RESEARCH TO POLICY: THE CASES OF CHAGAS DISEASE AND FOOT AND MOUTH ERRADICATION IN URUGUAY

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Background

Uruguay is a country of 3 million inhabitants, ranked number 32 in the world, according to the UN social development index (UN/UNDP, 1997), with a 4.5 to 1 relationship between the income of the richest and poorest 20%s of the population, and an illiteracy rate of 2.3% (PAHO, 1995). The population has almost completed the demographic and epidemiological transition (Omran, 1971), and is aging quickly. In 1963, 8% was above 64 years of age, while by 1985 that figure had reached 15.7%. The two main causes of death are Cardiovascular Diseases (38.7%) and Tumors (22.7%). General mortality has decreased constantly since 1910, but due to the aging of the population, we should not expect a very rapid descent. Infant mortality, on the other hand, fell from 110,7 %o in 1910 to the present 17.5 %o. This figure is mainly due to perinatal mortality, with a rate of 15.9 perinatal deaths per thousand live births. There are socio-economic differences in this indicator, since public services report a 19.5 %o infant mortality rate, while the private sector reports only a 10.4%0 rate.

The country's economy is based on its agricultural production. In spite of that, there has been historically a divorce between the capital city, where half the population live, and the countryside, the generator of wealth, but also the place where living conditions in general and health indicators in particular are worst.

We have chosen two cases of successful interventions in an attempt to identify what was the role of research in the achievement of health goals, and on the other hand, what was the process through which research findings were used as the basis for decision-making. The pathologies we've selected (Chagas disease and foot and mouth disease), have relevant similarities and differences. One is of relevance in human medicine, while the other is important in veterinary medicine and both particularly affect the countryside; but while the former afflicts the rural poor, the latter affects the economy of cattle ranch owners, traditionally a well-off sector of society, since it seriously hindered international beef trade. These facts were not of minor importance in the very long policy-making processes that led to their control.

We think of scientific knowledge as a cumulative process, the sum of numerous contributions, their acceptance through varying processes and the interplay of researchers, informed users of research findings and decision-makers. The cases we shall analyze show this long process of research and policy-making till success was achieved. Using Carol Weiss's models, (Weiss, 1979) this could be a mix of the "knowledge" and "interactive" types of relationship between research and policy-making.

At a time when much is being said of a "new contract" between science and society (Gibbons,1999), we think it is interesting to see how at least in these cases, scientific knowledge has long tried to make its way to public knowledge, and draw attention to the problems it identified.

Scientific policy underlies this process, since society's and the State's approach to science and therefore, its funding, has had ups and downs through the century. In very general terms, the times for flourishing of scientific knowledge coincided with those of economic well-being (from the beginning of the century to the 50's), a predominance of positivistic thought in the ruling classes, and democratic governments. The darkest times, on the other hand, were those of the military dictatorship (1973-1984) when the scientific structure was dismantled, and the State alienated itself from citizens. With the restoration of democracy, new funding was allocated to Science, particularly Basic Sciences, many researchers returned from exile and social groups that had formerly been left behind were paid attention to.

Methodology

Two of this paper's authors were responsible for the conduction of the programs we study, so that much of the information derives from the analysis of their own experience. A careful literature review was made, paying special attention to grey literature as much as to that which appears in scientific journals and books.
The group met on different occasions in order to decide on a common framework and discuss the draft reports as they were produced. A special effort was made to identify different stages in policy -making and its counterpart in scientific research, which was not always easy in such long processes. An in-depth paper was written on each disease, which were later the basis of the present summary and comparison.

A- CHAGAS DISEASE

Four historical periods may be identified regarding this disease.
a) From 1923 to 1950 (pioneering times) the situation was characterized by :

- The generation of original knowledge, which contributed to the reconsideration of Chagas disease as a separate entity.
- The study of a health problem of the rural sector at a time when it reached its peak as a sanitary problem in the country.
- The importance given by Prof. Rodolfo Talice to research in his Department of Parasitology at the Universidad de la República.
- The existence of a well constructed network with clinicians in at least 12 of the 13 endemic districts.
- The presence of the subject in public debate, including newspaper articles in "El Día" in 1944, competing in importance with World War news.

