

# Two mothers discover GERD is inherited and pave the way for a cure

Elizabeth Pulsifer- Anderson

Pediatric Adolescent Gastroesophageal Reflux (PAGER) Association – Frederick, MD, USA

## How The Crazy Idea Developed

- In the beginning, there were a handful of parents who assembled to help each other cope with a frustrating disease.
- Eventually, those parents began to discover patterns that they didn't find in the medical literature
- Parents began to divide pediatric GERD into subtypes:
  - Inherited type which is severe and not out-grown
  - Food allergy or protein intolerance type
  - Gut motility, stomach stasis, intermittent pyloric spasms
  - Neurological, autonomic instability or GERD of prematurity
  - Mechanically induced GERD associated with low muscle tone, high abdominal muscle tone, constant supine posture, or lax ligaments at the lower esophageal sphincter



Support groups are much more than a place to whine – they can be a source of ideas.

## The Quest for a Cure Begins

Coming up with the idea was easy



It was just a matter of stumbling over something nobody else was in a position to notice.

As more parents joined the group, it became apparent that some families had a strong history of inherited disease.

The group began a newsletter and openly discussed the logical idea of inherited GERD in the publication

*"The word filtered back from the medical community that discussions of inherited GERD in the newsletter were giving the group leaders a reputation as crazy zealots"*



The group leaders decided to preserve their reputation by being selective about sharing this idea.

## The Many Hurdles

The biggest ones are attitudes



Develop rational drugs that do more than mask the symptoms of GERD for children and adults

You could be Here

Target current treatments to individuals based on genetic typing of the disease

You could be Here

Bring in a corporate partner to invent a genetic test that compliments clinical judgment and current testing

You could be Here

Identify the exact gene and begin to unravel the true cause of inherited GERD

Convince pediatricians and gastroenterologists to help find families for the study (10 years so far)

We are Here

Convince the peer reviewers for JAMA this isn't such a crazy idea (12 months in review)  
Published 7/2000

Collect samples and identify a section of chromosome 13q14 where the GERD gene is (2 years)

Use family trees to document inheritance patterns (6 months)

Find researchers who believe (3 years)

Find families with many affected members (12 months)

## It's an Attitude Thing...

The Good...

The researchers we found had already mapped genes for hereditary pancreatitis and familial Crouzon's Disease. They not only believed us, they were delighted to have an opportunity to map a gene for a third disease that was not considered inherited at the time.



JAMA editors were skeptical of an idea so far outside the paradigm. Statistical geneticists outside the team were brought in to review the submitted article.



The Bad...

One family was told that having two children with severe GERD was a 'guarantee' that the next pregnancy would not produce a child with GERD. It produced twins with GERD.



This incorrect prediction led the mother to renew her quest for open-minded researchers

The Useless....

In 2005 the North American Society for Pediatric Gastroenterology and Nutrition issued a press release stating that the concept of inherited GERD is now well accepted by most pediatric gastroenterologists. But, according to the same statement, even those who believe in the concept don't bother mentioning it to their patients and don't help recruit patients for the study.

...And the Ugly

A leading pediatric gastroenterologist was asked to comment on the JAMA article. He told a reporter from a major newspaper, "GERD is absolutely not genetic and the whole crazy theory was dreamed up by a couple of hysterical mothers with too much time on their hands who are imagining a genetic connection."



Sigmund Freud's grave

## Are YOU Open-Minded?

- ? Do you think of patient groups as needy and wanting things from you?
- ? Are you missing an opportunity to receive ideas from patients that might lead to breakthroughs rather than dosage tinkering?
- ? Are you and your colleagues open-minded enough to take advantage of the unique opportunities offered by a true collaboration with patients?
- ? Are you ready to go out today and find a laughable patient theory to test?
- ? Are you ready to work with a group that will find all your study subjects, raise funds and send you chocolate?

! There is no more powerful way of identifying unique research needs than brainstorming with patients and patient organizations.

Overheard at NIH

"When I hire researchers to look for a cure for disease, I try to find PhDs rather than MDs. Most MDs are trained to think they already know the answers... and most PhDs are trained to wonder whether we are even asking the right questions"



## Literature cited

Hu, Fen Ze MS; Preston, Robert A. PhD; Post, J. Christopher MD, PhD; White, Gregory J. BS; Kikuchi, Lee W.; Wang, Xue MD; Leal, Suzanne M. PhD; Levenstien, Mark A. BS; Ott, Jurg PhD; Self, Thomas W. MD; Allen, Gregory MD; Stiffler, Richelle S. LSW; McGraw, Caroline; Pulsifer-Anderson, Elizabeth A.; Ehrlich, Garth D. PhD. *Mapping of a Gene for Severe Pediatric Gastroesophageal Reflux to Chromosome 13q14*. JAMA 2000;284:325-334. [Context: Gastroesophageal reflux (GER) has not previously been widely regarded as a hereditary disease. Results: In these families, severe pediatric GER followed an autosomal dominant hereditary pattern with high penetrance. A gene for severe pediatric GER was mapped to a 13-cM region on chromosome 13q between microsatellite markers D13S171 and D13S263.]

## Acknowledgments

We thank the open-minded research team headed by Garth Ehrlich and Chris Post at the Center for Genomic Sciences, Allegheny General Hospital, Pittsburgh.



## Collaboration Opportunity

Is your company interested in developing a novel treatment or potential cure for acid reflux disease?

Please contact Beth Anderson, Director, Pediatric Adolescent Gastroesophageal Reflux Association at [gergroup@aol.com](mailto:gergroup@aol.com) or Garth Ehrlich at [gehrlich@wpahs.org](mailto:gehrlich@wpahs.org)

[www.reflux.org](http://www.reflux.org)

