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Neonatal bacterial attack-unraveling the mysteries of acid defense

Ian Munro Rogers*

Adjunct Surgical Faculty, AIMST University, Kedah, Malaysia

Correspondence*: Ian Munro Rogers, FRCS, FRCP, PGMedEdu, 21 Strathview Place, Comrie, Perthshire PH62HG, Scotland. **E-mail**: irogers2000@hotmail.com

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ABSTRACT

This review article examines how gastric acidity develops and is maintained during the first 4 weeks of life. An initial maternal transfer of gastrin is followed by progressively increasing baby gastrin, not yet restrained by the rising acidity. When negative feedback matures at around 17 days, there is a predictable and real temporary peak acidity which is followed by controlled and independent baby acid secretion.

INTRODUCTION

We have all made the same journey. The journey from a safe warm sterile protective place to a potentially cold hostile new environment surrounded by many dangers. In short, we have all been born! Not least of the dangers, we have faced is that of attack by other competing small forms of life-bacteria.

The first maternal gift

We enter the outside world gifted with protective but temporary systemic immunity from our mother (her first gift!) but, as far as gut infections are concerned, we are largely on our own. The major form of baby defense is, of course, gastric acid. Few bacteria survive acid exposure. The more acid-the better. This paper will outline the ways in which normal physiology ensures that neonatal acidity is maintained during the critical first month at levels that will have kept us all safe.

The second maternal gift-gastrin

My interest in this subject was awakened by reading a paper, written 80 years ago by Dr. Robert Miller, an anesthetist who in later life practiced in Texas, US [1] From a study involving 50 healthy new-born babies he had shown that a wave of hyperacidity occurred within a few hours of birth and gradually reduced over the next few days. In those pre-gastrin days, he correctly assumed that a chemical was being transferred from mother to baby during labor to cause neonatal acid secretion. It would be another 20 years before the acid-producing hormone gastrin would be discovered. [2]

Maternal gastrin rises progressively during pregnancy, peaks at labor then quickly falls within 30 minutes of birth.[3] The placenta has been found to have very high gastrin concentrations.[3] The implication was that it was transferred from there to the baby during labor.

In a historic paper in 1970 Bruckner et al. conclusively showed that, at least as far as the dog was concerned, all of this was true.[4] Gastrin was transferred and, what is more, it caused acid secretion in the fetus. Miller had been proved correct. This maternal gastrin gift no doubt is the explanation why gastric pH at birth is lower whenever maternal contractions in labor form part of the birth process-the placental transfer presumably aided by uterine contractions. [5]

The gastrin gift also was known to increase the maturation of the gut in general and the gastric mucosa in particular.[6] Mother was preparing you and me for an independent life!

The road to independence

What happens when maternal gastrin is metabolized and is no more? The half-life of the common form of gastrin G 17 is about 17 minutes. What happens to our baby gastrin? Like many discoveries, chance played a part in unraveling the mystery. Our group measured fasting cord gastrin levels at birth and at 4 days of age. The day 1 level was higher than the

maternal level and higher than the usual fasting adult level. Surprisingly, the day 4 level, by now entirely baby gastrin, was several times higher again. In addition, there was a strong statistical individual correlation between day 1 and day 4 in the 11 babies born by oxytocin induction. The 9 spontaneously born babies had a higher cord level and there was no individual correlation with day 4. We presumed that the maternal gastrin contribution may have been confined to the spontaneously born babies [7] (Fig.1).

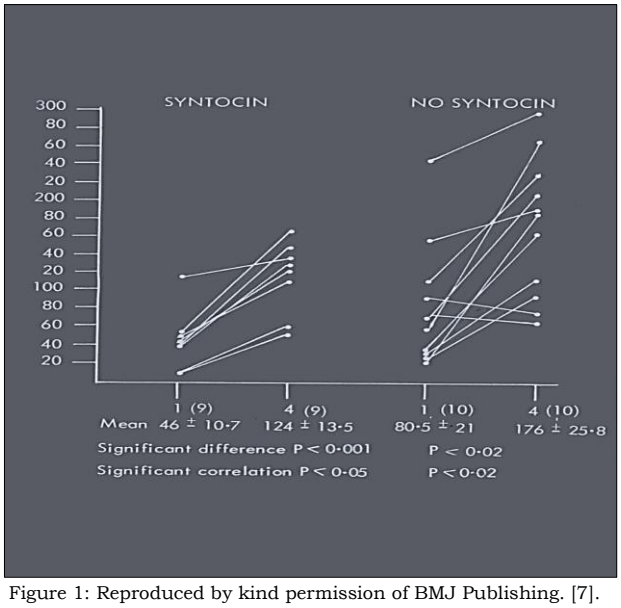

Figure 1: Reproduced by kind permission of BMJ Publishing. [7].

This was the first time that neonatal hypergastrinemia had been reported. Others soon after confirmed these findings.[8-11] Euler also reported that on the first day of life, there was no post-feed gastrin increase. The implication was that gastrin was being already maximally stimulated and feed could not stimulate it further.[12]

In our 1974 paper, we pointed to the possibility that the normal negative feedback between antral acidity and gastrin secretion did not apply. It had yet to mature. We did so because at birth the stomach is alkaline from swallowed liquor. On day 4, it was known that the fasting stomach was acidic. Thus, gastrin was rising hugely at a time acidity was also rising. The negative feedback did not appear to be working.[6] The baby was behaving like a mini-Zollinger Ellison syndrome.

In retrospect, immature negative feedback alone would explain the gastrin rise. It would also explain rising acidity. Both would be expected to peak when the feedback begins to be established.

