ECRONICON OPEN ACCESS

EC PAEDIATRICS
Thematic Article

Pyloric Stenosis of Infancy-The Y Chromosome, Hyperacidity and the Feeding Disease

Ian M Rogers*

46 Whitburn Road, Cleadon, Sunderland SR67QS, United Kingdom

***Corresponding Author:** Ian M Rogers, 46 Whitburn Road, Cleadon, Sunderland SR67QS, United Kingdom.
E-Mail: irogers2000@hotmail.com

Received: February 01, 2018; **Published:** March 09, 2018

Abstract

An analysis is made of the process by which primary hyperacidity and relative overfeeding has contributed to the modern understanding of the cause of pyloric stenosis of infancy. Reference is made to the paediatric contributions in the early part of the 20th century which have led to the present modern theory of cause.

It is concluded that male generated primary hyperacidity is the prime mover in causation with relative overfeeding especially with formulae milk as an important secondary factor.

Keywords: *Pyloric Stenosis of Infancy; Aetiology; Feeding Strategies; Seasonal Incidence; Primary Hyperacidity*

Abbreviations

PS: Pyloric Stenosis of Infancy

The pharmacology of Eumydrin is not completely understood. The pylorus is more responsive to changes of pH than to any other influence and I suggest that Eumydrin really acts indirectly by altering gastric secretion and hence the acidity of gastric juice. I wonder whether the line of treatment suggested by this idea had been explored.

Dr. R. E. Bonham Carter at the April 1951 meeting of the Royal Society of Medicine [1].

In 1951 the meeting at the Royal Society of Medicine attracted all the big guns. Denis Brown, David Levi and Dr. N. M. Jacoby all made contributions. Dr. Bonham Carters voice (I like to think of it coming from the back of the hall) attracted no further recorded comment and was lost in the mists of time.

Eumydrin was the propriety name for the modified alcoholic tincture of atropine popularised by Elizabeth Svensgaard in 1935 [2] and reputed to be directly absorbed from the tongue or buccal mucosa thus ensuring more secure absorption in the vomiting child. The atropine effect in reducing the vagal component of acid secretion, was well understood.

Another voice, that of Dr. Harold Weller is also recorded at the same meeting.

" I have many times observed typical gastric peristalsis and projectile vomiting in the first fortnight of life, and their disappearance under treatment with Eumydrin [1]. The really important word here is-many! There can now be little doubt that the acquired condition of PS is based on an inherited hyperacidity" [3].

PS babies have more acid, duodenal acid produces repeated sphincter contraction and sphincter hypertrophy and PS is born. PS is also created when acidity is unnaturally increased in new-born puppy dogs by pentagastrin injections to their mothers before labour [4].

The male predominance in this condition is no doubt due to the known increased acid secretion associated with baby boys and adult males [5-7].

The sex-ratio of 4-5/1 in favour of boys must have an explanation.

PS babies who survive the first few months with or without the standard temporary medical treatment are permanently cured. The peak acidity seen in normal development at around 3 weeks of age-appears to precipitate the presentation of PS in constitutionally hyperacid babies [8]. Not surprisingly problems with hyperacidity do sometimes arise in later life. The genes on the Y chromosome have clearly a part to play.

It is now becoming increasingly clear that the more frequently babies are fed-the more frequent PS. The earliest pioneers more than 300 years ago recognised that those babies had a great appetite and were often "crammed" with feeds [9-11]. They were initially vigorous babies with a birth weight above average [12].

The Y chromosome effect

The male gender in 80% of PS babies indicates an influence from the Y chromosome and, in particular, from the SRY gene-the gene which determines male gender.

The inheritance of PS is not obviously connected to Mendelian principles. Detailed family studies principally by Carter have concluded that it is inherited as a sex and environmental modified polygenic threshold inheritance [13]. Genomic wide assessments(GWASS) have revealed aberrations in multiple autosomal genes from chromosomes 2/3/57/11/12/16 (2 genes) and chromosome X [14]. No abnormalities have been reported in the Y chromosome.

