EUMYDRIN IN THE TREATMENT OF HYPERTROPHIC PYLORIC STENOSIS

AN ANALYSIS OF 40 CONSECUTIVE CASES

BY

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In the last few years the author has treated forty consecutive cases of hypertrophic pyloric stenosis with eumydrin (atropine methyl nitrate), which was brought to the notice of paediatricians in this country by Svensgaard in 1935. The analysis of this series has brought out certain points, which, had the writer realized them in time, would have improved the results. These factors are here discussed.

Clinical material

In order to review the results it is necessary to describe the clinical material. Every baby included was an undoubted case of hypertrophic pyloric stenosis. Diagnosis was based on the following points: (a) a history of large projectile vomits, associated with constipation: (b) visible gastric peristalsis: (c) in every case a palpable pyloric tumour, which varied in consistency under the examiner's hand: sometimes repeated examinations were necessary to elucidate this: (d) in thirty-four cases in which x-ray examination was carried out, delay in emptying the stomach. The delay, as usual, varied much in degree. In the majority it was marked, but in some clinically typical cases it was slight.

There were forty patients, nine girls and thirty-one boys, all treated at the Queen's Hospital for Children including two cases shown at the Royal Society of Medicine (Mackay, 1936). In half the cases, according to the mothers' history, projectile vomiting began under twenty-six days old, and the average age at onset was twenty-seven days (youngest seven days, oldest sixty-eight days). The onset of symptoms was usually sudden. In some babies small vomits occurred before the onset of projectile vomiting (probably independently of any pyloric obstruction), but these vomits have been ignored in calculating the averages. Probably those authors who state that vomiting is not uncommon in the first week have not made this distinction. The average duration of projectile vomiting before treatment was started was fifteen days (extremes three days and forty-two days, with one exception, in which it was said to be seventy-one days). In half the cases the vomiting had lasted less than fourteen days. At the beginning of eumydrin treatment the average age was forty-three days (half were under thirty-seven days, the youngest was seventeen days, the oldest eighty-six days). It is interesting to compare the age of these babies with the ages of 403 cases of pyloric stenosis admitted to the Hospital for Sick Children,

Great Ormond Street, between 1924 and 1930 (Paterson, 1931). The average age on admission to Great Ormond Street was forty-six days, so that this series does not suggest that diagnosis in London is now made at a much earlier age than ten or fifteen years ago. Paterson found that private patients, too, were diagnosed about the same age as his hospital cases.

The average weight at the beginning of treatment was 7 lb. 5½ oz. Only fifteen babies (37·5 per cent.) were over birth weight at the start of treatment; of the rest, three were under 6 lb. in weight. By Holt's standard (1926) the whole series averaged about 2¼ lb. under normal weight for their age.

As it chanced, fourteen out of forty babies, or 35 per cent., probably a higher proportion than usual, were suffering from some complication or were extremely feeble on admission. These complications included haematemesis, abdominal distension, collapse of lung with infection of that organ, pyrexia, boils, collapse of the baby, with irregular, somewhat gasping, breathing (symptoms usually attributed to alkalosis), prematurity and cyanotic attacks, and convulsions. All these complications were present before treatment.

The type of home from which the babies came may be judged from the fact that the hospital is in a poor district in the East End of London, and a large proportion of the fathers are unskilled or semi-skilled manual workers with small and often irregular wages, a material factor when considering the treatment of patients in their own homes.

Treatment adopted and its variations

All but two patients were admitted to hospital. An x-ray examination was made, usually on the day after admission, and generally eumydrin was not started until this was complete. Until latterly there was no fixed procedure as regards saline administration or gastric lavage, some babies receiving much saline and daily gastric lavage, some receiving neither. Feeds were given three-hourly, generally six feeds in twenty-four hours. Eleven babies, or 27·5 per cent., were fed on breast milk for all or a portion of the time of treatment. Failing breast milk, sweetened condensed milk was generally used, in a dilution (1 in 5 by volume) to provide 20 calories to each fluid ounce of feed; the feed being changed to dried milk when the baby was well on the way to recovery. The baby was given in the first few days rather less than his theoretical needs, but the aim thereafter was quickly to increase to an amount on which he could gain. A daily record was kept in the wards of food and fluid intake, but unfortunately some of these records were not preserved. The eumydrin solution (1 in 10,000 in water) was made up once a week, on account of its instability, and was given by mouth, usually half an hour, sometimes twenty minutes, before each feed. The first dose was usually 0·5–1·0 c.c. (0·05–0·1 mgm. per dose), increasing by 0·5 c.c. at each feed till a dose of 2·0–3·0 c.c., six times daily, was reached, i.e. 1·2–1·8 mgm. in twenty-four hours. Further increases were made if the vomiting was not checked. Only one baby was given eumydrin by lingual application of drops of 0·6 per cent. eumydrin in alcohol, as described by Wallgren (1940); this baby had one drop twice daily, or about 0·2 mgm. of eumydrin in twenty-four hours.

Results

(a) MORTALITY. Of the forty cases, five died during treatment; a sixth died of enteritis and pneumonia developed at home, i.e. four and a half weeks

after vomiting had completely ceased, and over seven weeks after the beginning of treatment. If this case is reckoned as cured of pyloric stenosis, then, on the basis of five deaths, the mortality was 12.5 per cent.: thirty-one cases, or 77.5 per cent., were cured by eumydrin, and four, or 10.0 per cent. more, were cured by operation after eumydrin had been tried for four to thirteen days. Of the five cases that died, four apparently responded to eumydrin, but developed an intercurrent condition: the fifth showed little response, was operated on on the thirteenth day, and, after operation, developed an enteritis of which he died. These cases are dealt with in greater detail later.

(b) VOMITING. Among the forty cases treated, the vomiting was stopped or markedly diminished by eumydrin in thirty-five or 87.5 per cent., though not all survived. These thirty-five showed a marked reduction in vomiting in an average period of 2.9 days: seven immediately, thirteen more within twenty-four hours, five more within two days, so that half the cases treated (twenty in all) had their vomiting much diminished in one day, and nearly two-thirds within two days. The longest period was seventeen days in a baby (J. van G., see page 4) acutely ill with a collapsed lung, and in this case much of the vomiting was presumably due to cough.

It is difficult to state the number of days within which vomiting due to pyloric stenosis completely ceased, for, when a careful record of all vomiting is asked for, the regurgitation of a drachm or two which would usually pass without comment is likely to be recorded as a vomit. In the thirty-one babies cured by eumydrin all vomits, big or small, were said to have ceased in an average period of twenty-five days. Of more value is the observation that, excepting for 'very small vomits,' or perhaps one or two large vomits in seven days, vomiting was stopped in an average period of ten days. For Svensgaard's (1935) cases, the comparable figure appears to be twenty-one days. In ten cases of the present series vomiting practically ceased within three days.

(c) GAIN IN WEIGHT. The thirty-one cases cured by eumydrin gained in the first week an average of 6.8 oz., and for five weeks an average of 6.9 oz. weekly. Of the whole series of forty, twenty-three gained 5 oz. and upwards in the first week, seven gained under 5 oz., nine lost weight, and one premature baby (J. W., page 14) had its true weight masked by oedema following excessive cooling of the body. The gain in weight of the babies responding rapidly to eumydrin was very good, for example, in the first week fourteen babies gained between 8 and 17 oz., and for a five-week period from starting eumydrin twelve babies averaged a gain of between 8 and 12 oz. weekly. It is interesting to compare these results with Svensgaard's. Her cases showed a loss of weight in the first week, and gained an average of 4.3 oz. weekly during an average stay of eleven weeks in hospital.

