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CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS AN ANALYSIS OF 145 CASES TREATED BY OPERATION

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In this paper an analysis has been made of 145 cases of congenital hypertrophic stenosis of the pylorus which have been treated by operation at the Royal Edinburgh Hospital for Sick Children during the twelve-year period 1922 to 1933 inclusive. In every case a positive diagnosis of pyloric stenosis was confirmed at operation, and no doubtful cases have been included in the series. Those treated by medical measures only, such as repeated gastric lavage, are not considered, although in a large proportion of the series treatment had been carried out in the medical wards prior to operation, with a view to improving the general condition of the patient. It is not proposed to discuss in detail the symptomatology of congenital pyloric stenosis, but merely to analyse the results of treatment in this series of hospital cases.

Sex and Age Incidence

Out of the total of 145 cases 125 were males and twenty females, representing a preponderance of males over females of 6.25 to 1. The 1931 census figures for

GRAPH 1.—Showing age on admission and age at first symptom for the total cases.

the general population show that the proportion of male to female births in Scotland is 1.02 to 1. This striking preponderance of males, which is so universally recog-

nized, is of great interest, as it is difficult to understand why a congenital malformation such as pyloric stenosis should show such a marked affinity for the male sex.

Graph 1 shows two curves: that with the unbroken line represents the age distribution on admission to hospital for the total cases, and the broken line shows the age at the first symptom. If these two tracings be compared, the interval elapsing between the first manifestations of the disease and the time when the condition was actually diagnosed will be obtained. It will be noted that in a large proportion of cases there was an interval of four weeks between the first manifestations and the admission of the child to hospital; in other words, there was a delay in treatment for this long period in a considerable number of cases. The average age on admission was found to be approximately $6\frac{1}{2}$ weeks, and the average age at which the first symptom occurred was 3 weeks. These figures apply to the total series, males and females, since it is impracticable to attempt a separate analysis of male and female cases owing to the very small number of the latter.

Place in Family

The following table shows the place in family of the cases in this series. It will be noted that more than half were first children, and a further 28 per cent. were from second and third pregnancies. No evidence was forthcoming of the occurrence of more than one case in a family.

Place in Family	Cases	Percentage
1st	77	56.6
2nd	23	16.9
3rd	15	11.0
4th	6	4.4
5th	7	5.1
6th	3	2.2
7th	2	1.5
8th	1	0.7
9th	2	1.5
No record	9	

Although this table suggests that congenital pyloric stenosis is an abnormality which has a peculiar selective incidence for the first-born, it is necessary before drawing any such conclusion to have controls with which to compare these figures, since it must not be forgotten that in the general population there is a much higher proportion of first-born children than, for example, fifth- or sixth-born. It is possible, therefore, that the preponderance of first children in this series is merely apparent and not real. For the purpose of control, the place in family of 150 infants admitted to the hospital for various complaints, other than congenital pyloric stenosis, was ascer-

tained, and the age and sex incidence of this control group was approximately the same as for the pyloric stenosis cases. The following table shows the place in family of the 150 control cases.

Place in Family	Cases	Percentage
1st	31	20.6
2nd	36	24.0
3rd	17	11.3
4th	18	12.0
5th	17	11.3
6th	9	6.0
7th	6	4.0
8th	6	4.0
9th	2	1.3
10th	3	2.0
11th	2	1.3
12th	0	0.0
13th	2	1.3
14th	0	0.0
15th	1	0.6

As a further control 230 records of newborn infants, supplied to us by Dr. T. Y. Finlay of the child welfare department, were examined to ascertain the place in family of each infant. The results of this investigation were as follows:

Place in Family	Cases	Percentage
1st	45	19.6
2nd	66	28.7
3rd	31	13.5
4th	30	13.1
5th	13	5.7
6th	10	4.3
7th	17	7.4
8th	6	2.6
9th	4	1.7
10th	3	1.3
11th	0	0.0
12th	1	0.4
13th	1	0.4
14th	1	0.4
15th	1	0.4
16th	1	0.4

From these tables it will be seen that the percentage of first-born infants is comparatively low when compared with the pyloric stenosis series—approximately 20 per cent. as compared with 56 per cent. The distribution of the controls shows at least one unexpected feature, inasmuch as the number of first-born was actually less than the number of second-born. This raises some suspicion of a degree of selection. We may reasonably assume, however, that with our controls as given, the first-born in the family is actually much more likely to be affected with congenital pyloric stenosis than the younger brothers and sisters.

