexia supervened after the fifth to seventh injection. The aqueous was less hæmolytic than the alcoholic extract, and the hæmolytic power diminished when the extract was heated to 100° C. for half an hour. The serum of animals injected with the aqueous extract was haemosozic when red corpuscles were suspended in aqueous extract or bile, but less so than the preceding extract in the case of bile. It had no hæmosozic effect on red corpuscles suspended in alcoholic extract, and had no effect on the ethereal extract. The serum mixed with bile produced a precipitate in the latter, which, though it did not settle at the bottom of the tube, did not pass through a paper filter.

In our first note we pointed out that, occasionally, the serum of animals injected with bile was not haemosozic but hæmolytic. We now found that, occasionally, the serum of animals injected with alcoholic or watery extract was hæmolytic instead of being haemosozic as is the rule. In some cases

the serum of animals injected with alcoholic extract was haemolytic when acting alone or mixed with alcoholic extract but unmistakably haemosozic when mixed with aqueous extract. Similarly, in some cases, the serum of animals injected with aqueous extract was haemolytic when acting alone or mixed with aqueous extract, but unmistakably haemosozic when mixed with alcoholic extract. The same serum, therefore, was both haemosozic and haemolytic.

Lastly, a mixture of our two haemosozic sera was not more haemosozic for red corpuscles suspended in bile than the more potent of the two sera.

NOTE AND REFERENCE.

¹ BRITISH MEDICAL JOURNAL, July 18th, 1903, p. 130. ² These experiments will be described shortly in the *Journal of Pathology*.

CAPSULE FORMATION BY DIPLOCOCCUS PNEUMONIAE IN CULTURE;

A POINT POSSIBLY OF USE FOR THE IDENTIFICATION OF THAT MICRO-ORGANISM IN PRACTICE.

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BEFORE a given micro-organism can be identified with *diplococcus pneumoniae*, one of the chief points to be determined is the presence of its capsule. For instance, as is well known, it is especially by dint of its capsule formation that the pneumococcus is distinguished from other virulent streptococci with which it is liable in other respects to be confused. But the pneumococcus forms its capsule only under certain conditions; and while the capsule can readily be demonstrated around the diplococci when they are present in sputum, blood, or animal exudation, it is rarely exhibited in cultures. Capsule formation, however, has been stated to sometimes take place in cultures of the pneumococcus in media containing tracheal mucus, and also in cultures in serum and in milk.¹ Be this as it may, in actual practice when capsules cannot be demonstrated around the diplococci in the original material, it is necessary before a given diplococcus can be satisfactorily identified with the pneumococcus to inject the micro-organism into a mouse and to demonstrate the presence of capsulated diplococci in the blood or exudation of the mouse *post mortem*.

The pneumococcus showing capsules in culture.

A few months since, when examining a specimen of the pneumococcus, I happened to make a subculture in gelatine and to incubate it at 37°C. On examining the culture next day microscopically after suitable staining I found that undoubted capsules could be seen around the diplococci. After seventeen to twenty-four hours at 37°C., the gelatine in the case of the pneumococcus becomes generally, but not always, uniformly turbid. To demonstrate the capsules the following procedure is used:

The gelatine used was 12 per cent. gelatine made as follows:—1 litre of distilled water is added to 1 lb. of minced beef. Boil for thirty minutes. Filter, add 12 per cent. of yellow-gold table (not bronze-gold table) gelatine, 1 per cent. peptone, and ½ per cent. salt. Make faintly alkaline to alkaline litmus paper with liq. potassae (B. P.) Add

white of egg and steam for thirty minutes. Filter, pour into tubes, and sterilize in the steamer for thirty minutes on two successive days.

A drop of the fluid gelatine culture is removed with a loop and spread over a cover-glass, dried over the flame, allowed to stand in alcohol for a minute, and then without drying transferred film downwards to a watchglass containing ordinary Ziehl's carbol fuchsin. The film is allowed to stain in the carbol fuchsin for from a half minute to three minutes at the ordinary room temperature. The cover-glass is then lightly dipped in a beaker of water, and after removal of the moisture from its upper side by means of a piece of filter paper (so as to enable a drop of oil to be placed on the cover-glass), the preparation is mounted on a drop of water on a slide. On examining the specimen with an oil immersion (one-twelfth or one sixteenth) clearly outlined, stained capsules can be seen around a good number of the diplococci.

It is important only to dip the stained coverglass lightly and rapidly into the beaker of water. If the specimen is washed in the usual way—that is to say, until all excess of stain is removed, the stain goes out of the capsules and they are invisible.

If several preparations are made it is advisable to renew the carbol fuchsin, which is much more efficient when first used.

While I have succeeded in demonstrating capsules in a one-day culture in gelatine at 37°C. in the case of five successive virulent specimens of the pneumococcus from different sources, six virulent streptococci which have been examined under the same conditions have failed to show capsules.

I believe, therefore, that this property of the pneumococcus of forming capsules in gelatine at 37°C. in one day may be applied for the identification of the micro-organism, and for its differentiation from specimens of streptococcus pyogenes. The point suggests itself as likely to be of use to those who are unable to make the animal experiment.

It should be added that it is difficult to get permanent specimens of pneumococcus showing capsules in gelatine at 37°C., as the capsules are less obvious in Canada balsam than in water, and tend rapidly to fade. The accompanying photograph, however, was made from a permanent specimen which was obtained by deeply staining with carbol fuchsin, only slightly dipping in water, and then, after drying, passing through xylol and mounting in balsam in the usual manner.

REFERENCE.

¹ Washbourn, Croonian Lectures, 1902.

ABSTRACTS OF

The Hunterian Lectures

ON THE

PATHOLOGY AND SURGERY OF CERTAIN DISEASES OF THE PANCREAS.

Delivered before the Royal College of Surgeons of England.

By A. W. MAYO ROBSON, F.R.C.S.,

Hunterian Professor.

LECTURE I.—SYMPTOMS AND DIAGNOSIS.

[AFTER some preliminary observations, Mr. Mayo Robson dealt with some anatomical, histological, and physiological considerations bearing on the pathology of the pancreas, and then went on to discuss the symptoms and diagnosis of diseases of the gland.]

DIFFICULTIES OF DIAGNOSIS.

As our knowledge of the functions of the pancreas both with regard to digestion and metabolism is becoming fairly well established, it would seem probable that any departure from the normal would lead to such considerable disturbance of function that the symptomatology of any of the diseases of the pancreas would be so marked as to make the diagnosis easy. But this is far from being the case for several reasons:

I. It is seldom the case that the pancreas is diseased without other organs participating. For instance, the relations between cholelithiasis and pancreatitis, between gastro-intestinal catarrh and catarrh of the bile and pancreatic ducts, between ulcer or tumour of the stomach and extension to the pancreas, between affections of the liver, colon, lymphatic glands, and duodenum and pancreatic disease.

II. Every function performed by the pancreas may be vicariously taken up by another organ except the glycogenic function, and that we are not yet certain about. The stomach can digest albumen, the salivary and intestinal glands have the power of digesting starches, and the bile and intestinal secretions can emulsify fats.

III. A considerable portion of the gland may be necrosed and cast off or otherwise disabled, and yet the portion remaining may apparently be sufficient to carry on the functions of the gland. For instance, in a case of my own, a patient who is now perfectly well, had necrosis of the pancreas, which I removed at operation. As may be seen, a good pro-