

Dr. Reinaldo de Menezes Martins: six decades dedicated to vaccination

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doi: 10.1590/0102-311X00200720

*Luiz Antonio Bastos
Camacho*¹

*Marília Sá Carvalho*²
*Reinaldo de Menezes
Martins* †

¹ *Escola Nacional de Saúde Pública
Sergio Arouca, Fundação Oswaldo
Cruz, Rio de Janeiro, Brasil.*

² *Programa de Computação
Científica, Fundação Oswaldo
Cruz, Rio de Janeiro, Brasil.*

† *Deceased.*

Correspondence

*L. A. B. Camacho
Departamento de
Epidemiologia e Métodos
Quantitativos em Saúde, Escola
Nacional de Saúde Pública
Sergio Arouca, Fundação
Oswaldo Cruz.
Rua Leopoldo Bulhões 1480,
8º andar, Rio de Janeiro, RJ
21041-210, Brasil.
luiz.camacho@ensp.fiocruz.br*

Reinaldo de Menezes Martins was a physician and PhD in Tropical Medicine. In his career as a pediatrician, for which he received numerous awards and accolades, he influenced the medical practice of generations of professionals as preceptor of medical residency and a respected leader among pediatricians. In the last two decades of his career, he expanded his dedication to the study of vaccines in public health, with significant academic output and pragmatic orientation, valued through consultancies for the World Health Organization (WHO), United Nations Children's Fund (UNICEF), Brazilian Ministry of Health, and the Immunobiological Technology Institute, Oswaldo Cruz Foundation (Bio-Manguinhos/Fiocruz). This interview aimed to focus on components related to vaccines in the biography of a workaholic who was so productive that he required great effort by himself and the interviewers to summarize his work. Dr. Reinaldo passed away in January 2019, leaving a legacy of inestimable contributions to evidence-based public health.



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Dr. Reinaldo de Menezes Martins (photo: Bio-Manguinhos Communication Advisory Board/Fiocruz).

Camacho Reinaldo, the purpose of this interview is to make an informal record of your long experience as a pediatrician, with an emphasis on your work in the field of vaccines.

Reinaldo A recently published biography of Dr. Zilda Arns ¹ presents part of my work in the field of prevention. At the time, we were attempting to implement oral rehydration therapy and facing problems with its acceptance, and even sabotage of the program [in oral rehydration therapy]. The book cites me several times because Dr. Arns and I collaborated for years. We worked mainly in the promotion of breastfeeding, oral rehydration therapy, preventive measures, normal delivery, and rooming-in. Immunizations were also part of this, but not as the “flagship”. This is just to cite my involvement in preventive measures in general, and not only in vaccinations.

Camacho When was this work with Zilda Arns?

Reinaldo Mainly in the 1980s, which economists considered a lost decade. How did my personal interest in the area of prevention and vaccines get started? I did not do a medical residency, and at the time few people did. We did public admissions exams for emergency medical services, and that was how I entered public service.

Camacho Was that in the 1960s?

Reinaldo Yes. And I felt useless in emergency services. First, because I didn’t have the aptitude to work in emergency care. In the emergency department, the person can’t think much, can’t stop to reflect, and that’s against my nature. So, I went to work in the Fernando Magalhães maternity hospital, and later in a public primary health care unit. It was the best thing that could have happened to me, because I felt useful there. It wasn’t happening in the emergency department, which was immediate, medical care for symptoms only, which didn’t solve anything. In the health post, I discovered that something could be done. I went to work in Gamboa, which was one of the poorest favelas in Rio de Janeiro, an area with a destitute population ². I treated young people at a youth shelter there. And they had no money. It was useless to write prescriptions. I was very frustrated at first, too, when I thought to myself, “*What am I going to do here?! Am I going to distribute milk?!*” So, there was milk there to distribute, and it worked as a strategy to vaccinate. We distributed milk, with vaccination as the condition.

Camacho Which vaccines were available at the health units at that time?

Reinaldo Very few. Smallpox vaccine, DTP (made by the Pinheiros Laboratory and which did not immunize properly against pertussis, but immunized well against diphtheria and tetanus). Vaccination began for measles, which was widespread at the time. There was also BCG... and I don't know if there was any other.

Camacho Was BCG still oral?