Birth Weight and Weight on Admission

Graph 2 shows the weight at birth and the weight on admission to hospital. It will be observed that the peak of the birth weight curve occurs at $8\frac{1}{2}$ lb.; this is of interest in that it demonstrates that the majority of infants born with stenosis of the pylorus are strong and healthy at birth, and tend to be above the average birth weight. The average weight of a newborn male infant is usually considered to be about $7\frac{1}{2}$ lb.; in this series

seventy-seven out of 121, or 63.6 per cent., of those regarding whom information as to birth weight was available weighed over 8 lb. The actual average weight at birth for the total series was $8\frac{1}{2}$ lb.

With regard to the weight on admission, the peak on this curve is at $6\frac{1}{2}$ lb., the average admission weight for the whole series being 6 lb. 6 oz. Thus it will be seen that the child usually comes to operation weighing nearly 2 lb. less than it did at birth. This loss of weight is all the more striking since it occurs at a time of life when the child should be rapidly gaining weight. Out of the total cases operated on only fourteen weighed more at the time of operation than they did at birth, and the average age of these children was unusually high—namely, 9 weeks.

First Symptom and Visible Gastric Peristalsis

The two outstanding symptoms associated with pyloric stenosis are projectile vomiting and constipation, and an analysis has been made of the frequency of the occurrence of each as the first indication of pyloric obstruction. In 129 out of the total of 145 cases, or 89.7 per cent., vomiting was the first and only symptom, the constipation not being noticed until a later date. In seven cases, or 4.8 per cent., constipation was the first symptom noticed, and in the remaining nine cases, representing 6.2 per cent., vomiting and constipation were reported to have begun simultaneously. As has already been mentioned, the average age at which the first symptom appeared was 3 weeks, the range varying from birth to the age of 9 weeks.

Visible gastric peristalsis was present in 141 cases, or 97.2 per cent. of the total. Furthermore, it is probable that in the four negative cases visible peristalsis was present, but had not been evident at the time of examination. A palpable tumour in the region of the pylorus was detected in only thirty-five cases, representing 24.1 per cent. In all these, visible peristalsis was also present. From this analysis, therefore, we must conclude that a palpable tumour in the pyloric region is a comparatively infrequent sign of congenital pyloric stenosis, and reliance should always be placed on the almost constant sign of visible gastric peristalsis in coming to a positive diagnosis. The frequency of these two signs in this series may be conveniently shown thus:

	Present	Absent
Gastric peristalsis	141 (97.2 per cent.)	4 (2.8 per cent.)
Pyloric tumour	35 (24.1 ")	110 (75.9 ")
Peristalsis + tumour	35 (24.1 ")	110 (75.9 ")

Operation

The following table shows the number of cases of congenital pyloric stenosis treated by operation and by non-operative procedures respectively during the last twelve years.

GRAPH 2.—Showing birth weight and admission weight of the total cases.

