Prophylaxis of neotropical exanthematic typhus in Brazil

by

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The rational prophylaxis of a disease results from the best and deepest knowledge of it. That of Neotropical exanthematic Typhus in spite of what is known of the disease, is not easy in Brazil. One of the first difficulties is the want of culture of the majority of our country people. Now, it is principally in the country or in the districts of the city bordering on the country, that the fatal cases occur. They are usually "poor devils" ("unimportant people") but one is often impressed by the robustness of many of those who live around the large cities where hygiene, with some of its conditions has penetrated. But the fact of the disease having attacked persons of little social influence, explains why the problem has not yet been solved amongst us.

Man is, without doubt, infected by the strains VB, VA1 and VA2 of the Brazilian virus:

1st — in the country, in the thickets and woods.
2nd — in the house or its surroundings.

The first constitutes, usually, isolated cases of the disease; the second forms a part of domiciliary cells, with two, five, seven and even twelve cases in the same house.

Responsible for the first are the ticks, principally Amblyomma cayennense and Amblyomma brasiliense specially in the nymph stage, considering the habitual inheritance of infection in these arthropoda that infest wild animals. depositaries of virus, whose names and numbers we have already given in many articles.

Responsible for the second are the Cimex lectularius principally and the nymphs and larvae of ticks dropped in the vicinity of houses.

Bugs and even larvae in the neighbourhood of houses can lodge themselves in man (who may also be a depositary of the virus), in dogs, and in sheep that usually have the disease, unapparent, with the virus in the blood
for some time. These domestic animals as everyone knows, are messmates of man in the interior of Brazil, often sleeping, some of them, with him in the same bed or under it. Therefore, the complete and rational prophylaxis of the disease, amongst us, would include the following measures: —

1st — *The clearance of ticks from the infested zones.*

At first sight this advice may appear to be contrary to sense. We felt this when talking, one day, to a high administrative functionary of Brazil; he could not help smiling and then bursting into laughter at the idea of exterminating the ticks, not only in certain zones of the State of Minas, as also in those of any state of Brazil. We gave the example of the United States of North America, in the fight against the Texas fever or "Piraplasmosis bovina". Of course, if anyone had spoken of exterminating the mosquitoes in Rio de Janeiro or rather, a determined species of mosquito in Rio de Janeiro, before the Oswaldina era he would have been labelled, as that scientist was in the beginning, an imposter or a madman. Nevertheless the campaign of Oswaldo Cruz was a triumph for Brazilian science. The extinction of the _Anopheles gambiae_, in the North-East of Brazil, is a model of work of this kind and has saved thousands of our countrymen, attacked by malaria, from death. The tick baths would be multiplied, principally around the large cities where the disease has been localised: Belo Horizonte, Sabará, Teofiló Otoni, Pitangui, Araxá, Pomba, Aiuruóca, São Paulo, etc. One day it may be possible, by generalising this measure to make the thickets of Minas Gerais, São Paulo and Rio de Janeiro, over poorer and poorer in ticks. The benefits that the clearance from ticks would bring to the flocks and to man would be enormous. Bleeding and the consequent anaemia in cattle that live in fields infested with ticks is a subject already studied and resolved in veterinary art. It is unnecessary to mention the other diseases that the "Ixodidae" cause in cattle and horses, that although immune themselves to the typhus carry ticks, infected with the virus VB, VA1 and VA2 of neotropical exanthematic typhus, letting these arthropoda fall in the proximity of houses, yards, footpaths and fields.

In 1935-1936, we insisted that at least around Belo Horizonte such a trial should be made. The bill n. 27 of 21-10-36, of the Municipal Council of Belo Horizonte, inspired by us, was directed, although very timidly, to this matter. We had hoped to get something more positive and energetic. But better little than to continue unarmed in this field.
The bill ran: —

Article One. The formation of pastures, or their use, in any form, in the urban, suburban or outlying districts of the Capital is forbidden. § 1st. The prefect may, however, authorise the formation of pastures in the suburban districts after consultation with the Directorate of the Public Health Department.

2nd. In the suburban and outlying districts the prefect may authorise the planting of grass for fodder, at the request of those interested after hearing the opinion of the Directorate of the Public Health Department.

