SOME OBSERVATIONS ON THE ADMINISTRATION OF T.A.B. VACCINE

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Preventive inoculation against typhoid fever has been used on an ever-increasing scale since its discovery by Wright and Semple in 1897. Until recently its efficiency has been accepted and its use has been standard procedure in the Armed Forces for many years. In the Army, doses of T.A.B. vaccine of strength $S.\ typhi$ 2,000 million and $S.\ paratyphi\ A$ and $B$ 1,500 million organisms per ml. are given on entry (0.2 ml.), after a period of one month (0.4 ml.), and again after a further interval of six months a third primary injection (0.2 ml.). Thereafter annual booster doses (0.2 ml.) are given.

All Army medical officers are aware that unpleasant reactions to T.A.B. may develop after the initial dose. Furthermore, Felix (1), besides pointing out that the reactions have a decided nuisance value, states that they do not confer more adequate protection. Side effects following the second dose also occur and may be more severe than following the first (2).

It was our aim to find the average response to a third dose of T.A.B. and how it compared with previous injections. This group we chose because we thought that such men would have minimal symptoms, having already had two primary doses in the previous twelve months. Further, we were anxious to discover the effect of the administration of alcoholic beverages when given with T.A.B. It is popular belief that alcohol may increase the side effects of vaccination, this view being particularly prevalent amongst medical officers. Actual evidence of this point is rather scarce, although Bamforth (3) states that alcohol appears to "intensify post-vaccination headache."

Half of our subjects received alcohol in the form of beer or whisky, the choice being left to the individual, although those unused to its effects were excluded from the "alcoholic" group. The amount of alcohol given (two pints of beer, proven strength 5 per cent. alcohol, or whisky, four ounces of 40 per cent. alcoholic content) was considered to be within reasonable limits of what a young recruit might drink, having regard to his age and finances. The two forms of alcohol in the above amounts were of approximately equal alcoholic content.

METHOD

Our 60 patients, i.e., 30 controls and 30 "alcoholic," were fit convalescent hospital patients drawn from three infantry battalions and supporting arms.
They were all due for the third T.A.B., the interval since the second being from five to twelve months. The vaccine used was the standard type "A" (alcohol-killed and alcohol-preserved organisms) (4) because of the milder reactions produced and its proved satisfactory property of antibody production (1). The injection was accurately measured in all cases by means of a "tuberculin" syringe; each was given at the same time of day by the same medical officer, using a similar needle, the site being subcutaneously at the insertion of the left deltoid muscle. For twenty-four hours before injection the patients were placed on four-hourly T.P.R. charts in order to establish a normal base-line. Subjects were allowed to be up and about thereafter, but were given no duties. T.P.R. charts were continued for a further forty-eight hours, and during this time each was seen twice and questions regarding side effects asked, while inquiries were also made as to the effects of previous inoculations and the conditions under which they were given.

In addition, the "alcoholic" group received two ounces of whisky or one pint of beer on two occasions after injection, at intervals of two and six hours.

The heights and weights of all subjects were recorded.

RESULTS

The following side effects were noted:

1. Pyrexia. This occurred in 30 of our total number of subjects, i.e., 50 per cent. There being 15 controls and 15 "alcohols" affected. Pyrexia was mild (99 to 100° F.) in 12 of the 15 "alcohols" and in 8 of 15 controls. Moderate fever (over 100° F.) was found in 3 "alcohols" and in 7 controls. The highest recorded temperature was 102.2° F.

| Group   | No. of pyrexial reactions | Mild (99-100° F.) | Moderate (100° F.+)
|---------|---------------------------|-------------------|---------------------
| Controls| 15                        | 8                 | 7                   |
| "Alcohols" | 15                        | 12                | 3                   |

In both groups it seemed that febrile responses were, not unreasonably, more common in those below average weight. The average of each group was practically identical, and of the whole 60 was 141½ lb. (Average weight of 18-year-old men is 149½ lb. (5), which shows our selection to be somewhat under average.)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of pyrexial subjects under average weight</th>
<th>No. of pyrexial subjects of average weight or above</th>
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</thead>
<tbody>
<tr>
<td>Controls</td>
<td>11 (73%)</td>
<td>4 (27%)</td>
</tr>
<tr>
<td>&quot;Alcohols&quot;</td>
<td>9 (60%)</td>
<td>6 (40%)</td>
</tr>
<tr>
<td>Total</td>
<td>20 (66%)</td>
<td>10 (33%)</td>
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</table>
The average weight of the pyrexial subjects of both groups was 138.5 lb. and that of the apyrexial was 144.5 lb.