Carlos Chagas' surprising findings of 1909 summarized the description of Trypanosoma cruzi (Chagas,1909). In Uruguay, the newly formed Chair and Department of Parasitology in the Medical School, started looking for the vector and for the disease, which was already known as Chagas disease.
The first evidence of the presence of Trypanosoma cruzi in Uruguay was published in 1923 (Gaminara, 1923). Dr. Rodolfo Talice developed national knowledge on the subject, with the clinical finding of the disease and an exact description of its Epidemiology. (Talice et al.,1937). In 1940 the same author, together with Costa, Rial and Ossimani, published what was to become a classic monograph (Talice et al.,1940) encompassing, among others, clinical, epidemiological, parasitologic and prophylactic

aspects of the disease. This monograph, and the works of the Argentine researcher Mazza , allowed for a re-evaluation of the disease entity (Mazza, 1926; Errecart, 1945).

Guerreiro and Machado in Brazil (Guerreiro & Machado,1913) developed the technique for complement fixation . Uruguayan researchers worked along this line from 1940 to 1950.

The main research group was based at the Parasitology Department of the Medical School at the Universidad de la República, in Montevideo, but related to a large network of clinicians in the endemic areas. The team in the Parasitology Department never exceeded the number of 10 people, but they worked as full-time researchers/professors in an adequate environment .

b) From 1950 to 1972 (the early control phase), research production was of lesser academic importance than in the previous period, though some of its contributions were useful for the control of disease in the country.
The most relevant paper of the time was Osimani, Verissimo & Baycee Carbonell's report on disease profilaxis with Gamexane, published in 1950 (Talice et al.,1952; Osimani,1959). The technique had been previously described by Dias and Pellegrino (Dias et al.,1948). Although the Gamexane spraying experience was successful, it was not repeated till 1972, and only in a very limited number of places.

There was also research on clinical manifestations, such as chagasic cardiopaty, megacolon and pathology

Operational research carried out in this period was the basis for the future control of Triatomineae in the country. It provided necessary knowledge, validating research previously carried out in Brazil and Argentina, but under local conditions, and mainly because they were carried out by researchers who later on became members of the control program.

The Parasitology Department was still the main research center in the field, but with a smaller number of members, and working conditions changed as funding decreased, till at the end of this period full-time positions had practically disappeared. The organic relationship with clinicians from endemic areas also disappeared during this time.
The subject did not attract political attention during a period of growing economic deterioration and social unrest, and this was accompanied by scarce research in the field.

c) The first organization of a control program covers the period from 1972 to 1983. The military took over in 1973 and ruled the country till 1984.This was the worst time for Uruguayan science, and Chagas research was no different. The military government banned numerous scientists, who were either imprisoned or exiled, and the University budget was drastically reduced. Since this was a time of fast development of biomedical and basic science all over the world, a large gap was generated, not yet bridged.

In 1972, a series of circumstances triggered the implementation of a control program in the Hygiene Division of the Ministry of Health:

- Aedes aegypti was eradicated from the country in 1958, and that left a vertical structure with experience in vector control, with very few tasks to perform.
- Solon Verissimo, the author of the first antitriatomineae fumigation in the country, and the person who had been in charge of other later focal treatments, returned to Uruguay after working abroad with PAHO for several years.
- The success achieved in controlling other pathologies (rabies, TB, immunopreventable diseases) through sanitary campaigns and/or programs, made it easier to obtain resources for new eradication programs.
- The existence of a similar program in Argentina for over 12 years.
- The presence of members of the Parasitology Department in key political positions at the Ministry of Health

The program was created by a Resolution in 1972. It was conceived as an intersectoral effort, since it included contributions from the Ministry of Health, the Pan American Health Organization, the University through its Parasitology Dpt. and local governments It functioned as planned during 1972 in Artigas, the area of greatest endemicity, but two events changed this in 1973: the death of Dr. S. Verissimo, and the coup d'etat which subverted all priorities and removed many national and local authorities. There followed ten years of extremely poor performance in 5 out of the 13 endemic Departments, including numerous technical errors.
To this we must add that by 1982 the economic model sustained by the military regime collapsed, which led to unprecedented budget restrictions, and the consequent decrease in resources for research and health care.

d) From 1983 to 1997 (definite control period), knowledge was generated by a new generation of researchers, who had to fill the vacuum left by the dictatorship. Available resources in terms of equipment, materials and funds were minimal.

Research was mainly applied and operational, in Epidemiology of vectoral transmission and Eco-biology. There was a strong interaction among members of the National Program for the Control of Chagas Disease and the Parasitology Department in the Medical School, as well as with research units in other University Schools. Some of these new actors include the Entomology, Genetics and Parasitic Biology Dpts. of the School of Sciences, the Biochemistry Dpt. in the Medical School and the Quantic Chemistry Dpt. in the School of Chemistry, (all of them in the Universidad de la República).