In considering the progress of a child great importance was given to the weight and general condition as well as to the vomiting, for a baby might improve considerably although continuing to vomit much. For example, two babies gained $5\frac{3}{4}$ and $5\frac{1}{2}$ oz. in the first week, though there was little obvious reduction in vomiting for six and ten days respectively, and both gained an average of over $6\frac{3}{4}$ oz. weekly for the five weeks after starting eumydrin. Excessive saline administration sometimes rendered the weights erratic and obscured one valuable check on progress.

(d) COMPLICATIONS OTHER THAN TOXIC EFFECTS. Complications already existing before treatment was begun have been mentioned. After admission seven babies developed diarrhoea in hospital (including one terminal diarrhoea), and of these four died (page 13). Four developed bronchitis, one otitis media (G. N., page 4), one a nasal discharge, and one (admitted with a collapsed lung) pneumonic changes in the collapsed lung immediately after admission (J. van G., page 4). All these made good recoveries. Two

babies (P. G., page 5, and B. L., page 5) had minor skin infections (boils and a papular eruption) on admission, and one (J. W., page 14) developed a small abscess in hospital. Two (G. N., page 4, and E. W., page 4) had haematemeses before eumydrin was given: two more (A. H., page 9, and E. C., page 14) developed it in hospital: one of the latter died (E. C., page 14). Two developed oedema, one (J. W., page 14) as a result of chilling, and the other (E. C., page 14) presumably from excessive fluid administration.

Progress of babies with a complicating condition on admission

Of the fourteen babies suffering from some complication before eumydrin was started, nine were cured by eumydrin, one by operation, and four died.

J. van G., male, aged twenty-four days, weight 6 lb. 15 oz., was admitted with the right lung collapsed, probably from aspirated vomitus. This baby was very ill in the early stages of treatment with infection of the lung, pyrexia, rapid breathing and cyanosis, and almost certainly would not have survived operation. His maximum dose of eumydrin solution was 5 c.c. six times daily (3.0 mgm. in twenty-four hours) and his food was chiefly sweetened condensed milk (1 in 5 by volume). His fluid intake was fairly liberal. Vomiting nearly ceased in thirty-two days, but not entirely for 106 days (fifteen weeks), and it was probably precipitated by cough for most of that time. In the ninth week of treatment the stomach was washed out and there was no residue. He was in hospital for eighty days on account of his lung condition, and ultimately made a good recovery. He gained an average of 5.6 oz. weekly for the first five weeks of treatment.

D. H., male, aged thirty-nine days, weight 7 lb., was admitted collapsed, wasted and approximately 3 lb. below birth weight. He had irregular and somewhat gasping respiration during the first twenty-four hours, i.e. symptoms presumably due to alkalosis. His maximum dose of eumydrin was 5 c.c. before each feed, and his food was sweetened condensed milk (1 in 5), with little fluid over and above that given in his feeds, except on the first day, when he had 10 c.c. of saline given subcutaneously. He improved fairly rapidly under eumydrin treatment. It is unlikely that surgical treatment could have saved his life. His average gain for five weeks was 5.5 oz. weekly, and the gain would have been larger had he not been underfed after discharge from the ward on the seventeenth day of treatment.

G. N., male, aged seventy days, weight 7 lb. 2½ oz., had had an unsuccessful Rammstedt operation at forty-six days old, which had failed to relieve the pyloric obstruction. He was having daily salines and gastric lavage and was steadily losing weight (about 1½ lb. since operation). He was suffering from pyrexia, haematemeses and poor appetite when started on eumydrin. His maximum dose of eumydrin was 2.5 c.c. six times daily, and his food was breast milk. He was given daily gastric lavage, and subcutaneous salines for the first twelve and nine days of drug treatment respectively. Vomiting was markedly reduced within twenty-four hours and he gained an average of 9 oz. weekly for the five weeks after starting eumydrin, in spite of developing otitis media.

K. S., A. T. and E. M. all had some abdominal distension or fulness before starting eumydrin: the first two did well, the third died (E. M., page 13).

E. W., female, aged thirty days, weight 7 lb. ¾ oz., had haematemeses on admission. Subcutaneous saline (about 5 oz.), was given daily for the first six days, and vomiting was not markedly reduced for six days, i.e. until the time when the fluid intake fell. Her maximum dose of eumydrin was 3.5 c.c. six

times daily, and her food was sweetened condensed milk. She gained an average of $8\frac{1}{4}$ oz. weekly for the first five weeks on eumydrin.

E. F., J. D. and E. C. had some pyrexia, without obvious cause, before the start of treatment. The last two died (J. D., page 13, and E. C., page 14).

J. W., a premature baby with a cyanotic attack with cessation of breathing before admission, died (page 14).

B. M., male, aged twenty-nine days, weight 6 lb. 6 oz., was wasted, feeble and sucked badly. He was given excessive subcutaneous saline (5 to 11 oz. daily), and his maximum dose of eumydrin was 5 c.c. six times daily. His vomiting was not much reduced until ten days after the start of eumydrin, and did not cease entirely until two months after the start of treatment. His haemoglobin was 46 per cent. (Haldane standard). In the fifth week of treatment he was given gastric lavage; the stomach was then emptying normally, and the lavage did not diminish the vomiting, but his appetite improved, perhaps as a result of the lavage, with a concurrent improvement in rate of gain in weight.

P. G. was suffering from boils. Eumydrin failed to cure him, and he was cured by operation (see page 8).

B. L. had a papular rash and blepharitis. She gained an average of $5\frac{1}{2}$ oz. weekly on eumydrin.

Factors influencing the results of treatment

It is notorious that in cases of pyloric stenosis treated in hospital, the biggest cause of mortality is often infection acquired in hospital. To this the present series is no exception. Of the five babies who died, four had diarrhoea. But setting aside this subject, let us consider what factors can be shown to influence the response to eumydrin in the individual baby, as this should be of material help in deciding the line of treatment for each patient.

(a) SEX. With the small numbers available in this series it is not possible to say whether or not with eumydrin treatment there is any difference in prognosis for the two sexes. All five cases which showed no response to eumydrin were boys, but as boys made up nearly 80 per cent. of the total number no significance can be attached to this fact, especially since, if rate of gain in weight is considered, it is found boys gained slightly more rapidly than girls—the average gain in the first week was 7.2 oz. for the boys and 5.8 oz. for the girls. So far as this goes, it bears out Svensgaard's (1935) view that sex plays no part in the prognosis.

