fixing, to an abnormal degree, the length of the muscles of the limb at all the intermediate positions through which the moving part passes. In this way the effects of diminished voluntary power are enhanced in degree on account of excess of plastic tone, which is no longer adequately controlled by the cerebral cortex. In fact this defective control is not infrequently the greater disability, and on account of it the voluntary motor pathway may be unable to function to the full extent of which it is capable. This desideratum is attained by removing the plastic tone entirely, when the rigidity of the muscles disappears. The result is that the initiation and the execution of voluntary movement are both improved.

Dr. Royle found that one patient, with a gunshot wound of the cerebral cortex, who illustrated the presence of excess of plastic tone to a striking degree before the operation, was able to inhibit the tone of the extensor muscles of the knee following ramisection. He was unable to flex the knee voluntarily, but he could inhibit the tone of the muscles sufficiently to let the leg fall into the flexed position. This was impossible prior to the operation. In other words, this patient was unable to inhibit plastic tone. After ramisection he was able to inhibit the contractile component of tone which alone remained. This patient illustrates that the cerebral cortex normally inhibits both components of postural tone, and that injury may affect the control over the plastic component to a greater extent than that of the contractile element. This accounts for the marked improvement in control which follows sympathetic ramisection.

Consideration of these facts reveals the far-reaching influence in the interpretation of the functions of the cerebrum and cerebellum the further investigation of the central control of muscular tone is likely to exert.

[Hunter was in the midst of his experimental work when he received the invitation from the American College of Surgeons to deliver the Murphy Oration in New York. He and the team of collaborators who were inspired by his enthusiasm were preparing to investigate a host of problems—anatomical, physiological, pharmacological, and clinical—suggested by this work; and it was with the utmost reluctance that he left his laboratory last September. But he realized the value of a personal exposition of his results, and felt it his duty to accept the invitation from America. He fully realized how profound a revolution his work was destined to create in anatomy and physiology; and it is unspeakably tragic that he was not permitted to develop these investigations himself.

I refer to these matters to call attention to the fact that circumstances forced Hunter to make the two announcements of his results at times when he realized their incompleteness. One of these I have just mentioned—the call to New York just at the moment when he had got a clear vision of the host of fascinating problems, the solution of which seemed to be made feasible by his working hypotheses. The first announcement of his work on the sympathetic was made in 1923, during the visit of Sir William MacEwen to the British Medical Association in Australia. The work was then still in the early experimental stage; but as the results were being applied to surgery it became necessary to explain the purpose and the principles underlying it for the guidance of those surgeons who felt it their duty to make use of a procedure that seemed to afford a certain hope of alleviating the chief troubles of the spastic paralytic patient.

Hunter had become keenly interested in the problems of the influence of the sympathetic upon visceral functions (which have not been discussed in these lectures); and if he had lived he had intended to embark upon a far-reaching inquiry as to the similarities and differences between the non-striated, cardiac, and striated muscles, and to correlate the actions of the sympathetic system on all three kinds of muscle.

In preparing these lectures for publication I have made free use of the work of Dr. T. K. Potts, published in the *Journal of Anatomy* (January, 1925), and the reports of the Murphy Oration in *Surgery, Gynecology and Obstetrics* (December, 1924); and I have to express my thanks to the editors of these journals (Sir Arthur Keith

and Dr. Franklin H. Martin) for their generosity in allowing me to quote freely and copy illustrations. The drawings illustrating these lectures were made by Mr. T. Poulton, mostly from illustrations selected by Hunter himself. Dr. John Beattie and Miss Audrey Russell made special dissections for me to check some of the anatomical points in the relations of the sympathetic rami in man and the fowl. Professor Hunter is in no sense responsible for Figures 2 and 14, which I constructed to give pictorial expression to the implications suggested in his argument.—G. E. S.]

REFERENCES.

²² *Brain*, 1922. ²³ *Ibid.*, 1921, p. 307. ²⁴ *Lancet*, 1923, p. 644. ²⁵ *Brain*, 1924, p. 178. ²⁶ *Ibid.*, 1923, p. 189. ²⁷ *Journ. Physiol.*, 1905, p. 369.

