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By Conner Gorry

Dr Vicente Vérez Bencomo is a world-renowned scientist who led the team that discovered and developed the Cuban *Haemophilus influenzae* type b (Hib) vaccine using a synthetic antigen – the first of its kind in the world. Educated in Cuba, Russia, and France, Dr Vérez has received numerous awards for his groundbreaking work, including the World Intellectual Property Organization's Gold Medal (2005), and the Cuban National Chemistry Award (2006). The Cuban Hib vaccine is undergoing evaluation by the World Health Organization for vaccination packages for use in the developing world.

Dr Vérez has published widely in international scientific journals of impact and is the Cuban representative to the International Carbohydrates Organization and Senior Member of the Cuban Academy of Sciences. He is currently Director of the Center for the Study of Synthetic Antigens, under the aegis of the University of Havana's Chemistry Department.

He sat down with **MEDICC Review** to talk about the global burden of *Haemophilus influenzae* type b, what motivates him as a scientist, how synthetic antigens might be applied to other vaccines, and what he is currently working on.

MEDICC Review (MR): Tell us about your team's development of the *Haemophilus influenzae* type b vaccine using a synthetic antigen. What might it mean for other vaccines?

Vicente Vérez (VV): First of all, conjugated vaccines are complex; they are produced using complex and costly technology.

So even though *Haemophilus influenzae* type b (Hib) is important for the world, recommended even in the Extended Immunization Program (EIP), the cost is what largely prevents this vaccine from reaching all children. [The Cuban Hib vaccine currently costs about USD\$12 for the full, four-shot course – twelve times what most developing countries spend per child on general immunizations, Eds.].

In this case, where we know the vaccine works, but expensive technology keeps it from reaching the whole world, we have two possible avenues for development. One is to try to simplify that same technology to reduce costs.

Work has been done on this for years and there has been some progress. The other is to look for alternatives; one of those alternatives is to make a synthetic antigen.



Center for the Study of Synthetic Antigens

MR: But the price of this vaccine is still prohibitive for many public health systems. Is there hope for making it more affordable?

VV: We're now scaling up production, so we're really going to have the capacity to lower the price. In my estimation, production will continue to grow and should

reach 50 million doses a year. [Cuba currently produces around 10 million doses a year; domestic demand is fewer than one million annually, Eds.]. This is positive, it's hopeful, since it's another alternative for *Haemophilus* vaccine production; even if the money was available to vaccinate all the children in the world tomorrow, current production wouldn't be enough to satisfy demand. In other words, it's important to have other alternatives.

MR: How about the synthetic polysaccharide used in Cuba's Hib vaccine, specifically?

VV: These polysaccharide vaccines, above all conjugated polysaccharide vaccines – *Haemophilus*, *pneumococcus*, *meningococcus* – work very well against their target diseases, offering a technological alternative for vaccine development: making a synthetic polysaccharide, without the use of bacteria.

When we started, the know-how for synthesizing a fragment of a known polysaccharide existed and the technology had been developed, but it was a concept that had yet to be proven. With *Haemophilus*, we found the opportunity to search for a competitive and potentially more economical technology. And this was what we tried to do for 15 years. After a lot of hard work, we succeeded. We discovered a set of synthesis-related factors and perfected the production process that made it possible for us to make a very competitive product.

After that, we set out to demonstrate clinically that it worked. And we did it, we demonstrated it clinically and we were able to use it in Cuba, and that really cleared the way, because many people who didn't believe in them before, now believe in synthetic vaccines. Above all, the transnational companies didn't believe, but now they do. This doesn't mean that all vaccines

will become synthetic vaccines right away. This just means there is an interesting, competitive alternative and not only for *Haemophilus*, but for others as well. This is what I think our scientific results really did – they opened up alternatives.

MR: Apart from the National Immunization Program in Cuba, is the Cuban Hib vaccine currently used in other countries?

VV: Our vaccine already forms part of the pentavalent vaccine. This is a much better vaccine because it immunizes at the same time against five diseases, including hepatitis B [the other three are diphtheria, tetanus, and pertussis, Eds.]. The pentavalent vaccine is on the market in some places already, and the *Haemophilus* vaccine alone is also on the market in some places – Venezuela, Bolivia, Argentina, in certain Asian countries, in Vietnam; it's also being marketed in Russia.

