Since 1964 a number of trials of anticoagulant therapy have been carried out in which treated and untreated patients were divided into two groups by random selection, but many of these have not been "double blind."24-28 Such "double blind" studies as have been carried out have not been in complete agreement. G. Aspenström and K. Korsan-Bengsten29 concluded that there was no difference in mortality between patients treated with long-term anticoagulants and untreated controls. C. Merskey and A. Drapkin in their preliminary report came to a similar conclusion,30 though their study is not yet complete. E. A. Loeliger and colleagues found no difference in mortality but a higher rate of reinfarction in the untreated patient,1 while O. J. A. T. Meuwissen and colleagues found significant benefit from anticoagulant therapy in their patients.31 An international review group has recently analysed the records of 2,205 males and 282 females included in nine controlled trials between 1950 and 1965 and could not reach an agreed decision. The only conclusion that can be drawn from these studies is that if any beneficial effect exists it must be marginal.

In their critical review of the published work up to 1960, Sir John McMichael and E. H. O. Parry concluded that the value of long-term anticoagulant therapy was unproved, and this remains true today. They showed that the prospect of surviving for five years after recovery from an acute myocardial infarct was 66% in untreated patients under the age of 60, being worse with increasing age and complications and better with improving social circumstances and completeness of recovery. The figure varies from 80% in the doctors studied by J. N. Morris and his colleagues32 to 30% in elderly patients.33 A reduction in mortality must be the main criterion for the success of anticoagulant treatment. Though the recurrence rate of infarction is also of importance, this is much more difficult to assess. In some of the reports recording favourable effects of anticoagulants patients in the control series did not survive as long as the established mean for untreated patients. Conversely it has been pointed out that mortality figures in some series of patients treated with anticoagulants are less than a life insurance company would expect for a healthy population of the same age and sex.34

In other studies the action of anticoagulants is said to be favourable only for the early years of treatment.35 If the action of anticoagulants is to prevent arterial thrombosis there is no reason why this prophylactic action should cease. It has been shown too that mural thrombi over infarcts occur with equal frequency in patients on anticoagulants as in those not receiving any specific treatment.36 At the same time it must be remembered that recurrent thrombosis is responsible for only little more than half the deaths following myocardial infarction.37 Other factors include the thickening of atheromatous plaques and subintimal haemorrhage.38 Falls in blood pressure may also be responsible by reducing perfusion through critically narrowed vessels.39

The disillusionment in long-term anticoagulant prophylaxis receives further support in a recent report by A. J. Seaman and his colleagues.38 This was a double-blind study of 256 patients over an average period of six years, and it showed that long-term prophylactic anticoagulant therapy after acute infarction did not reduce either the mortality or the recurrence rate of infarction. In fact, more of the treated patients required admission to hospital. It is agreed that long-term anticoagulants are of no benefit to women. Any benefit to men is unproved. The physician must therefore weigh these dubious advantages against the potential risks of his treatment.

Most of the haemorrhagic complications occur while the patient's prothrombin levels are in the desired therapeutic range. The hazards of anticoagulant therapy are significant even in the most experienced hands. The reported incidence of bleeding among patients on anticoagulant therapy is up to 40% in those who are ambulant, though it is only serious in 2% to 10% of patients.39 In the series reported by C. J. Bjerkelund40 lethal haemorrhage occurred in 4 out of 118 patients on anticoagulants.

While anticoagulants are of value in the treatment of venous thrombosis, this is not true of arterial thrombosis whether cerebral thrombosis41 or occlusive arterial disease of the legs.42 The inherent dangers of this form of treatment together with the absence of any evidence of benefit indicates that the time has come to abandon the long-term use of anticoagulants after myocardial infarction.

**Holiday Typhoid and T.A.B.**

As a result of hygienic measures, vaccination, and chemotherapy enteric fevers are nowadays less common and less severe than they used to be. But they can still be a menace to travellers, especially to holidaymakers, who are apt to take too few, if any, precautions against them.1

In the last decade the World Health Organization has conducted a series of controlled field trials in four countries where enteric infections are endemic.4-8 These trials have proved at least two things. Firstly, it is possible by means of a monovalent typhoid vaccine to protect people to a large extent against typhoid fever. Secondly, no laboratory method of assaying a vaccine gives results that can be correlated with those of a controlled field trial in which incidence of typhoid is compared in vaccinated and unvaccinated persons. Paratyphoid fever is
in a different category. No controlled trial with a paratyphoid
A vaccine has yet been reported, and in at least two trials paratyphoid B vaccine has been ineffectiv.6

