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POLIOMYELITIS IN IRAN

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In Iran, there was a deeply rooted belief, that poliomyelitis was totally absent from the population, in contrast with the relative prevalence and the severity of paralytic forms among foreigners coming from "infected" countries, and having lived for only a short time in Iran.

As the rumour of the dangerous importation of the infection by these foreigners gained ground, we included, in 1954, the study of poliomyelitis in a comprehensive serological survey on the presence of the various viruses in Turkey, Iran and Afghanistan, which we carried out with the collaboration of the Maryland University and the Walter Reed Army Institute of Research.

The results of the examinations of the first serum samples taken in Iran were clear enough not to necessitate, for the time being, this serological research to be pushed further. In Teheran itself, the first fifteen sera examined, taken from the age-group over five years, showed all poliomyelitis antibodies, fourteen of which against the three types of virus and one failing to show antibodies against type III alone. Out of eleven sera, in the age-group one to five years, all showed antibodies against two types at least and five against all three types. Still more striking were the results of the examinations carried out in rural areas as, for instance, those from the small village of Akinlou, in Kurdistan, which is completely isolated and therefore no recent importation of the infection could be made responsible; out of thirty-five children or adolescents (from six to twenty years) all without exception showed antibodies against the three types; out of ten children aged less than five, eight were already triple positive.

This survey was sufficient to show that the status of poliomyelitis was the same in Iran (and in Turkey and Afghanistan as well) as in the other countries with a still insufficiently developed health organization. Infection has undoubtedly been prevalent for thousands of years. It was extraordinarily widespread so that nobody in the country could escape contamination.

It seemed difficult to admit that infection could be so general among the whole population without paralytic manifestations, at least in young children, especially as it appeared that contamination occurred yearly.

It was therefore admitted that:

- either contamination in Iran occurred so early that children became infected before the age of six months, at an age where research carried out in other countries had shown that the disappearance of maternal antibody was completed. An early contamination under the protection of transplacental antibodies could produce infection without disease with consecutive immunity. The popular practice of giving a sugared water feeding-bottle all day long, at a time when Teheran was not provided with chlorinated water and when few mothers in villages thought of boiling the djoub water, was the basis of this assumption.

- or the rate of antibodies in adults, constantly reinfected, was so high that mothers were able to transmit to their children a quantity of antibodies which took longer to be eliminated and thus protected children beyond the sixth month.

- or the polioviruses were in Iran less pathogenic than elsewhere; such an assumption was inconsistent with the severity of paralytic cases in foreigners who contracted the infection in the country.

- Finally, the last possibility: infantile paralysis existed in Iran, although not diagnosed, as was previously asserted by some clinicians, first of whom our friends Garribe and Ameli are to be mentioned, and to whom in our opinion falls by right the title of discoverers of infantile paralysis in Iran. In fact, this possibility was undoubtedly the most probable.

Since the last war, J.R. Paul and his collaborators, while studying the incidence of paralytic poliomyelitis among the allied Expeditionary Forces in the Middle East, which was ten times higher than that recorded among troops stationed in Europe and the United States, noticed that the disease, which had been until then ignored by clinicians, also among the population. In the course

of a long study carried out in Cairo later on, Paul and his collaborators showed the prevalence of paralytic poliomyelitis among the Egyptian population. On the basis of their own clinical observations, they proved that, although paralytic poliomyelitis did not practically exist in adults, it reached in young children a prevalence equal to that observed in the USA (average from 1932 to 1946).

In 1956, our collaborator R. Pournaki left for Paris where he spent one year in the Virus Section, with Mr. Lépine. On his return, early in 1957, he organized with A. Boué our virological service and as from September of the same year, this service was able to start the type of work of which Pournaki has set forth the techniques. In order to define the conditions of poliomyelitis in Iran a survey was carried out with the object of:

- (1) resuming on population samples, on a wider scale, our survey of 1954;
- (2) assessing the prevalence and if possible the rate of maternal antibodies in newly-born infants;
- (3) research on the speed of disappearance of these antibodies during early life;
- (4) proving the precocity of contamination;
- (5) demonstrating the absence or presence, and in the latter case trying to define the prevalence, of paralytic poliomyelitis.

