being done subperitoneally as much as possible. The duct is ligatured and divided, the stump being aseptically either by the cautery or by the application of a 1 in 500 solution of perchloride of mercury. The peritoneum is now sutured over the top of the duct. There is usually little bleeding, and that is easily arrested by sponge pressure or by one or two ligatures.

Unless there be oozing, or unless the wound has been infected by pus or gall-bladder secretion, drainage may perhaps be thought unnecessary, but the adage, "When in doubt drain," is a good one, and it can do no harm to leave an efficient drainage tube in the right kidney pouch for twenty-four or forty-eight hours after extirpation of the gall bladder. Packing with iodoform gauze in these cases is better than using a tube, as it serves the double purpose of arresting oozing from the lacerated liver and acting as a drain.

Cholecystenterostomy consists in establishing an artificial opening between the gall bladder and intestine, preferably the duodenum. The first operation was performed by Winiwarter, in 1880. In its place it is an extremely useful operation, but as it leaves the cause of the obstruction unremedied, it ought not to be resorted to, except occasionally, where a more radical operation is impracticable or inadvisable. Dr. Murphy, of Chicago, favours the procedure before other methods.

My own conclusions are that the operation is indicated :

1. In biliary fistulæ, depending on stricture or other permanent occlusion of the common duct.
 2. Very occasionally in cancer of the head of the pancreas or malignant tumour of the common duct, leading to chronic jaundice and distended gall bladder; but in such cases the mortality will necessarily be so high that the justifiability of the operation is questionable.
 3. Occasionally in impaction of gall stones in the ducts, where the patient is not in a fit condition to bear the more prolonged operation of separating adhesions, and crushing or removing the concretion by choledochotomy.
 4. In certain cases of obstruction of the cystic duct where cholecystectomy is impracticable.
- Contra-indications.*—1. In any obstruction of the bile ducts which can be cleared away with reasonable probability of success.
2. In malignant disease of the head of the pancreas or common bile duct, leading to distension of the gall bladder, the mortality is so great (8 operations with 7 deaths) that it is hardly worth doing.
 3. In contracted gall bladder, where it is impracticable to insert the button.
 4. Where there are extensive adhesions which would lead to kinking of bowel.
 5. In very large gall bladder with obstruction of the cystic duct, where cholecystectomy should be done.

The operation may be performed (a) by means of simple suture, (b) by means of my decalcified bone bobbin, (c) by means of Murphy's button. I decidedly prefer to make the union by means of the Murphy button, both on account of its efficiency and the expedition with which it can be used.

The operation of cholecystenterostomy is performed through the same incision as is made for cholecystotomy, and after the gall bladder has been aspirated and the intestine clamped either by an india-rubber tourniquet or by intestinal clamps the junction is effected. If sutures be employed a semicircle of interrupted silk sutures is inserted to unite the contiguous serous surfaces of the gall bladder and gut, the viscera are then opened, and the mucous margins of the two openings are united by interrupted catgut stitches, after which the circle of catgut stitches and then the circle of serous sutures is completed. If the bone bobbin be used two continuous sutures only are employed, a silk stitch to unite the serous surface one-third or half an inch from the visceral openings, and a catgut suture to join the mucous margins of the visceral openings.

The whole process occupies a very short time, and is really very simple; it is, however, necessary to bear in mind that the button has to separate by causing the approximated margins of the openings to slough, and that the true bond of union is only slight at first, so that it is well to keep the patient absolutely quiet for at least a fortnight, lest the new bond of union should give way and permit of extravasation of the visceral contents.

In considering the question of cholecystenterostomy it has to be borne in mind that the operation can only be done when the gall bladder is of moderate size or dilated, and that it is inapplicable to the difficult class of cases where a gall stone is impacted in the common duct and the gall bladder is atrophied. When it can be done the anastomosis should be

made to the duodenum, but if preferred a free loop of jejunum may be selected and brought over the hepatic flexure of the colon. In only exceptional cases should the anastomosis be made between the gall bladder and colon.

From a report up to date which Dr. Murphy has been so kind as to furnish me, cholecystduodenostomy has been performed with the aid of the anastomosis button in sixty-seven non-malignant cases, with only three deaths. My own cases are eleven in number, with one death.

Choledochostomy is the term applied to the direct surface drainage of a dilated bile duct, of which Iverson and I have each had a successful case. The operation was first performed by Terrier.

Where it is impossible to clear the ducts, instead of performing choledochostomy, the operation of choledochenterostomy may be done, the union of the dilated duct to the duodenum being made by means of a Murphy's button. The operation was first performed by Sprengel.