THE EARLY DIAGNOSIS AND TREATMENT OF PYLORIC STENOSIS IN INFANTS.*

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A CLEAR understanding of the nature of pyloric stenosis in infants and the recognition of the importance of early diagnosis, and so treatment, are most essential. We are quite sure that if the condition could be recognized early many lives would be saved. It is more common than is usually thought. By pyloric stenosis we mean a great hypertrophy of the circular and longitudinal muscles which control the passage of food from the stomach to the duodenum. The muscle here becomes enormously thickened and hypertrophied, so as to block the pyloric canal. The consequence of the block is that the stomach wall also increases in thickness and size as it tries to force its contents through the constricted opening into the duodenum. The food, not being able to pass through the pylorus, is forced the opposite way up the oesophagus, and we get the forcible vomiting so characteristic of the disease.

DIAGNOSIS.

Sex.—In the great majority of cases the infant is a boy, but the cause of this is quite unknown. This fact, however, is a help in diagnosis. Eight or nine out of ten cases are boys.

Place in Family.—Many cases occur in the first-born; this looks as if the mother had not been able to produce a perfectly normal infant, but one different in some way. There is, by the way, a special liability of first-born children to abnormalities.

Age.—The condition is often called "congenital hypertrophic pyloric stenosis." This term is somewhat misleading and wrong, for the infants are, for a time anyhow after birth, perfectly well, and they show no symptoms till they are a few weeks old.

Symptoms do not appear till the infant is at least two weeks old, and the commonest time for the vomiting to start is from two to four weeks after birth. The vomiting seldom starts for the first time after the age of six weeks.

Vomiting.—This is perhaps the most characteristic sign, but only when the vomiting takes on the character peculiar to the disease. The vomiting is forcible, and the food is shot out of the mouth, even also down the nose, and finishes well away from the infant, as he lies in his cot. The infant does not vomit after each feed, but usually twice or three times a day, but when it does vomit more than one feed comes up at a time. The infant who vomits after each feed does not usually have pyloric stenosis. The vomit often has much mucus mixed with the food, showing that the stomach has become inflamed.

Constipation.—As the vomiting begins the infant becomes constipated to a marked degree. The bowels are only moved by enemata, and then only a little at a time. The reason being that little food gets through the pylorus. The intestines become atrophied from disuse, and this is a bugbear after operation, when the food gets through the pylorus

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into the intestines. The vomiting of ordinary digestive disturbances is associated with diarrhoea, not constipation.

Wasting becomes rapid simply from lack of food and fluid, which are not retained, and the child may easily lose 4 or 5 ounces a day. Another characteristic sign is that the baby is greedy for the feeds and takes them well. This is quite unlike the ordinary dyspeptic infant.

Peristalsis.—Waves of peristalsis may be seen passing across the abdomen, due to contractions of the stomach, and they are best noticed while the baby is having a feed. This peristalsis may be seen in other conditions, but it is specially well marked in pyloric stenosis.

Tumour.—The pyloric tumour is usually situated about an inch above the umbilicus, under the right rectus. Some observers state that they can feel the tumour in a high percentage of cases. Personally, we lay little stress on this, as it is often an exceedingly difficult matter to feel the pylorus. The infant is generally cross and holds the abdomen too rigid, and even under the anaesthetic the tumour frequently cannot be felt, as it may be placed deeply under the liver. The failure to feel the hypertrophied pylorus should not prevent a diagnosis of pyloric stenosis.

The reason that cases of pyloric stenosis are often not recognized, or recognized late, is that the food is thought not to agree, and that it is in consequence of this the infant vomits and wastes.

Two things may occur in infant feeding: the baby's food may be wrong and the baby right—this is the commonest thing to happen; or, as in pyloric stenosis, the food is right and the baby wrong. A baby with pyloric stenosis is weaned from the breast because he vomits; the food is thought to be wrong. The vomiting, however, persists, no matter what food is tried, and the breast milk is lost. A baby should never be weaned without a very definite and good cause.