	1922-1928	1929-1933
Operated on	40	105
Not operated on	40	25
Total... ..	80	130

These figures demonstrate quite clearly the striking increase in popularity of operative treatment in this condition; during the years 1922 to 1928 only 50 per cent. of the admissions to hospital were subjected to operation, whereas in the later period, 1929 to 1933, 80 per cent. were operated on. Another interesting feature is the larger number of cases in the later group than in the earlier one. It will be seen that in the seven-year period 1922 to 1928 the total number of cases of pyloric stenosis admitted to hospital was only 80, as compared with a total of 130 in the shorter period 1929 to 1933. If the average yearly admissions be compared in the two groups it is found that approximately eleven cases were admitted each year between 1922 and 1928, and a yearly average of twenty-six between 1929 and 1933. Whether this increase in numbers in recent years is due to the fact that congenital pyloric stenosis is being more generally recognized, or whether the condition itself is actually occurring more frequently, it is impossible to say, but there does not appear to be any good reason to suppose that this congenital abnormality should be more frequent at the present time than it was ten years ago.

The operation performed was the simple procedure of dividing the pyloric musculature, as first advocated by Rammstedt. Rammstedt's operation has now been carried out almost as a routine measure in the hospital for a number of years, and has been found to be the simplest and most satisfactory. Whenever possible the operation is performed under local anaesthesia, and the child is given a feed while it is actually in progress.

In the present series local anaesthesia alone was employed in 111 cases, or 76.6 per cent. of the total. In seventeen cases, or 11.7 per cent., the operation was begun with local anaesthesia, but it was found necessary to supplement this with a little general anaesthesia during the handling of the stomach. In the remaining seventeen cases the operation was performed under a general anaesthetic.

Operation Mortality

In view of the almost universal adoption of operation as the most satisfactory treatment in the majority of cases of congenital pyloric stenosis some facts regarding the mortality must be given. By operation mortality we mean patients who died apparently as a direct result of operation or of some operative complication. In this series thirty-six patients died as a direct result of the operation, representing a mortality rate of 24.8 per cent. The number of days which elapsed after operation before death occurred is shown as follows:

Days	0	1	2	3	4	5	6	8	9	10	11	13	14	19	21	31	34	Total
Cases	2	4	5	1	2	1	5	2	4	2	2	1	1	1	1	1	1	36

From this it will be seen that more than half of the patients died within one week of operation, and three-fourths within ten days.

The following table shows the number of operations performed and the mortality rate for the various years. These figures suggest that there has been comparatively little reduction in the operation mortality rate during the

past ten years, although admittedly the number of cases included in the earlier group (1922 to 1928) is too small to enable accurate conclusions to be drawn regarding the success of operation.

Operation Mortality in Various Years

Years	Cases	Deaths	Mortality per cent.
1922-1928	40	11	27.5
1929	18	7	38.9
1930	22	7	31.8
1931	22	5	22.7
1932	28	3	10.7
1933	15	3	20.0
Totals ...	145	36	24.8

Cause of Death

The various causes of death were: collapse 24, or 66.6 per cent.; enteritis 9, or 25 per cent.; sepsis 2, or 5.6 per cent.; peritonitis 1, or 2.8 per cent. The "collapse" cases are of special interest in that no definite pathological abnormality could be discovered at necropsy. Most of the patients in this group appeared to survive the actual operation quite satisfactorily, but within a comparatively short time showed signs of extreme weakness and, in spite of the administration of a variety of stimulants, failed to survive. It is a true description to state that these infants simply "faded away" for no apparent reason.

In an endeavour to discover some reason for the alarming operation mortality the cases which failed to survive have been compared very closely with the others, in the hope that some feature might present itself which would give us a clue for assessing operation risk in this condition. Unfortunately we have not been able to arrive at any very definite conclusion as a result of this investigation. It was thought, possibly, that several factors might be concerned in operative risk, and it will be of interest to consider each of these separately. First of all it occurred to us that the weight of the infant at the time of operation might have some bearing on the success of the treatment—the larger and less starved the infant the better the prognosis. This, however, was found not to be the case, since the average weight at operation of those patients who failed to survive was found to be 6 lb. 4 oz., as compared with 6 lb. 10 oz. for those who survived. This slight variation cannot be regarded as significant when dealing with a comparatively small series. If we compare the birth weights and the operation weights of the survivals and non-survivals, it is found that the loss of weight has been practically the same in both groups. In the fatal cases the average loss of weight since birth was 1 lb. 13 oz., as compared with an average loss of 1 lb. 15 oz. in the survivals. These figures suggest that neither the actual weight at operation nor the rate of loss in weight since birth has any appreciable influence on the operation mortality. It must be realized, however, that when dealing with a small series such as this it is probably unwise to draw any definite conclusions from such figures.