PAHO published numerous articles with original data from Uruguay. A special issue of the Uruguayan Medical Journal, dedicated to Chagas disease was particularly relevant.

In 1983 the Direction of the control program was changed, and the agreement between the Ministry of Health and the Medic al School came to an end, so that the former began carrying out its own laboratory work in the Parasitology Dpt. of its renewed Public Health Laboratories.

Different training activities were carried out with health personnel of endemic areas, and there was support from the Human Health Regional Program (Programa de Salud Humana,1982) fostered by the Interamerican Development Bank (IDB) and the Universidad del Salvador in Argentina.

The main achievements in this time were:

- A renewed dissemination of the subject among clinicians in the endemic area.
- A sensitization of authorities which led to passing Decree Nº 193/85, mandating serological screening for Chagas in every blood donor throughout the country.
- Setting up of laboratory capacity sufficient to support a program of seroepidemiologic surveys aimed at a situation diagnosis, and serial assessment of the control measures.

In 1985 a National Seroprevalence Survey was carried out, supported by WHO 's Special Program in Research and Tropical Diseases, the World Bank , UNDP and PAHO. (Salvatella et al.,1989). This survey's results constituted the baseline for future follow-up surveys.

In 1985 and 1991 Triatoma infestans was eradicated in Artigas and Soriano(Salvatella, 1991). In 1991 the Program was relaunched, since it was included among the prioritary health programs of the second democratic government. Positive circumstances for the program were:

- A change in local PAHO policies, which opened the road for greater external cooperation.
- The fact that the Minister of Health belonged to a party whose constituency was mainly based in the countryside.
- The participation of one of the main researchers in the field in writing the health program for that same party, and his presence as head of the program at the Ministry of Health.
- The Intergovernmental Initiative for the Southern Cone for the Elimination of Triatoma Infestans and the Interruption of Transfusional Transmission of American Tryponosomiasis, launched in the III Meeting of Southern Cone Health Ministers, which took place in Brasilia on August 1991. This united the Chagas programs of Argentina, Bolivia, Brazil, Chile , Paraguay and Uruguay.
- A renewed participation of Uruguay in the international arena due to a larger number of publications and two large international meetings on Chagas Disease.
- The submission of a Law Project in the House of Representatives (Annex 3) intended to create a decentralized organization for the Chagas program, allocating autonomous funds to it. It was thought to be a tool for the complete eradication of the disease in the country. Though finally it was not passed, it focused country's attention on the subject.

Uruguay reported new cases of eradication (MSP,1994):Cerro Largo in 1992, Rio Negro in 1994, Paysandu in 1995, Salto in 1996 and Florida in 1996. In the other areas, domiciliary infestation indexes reached minimal values, with large sections of Rivera, Tacuarembo, Durazno, Colonia and San José where the vector was also eliminated.

The program was subject to international assessments. There have been three assessment missions so far. In 1994 the Chagas program carried out a serological survey (Salvatella,1999). Results showed that there was no more active transmission. Later partial surveys also showed results compatible with the descent or elimination of Triatoma infestans and an effective arrest of transmission. Based on these results, the II and III International Assessments of the Control Program (PAHO, 1997;PAHO,1998)

concluded that Uruguay had reached the interruption of transmission of T. cruzi, both vectoral and transfusional.

Uruguay was the first country to achieve this goal. The program Director during the period 1983-1994 received the WHO /Arab Emirates Award for this reason during the 50th World Health Assembly in 1997 (WHO,1997).

B-THE CASE OF FOOT AND MOUTH DISEASE

The history of Foot and Mouth Disease in Uruguay covers a period of 129 years; from the first documented diagnosis made in the country by Veterinarian B. Duprat in Montevideo, on June 8, 1870 (Magallanes, 1997) to the international recognition of the condition of "Foot and Mouth Disease free with vaccine" on May 1993, and "Foot and Mouth Disease free without vaccine" on May, 1996.

Uruguay achieved eradication of Foot and Mouth disease in the present decade, 25 years after the beginning of its control program. In 1961 the Government declared its willingness to fight against the disease through Law 12.938, but it was really after 1968, when the Foot and Mouth Direction (DILFA) was created in the then called Department of Livestock and Agriculture, that the first organized actions did begin.