Reinaldo When I went to work, BCG was already transitioning from oral to intradermal. Despite the limitation, the vaccines avoided a lot of disease. Especially the measles vaccine, even though the vaccine was quite reactogenic. But of course, we couldn't focus only on vaccines. To begin with, there were few vaccines. I remember that we didn't have medicines. I managed to get some medicines to distribute. Simple drugs, like piperazine for scabies. Scabies was widespread.

Reinaldo The widespread idea at the time in public health in general, with some exceptions, was that medicine had nothing to do with public health. The idea was that the problem is political, socioeconomic, and that medical measures are useless, that only basic sanitation could solve things, plus improved socioeconomic conditions. These were recommendations and ideas from people that weren't actually working out in the field. So, I wanted to prove to myself, and to others, that medicine can do something to benefit public health. Especially in pediatrics, which is a field targeted to prevention, almost by definition. This experience in the Gamboa neighborhood and in other favelas made me reflect on this reality and on how to implement preventive measures like vaccination. And what a struggle it was!

Marilia Why was it a struggle?

Reinaldo Because doctors were instructed not to vaccinate anybody while they were ill, and there were a lot of contraindications. At the time, Ciro de Quadros was conducting a smallpox vaccination campaign, and I asked him in a meeting at the Ministry of Health what the main causes of non-vaccination were in Brazil. He cited false contraindications as the leading cause. All of this made vaccination unfeasible. And people were surprised because the coverage rates were low. So, I wrote a little article that was published in *Pediatria Moderna* ³, saying that vaccines could be given to children with minor illnesses as long as they did not compromise the child's overall health status.

Marilia I personally experienced the introduction of all these issues in the public health courses at the Sergio Arouca National School of Public Health (ENSP/Fiocruz). I did my residency in public health and was part of all of this. I'm also the result of the effort to include prevention in clinical practice and medical practice in health posts, too, which wasn't part of the routine before. But the issue of vaccines, I remember, triggered a huge discussion at ENSP. The issue about vaccination via campaigns. I'm against campaigns. How did this discussion play out?

Reinaldo The vaccination campaign strategy had existed since smallpox, and the measles and polio campaigns came next. People that opposed the campaigns cited the use of campaigns to promote unscrupulous politicians. The campaign would be held, and then all the enthusiasm would disappear. Cuba had already held national vaccination days with huge success when they eliminated polio from Cuba. So, Sabin proposed holding national immunization day in Brazil. At that stage, João Batista Rizzi Jr. took office as Secretary of Basic Health Actions in the Brazilian Ministry of Health. And Rizzi marked a turning point in the immunization program. When there were campaigns, they were poorly planned, poorly organized. Except for smallpox, where Rizzi and Ciro de Quadros were involved, which was always well organized. Surveillance was very poor, and the vaccination coverage rates were very low for measles and other diseases, including polio. Polio was already an oral vaccine, as droplets, easy to administer. It was Sabin's idea, there was a technical basis to it, because he reasoned that flooding the country on a single day with the polio vaccine would crowd out the wild virus and would be more helpful than individual action. So, Rizzi said it was possible. I doubted it was possible at first.

Marilia Really?

Reinaldo Vaccinate the entire country on one day?! And Sabin even gave details: it should be on a Saturday. A weekend, preferably a Saturday, because it's harder for people to participate on weekdays. Detailed planning was done. But Sabin also wanted a study done, to compare before and after. It was an idea, let's say, out of place at that time. And it would all have to be done much more carefully, with a lot more science than Sabin was saying. He was a virologist, not an epidemiologist. At the time, the idea of holding a campaign ran up against huge opposition. People said it was a political ploy, a

one-minute wonder, that it was going to destroy the health posts. Rather than improving, focusing on campaigns was going to make things worse. In 1980, I was elected president of the Brazilian Society of Pediatrics and established a productive collaboration with Rizzi.

He was highly competent. He had worked in the field, the school under the SESP Foundation. These people occupied positions by working on the frontline. I met Rizzi while we were both working in the Maré favela. We spoke the same language, something that wasn't happening before. I resisted the national immunization days a little, because I thought they were impossible. I proposed a full week, but Rizzi said to me: *"No! It's possible to do it on one day"*. And he knew what he was talking about, because at this stage there was already a network [of primary care]. It wasn't as broad as today, but there was already a network. And the vaccine could also be applied by trained lay people. They didn't have to be specifically healthcare technicians.

Camacho Was the cold chain satisfactory at the time?

Reinaldo No, but it always improved for campaigns.