In concluding my lectures I must thank you, Mr. President, and my audience, for the kind forbearance which you have shown in listening to details which I fear may at times have been somewhat wearisome. My wish has been to show the importance of the subject I have taken up, and some of the results which may be looked for by appropriate surgical treatment, and if I have succeeded in exciting your interest and in making it evident that in the greater number of diseases of the gall bladder and bile ducts surgical treatment is well worth considering, after a fair, though not too prolonged, trial of medical means, my aim will have been accomplished.

REFERENCES.

- 1 *Cent. f. Chir.*, 1887. 2 *Annals of Surgery*, October, 1893

REMARKS ON THE MORPHOLOGY AND CHEMICAL PRODUCTS OF THE DIPLOCOCCUS PNEUMONIÆ, AND SOME RESULTS OF VACCINATION.

By A. G. AULD, M.D.

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In these remarks it is merely intended to give a brief summary of some of the results obtained, reserving the discussion of these and the mass of details to a subsequent communication.

Sputa were obtained from cases of pneumonia in various hospitals, at all stages of the disease. In every case the capsulated diplococcus was found. It always existed as a paired body, and it was invariably found in association with numerous other bacteria. An attempt was made to isolate these organisms by means of plate cultivations. The pyogenic cocci were nearly always found, especially the staphylococcus aureus. Various bacilli also were cultivated, some decolorising with Gram's solution. Inoculation of many of these bacilli was attended with negative results, but one of them induced an illness characterised by wasting and chronic diarrhoea. Further cultivations of this bacillus proved it to be the bacillus coli communis.

Special mention must be made of the circumstance that the bacillus septicæmiæ of rabbits is frequently found in human saliva. It looks like a diplococcus, but can easily be known by its characters and growth in gelatine and agar. If this organism gains admission to the culture, its intense septicæmic effect will be found in all sub-cultures. Its effects have frequently been mistaken for those of the diplococcus.

The diplococcus is a very difficult organism to work with. In the first place, it is by no means so easy to get a pure growth as might be supposed, it varies often in virulence, and the broth cultures must be quickly utilised (within two or three days), as the virulence quickly dies out. This refers chiefly to broth cultivations; if kept on blood the organism will always retain its virulence for a considerable period.

The rabbit is well known to be highly susceptible to this coccus, and this was the animal selected for the investigation, a few side experiments were also made on guinea-pigs.

Death always occurred from the second to the fourth day after inoculation of virulent sputum. Sputum taken at the crisis was less virulent, and that taken some days after the crisis produced a mild inflammation, and the animals frequently recovered. When the animals were allowed to die, cultivations from their blood were usually impure; the pyococcus aureus was a special source of impurity, and various other cocci and bacilli were found. These impurities may be introduced with the sputum injected, or, on the other hand, they may be absorbed *post mortem* from the animal's intestines.

To get a pure culture the animal should be killed within twenty-four hours after inoculation, and cultivations made from the blood. Even then failure may result. There is, however, a very delicate test (in fact the only one found) for the purity of the growth. On the surface of sloping agar a streak culture forms a very fine dew-like moisture, absolutely transparent with reflected light. If the slightest trace of opacity can be detected, the culture is impure. This may seem a very hard condition, but repeated trials completely fulfilled it. This dew-like growth might easily be mistaken for watery droplets on the surface of the agar. After a few days or a week the cocci begin to die, and then a slight opacity makes its appearance. In broth at 37° C. a cloudiness, without any film, appears after six or eight hours. This lasts for about thirty-six hours, when the cocci subside, and the broth again becomes transparent. On tilting the flask the cocci appear as a granular sediment, which runs down the bottom after the manner in which sand runs down an incline.

Examination of the agar or broth cultivations shows that the organism has changed its character. It has no longer a capsule (although on agar, capsules were occasionally seen in virulent cases), and it presents three forms. These are: single cocci, diplococci, and short chains (streptococci). The chains consist of from three to fifteen elements, but the great majority are composed of seven or eight cocci. These cocci are nearly spherical, but in most cultivations the individual cocci and diplococci are oval (often with pointed ends) or approach to short bacilli. The diplococci often remind one of a grain of wheat or barley divided in the middle. In the blood of susceptible animals the same varieties are seen, but surrounded by a capsule.

If a pure virulent culture from blood or peptone broth be inoculated, either subcutaneously or into the internal cavities, it produces at the site of inoculation intense congestion, exudation of sanguineous serum and fibrin. It never produces pus or any other lesion. Many observers have stated that purulent infiltrations have been formed (after the lapse of some time) by the diplococcus. This was also observed in these experiments, in some cases, after a week or two, but inoculations from the pus never gave a pure growth on agar. The conclusion cannot be avoided that in all such cases (as also in cases of purulent inflammations in man, set down to the diplococcus) other organisms are present, and unless the agar test be fulfilled the statements of these observers cannot be accepted.