The synchronous acid and gastrin rise after birth has been observed by others. Lucas in 1980 while documenting the effect of age and feeds on several neonatal hormones, found that at 13 days the high fasting gastrin levels fell, and for the first time, feeds produced a gastrin increase [9] (Fig.2). They offered no explanation for this phenomenon and simply reported their findings.

Moazam in 1984 made similar observations and commented that in the early weeks there appeared to be “an insensitivity” of the normal negative feedback between gastrin and acidity.[10]

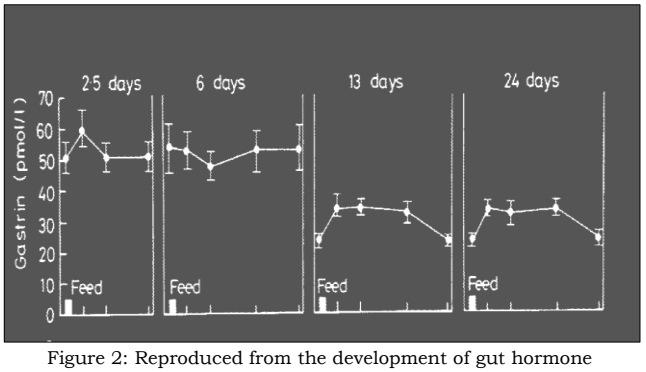

Figure 2: Reproduced from the development of gut hormone responses to feeding in neonates. By kind permission of BMJ publishers. [9]

It can be clearly seen in Fig.2 that the early fasting gastrin levels are elevated without an increase after food. Later, at 13 and 24 days, the fasting gastrin levels have reduced, and a post-feed increase has developed. These findings are consistent with early maximal gastrin and acid secretion. In the early week, feeds cannot stimulate gastrin further. In later weeks, with a sub-maximal gastrin secretion, feeds can produce an additional gastrin secretion [9] (Fig.2).

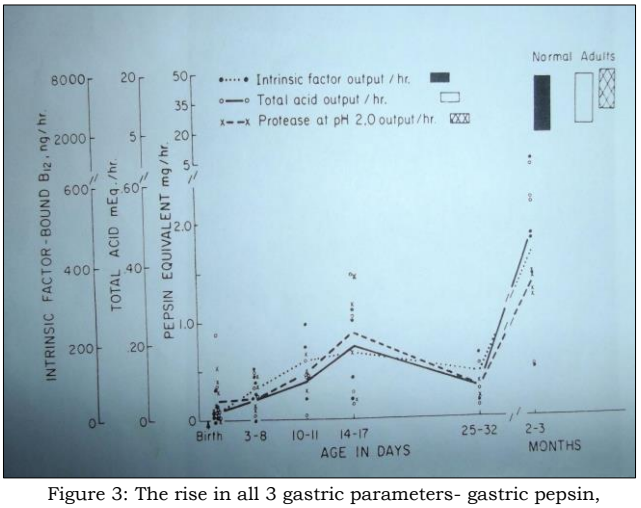

Figure 3: The rise in all 3 gastric parameters- gastric pepsin, intrinsic factor, and acid secretion peaks at between 14-17 days in normal term babies. Reproduced by kind permission of Springer Publishers. [13]

When feedback maturity is gained, there is a peak temporary acidity which thereafter falls as acidity becomes under gastrin control (Fig.3). The consequence during this phase of our lives is that the early temporary maternally induced acidity is maintained for several weeks at a time when baby acid secretion alone may be insufficient. The imputed insensitivity of the baby-gastrin/gastric acidity negative feedback is the key.

Acid independence at last

It was Dr. Miller who first described the relatively poor preparation of our gastric mucosa for the onslaught of milky feeds. The development of sufficiently mature gastric mucosa took time. It has been calculated that weight for weight, the milk consumed by babies would translate into 10-12 liters of milk in the adult. The baby's stomach has much digestion to do! [1]

The artificially elevated gastrin during the immature feedback time has another very important effect. All components of the cellular activity and structure of the gastric mucosa-parietal cells, intrinsic factor, and pepsin- all are stimulated to grow.[6] All reach a peak when feedback matures.

The development of our secure digestive system and our acid defense system against enteric microorganisms is now complete. We are (or should be) safely on our own. This development system is neat, smart, and efficient.[14] The temporary nature of hyperacidity means we are not necessarily encumbered with damaging hyperacidity in our adult years.

The end of our neonatal journey

Acidity and gastrin secretion now react one with another to establish mutual restraint and protect us in a dynamic way from excesses of either. The capacity of all the gastric mucosal elements- acid, intrinsic factor, and pepsin- are now already primed by earlier hypergastrinemia to equip us for our adult journey.

Our journey to complete independence is now over. Homeostasis and the internal milieu are preserved. Our adventure is complete.

Post-script

The temporary peak acidity achieved in all normal babies passes nearly always unnoticed. In babies who inherit a large Parietal Cell Mass, this peak may produce critical hyperacidity deemed by some, including the author, as the stimulus for frequent strong contractions of the pyloric sphincter which lead to pyloric stenosis of infancy (PS). By these means, the time-sensitive clinical presentation, male preponderance, and occasional later self-cures may be explained.

PS in a sense is the price to be paid for the acid bacterial defensive system in the neonatal period.[14]

The increasing use of acid-blocking drugs in the neonatal period clearly will carry the risk, theoretical and real, of promoting dangerous enteric infections.[15-17] It will also be a credible explanation for the recently reported fall in the frequency of P.S in Europe. [18, 19]

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