Article Two. The proprietors or tenants of uncultivated land situated in this zone are obliged to keep it clean, by cutting or burning the bushes and by keeping the woods, if any, fenced.

Article Three. The proprietors or tenants of uncultivated land or grass-land will be required to fulfil the preceding article within thirty days of notification.

Article Four. The infractors of the present law will be fined 200$000 (two hundred mil réis) for land situated in the urban district and 100$000 (one hundred mil reis) for the suburban and outlying districts, in cases of reiteration.

Article five. The Mayor is authorised to hely with the sum of 1:000$000 (one conto of reis) every person who constructs a tick bath, on his property, if this is required by the Public Health Department.

Article Six. The prefect is authorised to open a credit account up to a maximum of 20 contos of reis.

Article Seven. This law will take effect from 1937.

Article Eight. Anything to the contrary is hereby revoked.

As we see, it is not a decisive project, although it contains rational measures of prophylaxis for the Capital of Minas. But even this law was not carried out. To obtain results, and ten years is a sufficient time to show some, it would be necessary to make the baths compulsory for every animal, in the suburban and outlying districts, without exception of any kind, whoever the owner might be and whatever his social position.

For the environs of the capital of São Paulo there is also a law, passed by the municipal authorities and the work of Dr. Amancio Candido Esquibel on the results of its application, is significant.
The decree is as follows:—

Article one — The Directorate of animal Industry of the Department of Agriculture, Industry and Commerce, is authorised to fix the boundaries of the zone to be cleared of parasites, transmitters of exanthematic typhus.

Obs. This zone will include, initially, the municipality of São Paulo and those surrounding it.

Article two — From the defined zone no cattle, horse, ass, mule, goat, sheep, dog or other carrier of the parasite will be allowed to leave without the permission of the Directory of Animal Industry.

Article three — For the extermination of parasites the Directory of Animal Industry will have tick-baths built in the most convenient places.

Obs. Slaughter-houses and refrigerating-plants or other establishments that have a great number of animals, must build, within 30 days, the necessary tick-baths, in accordance with the design supplied by the Directory of Animal Industry.

Article four — The owners of animals enumerated in Article two, are obliged to pass them through the tick-bath every 20 days if the inspectors of the Directory of Animal Industry so determine.

Article five — For the private tick-baths the same rules will be observed as for the official ones.

Article six — Railways and Transport Companies are forbidden to take any animal, of those enumerated in article two, from the interdicted zone without the necessary transit license, given by the Directory of Animal Industry and the transport vehicles must be rigorously disinfected.

Article seven — The railways may accept animals from the Interior for the interdicted zone, by despatching them to stations indicated by the Directory of Animal Industry.

Article eight — Animals are not permitted to remain in open places, within the infected zone, on penalty of being confiscated.

Article nine — The cattle already in the interdicted zone will remain under the severe vigilance of the Directorate of Animal Industry.

Article ten — Functionaries of the Directory of Animal Industry and Public Health Department, will destroy all homeless dogs and all rodents found in the interdicted area and its neighbourhood.
Article eleven — The animals sent out of the infected zone will be labelled by the Directory of Animal Industry, noting their destination and the label will be sent to the Sanitary Service.

Article twelve — The Police will render any help that is required of them by the functionaries of the Directory of Animal Industry and the Sanitary Service, in the execution of this Decree.

Article thirteen — The cost incurred in the carrying out of this Decree, to the limit of 100 contos, will be met by obs. 4, of Article seven, of the Decree n. 6261 of the 30th of December 1933.

2nd — Measures against vagrant dogs, goats and other animals, carriers of the virus.

In previous articles, already published, we have enumerated the principal carriers of the virus of neotropical exanthematic typhus in Brazil.

Measures must be directed in the first place, against the house-dog (Canis familiaris). The unnecessary ones should be killed and those remaining kept for work or as pets, should be vaccinated every year with a type of mixed vaccine of the strains of Brazilian Virus of neotropical exanthematic typhus. The same for cats (Felis domesticus) and goats (Capra hircus). The other animals should be hunted or eliminated by poison to clear them completely from the neighbourhood of houses, and even of pastures and woods near houses. It is not difficult to hunt opossums, foxes, agutis, wildcats etc.