(b) AGE AND SEVERITY OF ONSET, AND AGE OF TREATMENT. Langstein in 1921 stated that if the symptoms of pyloric stenosis were fully established in the third week of life the prognosis for medical treatment was bad. On the other hand, Faxén (1933), after analysing 126 consecutive cases, all medically treated, failed to confirm this; he said that onset under twenty-one days old was not in his series associated with a longer total period of illness, nor, on the other hand, did early medical treatment appear to shorten the illness. These views were expressed before the days of eumydrin treatment. With eumydrin, Dobbs (1939) has emphasized that babies coming under treatment when very young respond less readily, thus supporting Langstein's view. This seems to be borne out in the present series, though, provided other conditions are favourable,

young babies may respond well. The two youngest babies both failed to respond and both were operated on (E. J., page 9, and B. D., page 9), the one was seventeen days old with three days history of vomiting, the other eighteen days with seven days history. Unfortunately both these babies had a high fluid intake which, as is shown below, was probably a contributory factor. The next in age was a twenty-two-day-old girl with a relatively small fluid intake, who did well. This certainly suggests that, with a much smaller fluid intake, the eumydrin might have had more effect in the first two. Of the five cases operated on because they failed to respond, four (P. G., B. D., A. H. and E. J., pages 8 and 9) were young babies, five weeks old or less, with the age of onset between eleven and twenty-two days old (the average age of onset for the whole series being twenty-seven days). On the other hand, the fifth case operated on after failure to respond to eumydrin (J. D., pages 9 and 13) was the oldest in the series, eighty-six days old at the beginning of treatment. In passing it is of interest that the youngest in the series, E. J. (page 9), who began to vomit at eleven days old, had two siblings, both of whom had been operated on for pyloric stenosis; a family history is considered by Langstein (1921) also of bad prognostic significance.

It is difficult to say whether or not rapidity and severity of onset influenced the results of drug treatment in this series. One is largely dependent on the mother's description for estimating the acuteness of onset, and both because of the uncertainties of history and on account of the other factors influencing progress, no final conclusion is possible. It is said that acute cases tend to come under treatment at an earlier stage in the disease because they are more readily diagnosed than more chronic cases. In this series there were twenty cases with a history of twelve days or less, and of these three failed to respond to eumydrin, and of the remaining seventeen all had the vomiting diminished by the drug, though four ultimately died. There were twenty cases with a history of fourteen to seventy-one days; of these two failed to respond and eighteen were cured by eumydrin. So that these figures afford little evidence for or against the view that severity of spasm, as indicated by rapid onset of typical symptoms, makes the prognosis less favourable. Except perhaps in the youngest babies it seems unlikely, however, that the severity of spasm or vomiting was a major factor in determining the outcome. The following two cases show at least that an acute onset need not mean a less favourable response, or vice versa:

A. A., aged seven weeks, with eight days history of vomiting, had lost 1 lb. in weight in four days, and had 'vomited every feed for five days,' but gained at the rate of nearly 8 oz. weekly, the vomiting being checked by only 2.0 c.c. of eumydrin solution six times daily.

On the other hand, J. D. (page 13), aged twelve weeks, a relatively chronic case, with over a month's history of vomiting, and said to have had only three large vomits in seven days before admission, failed to respond to 2.5 c.c. of eumydrin solution and was operated on.

The degree of delay in emptying the stomach, as shown by x-ray examination before treatment, did not appear to bear any relation to the subsequent course of the case: this is in agreement with the views of other authors.

(c) FLUID INTAKE. Food was given in a concentration to provide 20 calories to 1 fluid oz., as in breast milk. The fluid intake and the food intake per pound body-weight have been calculated for each day of the first week of treatment, and once a week thereafter, for all those babies for whom the data were available. For the first week full data were available for twenty-eight babies. The average food intake per day per pound of body-weight varied between 1.8 oz. (for two babies with poor appetites) and 2.9 oz. (for two babies of low birth weight); the average total fluid intake per day per pound varied between 2.4 and 4.9 oz. In this analysis the babies have been grouped in two series, according to the amount of fluid intake in excess of the intake with food in the first week: (1) those getting 1.5 to 2.2 oz. of fluid per pound body-weight daily, over and above the amount given in the feeds, (2) those getting 1.3 oz. or less of fluid per pound body-weight besides that given in the feeds. Thus if a baby received daily per pound body-weight 2.5 oz. of breast milk and 3.0 oz. of fluid in all, his extra fluid was 0.5 oz. and he would go into the second group.

(1) In the first group, getting the large quantities of fluid (an average of 1.8 oz. per pound body-weight daily of extra fluid), there were twelve babies. Four babies (P. G., J. D., E. J. and A. H., pages 8 and 9) were operated on because eumydrin failed to relieve the obstruction; the other eight responded, in that their vomiting was markedly reduced in an average period of $5\frac{1}{4}$ days. There were four deaths in the group (J. D., E. M., E. C. and J. W., pages 13 and 14), and only five of these twelve cases were cured by eumydrin. Only two of the twelve are recorded as having good appetites, and seven had poor or very poor appetites. In the first week of treatment there was an average loss in weight of 1.9 oz.

(2) Contrast with this the second group of sixteen babies getting much less fluid (an average of 0.6 oz. per pound body-weight daily of extra fluid). Fifteen cases were cured by eumydrin and the sixteenth (M. L., page 13) was responding well until he developed enteritis. He was operated on and died, after eumydrin had relieved the pyloric obstruction. In every case the vomiting was markedly diminished by eumydrin, and in an average period of 1.7 days instead of $5\frac{1}{4}$ days. Twelve babies had good appetites and only two poor appetites. The average gain in the first week was 8.5 oz.

Of the remaining twelve babies in the series, for whom full details of fluid intake are not available, nine are known to have had little or no subcutaneous saline, two had liberal daily salines, and the quantity of saline given to the twelfth is not known. Adding these eleven to the cases described above in order to increase the numbers in the groups (see table), we have: (1) a group of fourteen babies with very liberal fluid intake, nine apparently responding to eumydrin and five unrelieved by it, with four deaths (three of them babies with enteritis); (2) a group of twenty-five babies with relatively small fluid intake, all responding to eumydrin, with an average gain of 8.1 oz. in the first week, marked reduction of vomiting in 1.3 days, and one death of which the primary cause was an infection.

These results, unless they simply reflect a larger administration of fluid to babies in the poorest general condition or making poor progress, indicate an adverse effect of high fluid intake. Certainly all babies getting high fluid did not start in poor condition. In some of them, large quantities of fluid, chiefly

INFLUENCE OF THE AMOUNT OF FLUID INTAKE ON THE RESPONSE TO EUMYDRIN

Fluid intake	HIGH	LOW OR MEDIUM
Number of cases	14	25
At start of treatment:		
Age in days	39	45
Weight	7 lb. 3½ oz.	7 lb. 7 oz.
Number under birth weight ..	10	12
Responded to eumydrin: Number ..	9	25
Time in days in which vomiting was markedly reduced	4.8	1.3
Average gain or loss in first week ..	-1.0 oz.	-8.1 oz.
Cured by eumydrin: Number ..	5	24
No response to eumydrin: Number ..	5	0
Cured by operation: Number ..	4	0
Poor appetite: Number	8	2
Fatal cases: Number	4	1

as daily saline given subcutaneously, were pressed from the start, but on the other hand when infants continued to vomit and showed reluctance to finish their feeds the tendency was undoubtedly to continue subcutaneous salines, thus apparently continuing the vicious circle. The relative condition of the two groups at the start of treatment can in part be judged by a comparison of their average ages and weights. The average age of the group with smaller fluid intake was forty-five days and the average weight 7 lb. 7 oz.: the average age of the group with large fluid intake was thirty-nine days and the average weight 7 lb. 3½ oz.: i.e. the latter averaged six days younger and 3½ oz. lighter, which does not suggest their general condition was less satisfactory at the start of treatment. The same conclusion is borne out by a comparison of the notes on the clinical condition of the individual infants on admission. From a survey of the cases, the author feels in no doubt that a continued high fluid intake often produces poor appetite and also diminishes the effectiveness of the drug. The fact that all the five babies who failed to show any response to eumydrin received in extra fluid an average of 1.5 to 2.1 oz. per pound body-weight daily certainly suggests that a large fluid intake not only diminishes toxic effects but also diminishes the desired effect of the drug on the pylorus. The following are the cases that showed no response to eumydrin:

