Memorandum on immunological procedures which service personnel and their families may need at home and abroad.

W.O.
Code No.
11253

(Supersedes W.O. Code No. 6686)

WAR OFFICE

MEMORANDUM ON IMMUNOLOGICAL PROCEDURES

which Service Personnel and their Families may need at Home and Abroad

Prepared under the Direction of the Director-General, Army Medical Services

DON: HER MAJESTY'S STATIONERY OFFICE
1956

Price 2*s.* 6*d.* net

FIRST PUBLISHED — — — — OCTOBER, 1952

SECOND EDITION — — — — JANUARY, 1956

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(SO 8636)

IMMUNOLOGICAL PROCEDURES IN THE ARMY

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MEMORANDUM
ON
THE IMMUNOLOGICAL PROCEDURES WHICH SERVICE PERSONNEL AND THEIR FAMILIES MAY NEED AT HOME AND ABROAD

INTRODUCTION

1. The object of this memorandum is to provide in a composite form a ready reference of the present administrative and technical instructions relating to the types of immunization which Service men and women and their families may require in various circumstances at home and abroad.

2. It has been prepared primarily for the guidance of

(*a*) medical officers carrying out the immunological procedures, and

(*b*) medical officers and other personnel of the medical and nursing services responsible for the care and maintenance of syringes and the storage of biological products used for immunization.

3. The administrative instructions have been compiled from relevant Army Council Instructions, relevant paragraphs in Queen's Regulations and Regulations for the Medical Services of the Army, and War Office Memoranda, which must still be quoted as the appropriate authorities.

4. Technical instructions for carrying out different immunological procedures are approved by the Army Pathology Advisory Committee, and are notified from time to time in War Office Memoranda. Under no circumstances will these technical instructions be departed from without the prior sanction of the War Office.

5. The memorandum is divided into four parts, each containing a number of sections dealing with similar subjects. The paragraphs are numbered consecutively throughout.

6. As quarantine regulations of foreign countries alter frequently, and as improved technical procedures may be discovered as the result of research, it is inevitable that changes will occur. When necessary, amendments will be notified in Army Council Instructions or War Office Memoranda, and such amendments should be incorporated in this memorandum in order to keep it up to date.

7. This edition incorporates the revised regulations of the World Health Organization, agreed on 25-5-51.

SO 8636)

PART I

ADMINISTRATIVE INSTRUCTIONS RELATING TO THE CARRYING OUT OF IMMUNOLOGICAL PROCEDURES, DOCUMENTATION, CERTIFICATION, THE MAINTENANCE OF RECORDS AND THE ISSUE OF INTERNATIONAL CERTIFICATES OF INOCULATION

SECTION I

ADMINISTRATIVE INSTRUCTIONS FOR CARRYING OUT IMMUNIZATION IN THE ARMY

1. General

The different types of immunizing procedure which Service men and women, and their families, may need in various circumstances at home and abroad are described in this section. Instructions for documentation and certification are given in Sections II and III.

2. Army Inoculation Centres

With the exception of yellow fever inoculations, all inoculations are carried out at Army inoculation centres, which are located at medical centres and military reception stations. Yellow fever inoculations are only carried out at selected Army inoculation centres which are located in authorized military or civilian laboratories. ALL inoculations are provided free of charge for all ranks and their families, including those families who do not normally obtain medical attendance from Army sources.

3. Importance of Protection

Although acceptance of inoculation and vaccination is voluntary, officers other ranks and families must be made to understand that vaccination and inoculation are essential, not only to safeguard their own health, but also to protect the Army from epidemics which may seriously interfere with its efficiency. It is the responsibility of commanding officers to provide facilities for carrying out these recommendations, and for warning all who refuse that they may run an unnecessary risk of infection and thus become a danger to their comrades, to their units, and so to the whole force.

No officer or soldier will be prevented from going overseas because he has refused vaccination, but attention will be drawn to the fact that he will be subject to the prescribed quarantine regulations in any possible area through which he may be required to pass.

4. Protection against one or more of the diseases with which the International Sanitary Conventions are concerned may be demanded by the various countries to, or through which, Service personnel and their families may travel, depending on the route by which the country is reached. Apart from the unnecessary risk to health, non-acceptance may involve the individual and his family in considerable inconvenience owing to non-compliance with quarantine regulations.

The health regulations are now so complicated and change so frequently that it is not expedient to provide a ready reference to cover all contingencies. In cases of doubt the matter should be referred to the nearest administrative military headquarters (medical branch).

5. **Travel by Air**

Travellers by air are particularly likely to be required to produce evidence of inoculation and vaccination in order to satisfy international quarantine regulations. The requirements vary according to the countries traversed and should be investigated before undertaking a journey. In such cases the evidence of inoculation and vaccination must be recorded on the appropriate international certificate forms. (*See* Section III.)