The Y chromosome contains about 50 genes of which only 27 are male specific. The sex determining gene -the SRY gene- through a cascade influences many of the other autosomal genes.

It is possible that such an influence may be the reason why males have higher acid secretion. The genes which control the inheritance of the parietal cell are not known.

The phenotype which results from a polygenic inheritance such as height, facial characteristics etc. normally will have a range of values or intensities of presentations. Polygenic inherited conditions such as PS ought to display a range of intensities of presentations. It will not be all or none phenomenon.

As such we would expect to see mild forms of PS and more severe forms. Acute and intense presentations contrasting with mild, indolent forms which may not come to a full-blown case.

The clinical experience of John Thomson in 1921 and the more modern reports from MacKeown in 1952 and Gerrard in 1955 all testify that [15-17]:

1. The presentation does indeed vary from the most extreme to the most mild.
2. The condition does indeed come and go often within days.
3. Relative underfeeding is an important part of the non-surgical treatment.
4. Relative overfeeding precipitates the disease.

Zhang in 1993 corroborated the occurrence of symptoms that come and go -sometimes within a day [18].

In this way the occasional peaks in incidence of PS become more understandable. All that is necessary is a new surgeon or paediatrician with a special enthusiasm for the diagnosis of PS. Perhaps a more sophisticated ultra-sound machine. It is all to easy to dip into the formerly mild subclinical cases of PS and make the incidence higher. There are a lot of them about.

As far as Dr. Bonham Carter and the pH of fasting gastric juice is concerned, PS babies while more acid, share the same range as normal matched babies (See Figure 1) [19]. It is only when titratable acidities are measured that the much greater acidity in PS babies becomes clear. 21 PS babies and 13 matched controls were studied.

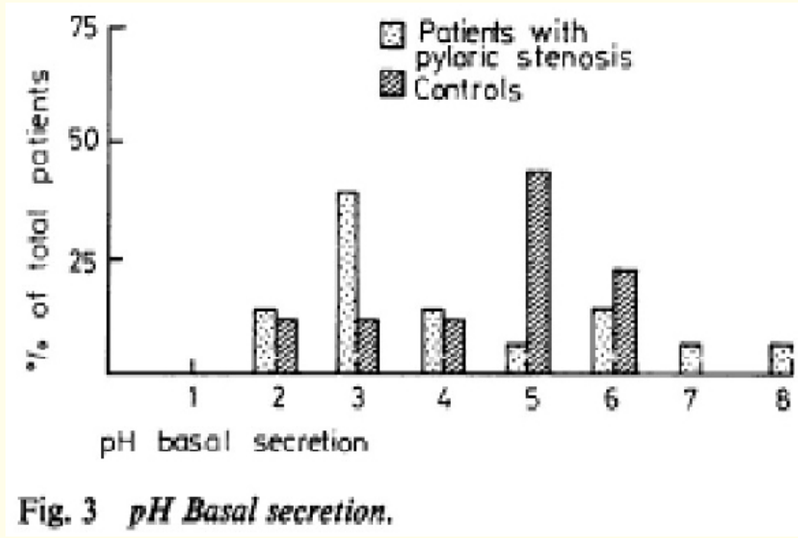

Figure 1: *pH basal secretion.*

The Y chromosome effect

The most effective way of promoting vigorous and frequent contraction of the pyloric sphincter is to feed the baby (Figure 2 reproduced by permission from M Schemann) [20]. In humans and in all animals, except cats, the interdigestive phase 111 activity is suppressed by a meal and strong and frequent pyloric sphincter contractions occur in the mixing process.

