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EDITORIAL

VACCINATION AND SELF-SUFFICIENCY

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The National Immunization Program has completed 25 years with two important victories: the eradication of smallpox and the control of poliomyelitis. Fifteen years ago, the Ministry of Health faced another equally serious problem, i.e., the lack of sufficient quantities of good quality (potency and harmlessness) antivenom sera. Since these sera are specific for the region, the only solution was to renew the production plants. The National Immunobiological Self-Sufficiency Plan was extended to vaccines, an area in which the initial inexperience led people to think that it would be simply necessary to increase and reform existing plants.

About 100 million dollars were invested, initially in 14 producers. A considerable fraction of these resources was lost due to inflation and to the bureaucratic incapacity that surrounds public laboratories. Today the production of vaccines is limited to five laboratories and success appears to be feasible for the goals initially proposed, i.e., the production of PNI vaccines sufficient to cover the child population and part of the population at risk.

This was not how the Butantan Institute understood the challenge since it was impossible to expand obsolete technologies that resulted in poor products. We understood that the goal was to do research in order to develop, to develop in order to produce and to produce in order to do research. Production was no longer simply a nationalistic effort to replace importation, but a goal for Society that would guide the flow of research towards development, permitting Brazil to participate in the world process of production of immunobiological agents. It was with this spirit that the Center of Biotechnology was created, one of the largest laboratories with directed research, today with a staff of 15 doctors, 5 doctoral students, 5 researchers with a Master's degree or working on it, who, side by side with 27 students ranging in level from scientific initiation to postdoctoral training, concentrate their activities on immunobiological agents and on other products for human health. The Center currently counts with about ten grants obtained from FAPESP, PADCT, FINEP, and PRONEX for a total of approximately R$ 3,000,000.00. A strong production and control sector was created in parallel.

The results of the R&D grants and of the investment of approximately R$ 28,000,000.00 in the Self-sufficiency Program are visible in modern plants with their own technologies and in products that have caused the WHO to make the following statement: *Please accept my congratulations on the changes you have made in the Instituto Butantan, bringing it to a place where it is poised to be a leader in the 21st century.*

VACCINE	BUTANTAN	FIOCRUZ	TECPAR	VITAL BRAZIL	ATAULFO PAIVA	SELF-SUFFICIENCY
DPT	+		started in 1999			1998: 80%
adult double diphtheria tetanus	+	+		tetanus in 1999		1998:100%
yellow fever		+				1998: 100%
BCG	+				+	1998: 80% 1999: 100%
Measles	started in 1999, vaccine in culture	+				1998: 100%
Poliomyelitis		(bottling)				1998: 100%
Rabies	+ started in 1999, vaccine in culture		+			1998: 100% 2000: 100% cell culture

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The production of vaccines is not a static process, not only because of the demand for new vaccines, but because of the development of more effective vaccines and vaccine combinations and the development of vaccines that can be administered by the oral or nasal route.

VACCINES BEING DEVELOPED AT BUTANTAN

- Meningitis BC (Lutz + Butantan + Fiocruz)
- Conjugated meningitis B-C
- Haemophilus b
- Pneumococci: conjugated polysaccharides (Butantan + Fiocruz)
- Pneumococci: recombinant psp A
- Rabies produced in cell culture
- Measles produced in cell culture
- Rubella produced in cell culture
- Influenza produced in cell culture
- Recombinant schistosomiasis (Fiocruz + Butantan)
- Acellular pertussis
- Recombinant hepatitis B vaccine with a prevalent Brazilian strain
- Oral recombinant antidiarrhea
- Leptospira
- Botulinic

In general it takes a decade to complete the development of a vaccine. Many of the vaccines mentioned should be ready for trials on volunteers as early as in 1999-2000. In addition to these, new combined vaccines will be assayed and placed in production: DPT-hepatitis b, DPT-haemophilus b, hepatitis-BCG (for newborns and for approximately 5% of the population which does not respond to usual vaccination against hepatitis B), and hepatitis B with the strain prevalent in Brazil.

These projects are combined with the production of heterologous sera against snake, scorpion and spider venoms, and now also against the killer caterpillar, against tetanus, diphtheria and rabies, for the control of transplant rejection (anti-thymocytic and anti-CD3 and CD18 monoclonals). Tetanus, diphteria and rabies sera will be replaced with homologous sera isolated from the plasma of donors. The program is now being extended to other biological drugs of high cost and social importance which include erythropoietin (already being produced), lung surfactant (being developed), botulin toxin (which can be used for muscle contractions, including in cases of chagasic megaesophagus), and natural and recombinant proteins for cardiologic use (vessel reperfusion and angiogenic induction).

Today Brazil is the major producer of vaccines in Latin America. Vaccines previously prohibitive because of their high price, such as hepatitis b vaccine, today can be produced for one tenth of their original cost. Not only do we have the capacity to satisfy the entire demand of Brazil in 1999, but we can export the surplus. With the new developments, we will be able to produce as many as 50 million doses per year.

All of this development has to go through field assays. Up to a short time ago the Brazilian population was used and abused to test vaccines produced in other countries, without receiving any advantage, when the vaccine was adequate (such as the one against AIDS), except purchasing it at the arbitrary price set by the producer. Today we are heading towards the other extreme, with vaccine testing having become a complex and slow process. Of fundamental importance is the collaboration of Centers linked to Universities, which should engage in the testing of new vaccines and in the monitoring of the results obtained with the vaccines applied, in order to prevent the enormous waste of resources and effort that occurred with the imported vaccine against meningitis BC.