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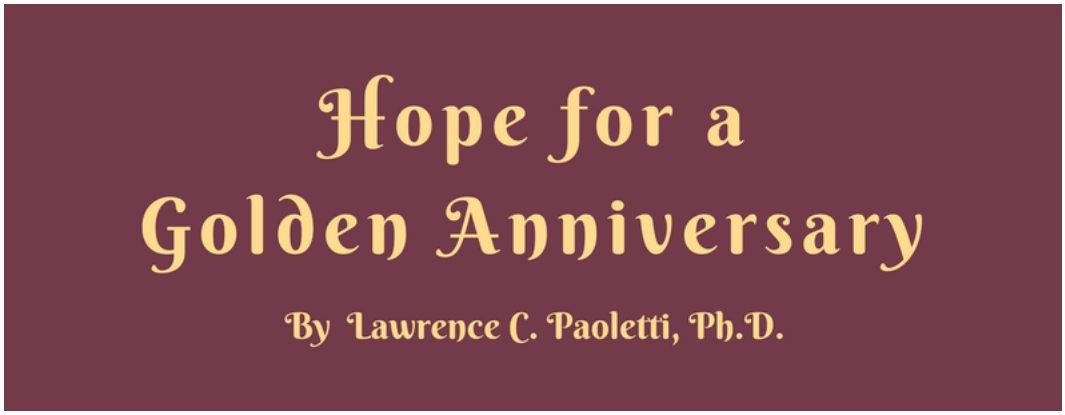


What if I told you a story of a story?

On October 27, 1993, I was one of the few chosen to deliver a presentation at the annual seminar program called the Proceedings of the Society of the Channing Laboratory. The Channing Laboratory (http://videocenter.brighamandwomens.org/files/dmfile/Speizer_Frank.pdf), then a division of the Department of Medicine at the Brigham and Women's Hospital in Boston, had a storied past as a premier research institute on infectious diseases in the city, if not the country. Past and present luminaries in the field attended the one-day event that showcased the recent achievements of laboratory scientists comprised of infectious disease epidemiologists and basic science researchers.

When I took the stage that day I had completed my postdoctoral training with Dennis L. Kasper (https://collections.countway.harvard.edu/onview/exhibits/show/maximizingmicrobiology/kasper) and Michael R. Wessels (https://connects.catalyst.harvard.edu/Profiles/display/Person/32348) at the Channing Laboratory, and I was a newly minted Assistant Professor of Medicine. More importantly, the data we accumulated over the prior 5 years on studies in animals of a new conjugate vaccine against group B *Streptococcus* (GBS), led to an all-important phase 1 trial in humans. I was about to present for the first time data from that clinical trial, and here is how I began my presentation:

> ***Today I'd like to tell you a story. The year was 1973. The place was the Channing Laboratory, Boston City Hospital, Boston, Massachusetts. The event was the annual Proceeding of the Society of the Channing Laboratory meeting.***
>
> ***Dennis Kasper, a postdoctoral infectious disease fellow with Dr. Edward H. Kass (http://oasis.lib.harvard.edu/oasis/deliver/~med00006), was listening to a presentation by Carol J. Baker (https://www.bcm.edu/people/view/carol-baker-m-d/b1666ae9-ffed-11e2-be68-080027880ca6), who was an infectious disease fellow with Dr. Maxwell Finland (http://www.nasonline.org/publications/biographical-memoirs/memoir-pdfs/finland-maxwell.pdf). The title of Carol's talk was: "Group B Streptococcal Infection in Infants: The Importance of Various Serotypes." Carol presented data that showed an increase in the number of neonatal cases of infection due to an encapsulated bacterial pathogen called Streptococcus agalactiae or GBS.***
>
> ***Later, Dennis and Carol chatted. They discussed the idea of combining her knowledge of the epidemiology of GBS and other encapsulated pathogens that caused meningitis in infants with his interests in bacterial polysaccharides. Their shared goal was to develop a vaccine to prevent GBS disease.***
>
> ***Today, I have the honor of presenting the results of Drs. Baker and Kasper's 20 years of dedicated and focused research toward the development of a vaccine against GBS disease and the results of a phase 1 clinical trial of this vaccine performed at Baylor College of Medicine.***

I concluded my concise presentation with these naïve words of high hope:

> ***I am optimistic that by the Silver Anniversary of that famous meeting between Drs. Kasper and Baker, we will be on the threshold of providing to clinics worldwide, a licensed conjugate vaccine against GBS disease.***

