

# VACCINATION AGAINST TYPHOID FEVER

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Vaccination against typhoid fever was first introduced at the end of last century and this prophylactic method has since been extensively employed in armed forces throughout the world. From experience in these forces it was soon claimed that this vaccine was very effective in reducing the incidence of typhoid fever and very convincing figures were published in support of this contention.

## *Doubts*

During the period between the world wars, however, doubts began to arise about the true efficacy of this vaccine, for it was found that attacks of typhoid fever were by no manner of means as uncommon in persons who apparently were adequately inoculated as was generally supposed, particularly when they were exposed to heavy risks of infection. It was then suggested that much of the apparent success of the vaccine in reducing typhoid fever in armies could be attributed to other improvements in hygiene, e.g. the chlorination of water supplies, which was introduced at about the same time as routine vaccination against typhoid.

The discovery of the Vi antigen, and the supposedly important role it played in protection as evidenced by animal experimental studies, led to efforts to improve the vaccine; and the alcoholized form of the vaccine, which is prepared from carefully selected, smooth, fully virulent strains of *S. typhi* in which the Vi antigens are effectively preserved with alcohol, was introduced. This latter vaccine, in certain countries, began slowly to replace the older (phenolized) type of vaccine, which was thought to be deficient in the important Vi antigen.

After the second world war still further doubts, as a result of experience in prisoner-of-war camps in North Africa, began to be thrown on the efficacy of typhoid vaccine. Typhoid fever was prevalent in some of these camps where there was gross overcrowding and poor hygienic conditions,

and evidence was obtained from some of them, where the risk of typhoid fever was high, which indicated that the vaccine was only of value in reducing mortality and not in reducing morbidity. There is, however, sound evidence from other recent sources to show that typhoid vaccine may be of definite though limited value in reducing the incidence of the disease. Thus, in 1943, a study of a group of men exposed to infection from a common contaminated water supply showed that the incidence of typhoid fever in the inoculated persons was only 1.1% as compared with 7.0% amongst the uninoculated.

On the whole it would thus appear that typhoid vaccine is of definite but limited value in that it may reduce both the incidence of typhoid fever and its mortality, but that the immunity it confers is only relative and will not withstand heavy assaults. The immunity would also appear to fade gradually, and hence the desirability of repeated booster doses at intervals of one to several years.

## *WHO Yugoslavia Report*

Recently the preliminary report of the World Health Organization on the strictly controlled field trials held in Yugoslavia on the value of typhoid vaccine has thrown some very valuable light on this difficult problem. About 48,000 subjects took part in these trials, which were carried out over the period 1954-56 in a district in which typhoid fever was endemic at the time. The subjects were divided at random into 3 comparable groups subjected to the same risks. One group was immunized with phenolized vaccine, another with alcoholized vaccine, and the third was given a control Flexner vaccine. The results of the trials were somewhat surprising. They indicated that, under the conditions of the trials and with the particular vaccines employed, the phenolized vaccine gave a 70% protection rate, whereas the alcoholized vaccine appeared to be no better than the

control Flexner vaccine, which theoretically should have given no protection to typhoid. This was despite the fact that the alcoholized vaccine on the whole gave a better Vi antibody response than the carbolized, thus suggesting that the inclusion of Vi antigen in the vaccine is not as important in man as suggested by animal experiments. The trials also showed that existing laboratory tests could not be correlated with the protection given by the vaccine in man, which indicates that at present we appear to have no accurate laboratory test for assessing the protective potency of typhoid vaccine for human use.

The important inference to be drawn from these trials is that the older carbolized vaccine appears to be of definite but limited protective value and the newer alcoholized vaccine of poor and doubtful value.

#### *South African Endotoxoid Vaccine*

What about the endotoxoid vaccine as prepared by the South African Institute for Medical Research and generally used in South Africa? This vaccine is prepared in a different manner to the carbolized or the alcoholized vaccines and, therefore, it is a different type of vaccine. It is prepared from carefully selected strains of bacteria, which are broken up by repeated freezing and thawing to liberate the endotoxoids, which are then detoxified by treatment with formalin.

The protective value of endotoxoid vaccine, the use of which appears to be exclusive to South Africa, has not been assessed by controlled field trials similar to those recently held in Yugoslavia. Available knowledge, however, including in particular the experience gained in the use of this vaccine in South African troops during World War II, indicates that this vaccine is at least as effective as the TAB vaccines then in use in the British and American armies.

#### *Other Considerations*

A minor disadvantage of typhoid vaccine, which occasionally may cause a little concern, is the fact that repeated doses may induce a hypersensitivity state to the typhoid antigens in certain subjects.

Another point to be considered is the possible provoking effect of typhoid vaccine when given to subjects who are incubating the disease. There appears to be definite evidence that, when given under such circumstances, the vaccine, presumably by inducing a negative phase, may have a harm-

ful action on the subject. This means that due care should be exercised when vaccinating in the face of an epidemic.

It has been shown that typhoid patients who have been successfully treated with chloramphenicol may fail to show a significant rise in the specific antibody titres. This indicates that a satisfactory immunity may not be acquired in patients in whom the disease has been aborted by chemotherapy. The practice has, therefore, arisen of giving such patients, as soon as they have sufficiently recovered from the disease, a course of vaccine inoculations. This, theoretically, would appear to be a wise procedure which may be of some value in preventing the patient from suffering a later reinfection.

#### CONCLUSIONS

From this summary of our present knowledge, it is obvious that typhoid vaccine should be used with discretion. Used under the proper circumstances, a potent vaccine is no doubt a very useful prophylactic agent but one of limited value. Its role in controlling typhoid fever should, therefore, be but a secondary one. The important measures to be taken for the public-health control of typhoid fever are the institution of proper community hygiene and the tracing of carriers. It is through these two basic measures and not through vaccination that typhoid fever has been virtually eliminated during the last half century in certain fortunate countries and it is on these measures that we must rely in South Africa. Vaccination is no doubt of importance in the armed forces and in certain selected portions of the population at special risk, e.g. in nursing and health staff and possibly in Natives in reserves as a temporary emergency when there are great difficulties in instituting proper hygienic measures. It may also be useful in other general emergency conditions, as in times of national disaster, e.g. floods. It is, however, doubtful whether general vaccination campaigns against typhoid fever in the civilian population do much good and, if such campaigns are instituted, they must never be allowed to give rise to a false sense of security and to cloud the issue by interfering with the adequate carrying out of the basic campaign of instituting proper hygienic measures and searching for carriers.

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