Reinaldo It wasn't ideal, but it was what we had. And I defended the national immunization days based on the reality: we had very low coverage. The prospects were that the low coverage would not be solved by routine vaccination. It was going to take a long time to structure the network. There were also technical reasons for this. Even if the health posts worked well, the national vaccination day was recommended to control polio. And one day they called me at ENSP, it was the main person against the idea, an excellent epidemiologist who did everything with the best of intentions, waging great opposition, and leading the whole group there at Fiocruz. There were also people against it for other reasons. Things like, *"Reinaldo, you're ordering everyone to get vaccinated for polio, and if something goes wrong, you're going to get sued"*. And there were also people that said, *"Polio is rubbish compared to malnutrition"*. *"You're spending so much money on polio prevention when there are other more serious problems, including malnutrition, and other diseases that are more serious than polio"*. My arguments were: first, polio prevention is easier, with a droplet; second, the reality: if we want to solve this coverage problem by structuring the health posts, it's going to take us ten or twenty years or more. We can't let people catch polio when there's such an easy way to avoid it⁴. But the group in favor of the immunization day prevailed. I should say, at the time, the President of Brazil was João Batista Figueiredo, who faced quite a lot of hostility from the medical field... in general. And I said, *"I'm collaborating with the Ministry of Health, with the immunization program. It has nothing to do with the government or politics"*. At the Ministry, I said, *"Collaboration by the Society of Pediatrics is guaranteed, as long as the campaigns aren't used for political purposes"*. That was a kind of trademark ever since the beginning, and that was rarely challenged. I already had experience with political interference, which only gets in the way and demoralizes. So, the program made its mark, the national immunization days made their mark with extraordinary success. Polio incidence plummeted.

Marilia I remember there was also some discussion that the campaign worked because [polio incidence] was already declining anyway.

Reinaldo Totally without basis!

Reinaldo There were localized polio outbreaks. The last one before the campaign started, which turned out to be bigger, was in the state of Paraná and had huge repercussions. So, Rizzi called a person who was opposed to the campaigns to do a cost-benefit assessment. The conclusion was that it was much cheaper to vaccinate with the campaign than with routine vaccination. Not to mention the result. And contrary to what many people feared, this gave the national immunization program great prestige, strengthened the preventive activities, strengthened the health posts that began to be better organized. The health post where I worked was an old house. The health centers began to be better equipped and furnished, more adequate.

Marilia And the cold chain, too, right?

Reinaldo The cold chain was improved, because before, the refrigerator was used to store everything, vaccines included. I remember a measles outbreak in the Baixada Fluminense [in Greater Metropolitan Rio de Janeiro] with cases in children who had been vaccinated, sometimes even with two doses. An inspection was done. There was everything imaginable in the refrigerator: sandwiches, soft drinks... The transportation was also inadequate, but the cold chain improved. A central cold chain headquarters was created in Caju [neighborhood in Rio de Janeiro], which contributed to adequate logistics. The national vaccination days also worked, because by this time Brazil had a com-

munications system that covered nearly the entire national territory. The television networks reached all states of the country. So, the message got out. Rizzi conducted highly adequate and detailed planning. He explained how to organize the waiting line. He was even ridiculed by part of the press. The result [of Rizzi's work] was that nobody doubted what had to be done on the day, and this had never happened before. When Rizzi issued technical notes and guidelines from the Ministry of Health, they were always crystal clear. The area of communication on vaccines also improved enormously.

Marilia I also want to touch on another component, which is the issue of technological development and Bio-Manguinhos, which also emerged at that time.

Reinaldo As I was saying, there are many components. In the early 1980s there was a shortage of vaccines, and diphtheria outbreaks began to emerge. I'll start with the vaccines' quality. I was in the Society of Pediatrics at the time. I publicized the Ministry of Health's activities to the pediatricians, and I remember a colleague who wrote to me about it. João Regis, who worked at the infectious disease hospital in Recife. I spoke with Rizzi, that I had always known that that triple vaccine didn't protect against pertussis, but apparently it wasn't protecting against diphtheria, either. Rizzi launched an investigation of the quality, but there wasn't any laboratory in Brazil capable of determining the triple vaccine's quality. So, the tests were done in Chile, and to our surprise, the vaccine didn't protect against diphtheria, tetanus, or pertussis.

Marilia Was it imported?