P. G., male, on admission aged thirty days, weight 7 lb. 14 oz. had boils on his legs. He was 12 oz. under birth weight. The stomach was washed out daily with normal saline, and he was given 10 to 20 oz. of subcutaneous saline daily. His weight owing to saline administration was increased by 10 oz. in two days before eumydrin was started. For the first week the food intake (sweetened condensed milk, 1 in 5) averaged, on account of poor appetite, only 2.0 oz. per pound daily, and his total fluid averaged 3.9 oz.: the extra fluid was therefore 1.9 oz. per pound body-weight daily. The maximum dose of eumydrin was 3.0 c.c. There was no reduction in vomiting. Weights were erratic on account of the large quantities of saline given parenterally. On the twelfth day instead of giving the drug by mouth 1 c.c. of eumydrin solution was given intramuscularly before feeds, but without relief of vomiting. On the thirteenth day a Rammstedt operation was carried out under local novocaine anaesthesia. During the operation the baby had a convulsion. The post-operative condition was poor with irregular breathing, but there was no laryngeal spasm and the Chvostek test was negative, so that there was no evidence

that the convulsion was due to tetany. It may have been due to novocaine (Bailey, 1940). From about the third day after operation progress was satisfactory.

J. D., male, aged eighty-six days, is dealt with on page 13. For the first week his average daily food intake was 2.4 oz. per pound body-weight, and his total fluid 4.5 oz., so that his extra fluid intake was high (2.1 oz. per pound). His appetite was poor. He was operated on after thirteen days on eumydrin on account of his failure to respond to the drug.

B. D., male, aged seventeen days, weight 6 lb. 8 oz., was in satisfactory general condition when put on eumydrin, and vomiting had started only three days before. Details of the food (breast milk) intake are not available, but he was given 5 to 15 oz. of saline subcutaneously each day during his six days on eumydrin treatment. The maximum dose of eumydrin was 5 c.c. There was no reduction in vomiting, he lost 9 oz. while on the drug, and he was operated on after one week. After the Rammstedt operation he still continued to vomit, though to a less degree. X-ray examination showed that there was now no delay in the emptying of the stomach. Vomiting temporarily improved when milk from another mother was substituted for that of his own mother, but did not cease until about seven weeks after operation.

A. H., male, aged thirty-five days, weight 7 lb. 8 oz., breast fed. For the first week his daily food intake averaged 1.9 oz. per pound body-weight, and his total fluid 3.6 oz., so that his extra fluid was 1.7 oz. per pound. He was given saline subcutaneously almost daily. There was no reduction in vomiting, and some haematemesis appeared. On the seventh and eighth days he was given gastric lavage without benefit. His maximum dose of eumydrin solution was 7 c.c. He was operated on with immediate relief of the vomiting.

E. J., male, aged eighteen days, weight 7 lb. 8 oz., was the third child in his family, and the first and second had also had pyloric stenosis and had been successfully treated by operation at the ages of three weeks and two months. There was no consanguinity of his parents. He had subcutaneous salines on the first day of treatment and thereafter rectal salines daily. His food intake (breast milk and sweetened condensed milk) averaged 2.4 oz. per pound body-weight, and his total fluid 3.9 oz., a difference of 1.5 oz. His appetite is recorded as 'very poor' when his fluid intake rose to 4.6 oz. per pound body-weight. The maximum dose of eumydrin solution was 6 c.c. There was no reduction in vomiting, and he was successfully operated on on the sixth day. This baby was a fully established case of pyloric stenosis when first taken to hospital at the age of sixteen days, and in addition the disease was familial, factors which, as already stated, Langstein (1921) considers bad prognostic signs for medical treatment.

(d) GASTRIC LAVAGE. Svensgaard (1935) has abandoned gastric lavage, whereas Dobbs (1939) found it of great value. Of this series, eleven cases were started off with gastric lavage daily or almost daily, for a week and upwards, three more were given one to four wash-outs before or at the outset of treatment and the remaining twenty-four were started without gastric lavage. Which cases fell into each category was, generally, a matter of chance.

1. Of the eleven cases given regular gastric lavage from the start, two (P. G., page 8, and J. D., page 13) failed to respond to eumydrin and were operated on; the average gain for the rest for the first week was approximately 6 oz. (as compared with an average of 6.8 oz. for all the thirty-one cases cured by eumydrin), so that in rate of gain this group showed no superiority over the rest.

2. Of the twenty-seven not started with regular lavage three failed to respond

to eumydrin (B. D., A. H. and E. J., page 9), one of these (A. H.) was then treated with lavage, but without benefit, and all three were operated on. Four other babies in this group (J. van G., J. C., B. M. and G. B.), who were ultimately cured by eumydrin, continued to vomit for eight days and upwards and consequently were given gastric lavage. In two of these (J. van G., page 4 and J. C.) this continued vomiting was apparently independent of pyloric obstruction, and there was no gastric residue removed two-and-a-half hours after a feed, nor was there any benefit from the wash-outs; the third baby (B. M., page 5) showed an improved appetite and gain, possibly associated with the wash-outs, though the stomach emptied normally; in the fourth case (G. B.), where there was still some delay in the emptying of the stomach one week after starting eumydrin, the institution of wash-outs coincided with a reduction in vomiting and a gain of $9\frac{1}{2}$ oz. in the second week of eumydrin treatment. This was the only case in which there appeared to be immediate and sudden improvement from the gastric lavage, and a single case cannot prove its value.

Dosage of eumydrin

The maximum dose of eumydrin given to a baby has varied from 2 to 7 c.c. of 1 in 10,000 aqueous solution given before each of six, or occasionally seven, feeds in the twenty-four hours, or 1.2 to 4.2 mgm. of eumydrin in the day. In twelve babies cured by eumydrin 2.0 or 2.5 c.c. has not been exceeded, whilst two appeared to require 5 c.c. The five cases which failed to respond to eumydrin (see pages 8 and 9) received 2.5, 3.5, 5.5, 6 and 7 c.c. respectively as their maximum dosage, and one (P. G.) was given intra-muscular injections of 1 c.c. of the solution before feeds without obvious effect. Larger doses might have proved effective, at least in the first two cases, but so far as the writer's limited experience goes, increases in dosage over 4 c.c. have usually seemed of doubtful value. There were only two babies (E. J. and A. H.) who were given 6 and 7 c.c. and in both cases these large doses, like the smaller, failed. In the single case treated with lingual application of the alcoholic solution (0.6 per cent.), approximately 0.1 mgm. of eumydrin given twice daily was accompanied by immediate reduction in vomiting. This dose was only one-sixth of the smallest 'maintenance dose' as given in aqueous solution.