Before DILFA's creation, 12 to 16.000 foci were registered annually, reaching 30.000 on epidemic years (Min. de Ganadería , 1966). According to the 1961 General Agrarian Census, there were at the time 86.314 rural estates.

Three historical periods may be identified during this long history:

1. From the appearance of the disease in the country to 1966, when the Foot and Mouth Disease Direction was created in the Department of Livestock
2. Disease control, to 1989, and
3. From 1990 to the present time.

Both research and action may be divided into three main fields:

a) Diagnosis
b) Vaccine production and control
c) Control and eradication program strategies

a) Diagnosis:

The pioneer in local research was Dr. Miguel Rubino, who already in 1927 carried out studies on the viability of virus on beef, on transmission mechanisms and prevention, using ovine blood as the substract for modified virus to be used in bovines, among other things. During the great 1943-44 epidemic, Government appointed an Honorary Commission, which based on Dr. Rubino's line of work, suggested the creation of an Institute equipped to carry out diagnosis, research activities and vaccine production. This was the origin of the 1946 Law.

Vaccines made at the time were used in dairy farms with excellent results. This experimental production was the basis for the establishment of the first commercial laboratories in the 50's, reaching a production of 10 to 12 million annual dosis by the end of the decade.
Only in 1956 did commercial vaccine production start in the country. Cattle farmers started using the vaccine individually (66% of the national bovine stock was estimated to be vaccinated in 1966) (Min . de Agric., 1978), which led to the development of an official system for the control of anti Foot and Mouth Disease vaccine by DILFA's lab.

The Veterinary School of the Universidad de la República also played an important role with its Center for Viral Type determination in foot an Mouth Disease, in its Department of Infectious Diseases. This center carried out diagnosis on samples sent from the field, using different techniques.

b) Vaccine production and control

Activities were initially concentrated at the Rubino Institute, until DILFA's offices and laboratories were ready in 1966.
It was only then that a real control plan was set up. The beginnings of vaccine control were difficult. Out of 10 laboratories producing or importing it, only 4 remained to produce vaccine that could be used in the campaign. DILFA's follow up of private labs was critical for the achievement of a good end-product.

Once the availability of enough vaccine of officially controlled safety and efficacy was ensured, the first massive vaccine campaign was launched on August 1968. By April 1969 the program covered the whole country .These massive immunization campaigns were preceded by intense dissemination and health education activities focused on cattle farmers.

Some of the vaccine production techniques used then were changed during the late 80's by new techniques developed by PANAFTOSA,(the Pan American Health Organization regional center against Foot and Mouth Disease). Field tests were carried out from 1972 to 1975 in Bage, Brasil. On 1977, the Uruguayan Department of Livestock, Agriculture and Fisheries signed an agreement with PANAFTOSA in order to test the performance of the oil-based vaccine made by the Pan-American Center, in a milk producing area with high disease incidence
Ten years later, an assessment showed that protection had been excellent. The oil-based vaccine showed no side-effects in terms of milk production and very few allergies.
From 1977 on , PANAFTOSA developed the technology for industrial production of oil-based vaccine in bovines and pigs and made it available for the countries.

c- Control and Eradication Program Strategies

From the onset of the campaign, farmers participation was considered prioritary. The strategy was based on the creation of neighbor or local committees, which at the end of the 60’s and early 70’s, reached 300, related to the approximately 77.000 cattle farmers identified by the 1966 General Agricultural Census

This situation varied in the 80's, among other reasons due to the migration of population to urban areas- there are now only 50.000 farmers - and private participation was reorganized through the Honorary National Commission of Animal Health (CONHASA). Participation also decreased as people refused to participate in government - sponsored activities during the military regimen.

Applied research was carried out at DILFA, which had both the labs and field services, plus the support of its Epidemiology and Statistics experts. This research included, among others, the following areas:

- Epidemiological characterization of different regions in the country
- Virus variants
- Immune studies with challenge tests using strains from the field
- Post-vaccine allergies
- Immune block due to the simultaneous provision of parenteral antiparasitic drugs and the vaccine.

Based upon this research, the first epidemiological characterization was made in 1978, providing guidelines for the modification of the campaign strategies.

In the mid 70's PANAFTOSA developed the theory of Ecosystems in Foot and Mouth disease, based on the prevailing production and socio -economic conditions in a region. This epidemiological knowledge allowed to design more appropriate strategies for the eradication in those areas where the disease had the greatest impact. It also had a great impact in the design of the River Plate Basin project, as it allowed for the recognition that an important region of Argentina , Brazil and Uruguay formed a single primary endemic area.