In like manner, it may be remarked that the morphology of the organism varies considerably. It is a curious circumstance that other cocci alleged to be the cause of pneumonia have always been capsulated organisms—for example, that described by Klein. How do these observers know that they have not been working with certain varieties of the diplococcus pneumoniæ?

In broth cultures the majority of the cocci die in a few days, but many of them retain their vitality at least for months, and new cultivations can be made from them. Some of these are often unusually large, stain very deeply, and are probably of the nature of arthrospores.

CHEMICAL PRODUCTS OF THE DIPLOCOCCUS IN RABBITS AND THE RESULTS OF THEIR INOCULATION.

The blood of inoculated animals which gave a pure growth on agar was used for these experiments. In one or two cases the organism was thereafter passed through a guinea-pig, when it seemed to acquire increased virulence. In all cases control inoculations were made. The injections were chiefly made into the pleural cavities, so as to obtain the characteristic local lesion. The animals so inoculated were always

killed as their symptoms indicated. There was nearly always severe pleurisy, the false membrane being grey or blackish grey. Congestion of the lungs was frequent; in two cases pneumonic consolidation of an entire lobe was found, the air vesicles being full of granular fibrin; and pericarditis was often present also.

MODE OF PREPARATION.

The local lesions, lungs, spleen, and blood were minced and pounded, and immediately placed in a large quantity of rectified spirit. The tissues were never taken from an animal which died after inoculation.

After standing for four weeks the spirit was filtered off, and the residue extracted with water. This was accomplished in twenty-four hours, and was assisted by an electrically-driven "shaker." The watery extract was filtered from the coagulated proteid, refiltered, and then, as also the alcoholic filtrate, evaporated *in vacuo* at 37° to 40° C. The concentrated liquids were then mixed, and thrown into a large excess (8 to 10 times their bulk) of absolute alcohol. A large precipitate fell, which was again extracted with absolute alcohol, filtered, and washed with alcohol. This precipitate was then dried at 37° C., and the resulting product was a very fine cream-coloured powder, which gave all the characteristic reactions of an albumose. It was soluble in water, completely precipitated by saturation with neutral ammonium sulphate, and gave a distinct biuret reaction. The entire quantity obtained from the lungs, spleen, and blood of six rabbits was less than three-quarters of a gramme.

The alcoholic filtrates were also added and evaporated *in vacuo* to a very small bulk at 37° C. This was again thrown into absolute alcohol and allowed to stand for ten days. It was again filtered, evaporated, and the residue washed with alcohol. This residue was thinner, reddish-yellow amorphous substance having a somewhat viscous consistence. It was agitated and re-agitated with ether, when a considerable quantity of fatty matter and free acid was dissolved out. The precipitate in ether was finally thrown into chloroform, and the final product was a yellow amorphous substance, nearly altogether freed from its previously viscous character. The quantity obtained of this substance amounted to 0.5 g. When tested it was found to be strongly acid, very soluble in water, and gave no colour reactions with Millon's reagent or potassio-mercuric iodide, nor was any biuret reaction given. Whatever else this substance contained, it was evident that it contained a large quantity of an organic acid. Both the ether and residue gave Uffelmann's reaction for lactic acid.

EFFECTS OF THE ALBUMOSE.

Both the albumose and organic acid were then tested on rabbits. The former was injected in doses of 0.02 gramme (1) intravenously (in saline); (2) into the chest; (3) underneath the skin of the ear. The result of the intravenous injection in a rabbit weighing 2,480 grammes was initial shock and fall of the temperature over 1°. In an hour or two the temperature began to rise, and in three hours had risen to 104.8° F. (the normal temperature of a rabbit is about 102.6° F.). Next day it had fallen to 103.4° F., and then gradually sank to the normal. No other pathological effect was produced, but the animal lost slightly in weight.

The result of the intrathoracic injection was very interesting. There was no initial depression, but marked dyspnoea soon set in. This continued and was accompanied by a rise of temperature to 103.8° in three hours. Next day the dyspnoea was still present, and the temperature 103.4°. On the third day the animal was killed. There was right-sided pleurisy, and the entire lower lobe of the right lung was completely consolidated. No other lesions were found. Inoculations were made from the blood, and the serum in the pleural cavities in solid and liquid media, and no growth whatever took place. The injection beneath the skin of the ear in a rabbit weighing 2,550 grammes gave the following results: The temperature slowly rose to 104° on the following day, and the ear was inflamed. Next day the ear was greatly inflamed and swollen, and a bloody serum issued from one or two cracks in the skin. The temperature rose to 106.2° on the third day. It then gradually fell, and the inflammation subsided, until on the sixth day it was nearly all gone. The animal lost 60 grammes in this time.