Treatment given in cases which responded favourably

The babies who responded really well to eumydrin in aqueous solution had treatment more or less as follows:—

1. The daily food intake for the whole of the first week added together averaged between 2.1 and 2.7 oz. per pound body-weight daily (this food containing 20 calories per fluid ounce).
2. The extra fluid in the first week did not usually exceed an average of 1 oz. per pound body-weight daily (over and above that given in the feeds), and might be cut out entirely after the first few days. During the first one or two days some extra fluid certainly diminished toxic effects.
3. Some had gastric lavage, some not, with little obvious influence on the results.
4. The maximum dose of eumydrin solution varied between 2 and 5 c.c.

given before each feed: the drug was begun with 0.5 to 1.0 c.c. in order to minimize the risk of toxic effects.

Below are given the histories of a typical case with good response (K. S.) and a typical case with poor response (J. K.) to eumydrin:—

GOOD RESPONSE. K. S., male, aged thirty days, weight 6 lb. 9 oz., breast fed. The baby on admission was thin and had some abdominal distension. The stomach was washed out before eumydrin was begun, and he was given 11 oz. of subcutaneous saline during the first twenty-four hours in hospital, and none thereafter. For the first week he received daily per pound body-weight an average of 2.1 oz. of food and 2.4 oz. of fluid. The maximum dose of eumydrin was 3 c.c. Vomiting was markedly less from the time the first dose was given, there were in all only four vomits in the first five days and none thereafter. He was eleven days in hospital, but had forty-six days' treatment. He gained 6½ oz. in the first week and an average of 8.1 oz. weekly for the first five weeks.

POOR RESPONSE. J. K., male, a twin, aged thirty-seven days, weight 6 lb. He was fed chiefly on breast milk. He did not begin to vomit until twenty-eight days old and was a typical case of hypertrophic pyloric stenosis. His condition was fairly good on admission. He had gastric lavage (with normal saline) daily for thirty-six days, and was given subcutaneous saline daily for thirty-one days. For the first week he received daily per pound body-weight an average of 2.2 oz. of food and 4.4 oz. of fluid in all. Appetite was poor and tube feeding was resorted to. Vomiting was markedly less in two days but was not stopped; it nearly ceased in thirty-four days. He was in hospital for forty-five days and had eighty-three days' eumydrin treatment. He gained 1½ oz. in the first week and an average of only 2½ oz. weekly for the first five weeks.

His twin sister, V. K., vomited from the first week of life, but her vomiting was not projectile, there was no visible peristalsis and when she died at thirty-seven days old autopsy showed her to have the first part of the duodenum much dilated, with a narrowing of the gut just beyond, so that at the junction of the first and second part of the duodenum the lumen just admitted a probe. The pylorus was normal. Dr. Alice King, under whom this baby was admitted, kindly allows the author to quote this case.

The first baby, K. S., had a relatively low fluid intake and no gastric lavage after the drug was started, his vomiting was rapidly checked, he had a good appetite and gained well. The second baby, J. K., had a grossly excessive fluid intake, and daily gastric lavage; vomiting, though much less, continued until after the salines were omitted. His gain in weight was slow. Incidentally, the family history of J. K. is interesting; both twins had a defect in the same region of the intestinal canal, in one case a stenosis of the duodenum with a normal pylorus, in the other a hypertrophic pyloric stenosis.

Toxic effects

Svensgaard's article in 1935 laid stress on the need of 'saline administration while the patient is still in a dehydrated condition,' with the object of avoiding the toxic effects of eumydrin, and paediatricians in this country have emphasized the same point. In Svensgaard's own series there were no serious toxic symptoms, but she mentioned one fatal case of eumydrin poisoning with hyperpyrexia, perhaps due to idiosyncrasy reported by Friedlaender. Monrad (1938) has had one death from eumydrin poisoning. The baby was having in all 3.5 mgm. of eumydrin daily and suddenly developed nystagmus, dilated

pupils, a high temperature, restlessness and convulsions. In a series of sixty-four cases treated with eumydrin Monrad has had nine cases of fairly severe toxæmia with high temperature in every case, and restlessness, nystagmus and convulsions recorded in two cases. The dose of eumydrin was 3·5 to 4·0 mgm. daily.

The toxic effects observed in the present series have been a rise of temperature, pulse and respiration rate, a bright red flush, slight dryness of the mouth, slight dilatation of pupils, abdominal distension and constipation. Fifteen babies in the series are noted as showing some toxic effect, which might be only a bright red flush lasting for an hour or more, or almost any combination of the above symptoms; e.g. one baby had a transient pyrexia of 105·4° F., without flush or other symptoms, another a flush and dry mouth without recorded pyrexia, another a flush, abdominal distension, dilated pupils, and rise of respiration and pulse rate, with the rectal temperature only 99·4° F. Usually the symptoms appeared in babies not having subcutaneous salines, and they were simply treated by omitting or halving the next dose of eumydrin. These transient symptoms in no way interfered with the baby's progress. It should be noted, however, that the initial dose of eumydrin was usually only 0·5 to 1·0 c.c. of the solution, i.e. 0·05 to 0·1 mgm.

There is one symptom, however, which may be of serious significance, and that is abdominal distension, a symptom also observed with atropine (Parsons, 1933), and all those using this drug should be aware of its possible dangers. Seven babies in this series are noted as having some abdominal fullness or distension, sometimes once only, sometimes on a number of occasions while on eumydrin, and probably transient fullness sometimes went unrecorded.

One baby (M. L., page 13) developed paralytic ileus. He was operated on during the course of enteritis, and paralytic ileus followed. Probably diarrhoea, perhaps on account of the resulting fluid imbalance, favours the development of this toxic effect, for the only other case of gross abdominal distension (E. M., page 13) was also in a baby with enteritis. This baby had some abdominal fullness necessitating reduction of the food intake, before eumydrin was given at all, and distension recurred and become severe with the onset of diarrhoea. In both cases the total dose of eumydrin was only 1·5 mgm. in twenty-four hours. In both cases severe distension could probably have been avoided had the drug been reduced when the toxic effect was first observed. The drug, moreover, in each case had markedly reduced the vomiting with a good gain in weight during the first week of treatment. Dobbs has also reported a case of paralytic ileus in a baby weighing 5½ lb. and given 7 c.c. of eumydrin before each feed, probably 4·2 mgm. in twenty-four hours. Although few reports of paralytic ileus following eumydrin treatment have been published the author has heard indirectly of some other cases in this country. In these, as in the author's case, the early and easily treated symptoms of abdominal distension were apparently ignored and the drug continued, perhaps in large doses, until the condition was irrecoverable. Abdominal distension is always an indication for immediate reduction, or temporary omission of eumydrin, and it would be a wise precaution when operation is undertaken after a course of eumydrin to omit the drug for twenty-

four hours before operation. Apart from the presence of toxic effects of the drug, which may be accentuated by diarrhoea, administration of eumydrin is not contra-indicated if a baby develops loose stools; in none of the cases in this series has eumydrin produced or worsened an existing diarrhoea; on the contrary, it sometimes produces constipation.