6. **Travel by Sea**

Ordinarily, personnel travelling by sea, whether in a draft or as individuals, will satisfy the various health authorities if they are protected against smallpox, and under the special conditions mentioned in para. 11 below, against yellow fever. Typhoid-paratyphoid (T.A.B.) inoculation is not normally required by quarantine regulations but is recommended for the individual's own protection (*see* para. 9 below).

When service personnel travel by troopship international certificates are not normally required except in the case of yellow fever inoculation and vaccination against smallpox.

7. **Smallpox—Vaccination against** (*See* Section XV)

(*a*) *Recruits.*—All recruits, irrespective of their vaccination history, will be vaccinated on enlistment. Readings will be made eight days after vaccination and if vesicle, pustule or scab formation is present, this fact will be recorded. If there is no visual evidence of a characteristic reaction the procedure will be repeated immediately; inspections will be made between the 8th and the 14th days. The appropriate results will be recorded in accordance with para. 86.

(*b*) *Re-vaccination*

(i) *Forces serving in the United Kingdom and in North-West Europe.*—Re-vaccination will be carried out every three years, adopting the procedure in sub-para. (*a*) above.

(ii) *Forces serving overseas other than in North-West Europe.*—Re-vaccination will be carried out every two years or at shorter intervals if demanded by local statute.

(iii) *Epidemics.*—In the presence of an epidemic or undue prevalence of smallpox, re-vaccination may be ordered by the local commander on the advice of his senior medical officer.

(*c*) *Before proceeding overseas.*—All troops and their families proceeding overseas other than to North-West Europe (from the United Kingdom or from North-West Europe) will be vaccinated not less than 14 days before sailing, unless already protected within the previous two years. *Infants* should normally not be vaccinated below the age of three months, but in the face of special risk, primary vaccination may be done at any age.

(*d*) *Precautions when combining vaccination with other inoculations*

(i) *Yellow fever inoculation MUST* precede *primary* vaccination against smallpox by an interval of at least four days in adults but 21 days in infants under nine months old. If for any reason *primary* vaccination against smallpox has been done first, there must be an interval

of 21 days before yellow fever inoculation is given. Where there is evidence of previous successful smallpox vaccination, yellow fever inoculation and re-vaccination against smallpox may be carried out simultaneously, but if time permits yellow fever immunization should always precede re-vaccination by at least three weeks.

(ii) *Inoculations other than yellow fever.*—These may be given at the same time as vaccination, but *not* in the same arm.

(*e*) Whenever Army personnel and families are vaccinated against smallpox, they will be issued with an International Certificate of Vaccination. The certificates to be used will be those printed by the Ministry of Health, or F.Med. 101.

8. **Diphtheria—Active Immunization Against** (*See* Section IX)

(*a*) Owing to the general prevalence of diphtheria in certain overseas theatres, all ranks of the Army will, on recruitment, be tested and, if necessary, actively immunized against diphtheria.

(*b*) *Procedure*

(i) A Schick test will be performed on all recruits to determine susceptibility to diphtheria.
(ii) The result of this test will be read on the fifth day.
(iii) Those requiring immunization will at once be given the first prophylactic injection.
(iv) Four weeks later, they will be given the second injection.

Note.—Infants and children under the age of eight years are immunized without Schick testing. It is recommended that immunization should begin when the infant is six months old or a little earlier.

9. **Typhoid-Paratyphoid Inoculation** (*See* Section VII)

(*a*) Immunization against enteric (typhoid) group of fevers and tetanus with T.A.B.T. is necessary for servicemen and women and their families proceeding anywhere outside the United Kingdom. They will be inoculated before arrival at the port of embarkation or air trooping centres, to ensure that they are as fully protected as possible before departure.

(*b*) *Recruits.*—To avoid unnecessary delays in drafting, and to ensure that draft finding units do not hold men for the sole purpose of inoculations when ready in all other respects for embarkation, all Regular Army and national service men and women passing through army basic training and selection units will be deemed to be required for overseas service on completion of training, even though they may not in fact be despatched immediately. Immunization will, therefore, be carried out before the completion of primary training.

(*c*) *Procedure*

(i) *Primary inoculation* will consist of two doses of combined prophylactic given at an interval of 4 to 6 weeks and a further dose which will be given 6 to 12 months later or *immediately on arrival overseas whichever is the sooner.*
(ii) Thereafter, yearly inoculation with one dose will be carried out so long as the individual is at risk.

Note.—Children under one year of age will not be inoculated with T.A.B.T.