Reinaldo At the time, the Pinheiros Laboratory, which was a small laboratory, made a good vaccine for diphtheria and tetanus, but not for pertussis. It was acquired by Sintex, which modernized the factory, but produced a vaccine with no efficacy. Rather than fixing the problems, Sintex closed its doors and left. We were forced to import vaccine. That led to two very important initiatives: the creation of the INCQS [the National Institute for Quality Control in Health/Fiocruz] to control vaccines' quality, and strengthening of domestic producers, specifically the Butantan Institute and Bio-Manguinhos. Together with the INCQS, they contributed to improving the vaccines' availability and quality. Sanitary control was a disaster, and I'm not going to spare words. Anvisa, the regulatory agency at the time, was a disaster, a rat's nest. It was bald-faced corruption with no credibility. Starting with Adib Jatene as the Minister of Health, [Gonçalo] Vecina headed Anvisa, and there was a turnaround, and other people subsequently carried the process forward. This contributed to improving the production process. Now, in order to produce according to Anvisa's requirements, which follow international standards, a serious problem is created for manufacturers in developing countries, not just Brazil. We don't have the multinationals' resources to compete. Meanwhile, the WHO only acknowledges Anvisa as the single reliable agency, fit to qualify vaccines. So, there's a game of requirements, which would be fine if the manufacturers were receiving the necessary resources. But in recent years the requirements have increased and the resources have shrunk, creating an impasse in production. But that's already the end of the story. The strengthening of the immunization program is due to a lot of measures. One of them alone would not be capable of sustaining the program. The National Immunization Program's prestige is due largely to the polio campaigns, and later other diseases. Besides, even today it's not possible to eliminate the campaign style for certain situations. For the measles outbreak now in the North of Brazil, we're going to have to conduct campaigns, vaccinate the population of all ages, otherwise we won't control the outbreak. If it's limited to single interventions, measles will continue to spread there, as it did in the Northeast just a few years ago. We took a long time to eliminate measles from Brazil's territory because of the outbreak in the Northeast, and now we also have the problem on the border with Venezuela and cases from Europe.

Reinaldo Epidemiological surveillance also improved. Everybody complains about surveillance, but I think it's great, because I remember how it used to be. There's no comparison! You now have information that may even have flaws, but it's coherent information on the occurrence of diseases of mandatory notification. There used to be nearly nothing, and the data were not reliable. And now they are reliable.

Marilia All this part of capacity-building and training was the result of this time, too. It was the training activities in the vaccination program and epidemiological surveillance. I am very proud, because I participated in the team that assembled the training materials, and even today these materials are recycled and reused. This even impacted the health services from within.

Reinaldo The Ministry of Health's manuals helped a lot. I had the honor of coordinating some of these manuals ⁵. The vaccination manual was always very thin. I think it could have been thicker. But there's the manual for the CRIEs (Reference Centers for Special Immunological Products) to serve special populations, and each of these activities has a manual ⁶. The manuals are very helpful as basic documents for the training activities, and they're revised periodically. The epidemiological surveillance manual has just been revised. It's a complete set that includes human resources, training, and everything else.

Camacho At the time of smallpox vaccination, we had to cope with highly reactogenic vaccine. When did the adverse events begin to gain greater visibility?

Reinaldo I'm not an expert in crowd psychology, but I think that every movement, even the best movement in the world, generates a counter-movement. If it doesn't generate a counter-movement, it's because the idea is not important or nobody cares. But when the idea is formulated, for every action there's a reaction. Ever since the first vaccinations in England, the smallpox vaccine encountered enormous opposition from anti-vaccine groups.

Marilia In Brazil as well, right?

Reinaldo The opposition was a lot heavier than today, despite the "fake news" now, among other reasons because there was some basis to it. That's the worst kind of problem, when they have some basis. When there's no basis, the "fake news" eventually dissipates by itself. The smallpox vaccine at that time [late 18th century] was hand-produced and contained contaminants. Vaccination was sometimes done person-to-person, so other diseases could be inoculated. The opponents had some basis for fearing vaccines. There's no denying that there were side effects, although the adverse events were hidden at the time. Nobody talked about them. When vaccines came to Brazil, there was also a group for and a group against. I think the internet makes a lot of noise, but the overall effect, with some exceptions, is not that big, because the ideas and news are so outlandish, so absurd and baseless, that they eventually dissipate on their own.