Lindberg (1925) has shown that if a given dose of atropine is continued the rate of elimination increases, so that a progressively larger dose is needed to produce toxic symptoms. The same probably holds true of eumydrin. Lindberg has said of atropine, and recently Wallgren (1940) of eumydrin, that toxic symptoms are more likely with an aqueous solution taken into the stomach, than by the lingual administration of an alcoholic solution. They state that, when an aqueous solution is given uncertainty of effect is produced by vomiting, varying dilution from gastric retention and varying potency of the solution from deterioration with keeping; and that the dose necessary for control of vomiting is much smaller when the alcoholic solution, absorbed through the tongue, is given.

Fatal cases

The following are the histories of the five babies who died:

J. D., male, aged eighty-six days, had some pyrexia on admission, was lethargic, wasted and weighed 7 lb. 9 oz. He had thirty-one days' history of vomiting, but was said to have had only three large vomits in the seven days before admission. He was fed on breast milk and sweetened condensed milk and his maximum dose of eumydrin was 2.5 c.c. He had large quantities of subcutaneous saline daily (an average total fluid intake of 4.5 oz. per pound body-weight daily for the first week), and daily gastric lavage. Though vomiting diminished, the obstruction at the pylorus persisted, as shown by the presence of 4 to 9 oz. of food in the stomach two-and-a-half hours after a meal, and consequently surgical treatment was adopted. His weight was erratic on account of the large amounts of saline given, but his general condition at the time of operation, thirteen days after the start of eumydrin, was better than on admission. On the third day after operation the stools were fluid, he rapidly became dehydrated and died next day of enteritis contracted in hospital. In this case eumydrin probably failed on account of the excessive fluid intake, but death was due to cross-infection after operation.

E. M., female, aged thirty-six days, weight 6 lb. 8 oz., had some abdominal distension on admission and was 12 oz. under birth weight. The food was sweetened condensed milk (1 in 5), and the total fluid intake for the first week averaged 4.4 oz. per pound body-weight daily. The maximum dose of eumydrin was 2.5 c.c. The vomiting was markedly less within twenty-four hours and she gained 6½ oz. in the first week. About the end of that week she developed diarrhoea at a time when the writer had gone on holiday. By the middle of the second week there was marked abdominal distension with fluid stools and vomiting. Eumydrin was continued. A Rammstedt operation was done on the fourteenth day when the baby was very ill with gastro-enteritis and abdominal distension. She collapsed and died the same night. In this case, in spite of a high fluid intake, eumydrin would presumably have cured the baby had it not been for cross-infection. Diarrhoea apparently precipitated the distension caused by eumydrin. Death was due to gastro-enteritis and to operation, and was probably accelerated by the abdominal distension.

M. L., male, aged thirty-seven days, weight 7 lb. 13 oz., started treatment

when in fairly good general condition, and was fed on sweetened condensed milk. He appeared to be responding well to 2.5 c.c. of eumydrin with an average daily fluid intake of 2.9 oz. per pound body-weight, and gained $7\frac{1}{4}$ oz. in the first week. In the second week he developed acute enteritis, probably from E. M. (see above) who was in the ward at the same time, and by the fourteenth day he had lost 12 oz. in weight and the abdomen was distended. In the absence of the writer, the abdominal distension was not taken as an indication to reduce the eumydrin, and on the twenty-first day the baby was operated on. The stools were fluid, the abdomen grossly distended and the baby acutely ill. He died next day with paralytic ileus. Death here, too, was primarily due to enteritis in a baby previously responding to eumydrin. The ultimate cause of death was paralytic ileus. The paralysis of the gut must be attributed to a combination of factors: (a) enteritis, (b) continued administration of eumydrin after the appearance of distension, and (c) the inevitable handling of the grossly distended gut at operation.

E. C., male, aged sixty-one days, weight 8 lb. 1 oz., was breast fed, and, though thin, in satisfactory condition on admission. Nevertheless he was given saline subcutaneously daily, and for the first week the average daily fluid intake totalled 4.4 oz. per pound body-weight. He did well at first on 2.5 c.c. of eumydrin, but, probably on account of the excessive fluid intake, vomiting recurred on the eighth day, and there were some large vomits daily. Three weeks after treatment started there was a sudden deterioration in the general condition, ushered in by some small vomits containing blood. Next day the baby was collapsed and oedematous, with constant dribbling vomits, and he died the same day. The excessive fluid intake was probably the cause of death in this case. Post-mortem examination showed only oedema of the tissues and some free fluid in the abdomen in addition to wasting and the typical changes in the pylorus.

J. W., male, aged thirty-three days, weight 5 lb. 6 oz., was a premature baby. He had had a cyanotic attack with cessation of breathing in the maternity hospital before admission to the Queen's Hospital. His maximum dose of eumydrin was 3.0 c.c. and he, too, received excessive quantities of saline subcutaneously. He developed a small abscess in the buttock. Four days after starting treatment his temperature fell to 93° F. and he was found collapsed. Thereafter he did badly. Next day he was oedematous as a result of the chilling, and he died with diarrhoea about two weeks later.

Thus the primary cause of death in three out of the five cases was an infective diarrhoea acquired in the hospital, and in two cases a contributory cause was failure to reduce the eumydrin when abdominal distension was observed, leading in one case to paralytic ileus. In one case the cause of death was uncertain, but was probably excessive fluid administration. In the premature baby a subnormal temperature and oedema were followed by a terminal diarrhoea.

Duration of treatment

The average duration of eumydrin treatment for the cases who recovered was fifty-six days, eight weeks exactly. Probably this was unnecessarily long. The average duration of treatment in fifteen cases successfully treated by Braithwaite (1938) was five-and-a-half weeks (extremes two-and-a-half and twelve weeks). Still stated in 1923 that with cases medically treated gastric lavage was generally required for three to four months, which would make the

baby, say five months old at the end of the treatment, i.e. when spontaneous recovery occurred. Four cases in the present series were stopped in less than four weeks; three (A. H., B. W. and B. L.) stopped after seventeen, twenty-three and twenty-seven days respectively at the ages of eighty-two, ninety-three and seventy-nine days, and had no return of vomiting; the fourth (J. P.) stopped after twenty-four days when seventy-one days old, had two vomits in the next seven days and a sharp recurrence of symptoms in the week after, for which he was re-admitted and given a further course of treatment. After this case the tendency was to leave well alone, and keep the baby on the drug a good deal longer, only reducing it gradually. In about half the cases the drug was stopped under three months old, i.e. much younger than spontaneous cures can usually be expected. The apparent carry-over of eumydrin effect is interesting and is discussed later.

Time in hospital

All but two babies were treated as in-patients. The average time in hospital for the in-patients successfully treated with eumydrin was twenty-eight days; seven babies were in for seven to eleven days; fourteen for twenty-one days or less. Of the rest, two were kept in for several weeks after being ready for discharge because of illness in their homes; two were from hostels for unmarried mothers, and, on account of difficulties in supervision in the hostels were kept in hospital for fifty and sixty days respectively, and one baby admitted with collapse of lung followed by pneumonia (J. van G) was in for eighty days on account of his lung condition. These five cases, averaging fifty-four days each in hospital, would most probably have been in as long if treated surgically. If these are excluded, the average stay of the rest was twenty-three days. With more knowledge of the drug, this time could be much reduced.

