On the real cause of pyloric stenosis of infancy

An interview with Ian Munro Rogers, School of Medicine, Asian Institute of Medicine, Science & Technology, 08100 Bedong, Kedah Darul Aman, Malaysia.
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[Interviewed 4 Feb 2008; manuscript received 6 Feb 2008; accepted and published 11 Feb 2008]

Abbreviations: PS – pyloric stenosis; ESP – E.S.Prakash; IMR – Ian Munro Rogers

Background: Dr.I.M.Rogers has put forth the hypothesis that the inheritance of a higher than normal parietal cell mass and the ensuing hyperacidity is the primary cause of pyloric stenosis (PS) of infancy. See ref. [1] Rogers IM. The true cause of pyloric stenosis is hyperacidity. Acta Paediatrica 2006; 95: 132–136 available at http://www.blackwell-synergy.com/doi/pdf/10.1111/j.1651-2227.2006.tb02197.x. In this interview, Dr. Rogers answers some questions that come in the wake of this hypothesis.

1. ESP: If the hypothesis that hyperacidity is the ultimate cause of PS of infancy is correct, then, patients with pronounced hyperacidity (example, patients with Zollinger-Ellison syndrome) should also develop this complication. Your comments on this.

IMR: Patients with Zollinger-Ellison syndrome usually have acid-induced peptic ulcers – normally duodenal ulcers which perforate and bleed. Some of them will have PS or rather duodenal stenosis. I think newborns with hyperacidity are a different kettle of fish in the sense that the pyloric canal is very narrow, and even a small further reduction due to acid-induced pyloric sphincter hypertrophy would be enough to precipitate functional stenosis. At this point, other factors which further increase acidity begin to operate and a self-perpetuating process begins, culminating in PS. In a sense, this condition occurs because the rate of pyloric narrowing due to acid exceeds the rate at which age related widening of the pyloric canal occurs. This may be the reason why this condition presents within 3-4 weeks (a narrow interval indeed) of birth. Further, hypergastrinaemia, a phenomenon known to occur at this time (as alluded to my in my review [1]), is also likely to facilitate hypertrophy of the sphincter.

2. ESP: You have mentioned in your review [1] that in babies with PS, the negative feedback relationship between fasting gastrin and acid secretion is not evident until the third week of life. Is this also true for normal babies? If so, what does this indicate?
IMR: Yes, it is true for normal babies. In papers from Dr. MacGuigan's laboratory, Florida, USA [2, 3], normal babies were found to have hypergastrinaemia without postprandial elevation in gastrin up to 2 months of age. Between 3-4 months, fasting gastrin levels had fallen and postprandial gastrin responses became evident. The implication is that from birth to 2 months of age, gastrin is maximally stimulated and hence can not become higher when exposed to constitutional hyperacidity or after ingestion of a protein containing formula [2].

3. ESP: Are there any studies of plasma levels of secretin (the major humoral mediator regulating meal stimulated secretion of bicarbonate rich secretions from the gastrointestinal tract) in neonates with PS? The question comes as defects in neutralizing the effects of gastric acid might also predispose to the hyperacidity that you consider the prime pathogenetic mechanism in PS.

IMR: In 1975, we published a study [4] in which we evaluated the secretion of secretin in neonates. Curiously, the rise between day 1 and 4 was similar to that observed with gastrin. I know of no more investigations of secretin levels in neonates.

4. ESP: Is hyperacidity a consistent feature of PS of infancy?

IMR: Strangely, there have been very few studies of gastric acid secretion in PS. In 1979, we first reported basal hyperacidity in babies with PS compared to normal babies [5]. Heine et al [6] reported higher histamine induced gastric acid secretion in babies with pyloric stenosis before and 1 week after pyloromyotomy.

5. ESP: Is there evidence that a high parietal cell mass is inherited?

IMR: Babies with PS do secrete more acid than normal babies, and this persists after pyloromyotomy [6]. Supporting evidence for primary acidity is the observation that babies who are vomiting and are alkalotic at this age invariably have PS. The condition is strongly familial; it is much more common in males compared to females (4:1) as duodenal ulcers are in adults. Long term studies have documented problems with hyperacidity long after pyloromyotomy. Preterm normal male babies have been shown to secrete more acid than maturity matched female babies [7]. Thus, while there is no direct evidence of supernormal parietal cell mass, available evidence is indeed consistent with this theory.