(*d*) *Lapsed immunization.*—When there has been a failure to maintain immunity by the above means it may be re-established by administering a single dose, provided the lapsed interval does not exceed three years. For intervals over three years, dosage to re-establish immunity will be as for primary immunization.

10. **Tetanus—Active Immunization Against** (*See* Section VII & VIII)

(*a*) All Service personnel will be protected against tetanus by active immunization. This protection, while not imperative for them, will also be offered to Service families proceeding outside the United Kingdom.

(*b*) *Procedure—see* para. 9

Note.—Only *documentary* evidence is acceptable as proof of primary immunization.

11. **Yellow Fever Inoculation** (*See* Section XVI)

(*a*) *When required.*—Personnel entering, leaving or proceed ng through the African and South American Yellow Fever Endemic Areas must be protected against Yellow Fever. The inoculation should be obtained not less than 10 days and not more than 6 years before entry and exit. The area consists of all African Territory lying between latitude 15° North and latitude 10° South and the whole of the Sudan and Eritrea. All South American Territory lying between latitude 15° North and latitude 15° South is also included. These areas may be modified from time to time and for the latest information the nearest Military Medical Headquarters should be consulted. Personnel leaving the African and South American Yellow Fever Endemic Areas by any route will be in possession of a valid International Certificate of inoculation against Yellow Fever. Personnel from countries outside the yellow fever endemic area disembarking in *Egypt* from westward bound troopships or other vessels which are routed through the ports of Massawa or Port Sudan must be in possession of a valid international certificate of inoculation against yellow fever. This may apply to some personnel from FARELF posted to MELF.

(*b*) Inoculation will be performed *before* emplaning or embarking. In exceptional circumstances individuals proceeding *by sea* direct to a colony in the endemic zone need not be inoculated until arrival, but if the journey involves further movement between colonies within the zone, they are liable to delays if not protected.

(*c*) All officers likely to travel by air at short notice through the yellow fever endemic area will arrange for their inoculation well in advance to avoid delay. This is more than ever necessary with the tightening of all government quarantine measures.

(*d*) Yellow fever vaccine is extremely perishable and requires special storage and technique in preparation. This inoculation is only carried out by appointment at specially selected centres. A list of these is available at military administrative headquarters (medical branch).

(*e*) Yellow fever inoculation is unlikely to be followed by any reaction and only one attendance is necessary. There is no lower age limit ; inoculation may if necessary be given in the first week of life at full dose. It is however desirable to avoid this inoculation, if possible, in infants under nine months of age. Inoculation affords protection for a period of six years.

12. **Typhus Inoculation** (*See* Section XIV)

(*a*) This is required in special areas as notified from time to time.

(*b*) Immunization consists of a course of three injections at weekly intervals. In endemic areas maintenance doses will be given annually. In the presence of an epidemic, "boosting" doses should be given at intervals of three months. Inoculation should not be done under the age of one year.

13. **Plague Inoculation** (*See* Section XIII)

This may be required in special circumstances. Primary inoculation is with two doses at 10 to 14 days' interval ; individuals at risk will be re-inoculated with a single dose at six-monthly intervals.

14. **Cholera Inoculation** (*See* Section XII)

This will also be required in special circumstances. Normally primary inoculation is by two doses at an interval of 7 to 14 days. Re-inoculation is performed by a single dose at six-monthly intervals. Cholera inoculation need not be given to children under one year of age.

15. **Personnel on Leave from Overseas**

Commands overseas will ensure that personnel returning to the United Kingdom on leave, temporary duty, etc., are fully protected so that no inoculations or vaccinations fall due during their absence from the overseas command, leading to delay in their return.

16. **Personnel Transferred from One Command to Another**

Commands overseas despatching personnel to another command overseas will ensure that the requisite protection is afforded. This applies to B.A.O.R. when despatching personnel to the United Kingdom for onward transit to other stations overseas.

17. **Despatch Overseas of Personnel who have Refused Vaccination or Inoculation**

Refusal of vaccination and/or inoculation is no bar to an officer, other rank or military family proceeding overseas. In exceptional circumstances, however, local authorities may refuse entry to, or transit through, the territory under their control to anyone who has not been immunized against a specific disease.

SECTION II

DOCUMENTATION AND MAINTENANCE OF RECORDS

18. Whether or not circumstances demand the issue to individuals of International Certificates of Vaccination or Inoculation (referred to below), the following Service recordings will always be made.

(*a*) *Inoculation and vaccination*

(i) *Officers.*—A.B. 439. The appropriate page of A.B. 439 and F.Med. 4.

(ii) *Other Ranks.*—A.B. 64 (Part 1), Medical pages and F.Med.4.

(*b*) *Refusal to be inoculated or vaccinated*

(i) All will be published in Part 11/III Orders (Officers as Sec. "A" occurrences).