TREATMENT.

The treatment of pyloric stenosis in infancy may be either medical or by operation. It is only within recent years that the real value of operative treatment has been recognized. Directly the condition is diagnosed we are quite convinced that surgical intervention alone will give the best results. In the past much valuable time has been lost by trying medical treatment. Medical treatment has undoubtedly been successful in a certain number of cases, but it is not improbable that some of the cures were really cases of pyloric spasm, and not hypertrophic stenosis. It is doubtful if cases of well marked hypertrophic stenosis are often cured except by operation. As already stated, the condition found is one of true hypertrophy of the pyloric ring, producing obstruction to the outlet from the stomach. Any treatment to relieve this must provide a free exit from the stomach, and experience has shown that this can only be satisfactorily obtained by operation. Further, the ideal operation is obviously one that restores the continuity of the alimentary canal through the pylorus.

Rammstedt's Operation.

The best procedure at the present time is that described by Rammstedt in 1912, and taken up in this country in 1918. This operation consists in transperitoneal incision of the hypertrophied pyloric ring, leaving the mucous membrane intact, thereby restoring the continuity of the alimentary canal. This method has now become widely adopted, and we ourselves are so convinced of its superiority that we carry it out in every case where surgical treatment is decided upon. To anyone familiar with the technique it is easy and quick to perform, and has such obvious advantages over other methods of treatment that it has received almost universal approval, whilst the fact that no suturing of the stomach or intestine is necessary makes it an extremely simple operation. Further, we have met with no cases of recurrence of symptoms necessitating a second operation, as has been recorded after other methods of treatment.

Once operation has been decided upon the pre-operative preparation of the patient is of considerable importance. If the child is in good condition we advise operation at the earliest possible opportunity, as nothing is to be gained by delay. In those cases, however, where symptoms have been

present for some time and the child is in a semi-starved condition a delay of perhaps twenty-four hours is justifiable to introduce fluids and thereby improve the chances of success. All cases are treated as urgencies once the diagnosis has been made. Prior to operation fluid in the form of saline and 2 per cent. glucose is introduced into the body by the rectum and subcutaneous injection, and the infant's weight can by this means be raised by as much as 6 ounces in the twenty-four hours. The stomach is washed out with saline to rid it of curds and other offensive contents; this also renders the stomach itself more healthy.

At the time of operation the child is warmly clad and laid on a hot-water bottle in a well heated theatre. All these details are of importance as they help to minimize shock in an infant which has often little reserve power to spare. With regard to the anaesthetic, we now as a general rule prefer warm ether. We have found this more satisfactory than local anaesthesia and gas and oxygen, owing to the poor relaxation so frequently obtained, which adds to the difficulties and time occupied in the operation.

The abdomen is opened by a $1\frac{1}{2}$ -inch incision above the umbilicus to the right of the mid-line. The dilated stomach usually presents and is gently delivered through the wound, the pylorus being thereby readily identified. The stomach is then held by an assistant, and this both draws down the pylorus and leaves the operator the free use of both hands. The pyloric ring, which appears as a hard white cylindrical swelling, is incised longitudinally along its upper border with a sharp scalpel. In this situation there are usually no vessels of any size and the bleeding will be practically negligible. The incision is carefully deepened with a blunt dissector till the mucous membrane beneath bulges freely into the gap. In this, the essential step of the operation, two dangers must be watched for: First, haemorrhage, and this can be avoided by making the incision as described, whilst any vessel that may be cut should be under-run and ligatured. Secondly, if the incision is prolonged too far into the thin-walled duodenum the mucous membrane may be wounded and result in leakage of the contents; this can be avoided by dividing the muscle with the blunt dissector rather than with the scalpel.

Having successfully completed this stage and seen that there are no bleeding points, the stomach is returned to the abdominal cavity and the wound closed, saline being introduced into the peritoneal cavity meanwhile. With ether anaesthesia little difficulty will be found in closing the small incision, and the whole operation should take less than ten minutes to perform.