3rd — Pastures, fields and woods of little economic value should be burnt annually, principally those on the boundaries of the cities where there are many residences. The fires in the dry cold season will destroy a certain percentage of ticks in the larvae or nymphic stage.

Besides driving away small animals, carriers of the virus, this annual burning of the vegetation will naturally prevent cattle and horses from coming into the neighbourhood of houses in search of food and there dropping the infected arthropoda.

Of course this burning must be directed and limited to places where the crops will in no way be affected.

4th — A real propaganda against neotropical exanthematic disease, amongst the urban and rural population of the infested zones must be made by:

a) local talks with protographs and graphs.
b) cinema with appropriate films.
c) short articles in newspapers with a wide circulation.

d) pamphlets, written in simple language, with photographs of serious cases and the percentage of deaths in these cases.

e) showing the part played by dogs, cats, goats and wild animals, bugs and ticks in the dissemination of the disease.

5th — Fight against all the vermin in the homes and around them.

6th — Show that infection by ticks, can certainly be avoided, if they are removed within 12 or 14 hours, from the time they stick to the patient’s body. It is sufficient to make a good search on these persons returning from the woods and remove the ticks by any means, even homely ones.

7th — Advise the use of D.D.T. Gammexane and Toxafeno for the expurgation of the animal’s houses and prevent the ticks from fixing themselves on man or animal by the use of these powerful insecticides.

8th — Advise preventive vaccination for the disease, principally of those persons who, working in places where the disease is endemic, are subject to repeated and numerous bites of ticks and bugs. The vaccine should be made with various strains of the virus V.B. of Brazil. The ideal would be for each State, where the disease has been found, to establish an Institute or a section of the Institute destined to fabricate vaccine. This, in fact, was our plan, when we organised the Ezequiel Dias Biological Institute in Minas Gerais. It would perhaps be convenient for a commission of Brazilian technicians to study the problem and standardise the method of preparation in the country.

To gain an idea of the quantity and variety of types of vaccine used to-day, it is sufficient to read the publications of Clavero del Campo and Peres Gallardo, from 1941 to 1943 and D. Albaladejo, 1941.

The types of vaccine are many and there are still variants for other animals, with other drugs but fundamentally with the same principles of technique.

The Spencer-Parker type of vaccine which we used for some time, is certainly a good product and has to its credit fifteen years of service in the United States. This was the type of vaccine we intended to make in the new pavilion of the Ezequiel Dias Biological Institute in Minas Gerais, before knowing the Cox type of vaccine and technique which is simpler, less dangerous and apparently just as efficient. We even had a long correspondence with the great North American technician R. R. Parker about the organisation of the work in the Hamilton Institute, Montana, U. S. and the techni-
que of preparing the product on a wide scale. He sent us photographs, drawings, plans and a detailed description of how the work is carried out in that great North American Institute.

The preparation of Spencer-Parker vaccine is difficult, requires special installations, a sure and exact technique against the dangers that those who work on it are exposed to, a great apparatus for breeding ticks on a large scale. Naturally when one devotes himself to this work, it appears to be simple and really in Montana everything must be splendidly organized for the production of vaccine in great quantities. But it was not so in the beginning, as Parker observes. Those who work with the Exanthematic group know that the danger in manipulation lies first in the habit of working with highly virulent material, which causes the assistants, after a certain time, to commit some fatal carelessness; and not a few lives have been sacrificed. We believe that no other disease has cost so many lives dedicated to its investigation.

The second danger is in the treatment of the carrier arthropoda. The virus itself, the patients, the infected animals, the dead bodies are dangers relatively easy to overcome. The arthropoda area not. They are, in fact, by their size and number and certainly by the extreme virulence of the microbe, a real and constant danger, difficult to overcome. Almost every case, and they are many, of infection in the laboratory by virus of the diseases of the exanthematic Typhus group, was in consequence of careless manipulation of infested arthropoda.

In addition to a sure technique, it is necessary to maintain constant vigilance over everybody and everything, to prevent regrettable accidents in ordinary research laboratories, where these carriers are being studied. For these reasons, if we had to use a type of vaccine, in the present stage of our knowledge in Brazil, we should prefer the Cox type, a product of comparative simplicity, in its preparation and control.