The author early on gave directions to one mother in the out-patient department for her baby's treatment at home. Unfortunately, the mother had been told by another doctor before her visit to hospital that operation was essential, and she never attended again. Two other babies have been treated to a conclusion without admission. In one case directions were simply given in the out-patient department, the baby recovered, but treatment was irregular and progress slow. The other mother with her baby attended in a ward daily for the first five days for instruction, and her infant made excellent progress. It should be noted that in spite of the fact that the parents were for the most part in poor economic circumstances, the mothers of nearly all babies successfully coped with the treatment at home after the initial period in hospital.

Discussion

'The pylorus will open up spontaneously in time and the child recover, provided he does not die in the process. When recovery occurs in this way we know, from the results of post-mortem examination, that the muscular coat remains thickened for a long time after its action has become quite normal.'

. . . 'When once the gain in weight has begun, it is usually rapid and continuous and the child is soon practically well.' So wrote that careful observer, John Thomson, in 1925. If cessation of vomiting is fairly sudden, so also is the onset of projectile vomiting. Not infrequently the mother can say to an hour when projectile vomiting started. The hypertrophy of the muscle obviously cannot develop suddenly, yet within three days of the onset of vomiting, the typical pyloric tumour may be felt. The present writer has seen a baby with all the typical symptoms and signs of pyloric stenosis suddenly cease to vomit without treatment, and progress normally for between one and two weeks, only to have a sudden return of symptoms, which were then cured by the Rammstedt operation. Again if a baby with pyloric stenosis develops a severe gastro-enteritis the vomiting may cease to have the typical projectile character, visible gastric peristalsis may greatly lessen and the pylorus may no longer be palpable. These facts can only be explained by supposing that it is spasm of the hypertrophied muscle which determines the presence or absence of the typical symptoms, that this spasm can appear and disappear suddenly, and that some unknown factor spontaneously causes a disappearance of spasm, it may be fairly suddenly, say between three-and-a-half and five months old, in those babies that survive as long. Obviously eumydrin, like atropine, can remove this spasm. In this series eumydrin was probably continued unnecessarily long, yet in about half the cases the drug was stopped when the baby was between five weeks and three months old, and there was no recurrence of symptoms, and this is much younger than a spontaneous disappearance of symptoms can generally be expected. Lindberg (1925) using atropine in alcoholic solution states that a single course of only one to three weeks stopped the symptoms for good in some of his cases. Again, there seems a curious 'carry-over' of the influence of eumydrin: toxic symptoms, such as flush and pyrexia, are transient, usually disappearing in a few hours, so one would expect the effect of the drug on the pylorus would last about a similar length of time, and it seems unlikely that a small dose of eumydrin, given once or twice in twenty-four hours, and producing no toxic effects, can exert an anti-spasmodic effect for the whole twenty-four hours. Yet Lindberg (1925) gave his alcoholic solution of atropine once to five times daily with satisfactory results, and Wallgren (1940) successfully treats his cases with one dose in twenty-four hours of 0.1 to 0.5 mgm. of eumydrin in alcohol applied to the tongue. Following his article, the writer has treated a single case with two doses in the day of 0.1 mgm. each, with extremely satisfactory results. Not only may the effect of one small dose last for a day but vomiting may be checked for many days after the drug is stopped. When J. P.'s medication was stopped after twenty-four days' treatment there were only two vomits in the first week, followed by a sudden relapse in the second week. Dobbs describes a case in which the drug was stopped after twenty days' treatment. There was no vomiting for eighteen days, and thereafter a return of vomiting. Rinvik (1940) has had cases showing recurrence apparently twenty to twenty-nine days after eumydrin was stopped. These facts taken together suggest that temporary allaying of the spasm may allow the disappearance of the factor causing it for a longer or shorter period.

Does a temporary anti-spasmodic effect break some vicious circle which produces the spasm? Perhaps the opening of the pyloric canal allows a return to normal of some chemical balance in the stomach.

Two facts seem to prove that eumydrin exerts its anti-spasmodic effect on the pylorus after absorption into the blood stream and not (as when instilled into the eye) by direct action at local nerve endings. These are: (1) that lingual application of a drop or two of the drug in alcoholic solution will check vomiting; (2) that excessive parenteral saline diminishes the effectiveness of eumydrin presumably by hastening elimination. Perhaps the action of eumydrin may help to elucidate the mechanism of normal physiological control of the passage of food through the pylorus (a subject on which, as Vertue (1939) has pointed out, views are still conflicting), as well as the pathogenesis of hypertrophic pyloric stenosis.

A high fluid intake appears to diminish all the effects of the drug. Not only this, but excessive fluid administration is likely to be accompanied by failure of appetite. Thus, though a fairly liberal fluid intake immediately before eumydrin is started will diminish the toxic effects, a continued high intake is contra-indicated, and was, probably, the cause of the failure of the drug to relieve spasm in five cases, and of its relatively slow action in others in this series.

The most dangerous toxic effect is probably abdominal distension. The two cases of acute abdominal distension in the series were suffering from enteritis at the time. The distension may have been caused by fluid imbalance resulting from the diarrhoea, but a large fluid intake did not prevent the distension. The distension was accompanied by continued pyrexia, possibly due to the drug, but there was no red flush, or dilated pupils, another instance of how the various toxic effects occur singly or in different combinations.

The number of cases here published, forty in all, is not large, and obviously the mortality rate in a series of this size may be misleading, so it is worth adding together the results of several workers in this country. Taking all the cases yet published in series of twenty-one and upwards [Braithwaite (1938), twenty-one cases; Dobbs (1941), forty cases; Vertue (1939), twenty-one cases; present series, forty cases], we get 122 cases with fourteen deaths, a mortality of 11·5 per cent.; ninety-three cases or 76·2 per cent. were cured by eumydrin, and fourteen or 11·5 per cent. by operation after a course of eumydrin treatment, and one or 0·8 per cent. by another drug. The great majority of the 122 cases were hospital patients. Lightwood (1939) and Findlay (1938) have published a further seventeen cases cured by eumydrin with no deaths.

Because of the risks of hospitalization in most countries, a distinction is usually drawn between the mortality rate of hospital cases and the mortality rate of private patients (Thomson, 1925; Herzfeld and Wallace, 1935). The unpalatable but well-known fact that the main mortality in most large series of cases in this country is often due to infection acquired in hospital was well brought out by Paterson in 1931. In the Hospital for Sick Children, Great Ormond Street, the year's mortality had never dropped below 21 per cent., and for the seven years 1924 to 1930 (403 cases in all), it remained roughly stationary