(ii) *Officers.*—The appropriate page of A.B. 439.
A.F. B 199A (Section 32).

(iii) *Other Ranks.*—A.B. 64 (Part 1), Medical pages.
A.F. B 200.

(*c*) *Inoculation or vaccination after previous refusal*

(i) Publish a Part II/III Order (Section A occurrences for Officers) stating that inoculation and/or vaccination has been accepted subsequent to a refusal.

(ii) Officers—enter the occurrence on AB 439 and AF B199A Section 32).

(iii) Other Ranks—enter the occurrence on AB 64 (Part I) and AF B200.

(*d*) *Recording of inoculation and vaccination in AB* 439, *AB* 64 (*Part I*) *and on F.Med.* 4

The following details will always be recorded and initialled by the medical officer carrying out the inoculation.

(i) Type of vaccine given—recognised abbreviations may be used, *e.g.*, T.A.B. for typhoid-paratyphoid vaccine and T.T. for tetanus toxoid.

(ii) Dosage.

(iii) Date of inoculation.

(iv) When specially ordered, the batch number and the name of the manufacturer. This will *always* be given when yellow fever vaccine has been administered.

The following are examples of the manner in which inoculations will be recorded :—

T.A.B.T. (I) 1.0 ml. 3 August 55. A.B.Capt.
T.A.B.T. (II) 1.0 ml. 31 August 55. A.B.Capt.
Yellow fever 0.5 ml. 1 September 55. X.Y.Major.
(Wellcome, Batch No. 278.)

When recording the results of *vaccination against smallpox* (*see* Section XIV, para. 83) only the following descriptions will be used :—

Primary Vaccination (Successful) ..	abbreviation	P.V.(S).
Revaccination (Successful)	,,	R.V.(S).
Insusceptible to Vaccination ..	,,	I.T.V.

Note.—Abbreviations will not be used on international certificates. It will be stated whether vaccination is primary or revaccination and, if primary, whether successful.

(*e*) *Maintenance of Unit Records.*—It is the responsibility of commanding officers to ensure that unit arrangements are adequate for the maintenance of up-to-date records of the vaccination and inoculation state of their units.

SECTION III

INTERNATIONAL CERTIFICATES OF VACCINATION AND INOCULATION

19. In certain circumstances it is necessary to provide additional evidence of vaccination or inoculation against the diseases with which the International Sanitary Conventions are concerned, *i.e.*, smallpox, cholera and yellow fever. International certificates will always be issued to personnel who have received inoculation against yellow fever and vaccination against smallpox, except in certain circumstances when special instructions will be issued from the War Office.

These certificates, *which must be in the officially recognized form*, are the only evidence of protection acceptable to the health authorities of the various countries concerned and inability to produce a valid certificate may result in considerable delay in quarantine, or in extreme cases, refusal to land.

The certificates for use by the Armed Forces will be obtained from the local Ordnance Stationary and Publication stores. With effect from 1-10-52 only three international certificates have been in use—vaccination against smallpox (F.Med.101), cholera (F.Med.102) and yellow fever (F.Med.103.)

Duplicate or typescript substitutes for international certificates WILL NOT be accepted.

International certificates, when issued, will be retained by the individual and will be carried, unless otherwise notified in Army Council Instructions, in the pocket on the back cover of the A.B.439 (for officers), and in the deep pocket at the back of the A.B.64 (for other ranks).

20. International certificates must be fully *completed* and *signed* by the medical officer carrying out the inoculation/vaccination. They must also bear the official "ARMY INOCULATION CENTRE" stamp. *Abbreviations will not be used on international certificates.* When indicating the date, the month will be written and not designated by a figure.

21. When families are inoculated by civil doctors, except in the case of yellow fever inoculation which must be performed at a recognized centre, official forms of certificate may be obtained from the nearest Administrative Military Headquarters (Medical Branch), or from the Ministry of Health, Whitehall, S.W.1. They must be signed by the doctor concerned and authenticated by the Office of the Medical Officer of Health of the local Health Authority, or by the Town Council, Urban or Rural District Council in whose area the doctor lives.

22. The validity of certificates varies with each disease :—

(*a*) *Smallpox* (F.Med.101) : valid for a period of three years, beginning eight days after a successful primary vaccination or, in the event of revaccination, on the date of that revaccination, but for service requirements, *see* para. 7.

(*b*) *Cholera* (F.Med.102) : Valid for a period of six months beginning six days after the first injection of the vaccine or in the event of revaccination within such period, six months from the date of that revaccination.

(*c*) *Yellow Fever* (F.Med.103) : valid for a period of six years, beginning *ten* days after the date of the inoculation, or in the event of re-inoculation within six years, on the date of that re-inoculation. Egypt has, however, increased the period which must elapse until the certificate becomes valid to twelve days.