Still, when is there a problem? There's a problem when there's a physician involved in the accusation. Once they asked me to analyze the situation in a town in rural Brazil that was against BCG vaccination. I already had experience with such situations, so I asked who the doctor was that was against BCG. I hit the nail on the head. There was a doctor there, widely admired in the town, who was against BCG, on grounds that the Americans didn't give BCG (which they don't give to this day). So, he also recommended to the townspeople, "*No, don't give BCG*". The situation was solved by talking to this physician, naturally. The case in England, the first more serious event along this line, involved a brain lesion following pertussis vaccine, which had some basis. A study by a highly prestigious individual, published in an important scientific journal, reported a brain lesion in a child who had received pertussis vaccine. After receiving pertussis vaccine, some children faint and become hyporesponsive, some have seizures. Many children have high fever. It's a vaccine that everybody hesitates about, even today. When he said there was a case of brain lesion from the pertussis vaccine, it affected the pertussis vaccination program in England. So, there was a serious pertussis epidemic with a lot of complications, and they started vaccinating again. Like what happened with Oswaldo Cruz, who vaccinated against smallpox. The population revolted, the epidemic wasn't stopped, and the population realized that people who had been vaccinated didn't catch smallpox, and that people who caught smallpox hadn't been vaccinated. So, vaccination made a comeback via a demonstration effect, which is the best argument against rumors, in other words, showing what happens in reality. The other serious episode was with Wakefield [English physician], relating autism to triple viral vaccine ⁷.

Marilia That was a fraud!

Reinaldo Yes, but nobody knew Wakefield had pulled a fraud. He was a prestigious doctor working in an important hospital in England, and according to what David Salisbury told me, who was health director in England at the time, he was a highly eloquent person who spoke well on television. And Salisbury, who is a very intelligent, very interesting man, made the mistake of polemicizing with Wakefield. The worst thing you can do in such a situation is polemicize, because you lend more credibility. That is, what he said must have a basis, otherwise the director of public health wouldn't come out to debate the subject. After the controversy, the triple viral vaccine coverage rates dropped in England. After that, there were measles and rubella outbreaks, and the coverage began to improve again. And once again, what happens in reality is the best response, which sometime takes a while.

Marilia And sometimes, meanwhile little children die.

Reinaldo Yes, epidemics caused by lack of vaccination. I remember that at first, nobody talked about adverse events. There was so much disease that there was no room to talk about an adverse event. Later the Ministry of Health hired me to do this manual on adverse events, which as far as I know is the first document or textbook of its kind in the world⁸. Nobody had a unified didactic document talking about adverse events with all the vaccines. I think Brazil was the first to produce one. And it says there, in plain letters: vaccines, like any product, have benefits, adverse reactions, but the vaccines that are used were studied, and a risk-effectiveness assessment was done. Nobody hid the adverse effects. This is very important and helps lend credibility to the program. I remember when there were the first cases of viscerotropic disease in 1998-1999, published in 1999, the evidence indicated that it was from the yellow fever vaccine. Rarely, the yellow fever vaccine can cause a serious adverse event. It's not actually a reaction, it's an invasion of the individual by the vaccine virus as if it were the disease yellow fever itself, for reasons still unknown. There was no genetic alteration to the vaccine virus, at least not genetic alterations that would explain the condition. Strangely, acquired immunity is not compromised in these cases. This disease has not been described in immunocompromised individuals, which is already a contraindication. But nothing was known about this until we did studies with an American called Steven Seligman who worked in a genetics group in infectious diseases at the Rockefeller Foundation. We were attending an immunology congress in Ouro Preto [Minas Gerais State] about five years ago... the talk, where the idea came from, by [Jean Laurent] Casanova, that has a lot of studies along this line of genetics and susceptibility to diseases. He refers to "monogenic holes", or small mutations that cause a disaster. So, we "devised" a research protocol for these cases, which we applied last year for the first time in a case in Macuco in the state of Rio de Janeiro. It's a well-documented case of viscerotropic disease in a young woman who was in serious condition but survived. We did a genetic study with skin biopsy, saliva and blood samples, informed consent. We collected saliva samples from the family and found that this apparently normal young woman had a double mutation in the interferon alpha receptor, which is the first barrier against the virus. The people from Rockefeller were excited, and an abstract from this paper is going to be presented at a congress in Europe. It includes the group from Bio-Manguinhos, who participated in the study. We discovered something that had never been described before. People suspected that it must be something related to the early immune response, an event that occurs right after application of the vaccine. But nobody really knew. Now in at least one case we saw it with the interferon alpha receptor. In the family, there was this girl who was homozygous, with the mutation, the parents were heterozygous, one brother without any mutation, and the other sibling was heterozygous. Only the homozygous individual cannot be vaccinated.