MR: One factor that is particular to Cuba's vaccine capability is its focus on "diseases of the poor" and improving population health in the developing world. Why is this?

VV: I think this is perhaps the most complicated part to understand. Somehow, it has been established that the academician is not related to the end result – curing people – because the leading motive in research is profit. And this is a tremendous contradiction in present day medicine – to make a profit from curing people. In the end, profit is the first priority and curing people ends up being a collateral result of the whole process. Given this dynamic, I think our science is truly different because it's not profit motive governing research and policy, but rather solving a health problem.

You can't be purely a scientist, completely removed from the humanistic approach that has been developed all these years [since 1959]. This humanism has become, at least in my case, the most important thing. And, when you're doing a thing like this – science – that can save peoples' lives, that can save a child's life...in my case, that child's life ends up being more important. I personally feel much more satisfaction when I say

At a Glance: *Haemophilus Influenzae* type b (Hib)

Hib causes serious infections including bacterial meningitis, pneumonia, epiglottitis, arthritis, cellulites, and osteomyelitis. The Hib bacterium is transmitted person to person through airborne mucus droplets released by coughing or sneezing. Children under five years old are at greatest risk; infants between four and 18 months are especially vulnerable.

Although it is a vaccine-preventable disease, some three million children a year develop illnesses caused by Hib, and between 400,000 and 700,000 die. The true disease burden of Hib-caused illnesses is hard to establish and may never be known since conclusive Hib diagnoses are still not made in many parts of the world. In addition to the Cuban Hib vaccine, there are four other Hib vaccines available internationally.

Source: *Bulletin of the World Health Organization*. 2007 July;85(7):501-68.

'there are children we saved with what we did' than 'we made a major scientific breakthrough,' although, as a scientist, discovering something important is comforting...but not really.

MR: I've noticed that your team has many women and young people...

VV: Yes, it's a young, motivated team; these things motivate them – facing the parents of a child to whom they are giving a vaccine, that was made by them, gives them a great feeling of responsibility and accomplishment about what they're doing, producing, and investigating. It's fundamental. These are real parents, with real children that are the most precious things in their lives...The science about which I feel most proud is above all, humane and very close to people.

MR: What motivates you as a scientist?

VV: Knowing that even though there's a vaccine, there are half a million children that die every year because of diseases related to *Haemophilus*; this is really the most important motivation, to be able to do something...

MR: In your opinion, what can the world do better? What can we do to help these children?

VV: This is complicated, because as I said to an American scientist after attending his lecture called *Vaccines against Poverty*, 'you can't eradicate poverty with a vaccine, it would be great if you could but you can't. Poverty is a social condition.' The intentions are good, but...it's not only a problem of vaccines, it's a combination of things. If you were to take the *Haemophilus* vaccine to every country around the world, the governments of those countries would need to be aware of the importance of that vaccine, the people would need to be aware of the importance of that vaccine, the human resources would have to be there to administer that vaccine and so on.

MR: Can you tell us what your team is currently working on?

VV: Yes. We're working on the *pneumococcus* vaccine. This is a much more complex vaccine and we're evaluating alternatives. Cuba doesn't have this vaccine. We have vaccines against two of the three bacteria that produce meningitis and bacterial pneumonia [*Haemophilus* and *meningococcus*, Eds.]. Then there is *pneumococcus*, the main cause of pneumonia and of bacterial meningitis...it's really an important challenge because technologically, it's very complex and the incidence rate is very high: more than 30,000 cases in Havana. At the moment there is only one commercial vaccine, made by an American company. Because it comes from an American company, Cuba has no access to it [due to US government conditions placed on acquisition of US medicines by Cuba under the embargo, Eds.].

And we are also working on some cancer vaccines together with the Center for Molecular Immunology. In this case we're making synthetic antigens for cancer vaccines. We believe this is possible, that synthetic antigens really can be important there.

We're working against the clock, because, well, when you start to think how many people will get sick in one year, while you're toiling away on your research, when you think about those sick people...we'll keep on fighting to find solutions. 