We wish, however, to call attention to a point of capital importance, for preventive vaccination for neotropical exanthematic Typhus in Brazil. Long experience in the practice of epidemiologic problems of this group of diseases, teaches us that we must be very careful, before coming to rigid conclusions about the results of the use of the product.

The first thing we must resolve is the question of the doses and the reaction which the vaccine produces. It is one thing to vaccinate the employees of a private company, soldiers or technical functionaries of an Institute or official department; another thing entirely to vaccinate a group of ignorant individuals, sceptical regarding medicine and doctors, who must
take a product, an injection, to avoid the disease. And we must not forget that when the vaccine produces a reaction, rarely will the “caipiras” (yocels) return for a second injection; similar cases have occurred, even with vaccination for rabies in the Biological Institute Ezequiel Dias and we saw a child die from hydrophobia, because the second dose of vaccine having produced a slight local reaction; the father stopped the treatment.

It must also be remembered that severe cases of neotropical exanthematic Typhus in one locality are not numerous as are those of small-pox or yellow fever during an epidemic. The “caipiras” say it isn’t worth while to be pricked for a disease that kills only two or three people in a hamlet.

Outside the periods of epidemics, in so backward a place as the interior of the country, any preventive injection would be attempted in vain. To make one preventive injection in a healthy person is difficult, to make two or three is almost out of the question. We must not forget the distances to be traversed in the interior of Brazil with intercalary injections, as those, for example, of the Spencer-Parker type of vaccine, which, above all, often produces violent reactions.

The ideal would be a single vaccination with vaccine prepared from various strains of Brazilian virus by the Cox technique.

Another point, which our experience puts us on guard against, is the conclusion we draw of the prophylaxis of the disease due to the product. We have verified many times in Minas Gerais, the silence of the Centres, for several years, of severe cases of neotropical exanthematic Typhus, without any individual or general measure of prophylaxis having been taken. Here is an irrefutable and significant example:

The district of Gorduras is one of the great foci of neotropical exanthematic Typhus around Belo Horizonte. It is easy to reach, and having relatively few inhabitants, we were able to fiscalise it rigorously. In 1929 there were a few serious cases. In 1931, three serious cases were registered. From that date until 1936 no further case was registered, though no prophylactic measure, individual or collective had been taken. If we had vaccinated the people of that hamlet, we should certainly affirm and proclaim to the four winds the efficiency of our vaccine. Why did the focus remain silent, first for two years and then for five? To-day we can say that only the severe forms ceased, but numerous mild and unapparent forms of the disease continued, which also guaranteed the apparent silence of the foci.

These forms are maintained by the bugs (Cimex lectularius) and also by the ticks, inoculators of the strains VA1, VA2 and even V.B. in per-
sons who have lived in the locality a long time. It is this immunity which explains the spontaneous silence of the foci. Que day the resistance acquired by the patient is overcome, either by accidental inoculation of a greater quantity of the strain V. B. or by the loss of the immunity acquired for various reasons and the severe forms reappear in a few cases and often a single case in a whole locality where everyone is subject to the same bites of the blood-suckers, carriers of the virus, and where life is more or less the same for everybody. The serious cases, sporadic in the centres, may also be the consequence of new inhabitants, who have come recently from places free of the disease.

This spontaneous and apparent extinction of the foci should make us very careful and even reserved as to the conclusions we come to of the success of mass vaccination of the populations of the interior of Brazil, until we have a greater and wider experience of the product.

There is yet another difficulty to be overcome. If the preventive vaccines of the exanthematic group gave a lasting immunity, as for example the vaccine for yellow fever, it would be advantageous to immunise the whole population of a stricken zone. But in practice this is not so. The technicians of the Institutes that work with the virulent material, are subjected to revaccination every year, to guarantee immunity, nevertheless at end of two, three and even five years of revaccination they may get the disease although in a mild form.

Parker said, in 1935:

"The degree of this residual immunity appears to be greater in persons who have been vaccinated two or more successive years".

In 1941, he said:

"The degree of protection conferred varies with the individual, the relative virulence of the infecting strain, the number of successive years that vaccine has been administered, and perhaps to some extent with the age of the person vaccinated. The duration of any consequential degree of protection probably seldom exceeds the year of vaccination, except under certain circumstances and immunization each year is the only safe procedure."

In the interior of Brazil, this would be difficult; in research laboratories, it would not. A long sanitary propaganda is necessary to prepare for the work of immunization.