Reinaldo When we got this written result, we went to speak to the family. I asked Jean Laurent Casanova what instructions he would give on future vaccinations for the patient and her family members. He oriented us in writing, and Lurdinha [Dr. Maria de Lourdes Maia, head of the Bio-Manguinhos Clinical Advisory Board] told me we should have a person onboard, a specialist in primary immunodeficiency, to participate in the care for this girl in subsequent years. We studied just one case, and now we're going to study a case in Belo Horizonte [Minas Gerais State], whose sister received the yellow fever vaccine and died. The surviving sister received the vaccine and developed an illness but survived. We'll see whether the mutation is the same. It's quite possible that there is more than one mutation involved, and the idea, although it's not easy, I believe it's not impossible, is to find a biological marker that allows identifying these individuals and to include this in the neonatal heel stick test. At birth, or the first time the infant visits the health post. Our idea is to also produce a diagnostic kit as a way of convincing people. The proposal for this kit involved the need for a legal agreement, since it would involve a patent. That's where another major bottleneck comes in, one of the problems we're having now. My protocol for this stayed three months in the legal department at Bio-Manguinhos and Fiocruz. It doesn't involve any special expenses, and the cost is only a little more than BRL 200,000 (USD 38,000) a year. For a research project, this is very little. There's no risk for Bio-Manguinhos. If it doesn't work, the partnership can simply be suspended at any moment.

Marilia This account you just gave now is very interesting, showing fantastic capacity for Brazilian science, which has been belittled or sabotaged, and which also grew with the immunization program. I think we learned how to do research in this process, to assess cost-effectiveness, to assess

the impact of interventions. I'm an epidemiologist, so I see this side more... developing technology, developing measures in primary care. We have enormous capability, correct?

Reinaldo Yes, I have no doubt about capability, but we don't have enough experience. And we don't have a big enough critical mass. Meanwhile, other things are creating problems for our technological development that don't involve money. Money is important, of course. But the way things work here in Brazil, even with a lot of money it's not going to work well. It's inconceivable for a procedure that should take just six months to have taken three years!

Camacho Together with vaccination, surveillance was organized that worked well, and that also included adverse events. Could you talk a little about this?

Reinaldo Right, the polio program served as a model for various other things. It was the model for surveillance of adverse events. It was a learning process, too. When we look at the polio data associated with the vaccine, we see things that seem absurd. One period that had too many reports, later decreased. I didn't join this group starting with the first meeting. When I joined, I said, "*there has to be a case definition*". Every case was classified as a case, and there was no case definition. There was a sort of hypertrophy of polio notification associated with the vaccine. This trend decreased following the case definition, it became more consistent with the reality. Of course, every classification and every definition have limitations, but if there's no case definition it's confusing. When the decision was made to eradicate polio, polio surveillance increased, and so did the number of cases. That outbreak in the Brazilian Northeast [1986] that everyone talks about, I have doubt about it because surveillance increased at the same time. The search began for more cases. I remember that Bahia State had no polio reporting. So, they sent a group there, and it was full of polio that wasn't being reported. Sometimes the improvement in surveillance gives the impression that the disease is getting worse. The same thing happened with measles. As the measles immunization program increased, the number of cases also increased. It seemed absurd, but the reason is that surveillance was also improving.

Camacho It seems like the strides in surveillance became a byproduct of the vaccination campaign, and not the other way around, as it should have been.

Reinaldo True. When the national vaccination days began, the data were also very faulty. So, when the campaigns were starting, I proposed notification, too, by the services, not only by the health posts, but also by the network's hospitals. I remember that [Daniel] Becker said something very interesting: "*Reinaldo, you may also get a lot of cases that aren't polio, that will be reported. You're going to lose in quality, whereas these cases we're receiving are from referral hospitals, so there's no doubt about the diagnosis*". I don't have to know all the cases to know how the disease is behaving. The disease profile in the place allowed planning vaccination for children under five years of age. It was based on the data. It wasn't all of the cases, but there was a profile.

Reinaldo I think it's very important for immunization programs to be integrated with other public health activities, including in maternal-child health. I think we could improve a lot with better integration. But every time they took the initiative to propose decentralization of the immunization program, I was against it.

