STUDY OF TYPHOID AND PARATYPHOID INJECTIONS IN IMMUNIZED PERSONS

Communication by the Government of Viet-Nam

Importance of the Subject

It is essential that subjects be vaccinated as effectively as possible if the increase in paratyphoid B and of certain strains of the Eberth bacillus with less immunizing effect is to be halted. The consequence of this increase is an augmentation of cases of typhoid and paratyphoid fever in immunized persons.

There are, of course, certain difficulties in administering immunization. Some are of the opinion that three injections are excessive. In the schools, parents would agree more readily to TABDT immunization if it were administered in three injections, in the same way as immunization against diphtheria and tetanus, and it is obvious that to insist on four injections will only cause a drop in the number of persons immunized against typhoid. So far, it has been generally felt that it is better to immunize a child against typhoid fever in a mediocre manner with three injections only, rather than not to immunize the child at all.

The long-term consequences of such inadequate immunization are that the individual is poorly protected, and the community is confronted with the threat of an increasing predominance of paratyphoid B - a source of unsuccessful immunization.

Since the discovery of the antibiotics, and especially of chloromycetin, certain physicians believe immunization against typhoid to be less necessary, seeing that the disease has become definitely less serious in view of therapeutic progress. They therefore tend to reduce the number of injections or to dispense with immunization altogether.
The Seine Health Council, at its meeting of 9 March 1951, on the proposal of Professor J. Boyer, expressed an opinion in favour of the four-injection method with a follow-up injection a year later, whenever this system was possible, for the two reasons just discussed.

History of Immunization

The clinicians having noticed the infrequency of typhoid among people who had already had the disease, research was carried out with a view to combating it by immunization. In 1888, Chantemesse and Vidal inoculated animals with cultures of heat-sterilized Eberth bacilli, but it was Wright who, on the advice of Haffkine, first experimented with the vaccine on man in 1896. The results were fairly encouraging, but the vaccinal reactions were extremely strong, and there were even some deaths.

In 1914, on the eve of the war, immunization against typhoid fever was made compulsory in the French Army by the Leon Labbé Act, and during the 1939-1945 war it became general. The Vincent ether vaccine was then used and rendered great service. This has now been replaced by the Pasteur Institute TAB vaccine.

The Pasteur Institute TAB vaccine is an aqueous suspension of several strains of the Eberth bacillus and of the paratyphoid A and B bacilli killed by heating at 56°C.

As a result of immunization, in 1914, typhoid fever became rare, but the paratyphoid fevers - and particularly paratyphoid B - appeared, and it became necessary to include paratyphoid bacilli in the vaccine in order to bring down the mortality rate.

French troops were immunized several times during the war; furthermore, one of the consequences of the unhealthy conditions of trench warfare was to set up in the immunized subjects inapparent infections which reinforced immunity.

Thus it may be said that between the two wars, typhoid fever in man was rare.

Investigations carried on in a hospital for adults were practically always in the women's wards. This situation persisted up to the period preceding the last
war even though most of the men had not received any follow-up injections of vaccine for 20 years.

The following principle emerges: immunization against typhoid fever has a prolonged effect but this long duration is perhaps in fact the result of occult re-immunizations.

In the period between the two wars, however, a new phenomenon was noted: an increase in the number of cases of typhoid fever among immunized persons.

During the 1914-1918 war such a case was considered as extremely rare. Vincent put the rate at 0.25 per 1,000, which appeared to be very low. In 1932, according to Montel, this proportion varied between 0.2 and 2 per 1,000. The rate increased, however, and before the last war it was about 5 to 6 per 1,000.

In 1943 and 1946, Boyer, Tissier and Cambéssèdes established the figure of 7 per 1,000. Subsequently, the rates were 9 per 100 in 1945, 11 per 100 in 1946, 8 per 100 in 1947, 14.5 per 100 in 1948 and 15 per 100 in 1949. In 1950, almost one-fifth of the patients were people who had received three injections of antityphoid-paratypoid vaccine.

R. Bestian and Mme. Bestian-Caudère indicated in a recent work (August 1950) that in Marseilles 16.6 per 100 of typhoid cases developed in subjects who had been correctly vaccinated, and that 12.5 per 100 were persons vaccinated in an unsatisfactory manner.