It has been suggested that a monovalent vaccine would be
preferable to a multivalent. W.H.O. experts affirm that it does
not seem advisable to add to typhoid antigen (which is potent
and effective) an antigen of doubtful effectiveness that adds to
the reaction in the vaccinated person but does not necessarily
add to the protection against typhoid fever.7 In the U.S.A.
also there is a trend to change from T.A.B. to a typhoid
course,8 paratyphoid vaccines are thought there to be ineffect-
ive and to increase the incidence of reactions.9 This is perhaps
a challenge to the pharmaceutical industry in the United
Kingdom to make a potent monovalent vaccine. An acetone-
inactivated and acetone-dried vaccine is marginally more
effective than the traditional heat-killed and phenolized
preparation, but this might or might not be commercially
feasible. All things considered, it does not at present seem
essential to discard our time-honoured and successful T.A.B.
vaccine.

As to dosage, some have suggested that three doses are
unnecessary and that one dose is sufficient to give protection.
This may be wishful thinking. The reason why, for example,
one dose of a potent typhoid vaccine was as effective as two
doses in Guayanese children10 was probably that the inhabitants
of that area, where typhoid is endemic, had previously ingested
subinfective doses of typhoid and related organisms, so that
the vaccine was actually a secondary stimulus to a latent
immunity. There can be no justification for assuming that in
Britain there is any basal immunity to enteric infections. Two
doses of T.A.B. vaccine are therefore necessary for protection,
and three doses are even better.

The reaction to T.A.B. inoculation is sometimes trouble-
some, and any means of reducing it is welcome. Probably the
most successful method is to give the vaccine intradermally.11 12
It is generally agreed that an intradermal dose of 0·1 ml. is as
effective as a subcutaneous or intramuscular dose of 0·5 ml.
The British Army has for many years given its T.A.B.
(usually combined with tetanus vaccine as T.A.B.T.) intra-
dermally with great success.13

What advice, then, should be given on T.A.B. inoculations
to travellers going abroad on holiday? Those who have never
had any anti-typhoid immunization should have the full course
of three inoculations—two doses before travelling with
insistence that the third dose is necessary in 6–12 months' time.
Persons who have had the full course three years or more
previously should be given two doses of T.A.B. vaccine,
with an interval between them of 4–6 weeks. The traveller
who leaves his immunization until a week or two before
departure should be given one dose of T.A.B.—not two doses
within 10 days—and reminded that he should have the second
dose on his return from holiday. Those who have had the full
course of three inoculations within the previous three years
require only one reinforcing dose of T.A.B. vaccine.

For the reinforcement of immunity it is logical to assume
that, after primary immunization or after a reinforcing dose of
vaccine, protection is maintained for at least one year and
basal immunity exists for three years. Persons at risk (as
holiday travellers generally are) require a reinforcing dose
ever year, while those not at risk (persons remaining in this
country) should receive this one every third year. It is
advisable for people who only occasionally go to places
where they may be exposed to typhoid infection to keep their
basal immunity "topped up" in order to circumvent the necessity,
when they do decide to travel, of undertaking primary im-
munization aresh. Likewise, the traveller who pops over to
the Costa Brava every summer needs only one dose of T.A.B.
each time he buys his ticket—three or four weeks before
departure.

It is good to know that the Ministry of Health and Social
Security is planning to issue information to travel agents
and others associated with the tourist trade so that they can pass
on the appropriate advice to travellers.14

Surgical Treatment of
Thyrotoxicosis

Many clinicians regard subtotal thyroidectomy as the best
response for hyperthyroidism in young adults with enlarged
thyroid glands, but in different series1–5 the incidence of
hypothyroidism after operation has ranged from 5 to 36%,
and of hypothyroidism from 0 to 11%.6

The report by Dr. A. J. Hedley and his colleagues in this
week's B.M.J. (page 519) is a useful addition to our knowledge
on this subject. They surveyed 254 patients treated by subtotal
thyroidectomy in Aberdeen from 1946 to 1965. Of these only
198 (78%) could be identified despite a thorough search,
so that the total morbidity in the series could not be accurately
assessed. Data are presented on 146 of these patients operated
on in the same surgical unit and followed up for 2–21 years
(mean 9·3 years) after operation. At the time of follow-up
55% of the patients were euthyroid, 5% had equivocal
thyroid status, 27% had become hypothyroid and were
receiving some form of replacement therapy, 10% had
untreated hypothyroidism, and 4% were hyperthyroid. Thus

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