

The Hyperacidity Theory of Pyloric Stenosis of Infancy Revisited

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ABSTRACT

The process of scientific inquiry into the cause of pyloric stenosis (PS) of infancy has run an erratic course. Over 100 years ago, it was proposed that hyperacid stomach contents in PS were somehow implicated in pathogenesis. This theory was quietly forgotten over the years with hyperacidity being presumed to be caused by the passive accumulation of acid behind a closed pylorus. The later finding that outlet obstruction itself leads to active hypersecretion of acid further reduced the interest in primary hyperacidity as the cause. In 1951 Dr. Bonham-Carter made the clear proposal that primary active hypersecretion of acid was indeed the cause. He suggested that the antacid effect of the anticholinergic drug Eumydrin was the reason that it often produced a long-term cure. Given that the drug was prescribed only for a short time, he was also implying not only hyperacidity pathogenesis but was also logically suggesting a temporary developmental hyperacidity around 4 weeks of age-the usual age of presentation. Sadly his comments and those of his colleague Dr. Harold Weller were not taken up by his listening colleagues. The primary hyperacidity theory has recently been precisely articulated and is reviewed in relation to present alternative theories. It can easily be shown to explain all the mysterious clinical features of this condition, including the first-born and male predominance. It also explains the family history. This article is presented as a tribute to the simple deductive reasoning of those early pediatricians who held on to their clinical observations and did not let them go.

Key words: Etiology, neonatal hyperacidity, neonatal hypergastrinemia, primary hyperacidity theory of pyloric stenosis of infancy, pyloric stenosis of infancy

A MOMENT IN TIME

On April 27, 1951, the Royal Society of medicine met to discuss the treatment of pyloric stenosis (PS) of infancy. Prof. Sir Kenneth Tallerman C.B.E. was in the chair.

Denis Brown F.R.C.S., David Levi F.R.C.S. (soon to become a hero of 100 consecutive pyloromyotomy without mortality!) and Dr. N.M. Jacoby all made contributions. A more peripheral contributor, one Dr. R.E. Bonham-Carter, recently qualified FRCP (Bonham to his friends) spoke from the floor---

“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.”^[1]

Dr. Bonham Carters voice (I like to think of it coming from the back of the hall) attracted no further recorded comment. There was no follow-up.

Eumydrin was the propriety name for the modified alcoholic tincture of atropine popularized by Svensgaard in 1935^[2]

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and reputed to be directly absorbed from the buccal mucosa thus ensuring more secure absorption in the vomiting child. Although the atropine effect in reducing the vagal cholinergic component of acid secretion was well understood, it was thought that the therapeutic effect was to relieve sphincter spasm.

Another voice, that of Dr. Harold Weller is also documented 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!

Atropine inhibits acid secretion in the conscious dog. It does so by inhibiting both the vagal cholinergic effect and the gastrin effect but not the effect of histamine.^[3] It also has a direct negative effect on the acid secretion from the parietal cell itself.^[4]

DISCUSSION

To put this RSM meeting and those comments in perspective, it came when great advances had been made in treatment. Pyloromyotomy was increasingly recognized as the preferred treatment. Medical treatment was accepted as suitable for early cases with a short duration of vomiting and before signs of dehydration were evident.

By contrast, there were few scientific inquiries into causation. Natural curiosity may have been subdued by two factors.

The presumed impossibility of discovering a single cause which would explain all the multiple substantiated clinical features

The male predominance/the family history/the acid problems in later life/the spontaneous long-term cure if the baby survives the first 3 months/the complete disappearance of the tumor once the sphincter is rendered incompetent by a scalpel stroke/the persistence of the tumour many years after a gastroenterostomy cure/the first-born predominance and the presentation around 4 weeks of age with a possible spontaneous long-term cure if the baby survives beyond 3 months.

Why bother? A long-term complete cure was now available at the stroke of a scalpel

The pediatric physicians were understandably reluctant to compete in treatment with successful pyloromyotomy. The dangers of tachycardia and other cardiac irregularities from atropine treatment were real, and the medical cure could take a worryingly long time.

The surgeons were only too pleased to have a simple, satisfying quick enduring surgical cure at their fingertips. They similarly were not overly keen to complicate matters or rock the boat by investigating the cause.

It is thus not surprising that Dr. Bonham-Carters implied proposal that a primary hyperacidity caused this condition was not followed up.

The earliest recorded assertion that hyperacidity was causal was proposed by Freund *et al.* in 1903.^[5] Indeed in those days part of the accepted treatment alleged to work was to instill chalk-like alkaline fluids into the stomach after gastric washouts. Occasional unmeasured references are made to the acid nature of the vomitus, but it is likely that this was falsely supposed to be due to retention of acid rather than a primary overproduction.

pH measurements of the fasting juice are relatively crude. It is a logarithmic scale of the concentration of hydrogen ions. It is only in the past 50 years when titratable acidity has been measured that it has been shown that primary hyperacidity is present both before and after pyloromyotomy.^[6,7] Both basal acid production and stimulated acid secretion are increased.