The age at operation and the age at which the first symptom was noticed in those patients who died does not show any significant difference from the survivals, the average ages at operation being 6½ weeks and 6 weeks respectively, and the average age when the first symptom appeared being 3 weeks for both those who died and those who survived. These points of comparison between the deaths and the survivals are shown in the following table.

	Average Weight		Average Age	
	At Birth	At Operat'on	At First Symptom	At Operation
Survivals	8 lb. 9 oz.	6 lb. 10 oz.	3 weeks	6 weeks
Deaths ...	8 lb. 1 oz.	6 lb. 4 oz.	3 ..	6½ ..

As in the case of the survivals, local anaesthesia was employed for the majority of the patients who died. Of the thirty-six operation deaths, local anaesthesia alone was used in twenty-six, general anaesthesia in six, and in the remaining four both local and general anaesthesia were required. Thus it will be seen that the type of anaesthetic cannot be blamed for the operation mortality.

From this comparison of the deaths with the survivals it must be concluded that no significant fact has arisen which enables us to predict the chances of survival in any particular case.

In addition to the thirty-six patients who died as a direct result of operation, four others died within a comparatively short time of operation from other causes. One developed diphtheria with fatal consequences six weeks after operation, and a second developed septicaemia as a result of abscesses in both axillae, which had been caused apparently by the administration of subcutaneous glucose saline. The remaining two patients were discharged from hospital in good condition, but were readmitted some weeks later with severe enteritis, from which they ultimately died. These four cases have not been included under the heading of operation mortality, since it seemed probable that the operation had little or nothing to do with death in each case.

Operative Complications

Some operative complication arose in twenty-nine cases, or 20 per cent. Post-operative enteritis accounted for nearly two-thirds of the total complications, and as a result death occurred in nine cases. The frequency of the various complications was: enteritis, seventeen; severe vomiting, six; sepsis, three; bronchitis, two; acute parotitis, one.

The six cases under the heading of severe vomiting are mentioned on account of the severity of the symptom, since in each it was found necessary to substitute parenteral feeding for several days following operation, the patients being unable to retain anything in the stomach. One of these died. A number of patients suffered from occasional slight vomiting after operation, but these are not included under operative complications.

Length of Stay in Hospital

The length of stay in hospital of the patients in this series is shown in the following table.

Weeks ..	0-1	1-2	2-3	3-4	4-5	5-6	6-7	Over 7	Total
Cases ...	6	31	17	16	9	9	7	12	106

In this table only those patients who survived operation are included, as the length of stay in hospital of those who died has already been discussed. It will be noted that fifty-three patients were discharged within three weeks of admission; this represents 50 per cent. of the total. The patients who remained a longer time were those who had received preliminary treatment in the medical wards prior to operation, or who developed post-operative complications necessitating detention in hospital for long periods. The six patients who remained for less than one week are of interest in that they were treated as out-

patients, and after remaining under observation for a few hours following operation were allowed to go home, with instructions to report progress from time to time. The result in these cases was highly satisfactory. When the lengthy stay in hospital required for the medical or non-operative treatment of congenital pyloric stenosis is considered it must be admitted that on this score, at any rate, the operative treatment of the condition has a very definite advantage over the medical.

Comparison of Early with Later Group

An attempt has been made to determine whether congenital pyloric stenosis is being diagnosed more readily to-day than it was a number of years ago. For this purpose we have divided the cases in this series into two groups. Group 1: cases which were operated on during the period 1922 to 1929, fifty-eight cases. Group 2: cases treated during the period 1930 to 1933 inclusive, eighty-seven. In each group the average age at first symptom and on admission to hospital has been estimated, in order to note the length of time which elapsed between the first manifestations of the disease and the date when the patients were actually referred to hospital for treatment. The figures are shown in the following table.