The vaccine used must be of an approved type and the inoculation must be performed at a recognized yellow fever inoculation centre.

(*d*) *Typhus and Plague :* No international certificate required with effect from 1 Oct., 1952. (International Sanitary Regulations 25-5-51.)

23. When Service personnel travel by troopship international certificates are not normally required, except in the case of yellow fever inoculations, and vaccination against smallpox.

In all other circumstances such certificates may prove necessary and should be provided. They will, of course, only be required in respect of those diseases against which protection is demanded by the country to which the person is proceeding, or those countries through which his journey may be routed.

All personnel, liable to travel at short notice from country to country, and by means other than troopships, should request international certificates whenever they are inoculated, as otherwise re-inoculation may be necessary in order to furnish these.

PART II

INSTRUCTIONS FOR THE CARE, MAINTENANCE AND STERILIZATION OF SYRINGES. INOCULATION TECHNIQUE AND THE PROCEDURE TO BE FOLLOWED WHEN CARRYING OUT MASS INOCULATIONS

SECTION IV

THE CARE, MAINTENANCE AND STERILIZATION OF SYRINGES

24. The Choice of Syringes and Needles

Syringes for inoculation should preferably be of the all-glass type and of good quality. For *subcutaneous* and *intramuscular injections* they should not be of more than two millilitres' capacity, as it is impossible accurately to measure small doses in a syringe of larger calibre. For *intradermal injections*, an all-glass syringe of the tuberculin type is preferable.

All-glass syringes are easier to clean and sterilize than are those made of glass and metal (Record-type). They are less likely to break on heating, and they have no cement which may melt in the sterilizing oven (dry sterilization) or autoclave (wet sterilization). If properly cleaned and lubricated, they may be assembled before dry sterilization.

" Half Record " syringes are now available. They have the bottom nozzle-fitting affixed with a special alloy having a melting point in excess of 200° C., and they can, therefore, be sterilized in safety up to that temperature.

The only advantage of the ordinary Record-type syringe is its less fragile nozzle. It is more difficult to clean, and it is apt to break on heating, because of the unequal expansion of the glass and metal; moreover, the cement may melt in the hot air oven or autoclave. After boiling, glass-metal syringes usually take longer to cool than do those made entirely of glass. Record-type syringes must not be sterilised assembled, but " half Record " syringes can be so sterilized.

It is important to use only stainless steel needles of the best quality. They should combine flexibility and strength, and should be highly resistant to corrosion and tarnishing.

25. " Segregation " of Syringes

It is imperative that syringes used for inoculations should be kept separate from syringes used for aspiration of pathological fluids, and that no syringe which has once been used for animal experiments should subsequently be used on a human being.

Syringes and needles used for the Mantoux test are very difficult to render free from tuberculin, and their use for Schick testing may lead to false positive results in the latter. Traces of tuberculin may also explain some reactions encountered after inoculations. Accordingly, separate syringes and needles

will be used for each tuberculin dilution in the Mantoux test, and for B.C.G. vaccination, and these syringes will be used for no other purpose.

Syringes used in the Schick test for toxin and heated toxin (control) must be marked and kept distinct while testing is in progress. They should never be used for other purposes.

26. Instructions for the Cleaning and Preparation of Syringes for Sterilization or Disinfection

(*a*) *Cleaning New Syringes*

Before use, new syringes should be well washed in soap and water, using a test-tube brush for the barrel. Both piston and barrel are rinsed in clean water and dried with a fluffless cloth.

The piston is lightly smeared with liquid paraffin, by dipping the tip only of the piston into liquid paraffin contained in a wide-mouthed screw-capped 2 oz. bottle or jar, and rubbing the paraffin well over the ground surface of the piston with the finger. Excess of liquid paraffin must be avoided.

The piston is inserted into the barrel and worked backwards and forwards several times to ensure proper lubrication, and to make sure that the syringe is working smoothly and evenly.

(*b*) *Cleaning of Syringes After Use*

When vaccines and test products have been used, the syringe should be washed out with *cold* water, by sucking up and expelling the fluid several times, with the needle still in position. Syringes used, however, for the administration of antitoxin should be treated like infected syringes, in order to facilitate cleaning. After antitoxin has been administered, the syringe is immediately washed with a *cold* solution of 2 per cent. lysol (contained in a small enamel dish), by sucking up and expelling the fluid several times, with the needle still in position. Hot fluid will coagulate protein, and the syringe will then stick. Antitoxin sticks firmly to the ground surface of the piston and other irregularities in the glass, and its removal is facilitated by the use of lysol.