Reinaldo The people proposing this were not worried about the immunization program. They were worried about regional vaccine purchase agreements made by people that were later going to finance political campaigns. Either that, or the local program served as the decoy for the one proposing it. For example, varicella vaccine was introduced in Santa Catarina State, in Florianópolis, and I said: "*how are they going to deploy a vaccine like that in just one place?*". That's what they did, but it wasn't sustainable. I mean, that kind of action is only going to help destabilize the program.

Marilia Reinaldo, what about the dengue vaccine issue? What do you think?

Reinaldo It's a typical example of what happens with industry. Of course, it's a vaccine that interests a large share of the world. And it was sponsored by international agencies like the WHO. But the documents on the dengue vaccine, reading the articles and studying a lot of work that had already been published, raised a lot of doubts in my mind.

Reinaldo When the dengue vaccine appeared, the meetings at the congresses were to promote the vaccine! I think I was the only one talking about the lack of knowledge on various aspects of the vaccine. The vaccine is made in the live vector, the yellow fever vaccine, which has serious adverse events. Whether this dengue vaccine would lead to serious adverse events was not completely clear to me. The duration of immunity was also critical, because when there's a drop in antibody titers, the

incidence of serious dengue increases. The results of the studies left room for doubt. Even so, the vaccine was touted as something that had solved the dengue problem. I even spoke out in the immunization program, calling attention to the doubts and risks of introducing this vaccine on a large scale. It was later found that there was an issue ever since the beginning, of lower immunogenicity at younger ages. Then there was an issue of hemorrhagic dengue appearing at higher rates in children who had already received the vaccine, compared to unvaccinated children. So, the recommendation was now to vaccinate starting at nine years of age ⁹. I think, and I beg to differ, that the Brazilian Society of Pediatrics jumped the gun, because they immediately incorporated the vaccine into the vaccination calendar.

Camacho Did the SBIIm [Brazilian Society of Immunizations] follow suit?

Reinaldo The SBIIm did, too. But the SBP [Brazilian Society of Pediatrics] really impacted me, because it deals essentially with children, which is an age bracket in which the vaccine should not be used. Later this concept was expanded, to include not just children. Susceptible people that have never had dengue should not receive the vaccine either.

Marilia So, what is it for, right?

Reinaldo We were left with a vaccine with too many problems to be implemented routinely or applied on a mass scale. I favored a more localized study with longer follow-up, to clear up the pending doubts. But at this stage, I don't think there's much doubt.

Reinaldo There was a huge rush to present a vaccine as ready for use, and by the groups that allowed themselves to get involved too easily. So, this is another aspect that should worry us. To maintain neutrality is impossible, because whoever says they're neutral is a liar... but we have to at least seek neutrality.

Marilia And maintain the scientific quality. Read the article to the end.

Camacho Part of our immunization program's robustness was expressed in the formation and consolidation of a technical advisory committee in immunization (CTAI) respected and consisting of individuals with great experience, with renowned expertise ¹⁰. And you followed the experience from the beginning. How do you view the technical advisory committees in general, and ours in particular?

Reinaldo The committee gained strength over time. The ideal thing is for each state to have an advisory committee to review specific issues in each state, but at least at the national level we have a strong group. Is anyone neutral, is there anyone with no conflict of interest? I don't think so.

Reinaldo Everyone has a conflict of interest. I said this once at an international meeting. They wanted the people at CTAI not to have conflicts of interest, preferably people from the university community. I said, "*That's an illusion, because in Brazil at least, the only group we might be able to say is free of conflict of interest is Anvisa. All the others have some interest. What's important is transparency*".

Marilia Reinaldo, I think that wraps up the first reason for the interview. We have to reclaim the history we have, which is not always easy. And I think that was one of our objectives today. To revisit this history for the new generations to know what was done. I think that's why we're here on a Saturday. Because we believe in what we're doing.

Contributors

L. A. B. Camacho conducted the interview and transcribed and revised it. M. S. Carvalho conducted the interview and revised it. R. M. Martins granted the interview.

Additional informations

ORCID: Luiz Antonio Bastos Camacho (0000-0003-4656-1914); Marília Sá Carvalho (0000-0002-9566-0284); Reinaldo de Menezes Martins (*in memorian*).

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Submitted on 10/Jul/2020
Approved on 17/Jul/2020