It is interesting to survey the position at the present time.

At the "Inspection Générale des Services Techniques d'Hygiène de la Préfecture de Police" we were able to carry out a large-scale survey, the results of which we give below.

In the first place, it must be stressed that in all the surveys the diagnosis had been confirmed by medical inspectors of epidemics selected on the basis of their university and hospital qualifications and fully competent in the field of communicable diseases.

Doubtful cases were eliminated from the statistics, i.e. cases in which an access of fever without any particular clinical character was accompanied only by a positive
serodiagnosis without positive haemoculture, as may be observed in immunized persons suffering from non-typhoidal diseases.

Results

In 1951, 240 typhoid-paratyphoid infections were confirmed by the medical inspectors of epidemics. Of these:

116 were cases of typhoid proper - i.e. - 48.3%
115 were cases of paratyphoid B - i.e. - 48.3%, and only
9 were cases of paratyphoid A - i.e. - 3.4%

Of these 240 cases of dothienenteria observed in Paris, 42 occurred in persons who had been immunized (35 men and 7 women), i.e. 1.75% dothienenteria in immunized persons of both sexes.

In 1952, 219 cases of dothienenteria were confirmed by the medical inspectors of epidemics of the Police Prefecture. Of these:

89 were Eberth infections - i.e. - 40.7%
116 were paratyphoid B - i.e. - 52.9%
14 were paratyphoid A - i.e. - 6.4%

The survey showed that, of these 219 cases, 37 patients had been immunized (31 men and 6 women), i.e. 16.89% dothienenteria in immunized persons of both sexes.

Thus, among the 459 typhoid-paratyphoid infections observed in 1951 and 1952, we noted:

209 cases of Eberth infection - i.e. - 44.66%
231 cases of paratyphoid B - i.e. - 50.33%, and only
23 cases of paratyphoid A - i.e. - 5.01%

of which 79 cases were immunized persons, distributed as follows:

37 cases of Eberth infection - i.e. - 46.83%
39 cases of paratyphoid B - i.e. - 49.36%
3 cases of paratyphoid A - i.e. - 4.81%
It will be seen therefore that paratyphoid B which a few years after the last war accounted for about 10% of typhoid-paratyphoid infections, tends to become more frequent than typhoid fever proper.

In a fairly recent work entitled "Acquisitions Récentes dans l'Epidémiologie et la Prophylaxie des Maladies Infectieuses" (Recent Advances in the Epidemiology and Prophylaxis of Communicable Diseases), J. Boyer, L. Corre Hurst and M. Tissier made an epidemiological study of trends in typhoid and paratyphoid infections during recent years.

Our work may be regarded as helping to round off that of the above authors.

Explanation of the incidence of typhoid and paratyphoid in immunized subjects

Is this due to the substitution of TARDT for TAB? This is possible - but it is often due to the increasing incidence of paratyphoid B.

In fact, the vaccine immunizes more effectively against typhoid than against paratyphoid B and little by little, as a result of the immunization of millions of the male population, there has been a greater decline in the Eberth infections than in the paratyphoid B type.

There are less paratyphoid B bacilli in the vaccine and there are many more paratyphoid B strains than Eberth strains.

Conclusion

Should TAB or the ether vaccine be substituted for TARDT? It should be remembered that the ether vaccine is often not well tolerated.

It would seem that the tendency should be, as recommended by Professor Boyer at the Health Council, towards the method of four injections with a follow-up injection after a year.

Should a follow-up injection be given every five years, as suggested by some? There is less certainty about this, as experience shows that typhoid-paratyphoid infection produces prolonged immunity and that no typhoid infection is found in immunized subjects until a few years after immunization.
Certain workers have thought, since the discovery of the antibiotics, that immunization against typhoid was less necessary and that in any case incomplete immunization would protect the subject against the more serious forms of the disease. In fact, nothing is less certain.

Incomplete immunizations, moreover, have the disadvantage of increasing the number of cases of paratyphoid B.

We have adopted the following criterion: adults are considered to have been satisfactorily immunized when they have had three injections, and children when they have received four.