The first point was studied on the sera of fifty-two children under five years, adolescents and adults, belonging to all classes of the population. The results proved that our limited survey in 1954, which in fact aimed only at proving the presence of poliomyelitis infection in the Iranian population, could not give an accurate picture of the rate of the infection. While all subjects examined showed polio antibodies, only thirty-two out of fifty-two showed antibodies against all three types (instead of fourteen out of fifteen in 1954), sixteen against two types, and four against one type only. The prevalence of type I was demonstrated by the fact that only one subject out of fifty-two was deprived of antibodies against this type.

The second point was studied on the blood from the umbelical cord of 110 newly-born. Twelve showed an illegible result, ninety-eight a neatly interpretable result. Out of these ninety-eight newly-born, all without exception showed polio antibodies and fifty-one, that is to say more than half, against

the three types. Eight only lacked antibodies against two types, thirty-nine against one type. The prevalence of type I was made conspicuous by the fact that only one of the ninety-eight newly-born lacked antibodies against this type.

These results coincided exactly with those of the survey on the first point, the mothers transmitting obviously to their children all the various antibodies they had themselves.

The results of the research carried out on the third point showed that it was useless to grade the rate of these antibodies as had been planned.

Indeed, the research carried out in August 1958 on the speed of disappearance of antibodies in early childhood, in 200 children of Nikoukari dispensary, aged from two to twenty-four months, showed that the percentage of presence of maternal antibodies in the children was dropping rapidly so as to reach its minimum as from the sixth month, that is to say that this disappearance followed exactly the same curve as in the other countries where this point had been studied, as for example the European countries and the United States.

The same survey allowed us to study the reappearance of antibodies in children to elucidate the fourth point of our research, viz. precocity of contamination. The curve called the "triple negative", that is to say the complete absence of polio antibodies, starting as we have said from zero - as at birth no children were lacking maternal antibodies - to reach practically 100% at the ages six to nine months, returned to zero with extreme rapidity, passing by 75% as from the tenth month, 50% at the thirteenth month, 25% at eighteen months. As from two years, 85% of the children showed antibodies against one, two or the three types of virus. These figures added a confirmation to those previously published by J.R. Paul and his collaborators for the infantile population of Cairo in 1952, then for that of Morocco in 1955, by Gelfand and Miller in 1956 in Liberia, Barski and Lépine in 1956, later Delville and his collaborators in 1957 in the Belgian Congo. All these authors had noted the precocity of contamination, but our research proved, thanks to the method of finger-bleeding which enables the taking of samples from very young children, that contamination occurred still earlier than had been established by our predecessors.

Simultaneously with this serological survey, we were carrying out a work of systematic research of enteroviruses in the stools of children belonging to the same age-groups. We carried out on the one hand, periodical sample-taking from children of the employees of our small staff as from their birth; twenty-nine

children were thus followed up, thirteen of whom belonged to families accommodated at Pasteur Institute, under favourable sanitary conditions and sixteen to families living in poor and unhealthy workmen's wards. On the other hand, we took - from September to May which is known as the most favourable season in other countries for the spread of enterovirus - single samples of stools from 106 children less than four years of age at Nikoukari dispensary.

The results of the survey confirmed those of the serological survey. Before six months, six out of sixteen of the children examined were already enterovirus carriers; this proportion maintained itself roughly at the same rate until the end of the first year of age: nine out of twenty-three children aged between seven and twelve months were examined. But it rapidly rose during the second year of age: twenty-two enterovirus carriers out of thirty children aged from thirteen to twenty-four months, and maintained itself at high rates afterwards; thirteen children out of twenty-three during the third year of age, twenty-five out of forty-one in the fourth year. Out of seventy-five viruses isolated, thirty-three were studied for identification; out of these twenty-two viruses, eight were polio viruses, the other twenty-five belonging to the Coxsackie, Echos, etc. types, present in Iran as well as in the other countries.