6. ESP: Given your hypothesis, it is indeed surprising to me that the tumor does not disappear following gastroenterostomy; i.e., if hyperacidity were the primary cause of the growth of the pyloric sphincter, gastroenterostomy which allows drainage of acid should lead to a perceptible reduction in the size of the pyloric sphincter.

IMR: The extraordinary thing is that the pyloric tumour disappears within days of pyloromyotomy [8] and within weeks of successful medical treatment [9]. Regarding the failure of the tumor to regress following gastroenterostomy [1], it simply may be that unless the hypertrophied pyloric sphincter is divided, it can not relax or dilate with the passage of food. Further, a posterior gastroenterostomy may not drain the antrum well. A poorly drained alkaline antrum is a classical way of increasing gastrin levels -
especially after vagotomy, and thus the continuing presence of trophic factors such as gastrin may in addition explain the persistence of the pyloric tumor following gastroenterostomy.

7. **ESP:** Alternate causes for pyloric stenosis have been proposed; for example, a relative deficiency of neuronal nitric oxide synthase at the sphincter [10] may be primary to the condition - something like in achalasia. Your comments on this:

**IMR:** Deficiency of nitric oxide explains the pylorospasm. It does not explain the predominance of this condition in males; neither does it explain spontaneous self-cure after a certain age. The failure of this condition to recur after simply dividing the sphincter and the very good response to adequate medical therapy is also not explained. How does it explain the persistence and complications of high acidity after pyloromyotomy?

8. **ESP:** The observation that rats with an artificially narrowed pylorus secrete more acid and gastrin in response to a meal and the fact that gastrin producing antral cells become hyperplastic [11] in this model is interesting but in this instance hypergastrinaemia and hyperacidity are secondary to pyloric stenosis not the cause of it. What is your opinion?

**IMR:** First, the hypothesis that primary hyperacidity is the cause of PS is based on the premise that all babies are potentially at risk of acid induced pylorospasm at around 3-4 weeks; however, babies who develop PS are most vulnerable because the burden of constitutional hyperacidity proves too great. Secondly, in my review [1], I cited the study by Omura et al [11] to suggest that once PS is established, there are mechanisms that maintain hyperacidity. The authors [11] demonstrated hypergastrinaemia secondary to PS. Furthermore, there is evidence for a gastrin independent pyloro-oxyntic local neural reflex [12] that can induce acid secretion. Indeed, Talbot [13] has reported improvement in symptoms in patients with peptic ulcer induced gastric outlet obstruction treated with proton pump inhibitors.

9. **ESP:** Please tell us what you believe would be the most important research questions that need to be investigated in the management of infantile hypertrophic PS?

- **To evaluate the benefit of intravenous proton pump inhibitors after making a diagnosis of PS and while awaiting surgery.** Indicators of improvement would be reduced acid and volume loss from the nasogastric aspirate and a reduction in metabolic alkalosis. A period of 2 days is not unusual between diagnosis and surgery; this should allow an adequate appraisal. Retrospective data on patients undergoing surgery for PS on whom 2 acid base studies (preoperatively and intraoperatively) are usual would allow a comparison to be made with the acid base changes as a result of treatment with proton pump inhibitors. In adults who have high acidity and who vomit; i.e., adult pyloric stenosis, preoperative administration of proton pump inhibitors is standard therapy to reduce loss of fluids as well as acid. Indeed, in some instances, the alleged pyloric stenosis is functionally improved or cured by this treatment alone – so the question is why babies in whom acid base and volume homeostasis is less secure should be denied this treatment. I believe that the baby diagnosed early enough to have PS but without access to safe surgery would be advantaged by the...
sole temporary use of proton pump inhibitors while awaiting the enhanced possibility of spontaneous cure. That is my opinion.

ESP: Thank you very much Dr. Rogers for sharing your thoughts with us.

IMR: Thank you very much.

**Conflict of interests:** none declared.

**References:**


4. Rogers IM, Davidson DC, Lawrence J, Buchanan KD. Neonatal secretion of secretin. Archives of Disease in Childhood 1975; 50: 120-122. Abstract at http://adc.bmj.com/cgi/content/abstract/50/2/120


Editor’s note: I invited this manuscript from Dr. Rogers, reviewed and edited it. Both Dr. Rogers and I work in the School of Medicine, Asian Institute of Medicine, Science & Technology, Malaysia, but that wouldn’t affect my review and disposition of this manuscript – E.S.Prakash, Editor, Medical Physiology Online.