EFFECTS OF THE ACID RESIDUE.

The organic acid was also injected (1) intravenously; (2) into the chest, in doses of 0.1 gramme. No result followed the injection into the lung. In the case of the intravenous injection the temperature rose a little over 1° in the course of a few hours. Next day it had returned to the normal, and the animal remained well.

CHEMICAL PRODUCTS OF THE DIPLOCOCCUS IN ARTIFICIAL MEDIA.

Subcultures were made from different sources, and grown in veal peptone broth. As the commercial peptone used for the broth contains much albumose, it was resolved also to try cultivations in broth made without peptone, and the organism grew freely in this medium. In addition, an artificial serum was made containing pure alkali albumin, and the various salts which exist in normal blood, in their respective propor

tions. The serum was prepared according to the formula given by Dr. Sidney Martin in his anthrax investigations.¹ The reaction of the broth must be alkaline, to ensure a successful growth.

As soon as the organism has grown the previously alkaline medium becomes distinctly acid, and this acidity is permanent. After two days' growth the cultures were filtered through a Chamberland filter, and the clear toxin evaporated at 38° C. to a sixth of its bulk, thrown into absolute alcohol, and the copious precipitate obtained treated exactly in the same way as already described in the case of the tissue extraction. In like manner the alcoholic filtrate was evaporated and the residue purified. Both products in appearance and chemical reactions were exactly similar to those obtained from the tissues, one being an albumose and the other an organic acid, a lactic acid reaction being obtained. Injected into animals also they produced precisely similar effects to the tissue products. A large dose of the albumose (3 g.) was also injected into the peritoneum. The temperature rose to 105.4°, and continued high (nearly 104°) for about three days, and the animal lost greatly in weight.

An interesting result was obtained from the filtered broth without peptone. After two days' growth a distinct biuret reaction was obtained, which was entirely absent from the control broth, and in which no other proteid could be detected. A copious precipitate was also given with alcohol and ammonium sulphate. It seems evident from this important reaction that a proteid is formed by the organism from nitrogenous material, the proteid thus being excreted after digestion as an albumose. It is perhaps hardly necessary after this to add that the albumose was also formed in the artificial serum.

The views of Dr. Sidney Martin may be alluded to in this connection. He has explained the production of toxic albumoses in diphtheria and certain other conditions by the digestive action of the chemical enzyme or toxin produced by the organism on the albumins of the tissues or of artificial serum. The enzyme he supposes to exert this action outside the organisms themselves. Thus in the case of diphtheria the enzyme is absorbed from the lesion, and exerts its digestive action on the albuminous constituents in the spleen and elsewhere.

It must be said that the result in the case of the peptoneless medium is opposed to Martin's view. Even granting that an undetected amount of albumin was originally present, it cannot account for the quantity of albumose precipitated. It seems clear that the albumose must have been formed by the living bodies of the organisms. That it is formed by a chemical ferment from and outside the organism has not been proved by Martin. In order to do so it would be necessary to isolate the enzyme and show the direct conversion of proteid. As the enzyme is carried down by all precipitants of the albumose, their separation has never yet been effected (except of course by the action of heat, which destroys the enzyme at 70° to 80° C.). In the case of a disease like diphtheria, where albumose is found in a distant organ, presumably without the presence of bacilli, there is no reason why it may not be absorbed from the primary lesion.

It remains to be observed, however, that though (in the case of the pneumococcus) an albumose is formed by the organism, there is no adequate proof that this proteid is in itself a true toxin. The true toxin may in all probability be united to, or mixed up with, the proteid in some undiscovered fashion, as has indeed been supposed by several investigators, and this proteid may be an albumose, a globulin, an albumin, or a peptone.

VACCINATION AGAINST THE DIPLOCOCCUS: IMMUNITY: PRODUCTION OF AN ANTITOXIN.