		Group 1	Group 2
Average age {	First symptom ...	2.7 weeks	3.0 weeks
	Admission	6.4 ..	6.9 ..
Difference		3.7 ..	3.9 weeks

This table reveals that there is no significant difference between the early and later groups of cases; we must conclude, therefore, that the possibility of the presence of congenital pyloric stenosis in a vomiting baby is not being considered any more to-day than it was five to ten years ago.

Commentary

The most striking and disquieting feature which is revealed by this investigation is the high operative mortality rate, as it will be seen that approximately one patient out of every four operated upon for this condition may be expected to die as a result of the operation. As has been shown there is no unusual feature characterizing those infants who fail to survive operation. Furthermore, the majority who died did not suffer from any recognized post-operative complication, nor was any satisfactory explanation of death discovered post mortem. We must conclude, therefore, that nearly 25 per cent. of infants who come to operation for congenital pyloric stenosis are in such a weak state that they are unable to survive even the comparatively minor operative procedure which is adopted. In this series the operation was carried out with a minimum of disturbance to the infants. Local anaesthesia was employed in a high proportion of cases, and the majority of infants during the operation did not show any signs of distress, so that it may be fairly claimed that post-operative shock was reduced to a minimum.

It would seem, therefore, that if good results are to be obtained in the treatment of congenital pyloric stenosis, and if the operation mortality is to be reduced to a reasonable figure, it is essential that the condition should be diagnosed and treated at a much earlier date than it is at present. In so many cases we find that for a period of three to four weeks after the commencement of symptoms these infants are considered to be suffering merely from dyspepsia, and the feeding is changed every few days in the vain hope that the vomiting will cease.

Eventually, when the child is more or less *in extremis*, it is sent to hospital in a state of health which makes any form of treatment a dangerous procedure.

We would suggest that pyloric stenosis in infancy should be regarded far more than it is at present as an abdominal emergency, and it should be realized that the longer the delay in sending the child for treatment the less are its chances of survival. Admittedly, vomiting in infancy is a frequent occurrence, and is due, in the majority of cases, merely to some feeding defect or mismanagement; nevertheless, we believe that until congenital pyloric stenosis is considered as a possibility in every case of forceful vomiting in infancy the mortality from every form of treatment must remain at a high level. It is probable that if the condition were diagnosed within one week of the commencement of symptoms and sent for operation without delay, as in other cases of abdominal emergency, the operation mortality would be greatly reduced.

Summary

An analysis has been carried out of 145 cases of congenital hypertrophic stenosis of the pylorus treated by operation. The proportion of males to females in this series was 6.25 to 1. More than half of the patients were first children, and it is revealed that the last child in a large family very rarely suffers from this condition. This analysis shows that the birth weights of the infants concerned were somewhat higher than the normal average for males. The average weight at birth for all the cases in this series was $8\frac{1}{2}$ lb.

The first symptom noticed in the majority of cases was vomiting, and the average age at which it occurred was three weeks. Visible gastric peristalsis was an almost constant sign, whereas a palpable tumour in the pyloric region was noted in only 24 per cent. before operation. The operation mortality was 24.8 per cent., and there is no indication of any marked fall in mortality during the last ten years. The patients who failed to survive did not appear to differ significantly at the time of operation from the survivors, and in a high proportion of deaths no adequate cause could be discovered at necropsy.

The time that elapses between the first manifestation of obstruction and the admission of the patient to hospital for treatment is between three and four weeks, and there is no evidence to show that pyloric stenosis in infancy is being recognized any earlier to-day than it was ten years ago.