2. Duration of Pyrexia.—Periods of fever varied considerably, the limits being 4 and 56 hours. The average duration in the “alcohols” was 13 hours and in the controls 25 hours, three readings of 48 hours and over being responsible for this latter rather high figure. A fever lasting 24 hours or more was not uncommon, occurring in 20 per cent. of the 60 subjects.

3. Specific Symptoms.—In this group the commonest complaints were:
(a) Local pain at the site of injection,
(b) headache,
(c) gastro-intestinal upsets, mainly nausea and vomiting, and
(d) muscular pains in that order of frequency.

Local reactions were seen to some extent in almost 100 per cent. of cases and were generally mild.

Headache occurred in 13 of the “alcohols” and in 16 of the control group. Two “alcohols” said that their headaches were severe, but neither was kept awake at night or asked for analgesics.

Nausea was an infrequent symptom, occurring in only 6 subjects—2 “alcohols” and 4 controls, vomiting accompanying in one of the latter.

Muscular pains were complained of by only one subject, these being confined in him to the lower limbs.

Time of onset of symptoms varied widely within each group, occurring from 2 to 24 hours following the injection. Most subjects with reactions began to experience symptoms either 7 or 8 hours from the injection, i.e., 9 or 10 p.m., or on the following morning. Rarely symptoms were delayed for 24 hours or occurred within 2 or 3 hours of injection.

SUPERVISION OF PREVENTIVE INOCULATION

Memorandum on Immunological Procedures (1952) states that the following precautions should be taken when T.A.B. is given:

1. Inoculation should be performed at a late hour.
2. A period of 36 hours off duty and confinement to barracks enforced.
3. A warning against the drinking of alcohol should be given.

Of our group 68 per cent. stated they had not been warned of the possible effects of alcohol, and nearly 50 per cent. claimed that they had no time off after previous inoculations. Of course, many who had previous reactions would be likely to insist that they had not had ample facilities for rest, but what did strike us was the complete lack of uniformity in the precautions taken. Some were told to “walk it off,” others were put to cleaning barrack-room floors, supposedly to exercise the injected arm. Some also who were given injections in the evening were expected to be on parade the next morning, when symptoms may well be commencing, as we have shown.

Seven of our subjects—2 “alcohols” and 5 controls—declared that their reactions to the third T.A.B. were worse than those of the first or second. The
majority, as expected, stated that the after-effects were much decreased, and indeed 33½ per cent. of the whole group, apart from local pain at the site of injection, admitted to no trouble whatever.

**Discussion**

It has been stated (6) that T.A.B. "in rare cases gives rise to some pyrexia with even pallor and collapse." It would seem from this investigation, which is admittedly on a small scale, that this is far from true even following re-inoculation. As we have shown, moderate pyrexia and headache often lasting many hours are quite common side effects following the third dose of T.A.B., even when subjects are on the lightest of duties. Reactions to the first and second inoculations of the primary series are generally much worse (2).

Furthermore, it does not seem that moderate amounts of alcoholic beverage consumed after T.A.B. injections have any appreciable effect. One would be inclined to suppose that the effects of alcohol and T.A.B. following the initial and the booster doses might also be no greater than the effects of T.A.B. alone. The only symptom in our group which seems to have been accentuated in any way is the very immeasurable headache, which two of the "alcohols" described as severe.

What does seem important is the varying instructions given to recipients as to how they should behave following immunization. Instructions set out do not appear to be followed. Admittedly it is difficult to put large numbers of men off duty, although one cannot help thinking that much trouble might be avoided in this way.

Granted, then, that even re-inoculation with small doses of T.A.B. may cause moderate reactions, how does this affect future policy? Surely when one considers (a) that chloramphenicol is a remarkably effective drug in the treatment of the enteric fevers, (b) that injections of T.A.B., apart from causing unpleasant and worthless reactions, may rarely cause severe encephalopathies and encourage the development of poliomyelitis (7), (c) that the antibody titres produced by inoculation interfere with the serological investigation of enteric cases, (d) that some observers have cast doubts on the efficacy of T.A.B. inoculation as a protective measure, not only in the prevention of cases of enteric fever but also in moderating the clinical course of established cases (8, 9)—it is time to consider critically the value of T.A.B. and, if we use it, to ensure that instructions for the protection of recipients are carried out.

**Conclusions**

An investigation into the side effects of the third inoculation of T.A.B. vaccine was carried out. It would seem that:

1. Reactions of moderate severity may occur even when using small doses, particularly in those recipients under average weight.

2. Alcohol in moderate amounts had little effect on the severity of such reactions.
3. Precautions taken are, in fact, not uniform among units, and do not in most cases offer maximum protection from reactions. The question of the preventive value of T.A.B. is raised.

REFERENCES