Cultures in veal broth were continued for six generations. These were made several times to test the variability of virulence. Doses of one and two cubic centimetres were injected into the flank from these various cultures, but taking care that each growth was only two days old at the time of inoculation. From the weakest cultures no appreciable reaction was observed from these doses. Notwithstanding this, it was evident from the subsequent inoculation of virulent cultures, that they conferred some resistance. This was proved from the effect on control animals. It was then found that if a cubic centimetre from the second and third generations of a culture of a standard virulence was first injected, and after two or three days the same dose given of the first generation that the animals afterwards survived doses of sufficient virulence to cause death in control animals in thirty-six hours. The result of this virulent inoculation in the vaccinated animals was a marked reaction, the temperature

rising to 105° F. or even 106° F. But no further signs of illness were shown, and the animals partook of their food as usual. After the fourth or fifth day, the temperature generally fell quickly, and no further reaction was obtained with subsequent injections. The filtered broth cultures were also tried. Compared with most other diseases, the broth toxin of pneumonia is feeble. The clear filtrate was therefore evaporated *in vacuo* at 37° C. to small bulk. Only the toxin of the first broth culture was employed. Small doses of this concentrated toxin were injected in the same way into the flank, and gave a temperature reaction of one to two degrees. In this manner resistance to virulent cultures was conferred. Evaporation of the toxin is, however, a tedious process, and quite as good, if not better, results were obtained by injecting the alcoholic precipitate from the broth in the manner already described.

To obtain an efficient antitoxin, the animal must be perfectly immune, and the temperature must be got up to 105° or 106° F. This may be done by the final administration of virulent cultures, but much the best way is to employ larger doses of the concentrated toxin from a first cultivation or else the albumose.

As this part of the subject is merely touched upon in this communication, it may be added that the serum from two immune animals was made the subject of experiment. Injected in small doses ($\frac{1}{2}$ c.cm. to 1 c.cm.), complete protection was conferred from measured doses of moderate virulence injected at the same time, and life was much prolonged in the case of the most virulent doses.

I must express my indebtedness to Dr. Woodhead, Director of the Laboratories, for some valuable suggestions.

REFERENCE.

¹ Local Government Board Reports, 1889-90. I am also indebted to Dr. Martin for kindly supplying me with a quantity of dried serum alkali albumin.

THREE CASES OF INTESTINAL ANASTOMOSIS.*

By HARRISON CRIPPS, F.R.C.S.,
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CASE I. End-to-End Anastomosis of Ileum to Ileum.—The patient, a young woman, was under my care at St. Bartholomew's Hospital. Obstruction followed after an abdominal section for hysterectomy. A temporary enterotomy was performed by my colleague, Mr. Bruce Clarke. She recovered from this, but rapidly commenced to run downhill from malnutrition, for the obstruction was high up in the ileum, and all food only partly digested escaped from the enterotomy opening. All attempts to close this failed on account of the obstruction below. Ten weeks later I performed abdominal section. The strictured portion was found 7 inches below the enterotomy opening. The bowel was divided just below the obstructed portion, and again just above the site of the enterotomy opening, the intervening portion, about a foot in length, being removed and the ends united. I will not go further in the details of this case, for I mentioned them at the time in this Society. The patient recovered, and it may be of interest to know that from that time to this—nearly three years—she has been and remains in perfect health, without ache or discomfort, is thoroughly well nourished, and able to earn her own living.

CASE II. Double Anastomosis of Large and Small Intestine.—Mr. Y., aged 55, brought to me by Dr. Webber, had passed many years in India. He considered himself a healthy man up to eight months ago, when he commenced to suffer pain from time to time in the abdomen. The pain was of a paroxysmal character, and was referred to the pit of the stomach. It generally came on soon after taking food, but occasionally at other times. He has had two or three attacks of diarrhoea, but is more often constipated, and has never passed blood-stained mucus. He has not lost flesh, and has had no vomiting.

Examination.—Has a large, fat abdomen. On a line with the left nipple, about 4 inches below the ribs, a tumour can be felt the size of a large fist. It descends on inspiration, and admits of some mobility both from side to side, and from above downwards. It is possible to get the hand between the tumour, and what should be the position of the lower part of the stomach. The disease had been diagnosed as cancer of the stomach. Dr. Webber and I did not agree with this, and believed it to be the colon. The patient was extremely anxious that an operation should be done if there was the remotest possibility of giving him relief.

Operation.—In the presence of Dr. Webber, and assisted by my colleague Mr. Bruce Clarke, the abdomen was opened by an incision commencing 1 inch below the ensiform cartilage and extending to the umbilicus. On introducing the hand, and raising the omentum, the tumour was seen to be a mass of malignant disease in the transverse colon near the splenic flexure. Adherent to, and incorporated into it from an extension of the growth, was a coil of the ileum about 6 inches in length. The whole, together with adherent omentum, formed one mass the size of a cocoon. It was fairly movable, and could be drawn well up into the wound; the stomach was not implicated. The operation was continued by passing and clamping a piece of thin india-rubber tubing round the ileum on each side of the implicated loop, and about 3 inches free of it. The coi

* Read before the Medical Society of London, March 22nd, 1897.