The special interest of these results lies in the fact that they confirmed the extreme precocity of the contamination by intestinal virus in Iran and showed the prevalence of polioviruses among these enteroviruses. Contamination could occur in a non-negligible number of children whilst they were still under the protection of maternal antibodies, which confirmed the fact noted in adults that antibodies protect only against the disease, not against infection. This research also showed what enormous chances of contamination awaited the child as soon as he would start his autonomous life, that is to say from the age of ten months.

The last point of our research: to prove the presence of poliomyelitic disease, could be achieved thanks to the assistance of those of our colleagues who were kind enough systematically to direct to us the patients they had diagnosed as "poliomyelitis" and I must thank them here, especially our friends Mokhtar Zadeh and Ameli.

This study is still under way at the present time and the results we are submitting to you are up-to-date. Out of the 127 patients who have been sent to us, we have isolated forty-six times a duly identified poliovirus, i.e. four times type III, six times type II and thirty-six times type I, which proves once more the prevalence of the latter type in Iran.

Out of the forty-six cases, twenty-six represented a diagnosis of certainty in the scientific meaning of the word, that is to say, as explained by Pournaki, a perfect agreement of the serological response. The other twenty represented a presumed diagnosis, in the scientific meaning of the word as well, in fact such a strong presumption that the clinician may with good reason consider it a certainty.

But what could be said of the eighty-one remaining cases; two-thirds of the patients sent by the clinics with the diagnosis of paralytic poliomyelitis? Do the negative results of our examinations invalidate this diagnosis? In no case. In fact, it appears that it is only practically due to the fact that the examinations were made too late for the virus to be isolated. The report of the first Expert Committee on Poliomyelitis, which met in 1953 under the auspices of WHO has defined this question according to the research carried out in various countries as follows: "During the first ten to fourteen days after onset, practically every patient excretes virus in the stool. By three weeks after onset, approximately half the patients no longer excrete virus; by five to six weeks, only 25% of patients still excrete virus in the stool, and in a small percentage excretion may continue for twelve weeks."

The results of this research shed some light on the picture of poliomyelitis in Iran, but only partially. The virus, or rather the viruses, are extraordinarily widespread in nature and the children contract the infection very quickly. As in all countries where the health organization is still inadequate, this early contamination confers a strong immunity which protects adolescents and adults from the disease.

But so far we know nothing, or too little, about the incidence of the disease among young children at the age which, according to our research, has proved to be the age of contamination. Although the work of a few clinicians, showed clearly the presence of poliomyelitis in Iran and this was confirmed by the findings of our laboratory, yet its prevalence could not be determined.

The programme for the future of our common research clinic laboratory is clear and imperative; it must aim at determining this incidence of the disease, which is the only factor which would allow for an assessment of its relative severity and, as it will be seen later, to foresee the future and, possibly, organize it. As a matter of fact, the true incidence must include atypic forms: light (such as cases of facial paralysis recently referred to us by Mr. Mokhtar Zadeh) or violent (such as the bulbar forms referred to us by the same clinician), and furthermore the meningitis said to be "aseptic" in which we do not know yet the part played by poliomyelitis. As an indication, I mention out of 152 cerebro-spinal fluids received in 1338, for instance, 75, - i.e. the half-belonged to aseptic meningitis: unfortunately we received no stools or sera of these patients, which could have made possible the diagnosis of these meningitis.

It is obvious that in order to determine the true incidence of the disease, all our colleagues without exception, at Teheran at least, should search and detect systematically and notify all cases of this disease, the declaration of which is compulsory. This would be difficult to obtain, but as the most important factors for the assessment of the situation are the factors of severity and age, we hope, if the colleagues who have started this work with us would continued it and if others join them, obtain a picture sufficiently accurate of the present situation and observe its development.

As a matter of fact, the future waiting for us - we may say - unquestionably - is the following: The contamination by the poliovirus is mainly of hydric origin; the installation of a network of treated water distribution in Teheran and other towns in Iran will quickly modify the present situation.