We wish to record our thanks to the physicians and surgeons of the Royal Edinburgh Hospital for Sick Children, who have kindly placed their case records at our disposal. We also gratefully acknowledge the help of Colonel Harvey and Dr. Kermack of the Royal College of Physicians Laboratory for advice and criticism in the preparation of this paper.

Commemoration Day at Livingstone College, Leyton, was held on June 14th, when General E. J. Higgins of the Salvation Army presided over a large gathering and congratulated the principal, Dr. Tom Jays, and the college generally on the success of their work in providing training in medical subjects for missionaries. "I did not come here," he said in conclusion, "to appeal for funds, but the burdens of finance are pressing. We cannot all go to the mission field, we cannot all come to Livingstone College (most of us are too old), but there are lots of other things we can do, and I feel we could free the college from the burdens that are upon it through lack of money." The Rev. G. Harp of the Moravian Mission, Labrador, said that the year's training he received at Livingstone College had been very useful indeed, and he was most thankful for the help he had received. Dr. Jays said that this year they had had thirty-two students, seventeen of whom were at the college for the whole session. They depended very largely on students' fees to pay their way, and last year there was a deficit of £650.

AN IMPROVED METHOD FOR THE DETERMINATION OF BILIRUBIN IN BLOOD

BY

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Considerable inaccuracies are inherent in the test for bilirubin in the blood serum as an azo-derivative. We have always preferred, therefore, to call it a quantitative estimate¹ rather than a quantitative determination. The method, however, which owes its widespread use largely to McNee's investigations, continues to be employed chiefly because no better test has yet been found. One of the errors of the method is due to the adsorption of a varying quantity of pigment to the albuminous precipitate during the performance of the test. This objection has been partly circumvented by Thannhauser's modification.² A second error, which must not be neglected, appears in the colorimetric comparison of the azo-bilirubin solution with a standard solution. Our attention was especially devoted to this second error when we critically reconsidered the method. To use as a standard a solution of artificial bilirubin which has to be freshly made for every test is almost impracticable for several reasons. The cobalt sulphate solution we recommended differs considerably in colour-tone from the azo-bilirubin solution, and this makes an exact colorimetric comparison very difficult.* The ethereal solution of rhodanate of iron formerly suggested matches the azo-bilirubin slightly better in colour. The great and rapid change in concentration of an ethereal solution, however, is a serious drawback. A solution of potassium permanganate has been advocated, and this really gives colours which are better matched, but it provides no complete similarity. A permanganate solution, moreover, has the drawback of soon losing its concentration when the solution is weak, and this renders it necessary to make a fresh solution of the desired strength fairly often, thus diminishing the practicability of the method as a routine test. In order to circumvent these difficulties we resorted to carrying out the test in monochromatic light, avoiding in this way the difference in colour between the fluid for comparison and the fluid to be examined—a very disturbing difference in "white" light. This procedure really changes the colorimetry, which is the comparison of the intensity of two colours, into a photometry in monochromatic light, which is a comparison of two strengths of a qualitatively similar light.

Instrumental Modifications

Several more or less costly instruments constructed according to this principle have been recommended. We have used, with good results, one of the ordinary colorimeters common in many laboratories, and have covered the eye-piece with a light-filter. We chose Klett's colorimeter, the new model, in which the source of light is in the foot of the instrument. Schott's green light-filter (S. 53), which only transmits rays of 520 to 546 $\mu\mu$, was placed on the eye-piece. At first we employed the cobalt sulphate solution, originally described as our standard

* The concentration of the cobalt sulphate solution appears to be 2.16 per cent., and not 2 per cent., as we indicated in our publication *Der Gallenfarbstoff im Blute* (McNee, *British Medical Journal*, 1925, ii, 52). This difference from our former quotation is probably due to a mathematical error on page 17 of the above-mentioned publication, where the azo-bilirubin concentration is mentioned as being 1 in 250,000, and not 1 in 200,000 (cf. Rabinowitch, J. M., *Journ. Biol. Chem.*, 1932, xcvi, 163).