From TUMS® to Tragedy

In 2000, through a series of mergers, GlaxoSmithKline acquired TUMS. I can almost hear the boardroom discussion.

CEO: Well, gentlemen, TUMS is a good brand. Makes us a couple hundred million a year, but, I'm sure we can do better. Any ideas?

Joe: Problem is that "heartburn" is not something that people take very seriously. They only use TUMS when they need it.

Harry: Not true. Our promotion to medical organizations has paid off big time. All over the world, doctors are recommending TUMS as an effective calcium supplement to be taken every day.

Chief Scientific Officer: What? Are you kidding me? You marketing fellows have gone too far. Do you know that we have absolutely no evidence that TUMS can support bone density, or provide any benefit at all outside the stomach?

Harry: What are you talking about? The product is made of sugar and calcium!

CSO: And it's an antacid, for crying out loud! In order for calcium to be absorbed, it has to be ionized by stomach acid.

Harry. Picky picky. You scientists just don't get it. We're selling close to 40 billion bottles of this product a year. I don't hear any complaints from the sales group.

VP Sales: No, we're actually delighted. But we have an even better idea. Let's create a scarier name for heartburn, and make a prescription drug to treat it. When fluid comes up from the stomach into the esophagus, it's called reflux. What about Gastric Reflux Syndrome?

VP Marketing. Not scary enough.

CSO. Well, technically speaking, it is gastro-esophageal reflux.

VP Marketing: Add the word DISEASE and you've got it. Gastro-esophageal Reflux Disease.

CSO. Well, it's not really a disease; more of a condition or process.

VP Marketing: Nope, we're going with Gastro-esophageal Reflux Disease. GERD for short. Why didn't we think of this before? Doctors love an easy fix for a disease, and there are millions of people with heartburn I mean GERD.

And thus Tagamet® was born, followed by Zantac® and Pepcid®. These H2 receptor blocker went beyond the acid-neutralizing effect of TUMS to actually suppress acid production by the stomach. And they worked quite well.

Until other drug companies, who missed the blockbuster market for H2 blockers, upped the ante. If H2 receptor blockers *reduced* stomach acid production, by golly, there must be a way to stop it altogether.

Thus Prilosec, Prevacid, Protonix and Nexium were born. These are proton pump inhibitors (PPIs) that directly affect the ability of the stomach to produce hydrochloric acid. Since they were more powerful than the H2 blockers, and promoted with the most extravagant advertising campaign in pharma history, doctors wrote millions of prescriptions in the first year. By 2005, sales topped $13.9 billion in the US alone. [1] Worldwide, these drugs now account for more than $25 billion in annual sales. [2]

No one is going to deny the value of these drugs in acute care – for the treatment of ulcer or serious reflux disease, but the vast majority of sales fall into the inappropriate use category. This includes people who were prescribed a PPI for short-term use, but were never taken off the drug, as well as millions of people who self-medicate with over-the-counter PPI's. Prilosec (Omeprazole) and Nexium (are both available without a prescription.

Costco now has their own brand of Omeprazole. Disount coupons are available on line. Prilosec was buy one get one free at a local drug store last month. **THIS is a serious problem**, and except for a few editorials in GI journals, no one is talking about it.

So lets talk about it.

The Science

Antacids like TUMS and Rolaids™ act by neutralizing stomach acid to a small but significant degree. H2 receptor blockers like cimetidine (Tagamet™) raise the pH of the stomach from 1 to maybe 2. PPIs can increase the pH of the stomach from 1 to 5. And your science teacher will explain why that is more dramatic than it appears. You see, pH is a logarithmic scale, where each unit represents an order of magnitude. This means that PPI's basically (excuse the pun) stop acid production altogether.

The Side Effects

Your stomach secretes hydrochloric acid for a very good reason. Actually, a number of very good reasons. Stomach acid activates pepsin, an important digestive enzyme. Without pepsin, protein digestion is seriously impaired. Calcium and other minerals must be ionized by stomach acid in order to be absorbed. Thus PPI use is associated with increased risk for osteoporosis and fractures. The absorption of vitamin B12 is also reduced in the absence of HCL.

PPI's can affect the absorption and metabolism of a raft of prescription drugs. Manufactuers simply say: "May interfere with drugs for which gastric pH affects bioavailability;" which is good information for your doctor, but how is the average Walgreens shopper going to figure that out? Remember, the average 65 year old in America uses six Rx drugs in a year, many concurrently. PPI's can decrease the absorption of some meds and increase blood levels of others. With digoxin, a drug commonly prescribed for heart disease, this increases risk for a serious adverse effect including life-threatening arrhythmias.

PPI's decrease the activity of Clopidogrel (Plavix™), a common blood thinner. So think about this: Millions of people take Plavix or the generic version every day to prevent a heart attack or stroke. But even a slightly increased dose of their PPI (like some people would take on Thanksgiving) can completely inactivate this drug.

Then there's the infection issue. One of the principle functions of stomach acid is to destroy microbes that accompany our much of our food. So it was only a short time before it was apparent that people using PPI's were more prone to gastric infections, including clostridium Clostridium difficile (C. diff) a bacterium capable of causing serious illness or death.

There's more. Even perfectly healthy people can aspirate small amounts of fluid from the stomach into their airways. This commonly happens at night when we are lying down. Recent research suggests that, in addition to C.diff, the bacteria that cause pneumonia also find a happy home in stomachs of people using PPIs, which this accounts for the increased risk for pneumonia in this population. [3]

The main point
The likelihood of serious adverse effects increases the longer you take a PPI. Thus the FDA-mandated prescribing information states clearly that the drugs are only to be used for 14 days. This is insane for three reasons.

A. GERD is rarely a self-limiting disorder, without significant diet and lifestyle changes.
B. When patients stop their PPI, they experience a wicked side effect known as acid rebound that often sends them to the ER, where the standard of care is…... you guessed it, **another PPI**.[4]

Thus everyone (the drug companies, conventional doctors, pharmacies and retailers) are participating in an irrational vicious cycle with no apparent solution. To the average Joe, all the ads lead to one conclusion: "Hey, if these drugs work so well that I can wash my pizza down with a six pack of beer and not even burp, why not get 24 hour "protection" with timed release Nexium, now also available without a prescription.

If you think I'm being too cynical, the Nexium OTC website site actually states:

> Nexium® 24HR works by blocking acid directly at the source, giving you complete protection from frequent heartburn – no matter what triggers it.[5]

Of course at the bottom of the page, it states:

> Use as directed for 14 days to treat frequent heartburn. Do not take for more than 14 days or more often than every 4 months unless directed by a doctor. Not for immediate relief.

"As directed" by whom? Your next-door neighbor? An ad on TV or the discount coupon you got in the mail?

This "advice" is coming from everywhere. *The Harvard Health Newsletter* states:

> "If your symptoms are typical for gastroesophageal reflux (GERD, or simply, reflux), the first step is usually to try a medication such as omeprazole (Prilosec) or lansoprazole (Prevacid)."

I would argue that powerful drugs with common side effects are NOT the first step, and I wonder when this formerly useful publication became the Harvard Drug Letter. The first step, backed by published biomedical literature, is:

A. Diet and lifestyle changes: Avoid overeating. Eat slowly. Chew well. No eating on the run; especially not while driving. No food after 7:00 PM.

B. Aloe Vera, probiotics and possibly digestive enzyme supplements. [6],[7],[8]

Onward!

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