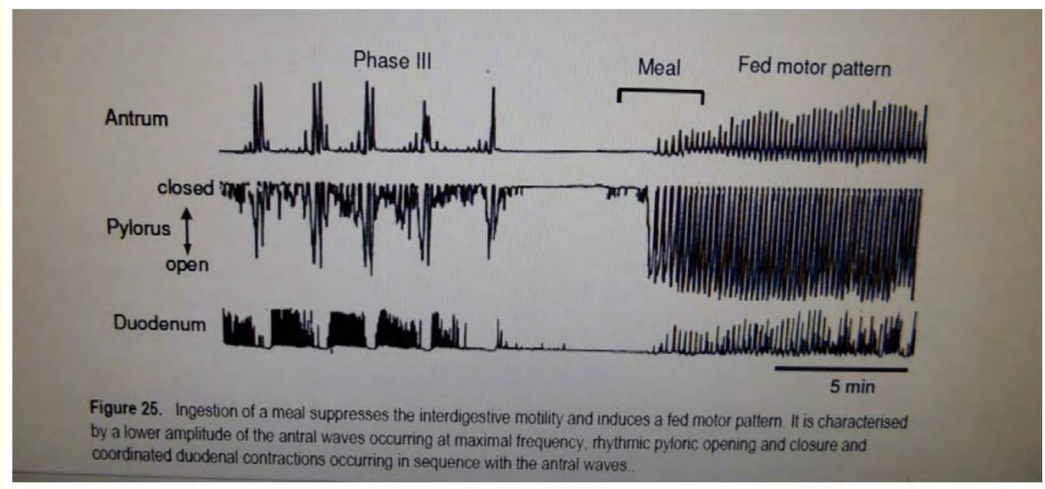

Figure 2: *Pyloric sphincter contraction is best developed after a feed. The contractions are stronger and more frequent than those occurring in between feeds (Phase 111) [20].*

The importance of the frequency of feeding in the genesis of PS was illuminated by 2 studies from Birmingham Childrens Hospital, UK.

The first study published in 1952 by McKeown., *et al*. examined 1059 PS babies born between 1940 - 1951. Just under half were born in hospital –the rest were born at home.

The home born babies presented with vomiting at a significantly earlier date- mean 21.6 days as compared to 27.1 days (SE of mean = 4). The authors conceded that the date of onset "was by no means invariably sharp"- the symptoms presumably coming and going in the beginning-but since there was no reason for this uncertainty to be unequally distributed, the findings were accepted.

The authors concluded that this revealed that post-natal environmental factors were the logical explanation but speculated no further [16].

A second Birmingham study in 1955 by Gerrard., et al. analysed 150 PS babies who had been fed 3 hourly or 4 hourly. They found that the 3 hourly babies presented significantly earlier than the babies fed 4 hourly. With the co-operation of the earlier authors they reviewed the feeding frequencies of the 1059 babies in the earlier study. Most of the hospital babies were fed 4 hrly. and most home born babies were fed 3 hourly. The place of birth itself had no discriminating value- it was the frequency of feeding.

The post-natal environmental influence was simply the frequency of feeds [17].

Both studies also confirmed that the size of the pyloric tumour varied directly according to the age of the baby another clear example of post-natal influences.

The second study also uncovered two further important facts.

1. Premature babies-sometimes for example 5 weeks premature- took only a few days longer on average to present with PS. It was again the duration of the post-natal feeding experience which was important both in starting and progressing the condition [17].
2. First- born babies only demonstrated their increased frequency from the 3rd week of age onwards. There was no difference in the first 2 weeks. One credible explanation is that the first born mothers in their natural anxiety were overfeeding and pyloric hypertrophy took at least 2 weeks before causing gastric outlet obstruction [17].

In an important paper from 1921, Dr. John Thomson of the Royal Hospital for Sick Children, Edinburgh reviewed 100 cases of PS during the previous 25 years 1894 - 1919. 58 had ended fatally. He concluded [15]:

1. The disease may be self-limited. He echoed the words of Robert Hutchison-that the pyloric lumen will eventually open up spontaneously and the child recover completely provided he does not die in the process [21].
2. Feeds must be restricted to 2 oz. or less and there should be warm water wash-outs once or twice a day. When babies had been treated with unsuitable feeding it was of the greatest importance to stop all feeding for 24 hours and use sub-cutaneous saline infusions. In other words restricting feeds was part of the successful treatment.
3. He recognized categories of IHPS- an acute form with sudden and violent symptoms: an ordinary form and (most importantly) the very mild case. He described these cases as not at all uncommon. They probably resolve simply by dietary restriction alone and may never come to medical attention. There appeared to be a continuum of degrees of stenosis. It was not an all or none affair. The least severe was the most common.
4. Of 33 survivors of either medical or surgical treatment aged from 10 months to 16 years the majority were above average in development and vigour. None showed signs of gastric derangement.
5. The work of Jacoby is also of particular interest in this matter. Although a pediatrician, he treated PS both surgically and medically. A similar mortality of 1% in 100 surgical and 100 medically treated babies was reported by him in 1962 [22].

Great importance was attached to the need for relative under nutrition as well as a precisely controlled body weight dosage of atropine therapy in the medically treated group. He commented on the poorly controlled body-weight doses of atropine which were given in those days. Too little meant no effect and too much meant dangerous tachycardias. Regular gastric washouts to empty the stomach were also part of the medical treatment.

Of special interest was his opinion that the babies most receptive to medical treatment were those thought to have a less intense degree of hypertrophy. Babies for example whose vomiting began on or after the 4th. week or in whom there has been a prolonged history without significant dehydration or electrolyte imbalance.

These findings are in keeping with Dr. John Thomson's "not uncommon cases" 40 years before which, in his hands spontaneously self-cured after a few days of food restraint or, in the words of Dr. Richard Dobbs , speaking at the Royal Society of Medicine in 1941. "*This gives the clue to the first principle upon which medical treatment is based. The disease is, we know, self-limiting in nature and, we shrewdly suspect, functional in origin. As the child may die in the meantime if left to cure itself, medical treatment is designed to hasten the natural process" [23].*

*"*The observations of the clinical and objective signs of PS coming and going are echoed in the more recent observations from Zhang et al. from the Westmead Hospital, Sidney, Australia from a data base of 212 PS babies. I quote [5]:*"*

"The diagnosis of IHPS can be difficult, as illustrated by the case histories. Diagnostic tests are not infallible, as is shown in case 2 where an ultrasound reported a 2.5 mm thick pylorus yet later the same day a typical pyloric mass was palpated and operated on. However, more often the data suggest that there is a prodrome in some patients during which there can be normal clinical, radiological and ultrasound findings. On eight occasions there was a normal initial ultrasound or barium meal in patients who subsequently had IHPS".

The frequency of those mild cases of PS can only be guessed at since, in practice, many will evade diagnosis and with food restraint, will self-cure.

Other associated pointers to the importance of relative overfeeding is the increased incidence with babies who are bottle fed. It is much easier to overfeed by bottle. Out of a data base of 91 PS babies Habbick from Saskatchewan, Canada found an ODDS ratio of 2.9. in favour of bottle fed babies [24]. Of particular interest is the direct relationship between the falling incidence of PS and the falling incidence of formula feeds in hospital from 1970-85. In the early part of the 20th Century it was recognised that the surgical mortality with bottle fed babies was much higher.

The seasonal incidence

Most reports have found that the incidence of PS increases in the summer months. Zamakhshary., *et al*. in 2011 reported on 1777 cases of PS between 1992 and 2014 from the province of Ontario, Canada [25]. They used the number of babies under 1 year as the denominator. 14.92/100,000 PS babies were born in June and 10.73/100,000 in February. The results were statistically significant [25]. A similar summer preponderance was reflected by Zhang., *et al*. from Sidney, Australia (AD) from a data base of 212 babies between 1984-92 [18].

Babies are well known to become dehydrated quite easily. One explanation may be since summer temperatures are hotter, thirst from relative dehydration may be causing an increased frequency of milk feeds.

Conclusion

In terms of causation there abides these two- Y chromosome associated hyperacidity and overfrequent feeding. The greater of these is hyperacidity.