The immunity conferred by the vaccine is precocious, but not definite or absolute. So it must be, for the resistance obtained with the living virus
itself in the centres of the disease, by the old inhabitants can be destroyed, in one stroke, by the strain V.B. killing the patients.

Here the Cox vaccine, according to the formula established by the author, has been produced regularly, with an efficient antigenic action by Dr. José Tostes, in the Public Health department of Rio de Janeiro, Niterói, according to the publication in the Review of Biology 1944.

Vigilance in the centres, of new arrivals and principally human carriers of the mild and unapparent disease as depositaries of virus capable of irradiating the disease, is necessary.

In a very interesting article, published in Brazil Medico 1945 as a complement to one he had already written in 1944, the notable Paulista researcher, Toledo Piza, advises:

1st Cultivation of the land, ploughing and tilling it.

2nd Felling of the local woods.

3rd Drainage of the lakes.

All this, naturally, to clear away the ticks. If it were possible to eliminate the virus from the districts around the inhabited zones, the disease would be exterminated, because it is from there that it penetrates into the interior of the dwellings, constituting mass domiciliary foci.

ZUSAMMENFASSUNG

Die rationelle Prophylaxe einer Krankheit hängt ab von der besten und tiefsten Kenntnis derselben. Die des neotropisch exanatematischen Typhus (Fleck-Typhus), trotz allem, was man von dieser Krankheit weiss, ist nicht leicht in Brasilien. Eine der Grössten Schwierigkeiten finden wir in den Entfernungen unseres Hinterlandes und in dem Mangel an Kultur unserer Landbevölkerung. Der Mensch steck sich sicherlich an mit den brasilianischen virus-Arten VB1, VA1 und VA2:

1. im Felde, in den Wäldern und in Gestrüpp;

2. in den Wohnungen und in deren Umgebung.

Die ersten bilden für gewöhnlich die Einzelfälle der Krankheit. Die zweiten gehören nicht selten zur den starken Herden in Wohnungen mit 2, 5, 7, 12 und sogar mit Fällen in demselben Hause. Verantwortlich sind für die ersten Fälle die Zecken (karrapaten), hauptsächlich der *Amblyomma cayennense* undder *Amblyomma brasiliense*, besonders wenn sie sich noch im
Puppenzustand befinden, wegen der gewöhnlich erblichen Ansteckung dieser Artropoden, welchesich an Waldtieren, Träger dieses "virus", anstechen.

Die zweiten sind verursacht durch den Cimex lectularius (Bettwanze), sowie durch Puppen und Larven der Zecken (Karrapaten). Welche in der Nähe oder sogar im Innern der Wohnungen herabfallen. Die rationelle und vollständige Prophylaxe unter uns verlangt folgende Massnahmen:

1. Vernichtung der Zecken in den angesteckten Zones, mittelst entsprechenden und verpflichtenden Massregeln, die ausnahmslos durchzuführen sind;
2. Kampf gegen herrenlose Hunde, Ziegen und andere Tiere, als Träger des "virus";
3. Verbrennung der Weiden, Felder und Burschwerk von geringem economischen Wert, besonders wenn sie and die Wohnungen grenzen;
4. Rationelle Propaganda gegen diese schwere Krankheit.
   a) durch lokale Vorträge, gestützt auf Photographien oder allgemein verständliche zeichnerische Darstellungen;
   b) durch das Kino;
   c) durch einfache Artikel, Welche den Gegenstand klar und deutlich her vorheben;
   d) durch entsprechende Flugblätter.
5. Bekämpfung von Wurmern im Innern und in der Umgebung des Wohnungen;
6. Beweisführung der sicheren Möglichkeit die Krankheit zu vermei- den, wenn man die Zecken vom Körper entfernt, spätestem 12 oder 14 Stun- den nachdem sie sich angehefter haben;
7. die Anwendung von DDT, "Gammexane" und "Toxafeno" anraten zur Desinfektion von Häusern und Tieren, um die Zecken zu bekämpfen;

Der Verfasser hätt einige Zeit mit dem Spencer-Parker-Impfstoff gearbei- tet. Heute empfiehlt or die Anwendung von originellen oder abgeänderten Cox-Impfstoff.