After being washed with water or lysol, the syringe and needle are returned to the tube in which they were sterilized. (*See* " Preparation of syringes for sterilization," para. 26 (*c*).)

Before being re-sterilized, the syringe must be thoroughly cleaned by being washed in warm, soapy water, using a test tube brush for the barrel. Antitoxin tends to adhere to the side of the barrel and must be removed from the flat surface at the nozzle end of the barrel, so as to prevent the syringe from sticking when re-sterilized. After being rinsed in warm water, piston and barrel are dried with a soft cloth, care being taken that no threads or fluff are left ; otherwise the syringe will not work smoothly. The cleaning technique is the same as that described for new syringes. The piston is lightly lubricated with liquid paraffin, which is well rubbed on with the finger. The syringe is then re-assembled, placed in its tube and the whole wrapped in kraft paper.

If several syringes of the same capacity are being cleaned at the same time, it is essential to see that each piston is inserted into the barrel belonging to it. An identification number should be engraved on the piston and barrel of every syringe, to ensure that the correct parts are fitted.

(*c*) *Preparation of Syringes for Sterilization*

(i) *By Hot Air*

The assembled syringe is placed in a glass tube of such diameter that the barrel of the syringe is a loose fit, but that the flange rests

on the top of the tube. The tube should be long enough to take the syringe when a needle is attached, without the point of the needle touching the bottom of the tube. The shoulder of the syringe may be wrapped with gauze or paper, so that the flange does not rest directly on the tube.

The tube with the syringe in position is wrapped in kraft paper. The paper is turned over and inwards at the bottom of the tube and twisted spirally round the tube, ending in a firm twist of paper at the top of the piston. The wrapped syringe is sterilized in the hot air oven as detailed below.

Alternatively, the syringe and tube may be wrapped in " cellophane ", when the details of the syringe are clearly seen through the wrapper. Sterilization in the hot air oven causes the " cellophane " to turn slightly brown, which is an indication that the syringe has been subjected to heat treatment.

As a further method, the whole syringe may be sterilized in a large tube plugged with cotton wool, the needle being protected as for separately sterilized needles. If this method is used, it should be borne in mind that " from certain brands of cotton wool, volatile substances are given off during sterilization. These condense on the tube." Such cotton wool must be avoided, and only absorbent cotton wool used, as it has been de-fatted.

(ii) *By Autoclaving*

The cleaning, lubricating and packing should be as for hot air sterilization, but the following precautions will be taken—

1. The syringes will be assembled wet.
2. Syringes will always be placed in wire baskets and not in a metal box.

It is necessary to take these precautions to ensure penetration by steam.

27. **The Sterilization and Disinfection of Syringes**

(*a*) *Procedure to Produce a Sterile Condition*

Complete bacteriological sterility can be achieved only by sterilization in the autoclave or hot air oven. Boiling in water for short periods will not destroy resistant spores.

(*b*) *Availability of Facilities for Sterilization*

Autoclaves are available in both hospitals and pathology laboratories, but hot air ovens only in laboratories.

Instrument sterilizers for boiling of syringes are available at M.R.Ss. and Medical Centres.

(*c*) *Sterilization by Hot Air*

The assembled and wrapped syringes are placed in the *hot air* sterilizer and maintained at a temperature of 160° C. *for not less than one hour*. Retention in the oven at this temperature for even up to 3 hours is strongly recommended. The sterilizer must have a reliable thermostatic control, and be provided with a thermometer, the bulb of which is near the syringes. The temperature must be checked and noted from time to time, to ensure that effective sterilization is carried out. The whole process should be under the control of a bacteriologist.

Syringes and needles are placed in the oven while it is cold ; the time of sterilization is *not less than one hour* after 160° C. has been reached. The

oven should be allowed to cool before the syringes and needles are removed.

(*d*) *Sterilization by Autoclaving*

If syringes are sterilized by autoclaving, a temperature of 120° C. (equivalent to a steam pressure of 15 lbs. per sq. inch) must be maintained for 20 minutes.

(*e*) *Disinfection of Syringes by Boiling*

If an autoclave or hot air oven is not available, or if ordinary glass-metal syringes are to be used, " sterilization " by boiling in water is the method of choice ; however boiling cannot be relied upon to destroy all spores. Although the addition of a little sodium carbonate to the water in which a syringe is boiled will ensure the destruction of spores, this practice is not recommended because the resulting alkalinity of the syringe may affect drugs or biological products to be injected. The action of the sodium carbonate will also materially shorten the life of syringes.

Syringes should be thoroughly washed before they are boiled ; boiling will coagulate and fix any protein in them.

The sterilizer : Commercial sterilizers are usually provided with a close fitting lid, and have a perforated tray inside. A saucepan with a lid is a satisfactory extempore sterilizer.