To secure success in these cases, rapidity in operating and the least possible amount of handling of the viscera are of vital importance. Both of these conditions are attained in the Rammstedt operation, and shock is thereby reduced to the minimum. The child should be given salines immediately after the operation, and fluids by mouth are allowed as early as possible. Whenever possible the mother should be encouraged to suckle the baby; this we regard as one of the most important steps in the after-treatment. A doubtful case may be brought through successfully if the mother's milk is available for the child. If breast-feeding is not possible, peptonized milk is likely to suit the baby.

PROGNOSIS.

The prognosis depends largely on the duration of symptoms and the condition of the child when submitted to operation. In early cases there is usually a rapid improvement immediately following operation. If the patient has been ailing for some time and there has been a progressive loss of weight and it is in a semi-starved condition, the mortality is bound to be high. Recovery after operation is uncertain in babies weighing less than 7 lb. As, however, the disease is becoming more readily recognized—and the symptoms are so typical that mistakes should seldom be made—the prognosis will become increasingly more favourable. With earlier diagnosis and opportunity to operate before the child is wasted and collapsed, the death rate should be reduced to less than 10 per cent. This ideal will only be attained when cases are recognized sooner.

In considering the results of treatment, statistics collected from the Hospital for Sick Children, Great Ormond Street, London, show that, during the years 1915-17, 54 cases were

treated, the majority without operation, and the total mortality was 80.5 per cent. Prior to the introduction of the Rammstedt operation in 1918, the operative mortality at this hospital was 100 per cent., not one single case having recovered after operation. In the following year, when the Rammstedt operation was adopted, it fell to 41 per cent. after surgical treatment, whilst in 1923 for 55 collected cases the operative mortality was 29 per cent.

During the past twelve months we have operated on 16 cases, with 5 deaths. This gives a death rate of approximately 30 per cent. Death occurred in 2 cases within twenty-four hours of operation, and was due to post-operative collapse in weakly and debilitated infants. In 3 cases it occurred four, seven, and twelve days later, and appeared to be due to gastro-intestinal disturbances and inability of the infant to assimilate its nourishment.

In cases with a long history it is not unusual to find the intestines small and shrunken when examined *post mortem*, and it appears that death is due to their atrophy from disuse and their failure to recover their digestive function. The average age in these cases was 7 weeks, and the duration of symptoms twenty-one days. The condition most commonly appears in the third week of life.

Whilst fully realizing that the figures here cited are too small to allow deductions to be drawn, they serve none the less to illustrate the average results of surgical treatment of the disease at the present time.

CONCLUSION.

We would conclude by again urging that, once the condition has been recognized, surgical aid should be sought at the earliest possible moment, for in operation lies the quickest and most certain chance of success.

After surgical treatment the infant usually shows rapid improvement and within a few weeks is frequently able to be discharged as cured. Medical treatment, on the other hand, may require months of careful attention, and the ultimate result is often uncertain. If recovery takes place after operation it appears to be permanent; in fact, the majority of those who recovered after operation in infancy are in later life a good deal above the normal weight for age.

A NEW TUBERCULIN.*

BY

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ORGANIC analysis is not likely to yield any single substance capable of producing antibodies to the tubercle bacillus, and if it is carried too far it is not even likely to yield any mixture of substances capable of antibody formation. The most efficient antigen is likely to be a suspension of entire or of pulverized bacilli in normal saline. There are technical difficulties in the way of obtaining ideal products, and these difficulties are aggravated when the antigen is required for immunization experiments or for therapeutic use.

Besredka's antigen is prepared at a high temperature, and most tuberculins are made from bacilli killed by heat. The analytical processes employed to determine the composition of tubercle bacilli mostly involve the use of heat, to kill the organisms if for no other purpose. Heat is required for extracting the acid-fast material from the organisms. I know of no simple solvent that can extract this substance without the prolonged action of heat. A number of observers have noted that hydrochloric acid added to a simple fat solvent is able materially to assist the process of extraction.