and averaged exactly one death in every four patients admitted. Of fifty private patients of the same average age operated on by the same surgeons and apparently supervised by the same physicians in nursing homes, however, not one died. But of twelve private patients of Paterson's admitted to hospital, again one in four died. Some children's hospitals in other countries have diminished their cross-infection rate far below ours, as witness the fact that Svensgaard reporting sixty-one cases kept an average of seventy-seven days each in hospital, lost only one baby from infection, a case of pyelo-nephritis, and is able to make a statement that astonishes a British paediatrician, namely that: 'the infant itself misses nothing by staying in the hospital.' A mortality rate of 20 to 25 per cent. is probably not unusual in children's hospitals in this country for surgically-treated cases (Parsons and Barling, 1933; Wallace and Wevill, 1934; Herzfeld and Wallace, 1935; Braithwaite, 1938), but a considerably lower rate can be claimed for some large series. In the last five years large series have been published by Thompson and Gaisford (1935), 209 cases; Jewesbury and Page (1937), 303 cases; and Tallerman (1938), 98 cases. The great majority were hospital patients, and among this total of 610 cases there were eighty-two deaths, a mortality of 13.4 per cent. If the mortality among large series of babies treated by the Rammstedt operation by trained hospital teams is, say, 13 to 25 per cent. in this country, we can be fairly sure that the total morbidity in the country averages considerably higher. With expert teams the direct operative mortality is known to be small, but a surgeon's opinion on the operative skill necessary is of interest. Lake has said: 'It is the type of operation in which only practice makes perfect . . . simple as it appears, there are many pitfalls for the inexperienced,' and few surgeons unconnected with a children's hospital can gain any large experience. Some of the immediate post-operative troubles occasionally met with are persistence of symptoms due to inadequate division of the muscle, haematemesis immediately following operation, particularly perhaps where there has been additional handling (for instance following accidental puncture of the mucous membrane) and cutting out of sutures in the abdominal wall, not to mention the risks inseparable from any major operation. Hence it is probable that in the country as a whole the direct operative mortality among babies treated by the Rammstedt operation is not small, and to this must be added the mortality from hospitalization.

The mortality of 11.5 per cent. for 122 cases, nearly all hospital or clinic patients, treated with eumydrin in this country compares favourably with anything heretofore achieved in large series of cases in Great Britain by operation. With the experience now being gained it should, however, be possible to reduce the mortality considerably, by treating cases without admission to hospital whenever possible, by avoiding excessive fluid administration and thereby improving the response to eumydrin and shortening the time in hospital, and by vigilance in avoiding dangerous toxic effects, such as excessive abdominal distension or hyperpyrexia.

In the Scandinavian countries it seems that eumydrin has already largely displaced other methods of treatment, and its use is spreading from there to

other countries (Türck, 1939; Landor, 1939). Svensgaard's mortality was 3.3 per cent. for sixty-one cases and Wallgren, using the drug in alcoholic solution, applied to the tongue, states that the total mortality rate of Gothenburg infants suffering from pyloric stenosis has been reduced to 1 per cent. for the past twelve years. So there is still much room for improvement in results in this country.

Simpler methods of treatment, if efficacious, are obviously preferable to more complicated ones, and eumydrin therapy is steadily growing in favour. Its wide adoption in this country should greatly diminish the total mortality from pyloric stenosis. Whether medical or surgical treatment is employed, success will always in large measure depend on the physician and his familiarity with the medical treatment involved.

In this series an aqueous solution of eumydrin has been used: it may be that an alcoholic solution in much smaller dosage for lingual application will prove the more effective method, as Wallgren (1940) holds. If drop doses are given by a mother with a pipette, there is, of course, the possible danger of double or quadruple the intended dose being given, though some practice with a pipette and plain water should render such errors unlikely. Nevertheless an aqueous solution in bigger volume will probably prove the method of choice at least when the mother's accuracy is doubted. In that case, the routine suggested is as follows: The baby, unless obviously dehydrated, should receive fluid by mouth only, perhaps 3 oz. per pound body-weight (inclusive of his feeds), in the first twenty-four hours, and thereafter only so much water, over and above that in his feeds, as he really wants to take. The food should be given in a concentration to provide 20 calories to one fluid oz.; sweetened condensed milk (1 in 5 by volume) is well tolerated if breast milk is not available, and can be changed to dried milk at a later stage. Within two or three days of starting treatment the full caloric needs should, if possible, be given, perhaps in six feeds in twenty-four hours. If feeds are vomited the author prefers not to repeat them. The eumydrin (1 in 10,000 in water) should be given half an hour before each feed, beginning with 0.5 to 1 c.c. and increasing by 0.5 c.c. at each feed to 2.5 or 3 c.c., and higher if necessary. No gastric lavage is necessary. It is probable that nearly all cases will respond to this regime. If, however, it fails and it is decided to adopt surgical treatment, it would be wise to omit the drug twenty-four hours before operation. In any case, toxic symptoms particularly abdominal distension, indicate a reduction of dosage; often the omission of one dose is all that is required. For distension a reduction of food may also be necessary. How long it is necessary to continue the drug is uncertain, but if it be reduced gradually, 0.5 c.c. at a time, there is little risk of an acute return of vomiting.

With such a routine it is clear that a cooperative mother, who is accurate and methodical, can certainly carry out the treatment at home under supervision. She needs to be instructed in careful measuring and in symptoms of overdosage, and, if her supply of breast milk is liberal, it may be better, though probably not essential, to teach her to express her milk in order to give the baby at first a measured quantity. Whatever the method of treatment employed in

hypertrophic pyloric stenosis, the results obtained must in part depend on familiarity with the method employed and its pitfalls, and in part the avoidance of the risks of cross-infection.

Summary

Forty consecutive cases of hypertrophic pyloric stenosis have been treated with eumydrin with a mortality of 12.5 per cent.; thirty-one cases were cured by eumydrin and four more by operation. Of the five deaths, four were due wholly or in part to enteritis contracted in hospital, and one was probably due to excessive fluid administration. Thirty-five babies showed disappearance of, or reduction in, obstruction at the pylorus after eumydrin treatment. Of the five which showed no response, all had a high fluid intake which was probably the factor which prevented the drug bringing about relaxation of the pyloric spasm. Excessive fluid intake was accompanied by a less rapid response to eumydrin, a slower gain in weight, and often by poor appetite. There was no evidence of benefit from routine gastric lavage. In those cases cured by eumydrin, vomiting was markedly diminished in an average period of 2.9 days, the babies gained an average of 6.8 oz. in the first week, and 6.9 oz. weekly for the first five weeks. The most serious toxic effect encountered in the series was abdominal distension, but there is no reason to suppose this would prove serious were it treated early by reduction of the drug. The drug was used in aqueous solution given by mouth six times daily. In one case only was it given by lingual application in alcoholic solution, which may prove the better method. It is suggested that temporary relief of the spasm at the pylorus may possibly break a vicious circle. The results here recorded should be capable of much improvement with increased experience of this method of treatment. Whereas a mortality of 25 per cent. is not unusual in this country among babies treated surgically, there has been a mortality of 11.5 per cent. among 122 cases treated with eumydrin reported by four physicians in this country.

A plea is made for the more widespread adoption of eumydrin, which has proved so successful in Scandinavian countries, for the treatment of hypertrophic pyloric stenosis in this country.

Sincere thanks are due to the house physicians who have cooperated in the work, as well as to the sisters and nurses at the Queen's Hospital for Children who, in addition to the anxious work of nursing young babies in hospital, have given much time and care to the record-keeping involved.

Postscript. One baby, the only one in the series still on eumydrin when this paper was finished, has since died at fifteen-and-a-half weeks old. She was twenty-two days old when she started treatment, the third youngest in the series (see page 6) and progressed well. She was the child of a fifteen-year-old unmarried mother who was evacuated. She was suddenly weaned after evacuation, grossly underfed on dairy milk, and was twice taken off eumydrin with return of vomiting. On the second occasion the child was re-admitted, but did not respond to medical treatment.

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