That is why we must firstly, and imperatively, describe this situation. Here it is for our clinicians to speak. I shall confine myself to point to the research which we have just narrated showing that the situation in Iran is the same as that described by international research in countries where - as in Iran - a large diffusion of the infection is present in the early childhood, that is to say a weak incidence* and mildness of paralytic poliomyelitis, which remains limited to early childhood.

*The Expert Committee on Poliomyelitis estimated - according to research carried out in various countries, that this incidence lies at one case for 1.000 contaminations (a proportion ten times lesser than that of USA for example). If we calculate the annual rate of increase of the infantile population in Teheran at 50.000 yearly, the incidence to which one might expect should be only about 50 cases yearly.

What is in store for us is what happened in all countries which in the past followed the development of health now followed in this country, that is to say stronger incidence and malignancy of paralytic poliomyelitis extending to all age-groups; appearance of familial, school, etc. epidemics. What is responsible for this transformation? Obviously the fall in the contamination rate as sanitary conditions are improving, by the double phenomenon of the rarefaction of contamination opportunities and the decrease of the number of carriers excreting virus, a decrease which lowers the prevalence of the virus in nature; and consequently irregular and late immunization of the population. This explains the extension of the disease to all age-groups and the appearance of epidemics, but not the increased malignancy and the increase of the number of cases.

Must one admit that the poliomyelitic disease is less frequent and serious than in the first years of life? Not at all; the statistics of the countries where poliomyelitis is "epidemic" show that early childhood is almost as frequently and seriously affected as the other ages. Can the protection against the disease by residual maternal antibodies become operative? Do our own research and those of others show that it may become operative? The reply to this is no.

Paradoxically, if we consider the enormous facilities implemented in the research on polio, we have no explanation of this phenomenon and we can only suggest hypothesis. Among them, the most attractive and at the same time the most credible is that of A.B. Sabin. The famous American specialist considers what he calls "the cipher or weak incidence of paralysis in early childhood is paradoxically associated with a large diffusion of the infection in early childhood" in countries with an inadequate level of health due to the presence in these countries of very numerous non pathogenic strains and weak virulent strains beside relatively few strains of strong virulence. The presence of the first would explain the prevalence of inapparent infections strongly immunizing, and that of the second the existence of mild forms, whilst the scarceness of the third would explain the very weak prevalence of serious forms, even in foreigners arriving in these countries without antibodies.

The increasing pressure of hygiene would tend to dispel those avirulent or weakly virulent strains, and spare the strongly virulent strains.

It is this fundamental assumption - which numerous experimental and epidemiological facts tend to confirm every day, - that led Sabin to the bold concept of vaccination by means of a virulent live poliovirus; bold because the vaccinees are in fact infected and carrying viruses, they spread them and the idea of seeing these viruses, so extensively spread, becoming virulent, has troubled many scientists.

In fact such a danger is not to be feared, as soviet hygienists perfectly understood it and apply at present the Sabin method on an enormous scale. In fact, it seems that the opposite is always occurring, as the avirulent strains are undoubtedly "mutants" permanently produced in nature by strongly virulent strains.

To conclude, one may ask what may be the best position for the practitioner and the hygienist in Iran, now and in the future.

At the present time, the problem of poliomyelitis is not posed to the hygienist, in comparison with the enormous urgent problems they have to face. It is already posed to the practitioner, to whom the question of vaccination is more and more frequently propounded by parents who are unwilling to let their children run even so dangerous a hazard as one in a thousand. The behaviour of the practitioner is easy to be defined: vaccination with one of the inactivated vaccines, now extensively available on the market, to be practiced as soon as the child reaches the age of disappearance of the maternal antibodies, that is to say at six months, will enable the child to cope afterwards with the minimum risks of natural contamination which will confer him final immunity.

The present conditions are ideal for vaccination by inactivated vaccine, as further "boosters" for the maintenance of immunity, could not be practiced thanks to early and certain natural immunization.

As for the future, it belongs to clinicians and epidemiologists, as already said, to set the time where the increase of the number of serious cases and the appearance of cases in older children and adolescents, will suggest the necessity of group vaccination by live poliovirus, and to put again in circulation these beneficial avirulent viruses which we are actually suppressing.