We noted that many subjects alleged to have been immunized had in fact been incompletely immunized and these were not included in the statistics.

We have not included the follow-up injection, since this practice is only irregularly followed in France.

Thus we have included in the statistics only correctly immunized subjects who have had the follow-up injection after one year.

We are led to the conclusion that in the Paris region a much smaller proportion of the population has been immunized against typhoid fever than is generally supposed.

*Graph I*  Typhoid and paratyphoid infections in the Seine "département" from 1935 to 1952 Curve established year by year.

*Graph II*  Typhoid and paratyphoid infections in the Seine "département" from 1935 to 1952.

*Graph III*  Typhoid and paratyphoid infections in the Seine "département" Monthly averages from 1935 to 1952.

*Graph IV*  Typhoid
Paratyphoid B
Paratyphoid A
Paris 1943 to 1952 Curve established month by month.

*These graphs were received too late to be added to the present document. They will be communicated to Member States as an Addendum to "A6/Technical Discussions/Typhoid/10".*
Graph V
Typhoid and paratyphoid A and B
Monthly averages observed in Paris 1943 to 1952.

Graph VI
Typhoid and paratyphoid infections at different ages
Paris 1943 to 1952.

Graph VII
Eberth in both sexes
Paris 1943 to 1952 inclusive
males = 808
females = 1,229.

Graph VIII
Paratyphoid B in both sexes
Paris 1943 to 1952 inclusive
males = 812
females = 1,155.

Graph IX
Date of appearance of typhoid and paratyphoid infections
after vaccination (1951 and 1952)
Curve established year by year.

Graph X
Date of appearance of typhoid and paratyphoid infections
after vaccination
Curve established by five year periods.

*These graphs were received too late to be added to the present document. They will be communicated to Member States as an Addendum to "A6/Technical Discussions/Typhoid/10"
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ADDENDUM

Graphs to be added to document A6/Technical Discussions/Typhoid/10, dated 6 May 1953 (see footnote on page 7).
Typhoid and paratyphoid infections in the Seine "département" from 1935 to 1952
Curve established year by year

Infections Typho-paratyphoïdiques dans le département de la Seine de 1935 à 1952
Courbe établie année par année

Graph 1
Typhoid and paratyphoid infections in the Seine "département" from 1935 to 1952
Curve established month by month

Infections Typho-paratyphoidiques dans le département de la Seine de 1935 à 1952
Moyenne mensuelle mois par mois

Graph II
Typhoid and paratyphoid infections in the Seine département from 1935 to 1952

Monthly averages

Infections Typho-paratyphoidiques dans le département de la Seine de 1935 à 1952

Moyennes mensuelles

Graph III

Typhoid and paratyphoid A and B

Monthly averages observed in Paris 1943 to 1952

Moyennes mensuelles des typhoïde, paratyphoïdes A et B observées à Paris de 1943 à 1952

Graph V
Typhoid, paratyphoid B, paratyphoid A, Paris 1943 to 1952
Curves established month by month

Typhoïde, paratyphoïde B, paratyphoïde A à Paris de 1943 à 1952
Courbe établie mois par mois

Graph IV

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Typhoid and paratyphoid infections at different ages
Paris 1943 to 1952

Infections thypho-paratyphoïdiques aux différents âges
Paris de 1943 à 1952

Graph VI
Eberth in both sexes, Paris 1943 to 1952 inclusive

Eberth dans les deux sexes à Paris de 1943 à 1952 inclus

Graph VII
Paratyphoid B in both sexes, Paris 1943 to 1952 inclusive
Paratéphoïde B dans les deux sexes, à Paris de 1943 à 1952 inclus

Graph VIII
Date of appearance of typhoid and paratyphoid infections after vaccination (1951 and 1952)
Curve established year by year

Date d'apparition des infections typho-paratyphoïdiques après la vaccination (1951 et 1952)
Courbe établie année par année

Graph IX

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Date of appearance of typhoid and paratyphoid infections after vaccination
Curve established by five years periods

Date d'apparition des infections typho-paratyphoïdiques après la vaccination
Courbe établie de 5 ans en 5 ans

Graph X