A piece of lint fastened to the tray of the sterilizer may protect the needle points during boiling, and prevent the syringe parts from moving about and hitting one another.

The sterilizer may be heated over a spirit lamp, or over a gas ring or hot plate. Electrically-heated sterilizers are very satisfactory.

The water : In districts where the water is hard, a film of chalk will collect on the syringe if it is boiled in tap water. Syringes coated with chalk are difficult to assemble, and soon become worn. Deposition of chalk can be prevented by the use of distilled water, rain water or softened water. Chalk deposit can be dissolved off all-glass syringes with weak hydrochloric acid.

Procedure : The piston and barrel of the syringe, the needle and a pair of dissecting forceps are immersed separately in cold or warm water (not above 50° C.) in the sterilizer. Syringes should not be dropped straight into water which is already boiling, or they may break.

The water is brought to the boil, and kept boiling for not less than *five minutes*. The lid of the sterilizer is then removed, and inverted on the table. The tray containing the syringes and needles is lifted out and placed in the lid by means of two pairs of sterile (flamed or boiled) forceps or, failing forceps, with clean, dry fingers, provided, however, that the handles of the tray are above water level. The water in the sterilizer is run off or poured away, the tray at once returned to the sterilizer, and the lid immediately replaced.

When the syringe is reasonably cool and dry, the barrel and piston are assembled with the aid of sterile forceps, or with clean dry fingers, care being taken to touch only the outside of the barrel and the knob of the piston. The needle should be fixed to the barrel by means of the sterile forceps, and should not be touched with the fingers.

After assembly, the syringe should be returned to the empty sterilizer and covered with the lid until it is used. It should not be placed in any other container, unless this is covered and has been previously sterilized ; neither should it be transferred to alcohol.

If an instrument sterilizer is not available, the syringe should be boiled in a saucepan fitted with a lid. After boiling, the water is poured off gently, the lid being held to retain the syringe inside. The saucepan should then be

left covered till the syringe parts are cool enough to assemble. If this method is used, it is an advantage to thread the needle through a piece of lint, to afford some protection to the point.

From start to finish, the boiling and assembly of a syringe need not occupy more than ten minutes.

It is sometimes suggested that the separate parts of syringes should be wrapped in lint before boiling, in order to prevent them from bumping against one another and getting mixed. This practice is not, however, recommended, partly because syringes so treated do not dry when the water is poured away after boiling and so have to be handled wet, and partly because it is not certain that the temperature of a syringe wrapped in lint reaches the boiling point of water. Loose fibres from the lint also adhere to the syringe.

28. The Sterilization of Syringes and Needles for Mass Inoculation

It is preferable that syringes and needles should be hot-air sterilized or autoclaved. When this is not possible, they should be boiled in an instrument sterilizer. (*See* Section VI—Mass Inoculation Technique.) In the latter instance, care must be taken to ensure that the contaminated exterior of an assembled syringe does not foul unassembled syringes and needles that have been sterilized. Moreover, the operator giving the injections should not assemble syringes with his own fingers, which may be soiled with blood from patients injected earlier.

29. Cleaning and Sterilization of Needles

When the syringe is cleaned, the needle is detached and well washed through with warm water from a small (2 ml.) syringe, which may be kept for this purpose if a number of needles are used. The mount of the needle is cleaned out with a piece of cotton wool on the end of a swab stick. The needle is then washed through again, first with water and then with alcohol (industrial methylated spirit), and allowed to dry. Drying may be hastened by placing the needle on a warm radiator or a hot plate.

The point of the needle should be examined under a hand lens, and, if necessary, is touched up on a fine Arkansas slipstone, lubricated with liquid paraffin or thin machine oil. The needle is washed again thoroughly in spirit and dried. The wire stilette, lubricated with a very small quantity of liquid paraffin, is passed through the bore to make sure that it is patent. The clean needle is finally inserted into a piece of narrow bore glass tubing, 2 inches long and placed in a small test tube of a suitable bore and length which is plugged with a twist of kraft paper or a piece of gauze (if cotton wool is used threads may adhere to the needle mount). The plug is forced down the tube, to hold the needle and prevent it from moving.

The tube containing the needle is then wrapped in a piece of kraft paper, and, if required, details of the length of the needle, bore, date, etc., written on the paper with lead pencil.

If " cellophane " is used, the relevant details may be written on a small piece of gummed paper which is fixed to the tube. The writing is easily seen through the transparent wrapping.

The wrapped needles are sterilized in the hot air oven for *not less than one hour* at 160° C.

The syringe and needle are assembled before use.

Many workers prefer syringes and needles to be assembled before sterilization by the hot-air method.