Acid accumulating behind a closed pylorus is not the explanation. PS babies have a primary inherited increased capacity to secrete acid.^[8] Indeed when acid secretion is increased in the fetus and neonate by giving pentagastrin injections to the pregnant bitches, PS indistinguishable from the human variety is produced in 28% of the 84 puppies. Even more puppies developed PS when the injections were also given to them directly.^[8a] Adults surviving PS more commonly suffer from problems with hyperacidity.^[8b]

Dr. Harold Weller’s statement is also worthy of further analysis. In those days clinical observations reigned supreme. Dr. Weller knew he was right. PS of infancy did come, and go, and eumydrin (an acid reducing agent) made it go.

There was a *dynamism* to this condition. It was not static. His observation, coupled to the time-related presentation of symptoms pointed to an age-related developmental mechanism. Neonatal hypergastrinaemia unchecked by rising gastric acidity causes a temporary peak acidity around 3 weeks of age before the negative feed-back matures and acid and gastrin secretion falls as a result.^[9,10]

It is only the PS baby with an already inherited enhanced acid secretory ability who falls victim to sphincter work hypertrophy from repeated acid induced contraction. In short, he develops PS.

Before this meeting and indeed after it, the pediatric establishment has otherwise been strangely silent on causation. The difficulty in equating so many clinical

features with one cause may have put them off. Perhaps an inherited primary hyperacidity similar to the increased parietal cell mass in the adult equivalent of PS-duodenal ulcer did not satisfy their need for a complicated explanation. For whatever reason, their corporate silence remained.

Thankfully the admirable Dr. Bonham-Carter and Dr. Weller had not read the script!

In recent years, other theories, predictably complicated, have emerged.

For example, an abnormal concentration of growth factors in the sphincter has been proposed. There are, for obvious reasons, no satisfactory control tissue samples. If they are more concentrated in the PS sphincter is because this is the mechanism by which a repeatedly acid-stimulated contracting sphincter hypertrophies.^[11]

Conversely, it is alleged that nitric oxide (NO), the muscle relaxant is present in reduced quantities in the sphincter. Again the control specimens have been postmortem normal sphincters at varying times after death.^[12] If NO is truly deficient why are the other gastrointestinal muscles not hypertrophied as well. Why just the sphincter?

The attempt to explain the condition on a genetic basis has also ground to a halt. The concordance rate between identical (monozygotic) twins is between 0.25 and 0.44.^[13] It is accepted that the inheritance of PS is multifactorial with a strong environmental influence.^[14]

The most astonishing observation is that not one of these 3 proposed causes attempts to explain the extraordinary established clinical features.

The primary hyperacidity hypothesis explains all of them.

Dr. N. M. Jacoby was another attendee at the 1951 RSM meeting. Some 10 years later he recorded a 1% mortality both in 100 personally operated pyloromyotomy, and 100 cases treated medically. The medical cases were considered less advanced. These mortality figures from medical treatment were a considerable advance in those days.

He made two very important observations^[15]

1. The dose of atropine needs to be accurately controlled with body-weight doses to avoid over or under dosage
2. Feeds should be temporarily stopped and restricted.

Sphincter work-hypertrophy requires both hyperacidity and feed-related gastric peristalsis. The peristalsis which churns

up and mixes the feed has been shown to be the most effective in producing high amplitude frequent sphincter contractions. Dr. Jacoby's observations on this topic were correct. Resting the stomach reduces the process of hypertrophy and encourages spontaneous cure.

3 hourly feeds produce a greater incidence of PS than 4 hourly feeds.^[16] The first-born predominance is only statistically apparent in the 3rd week of life-sufficient time for an anxious 1st time mum, to relatively overfeed.

CONCLUSION

The increasing availability of sophisticated, precise measurement devices, notably ultrasound, has gradually reduced the former reliance on continuous clinical observations. Yet accurate clinical observations, especially when repeated by the same observer (free from a shift system!), has been the bedrock of medical practice since medical practice began. This is particularly true in pediatric practice when the neonate has only his observable symptoms and signs with which to communicate.

Good examples of the essential contributions of precise clinical observations to the Primary Hyperacidity theory are provided in this manuscript by the contributions from Dr. Bonham -Carter, Dr. Harold Weller, and Dr. Jacoby.

A more comprehensive account of the evidence-based Primary Hyperacidity theory may be found in *The Consequence and Cause of PS of Infancy* Fred. Vanderborn MA and Ian Munro Rogers. FRCS Available from More Books(Lambert Academic Publishing0 ISBN 978-3-659-52125-6).

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OBITUARY: RICHARD BONHAM CARTER 1910-1994

Richard Bonham Carter was a pioneer in the diagnosis and clinical care of children with congenital heart disease; he was admired in Britain and internationally for his work.

Bonham (as he was usually called by his colleagues) was born into a family with wide ramifications, numerous members of which were and are prominent in public affairs. Graduated St. Thomas' Hospital Medical School, in London. 1 year after gaining his F.R.C.P. he attended the aforesaid Royal Society Meeting in 1951.

An appointment as House Physician to the Hospital of Sick Children, Great Ormond Street (GOS), was intended as a brief look at paediatrics, but it kindled an interest that dominated the rest of his medical career, during which he became one of the leading paediatricians of his generation. He was one of a dwindling number who practised for many years in the whole range of children's diseases. During the war he organised the provision of medical services to children evacuated from London. After enlisting he took part in the airborne drop at Arnham in 1944 where he was captured. The Cardiac Wing of GOS formally opened in 1988 was created largely due to his vision.

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