On 1985 a project was presented by Drs. Figares, Dias and Muzio including an updating of the law, which was the basis for Law 16082. In 1990, with the new law in place, Uruguay obtained funding for the eradication project from the Interamerican Development Bank (IDB) .

An important element for the consolidation of the country as a Foot and Mouth disease - free zone, was the sero-epidemiological national survey carried out in 1992.
The survey 's population included all bovines and sheep in the country. Samples were processed in the national public laboratory, and positive ones were reprocessed in PANAFTOSA.

On October 1989, with the cooperation of PANAFTOSA, and in coordination with the River Plate Basin Project, the national strategy was modified to bring it in line with that of the region. That meant changing the immunization strategy, using the oily adjuvant vaccine for bovines in order to achieve longer immunity, and ensuring high population coverage through direct control by government officials who made their rounds in periods not longer than 45 days.
The epidemiological background of the county advised to concentrate efforts in bovine immunization, since this was the main disease reservoir. This decision was initially questioned due to the number of ovine in the country (26 million at the time), mixed with bovines in the extensive breeding techniques used.

The last reported episode of disease was on June , 1995. On May 1993, Uruguay was recognized by the OIE as a Foot and Mouth Disease free with vaccine country, an in 1994 the second stage started, which meant the suppression of vaccination, reaching the condition of Foot and Mouth Disease free on May 1996.

Starting the second phase meant the complete elimination of virus handling, both in private laboratories and in the public sector. Given the effort industry had made to achieve good quality vaccines that could be exported, this was by no means an easy or consensual decision.

Epidemiological surveillance also increased, with participation of the whole veterinarian system (Public services, producers, private veterinarians, and agroindustries. 10-15 suspect cases have been reported annually from 1992 to 1998. Sanitary barriers were set up and when the illegal entry of stock was suspected, serological antibody presence tests were carried out.

An important tool to ensure compliance was the inclusion in Law 16.082 of a Fund to be used in case producers had to be paid because of measures adopted to eradicate an outbreak or another exotic disease. This Fund was generated by a tax of 0.21% of all exported animal products and by-products. By 1999 the amount accumulated in the Fund was considered enough, so that the tax has been temporarily suspended, but may be reactivated if there was any need.

In 1985, with the return of democracy, a new process started which ended up (sooner than expected) in disease eradication. All political parties voted together for the approval of Law 16.082 in 1989, in a consensus that did not occur in other fields and which remains to this day. Sanitary Emergency System was set up

C- CONCLUSIONS

We have seen two long research processes that finally led to successful control programs. There are some similarities in both cases, namely:

- The continuing existence of groups of researchers on the subject, which allowed for the accumulation of knowledge, even when solutions were not yet available, and the creation of a critical mass to continue the different lines of research.
- The varying availability of research funds and infrastructure which allowed for the work of these researchers.
- The permanence of both subjects in public opinion during many years
- The negative impact of totalitarian regimens both on science and program development
- The opposite situation following the overthrow of these regimes (not necessarily a lasting condition)
- The contribution of many different disciplines and approaches to the solution of the same problem
- A timely and appropriate use of international cooperation, particularly strong at the sub-regional level

Differences are also noteworthy:

- In the case of Chagas disease, science preceded action, as the affected population does not have economic or political power. It was necessary for scientists, who had gone into the subject because of scientific curiosity, to become active in political parties and at the Ministry of Health, which then introduced research findings into actual programs.
- Foot and Mouth disease, on the other hand, because of its economic importance, was a government priority and research was always included as part of the control plans.
- While much of Chagas research was supply-driven, in the case of Foot and Mouth disease much was demand-driven.
- Most Chagas disease research was University based, while government institutions were prominent in Foot and Mouth Disease research, though the University also participated, particularly in basic research.
- Financing mechanisms were also different. Whilst Chagas research was subject to severe budget cuts affecting the University for many years, Foot and Mouth disease research enjoyed better and more continuous funding

As a final conclusion we may say that there are many different roads leading to the successful use of research. In any case, though, it is a long process, needing continuity and a critical mass of committed scientist who may not see the application of their work in their lifetime.

Political will to undertake action is more easily achieved when those affected are found in the more affluent or powerful sectors of society, but this is not the only way, and the demonstration of the severity of a problem , and the possibility of its solution finally prompt action, if the whole society is made aware of it.

These two cases are also a good demonstration of the fallacy involved in the attempt to separate basic, clinical or public health research, or prioritize one over the other.

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