Bibliography

1. Proceedings of the Royal Society of Medicine. Discussion on the treatment of congenital hypertrophic pyloric stenosis. 1 volume 44 Section of Pediatrics. President-Kenneth H Tallerman (1951): 451.

2. Svensgaard E. "The medical treatment of congenital pyloric stenosis*". *Archives of Disease in Childhood* 10.60 (1935): 443.

3. Rogers IM. "New Insights on the pathogeneesis of pyloric stenosis of infancy. A review with emphasis on the hyperacidity theory". *Open Journal of Pediatrics* 2 (2012): 97-105.

4. Dodge JA and Karim AA. "Induction of pyloric hypertrophy by pentagastrin". *Gut* 17.4 (1976): 280-284.

5. Koster KH., *et al*. "ABO blood groups and gastric acidity". *The Lancet* 269.6880 (1955): 52-56.

6. Dodge JA. "ABO blood groups and IHPS". *British Medical Journal* 4.5582 (1967): 781-782.

7. Baron JH. "Studies of basal and peak acid output with an augmented histamine test". *Gut* 4 (1963): 136-144.

8. Ames Mary. "Gastric acidity in the first 10 days of life of the prematurely born baby". *American Journal of Diseases of Children* 100.2 (1960): 252-256.

9. Patrick Blair. Surgeon Apothecary. R.S.S. Phil.Tr. no 353 (1926): 631.

10. Observatio singularis de obstruction pylori. Opera Omnia. C.V1 Obs. Frankfurt, Joh. Bejerus (1646): 541.

11. Professor Dunn. "George Armstrong MD (1719–1789) and his Dispensary for the Infant Poor". *ADC Fetal and Neonatal Edition* 87.3.

12. Czeizel A. "Birthweight distribution in congenital pyloric stenosis". *Archives of Disease in Childhood* 47.256 (1972): 978-980.

13. Carter CO. "The inheritance of congenital pyloric stenosis". *British Medical Bulletin* 17 (1961): 251-254.

14. Svenningsson A., *et al*. "Genome-wide linkage analysis in families with infantile hypertrophic pyloric stenosis indicates novel susceptibility loci". *Journal of Human Genetics* 57.2 (2012): 115-121.

15. Thomson J. "Observations on congenital hypertrophy of the pylorus". Edinburgh Medical Journal (1921): 261.

16. McKeown T and McMahon B. "Evidence of post-natal environmental influence in the aetiology of infantile pyloric stenosis". *Archives of Disease in Childhood* 27.134 (1952): 386-390.

17. Gerrard JW., *et al*. "Infantile pyloric stenosis". *Archives of Disease in Childhood* 30.154 (1955): 493-496.

18. Zhang AL., *et al*. "Infantile hypertrophic pyloric stenosis: A clinical review from a general hospital". *Journal of Paediatrics and Child Health* 29.5 (1993): 372-378.

19. Rogers IM., *et al*. "Serum cholecystokinin, basal acid secretion and infantile hypertrophic pyloric stenosis". *Archives of Disease in Childhood* 54.10 (1979): 773-775.

20. Ehrlein H and Shemann M. "Gastro-intestinal motility".

21. Hutchison R. "The Schorstein Lecture on congenital pyloric stenosis". *British Medical Journal* 2.2597 (1910): 1021-1024.

22. Jacoby NM. "Pyloric stenosis. Selective medical and surgical treatment". *Lancet* 1.7221 (1962): 119-121.

23. "Discussion on pyloric stenosis in infancy". Proceedings of the Royal Society of Volume XXXV. Section for the Study of Disease in Children (1941).

24. Habbick BF., *et al*. "Infantile hypertrophic pyloric stenosis: a study of feeding practices and other possible causes". *Canadian Medical Association Journal* 140.4 (1989): 401-404.

25. Zamakhshary MF., *et al*. "Seasonal variation of hypertrophic pyloric stenosis: a population-based study". *Pediatric Surgery International* 27.7 (2011): 689-693.

Volume 7 Issue 4 April 2018