If any chemical substance could be found to dissociate this acid-fast substance from its union with other constituents of the bacillus, at a comparatively low temperature and without loss of time, it would make the protein constituents of the bacillus more easily accessible to simplesolvents, and would yield them up in a state more nearly resembling the parent substance. Phosphorus trichloride seems to have

this action, but it also reacts with the protein constituents of the bacilli. Very definite considerations led to the use of this reagent for the purpose of preparing a tuberculous antigen directly from living organisms. It is not always possible to foretell exactly what will happen when a new reagent is tested. A number of reagents were previously tried, with more or less futile or even alarming results. The process adopted is offensive, and must be conducted with due precautions for safety. Phosphorus trichloride gives a colour reaction with all bacilli and with other organic substances containing protein. The colour is purplish-brown. Enough water must be present to act catalytically; too much will interfere with the reaction, and there will be no reaction with absolutely anhydrous materials. Under proper conditions violent effervescence takes place, and a voluminous evolution of irritating fumes occurs, which cause coughing and headache, which may last for several days.

Although the original mixture is liquid, the end of the reaction is indicated by its becoming a firm pasty mass, which can be liquefied by the addition of water. All the bacilli can be precipitated along with the phosphorized fats by the addition of acetone. This precipitate is the basis of the tuberculin about to be described. Its antigenic action is feeble, but is much enhanced by cholesterin.

Sound guinea-pigs bear relatively large doses of tuberculin, but tuberculous animals are readily killed in thirty-six to forty-eight hours by comparatively small doses. A healthy animal bore a large dose of this new preparation with impunity. A seriously diseased animal also bore the same dose, and even appeared to be better twelve hours afterwards. Twenty-four hours later a second dose, even larger than the first, was given, and borne equally well. Forty-eight hours after the first dose a third dose was given, and next day the animal was markedly better in health. Clearly this substance had not the lethal property of old tuberculin towards tuberculous animals. Its therapeutic action on the same animal was then tried. A weekly dose was thereafter administered until all the enlarged glands became impalpable, while the animal actually became the healthiest and heaviest in the establishment. When it was at last killed no trace of the diseased glands could be found, but there were a few scars of healed tubercles in the spleen, and an area of perisplenitis. An emulsion of the spleen injected into another guinea-pig produced no disease.

The various strains of human and bovine tubercle bacillus differ in virulence, so a culture of bovine bacilli of well established virulence was obtained from the National Collection of Type Cultures for the purpose of the next experiments, which were performed on rabbits.

The rabbit never survives an infection of bovine tuberculosis, no matter how contracted. If the bacilli be inoculated subcutaneously into one of the hind limbs an insignificant glandular enlargement soon arises. After the lapse of a period, depending upon the mass of the bacilli inoculated, general symptoms supervene. General miliary tuberculosis sets in and rapidly kills the animal. On *post-mortem* examination none of the lesions shows any evidence of circumscription. They tend everywhere to spread diffusely.

Five young rabbits were each inoculated intraperitoneally with 5,000 million virulent bovine tubercle bacilli. One was kept as a control without subsequent treatment. In six days its temperature had risen two degrees, and in eleven days four degrees. Its weight varied, reaching a maximum in eighteen days; it died in thirty days, weighing exactly the same as at the beginning.

The second rabbit was treated with the new tuberculin. It gained weight for twenty-one days. It was accidentally injured, and died on the twenty-second day.

The third rabbit became ill five days after inoculation. On the eleventh day its temperature was 105.3° F. Treatment was then commenced. It gained weight for thirty-one days, but the temperature remained high, and it died on the fortieth day.

The fourth rabbit became ill one day earlier than the others. Treatment was commenced on the tenth day, and it died on the thirty-fifth day.

The fifth rabbit became ill on the sixth day. Treatment was begun on the eleventh day, but in this case human, not bovine, tuberculin was used. All the other rabbits were treated with bovine tuberculin. This animal trebled its weight in fifty-five days. The local infection soon became sharply delimited from the surrounding healthy tissues and began to heal. The animal was killed at that stage on account of my holiday arrangements. *Post mortem* the lungs showed large, well defined tubercles in process of healing.

* A paper read before the Birmingham Branch of the British Medical Association, November 20th, 1924.