My closing words that day reflected a profound unfamiliarity with the world and priorities of the biopharmaceutical industry. In my mind, we had made significant improvements to the first version of a GBS polysaccharide vaccine (http://www.nejm.org/doi/full/10.1056/NEJM198811033191802) by coupling it to tetanus toxoid, a protein with a long history of safe use in children and adults including pregnant women. We had shown in several animal models that the conjugate vaccine induced the right type of antibody (IgG) that killed GBS and it also protected against GBS disease. And now we

demonstrated that a conjugate vaccine (https://www.jci.org/articles/view/119042/version/1/pdf/render) (prepared with GBS type III polysaccharide coupled to tetanus toxoid) was safe and immunogenic in healthy adults. What more could any company need to move ahead with this vaccine? After all, the success of the first conjugate vaccine licensed for human use, *Haemophilus influenza* type b conjugate vaccine, was already well documented (https://www.cdc.gov/mmwr/preview/mmwrhtml/00041736.htm).

The answer to that simple question is actually quite complicated.

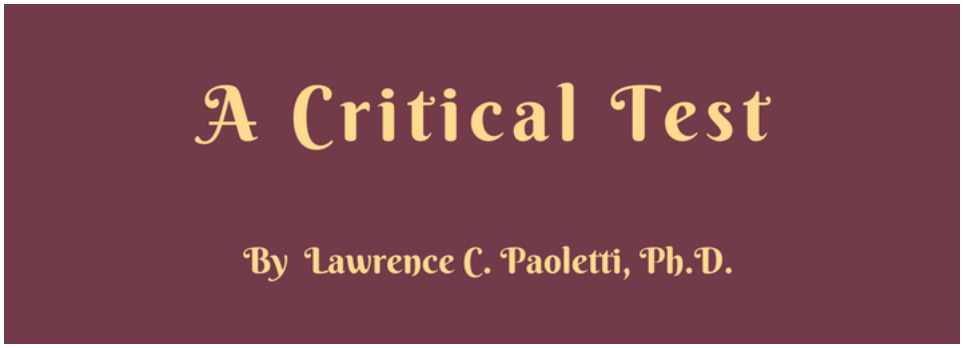
Suffice it to say that today there is a better acceptance (https://www.ncbi.nlm.nih.gov/pubmed/26307234) of vaccines administered during pregnancy, a greater understanding of the worldwide GBS disease rates (https://www.ncbi.nlm.nih.gov/pubmed/23973349), of emerging serotypes, and of disease-causing sequence types. We have refined assays to accurately measure the amount of functional antibody (https://academic.oup.com/cid/article-abstract/63/6/746/2389118/The-Protective-Value-of-Maternal-Group-B?redirectedFrom=fulltext) raised to vaccines. Importantly, there are more GBS awareness groups that disseminate information on screening and prevention measures to those who need it the most.

Today we have amassed a larger dataset on the safety and immunogenicity of GBS conjugate vaccines prepared by our group (http://www.nature.com/nrmicro/journal/v4/n12/full/nrmicro1552.html) as well as scientists at Novartis (https://www.ncbi.nlm.nih.gov/pubmed/26942345), now GlaxoSmithKline (https://www.gsk.com/en-gb/). That three very different groups (PATH (http://sites.path.org/cvia/our-disease-targets/group-b-streptococcus/)- an international nonprofit organization, Minervax (http://minervax.com/) - a privately held biotechnology company, and Pfizer (http://press.pfizer.com/press-release/pfizer-begins-phase-1-clinical-trial-evaluate-investigational-group-b-streptococcus-va) – a global biopharmaceutical company) share a common goal to bring a GBS vaccine to market, provides renewed hope that prevention of GBS disease is within reach.

What if by 2023 – the Golden Anniversary of that famous meeting between Drs. Kasper and Baker – the world has a licensed vaccine that prevented prenatal, perinatal and adult GBS disease?

And what if by 2033 we write stories about stories on how we made GBS disease history?

Click **HERE (/a_critical_test.html)** to read Dr. Paoletti's firsthand account of designing a test to determine if a GBS vaccine was safe for pregnant women and their unborn babies in:



Dr. Paoletti (https://connects.catalyst.harvard.edu/Profiles/display/Person/25737)'s research career focused on the development and testing of GBS conjugate vaccines. He is now a Research Associate at Harvard

Medical School and a paid consultant for PATH's GBS vaccine program.