30. **Disinfection by Hot Oil Method**

(*a*) *Syringes*

Sterilization by hot oil has been employed extensively for many years for the sterilization of all glass syringes which have been used only for injecting prophylactic vaccines, and which should therefore never be grossly infected. This method should not be used for the sterilization of syringes.

(*b*) *Needles*

This method has been used successfully for the sterilization of needles. These should be thoroughly cleaned and then immersed in Liquid Paraffin which has been heated to a temperature of 150° or 160° C. The temperature *must* be controlled by means of a thermometer.

When several injections are being given the needle should be sterilized between injections without removing it from the syringe by dipping the needle up to the middle of its mount in the oil at a temperature of 140° C. for a period of 10 seconds. Before recharging the syringe the needle must be cooled by dipping in sterile normal saline, if a live vaccine is being used.

A tin or a metal pot filled with liquid paraffin is held in a clamp and heated by a Bunsen burner. The peep light of the burner is usually sufficient to maintain the required temperature once this has been reached. When gas is not available a spirit lamp should be used. A thermometer reading from 100° to 200° C. dips into the oil, and should be held by another clamp on the same stand so that the bulb is in the oil but not touching the metal.

Care must be taken to ensure that the oil is not heated beyond the sterilizing temperature as it is liable to char and there is also danger of its igniting at higher temperatures.

There are three mechanisms by which sterilization of needles is achieved by this method. The metal needle rapidly reaches the same temperatures as the oil (in about one second) and most organisms are killed on exposure to this temperature for several seconds ; the fluid in the lumen of the needle boils and the steam has a sterilizing effect, and this steam when expelled forces out any infective material which is in the bore.

SECTION V
INOCULATION TECHNIQUE

31. **General**

With the exception of yellow fever, small pox and B.C.G. vaccines, the agents usually consist of sterilized cultures of the organisms concerned or of their chemically-treated products. They have all been tested for sterility before issue, and the dose determined by the various methods of standardization.

In order to minimize waste, vaccines and test products are sent out in rubber capped bottles holding several doses, or in multi- or single-dose ampoules.

In view of the labour involved in the preparation and standardization of vaccines and other biological products, every endeavour must be made to ensure economy in their use.

Only one bottle of any vaccine should be in actual use at any one time ; when not in use, the bottle should be kept covered up to protect it from dust and light. If the rubber cap on the bottle of vaccine gets into bad condition

through repeated punctures or any other causes, the bottle should be discarded as holes in the rubber may lead to contamination of the product.

Once a sealed ampoule is opened, it is highly undersirable, owing to risk of contamination, to reserve any portion of the contents for future use. If the whole of the product cannot be used at once on one or more patients, the unused portion should be discarded.

32. Filling of syringes

(*a*) *From ampoules*

Before opening an ampoule, any liquid lodging in the neck should be shaken down by a movement similar to that used in setting a clinical thermometer. A file mark should be made on the neck of the ampoule, which should then be swabbed with alcohol or tincture of iodine and broken off with sterile forceps. The ampoule is then held on the slant, the sterile needle inserted and the syringe filled.

(*b*) *From rubber-capped bottles*

The cap of a rubber-capped bottle should be sterilized by wiping it thoroughly with a sterile swab dipped in 70 per cent. alcohol, followed by the application of tincture of iodine. The bottle should be shaken thoroughly to ensure uniform dosage. After a session, any container which is nearly empty should be discarded. A sterile syringe is filled with a volume of air approximately equal to the quantity of the vaccine, etc., to be withdrawn, the needle is then pushed vertically through the cap, the bottle inverted, the air injected, and the requisite quantity of vaccine, etc., withdrawn. (To enable the contents to be withdrawn easily, some workers push a second needle, plugged with a sterile cotton-wool filter, through the rubber cap to act as an air inlet.)

33. Method of performing inoculations

(*a*) *Site of injection*

All prophylactic inoculations are given by the subcutaneous route, except alum precipitated toxoid (A.P.T.) for diphtheria, which is given intramuscularly.

(i) *Intradermal injection*

For the Mantoux test the site of election is over the upper third of the flexor surface of the forearm, or at the junction of the upper and middle thirds. For sensitivity and other diagnostic tests intradermal injections are usually given in the middle of the front of the forearm.

(ii) *Subcutaneous injection*

Subcutaneous injections should be made in a location where the skin is loose, the tissues yielding, and the veins scarce. The site most frequently employed is the outer aspect of the arm or thigh. The site of election for the injection of most vaccines is *over the insertion of the deltoid muscle*—inoculations given lower down the arm are likely to result in painful serous effusion.

(iii) *Intramuscular injection*

Intramuscular injections are best made into the deltoid or triceps for small amounts, and into the middle third of the lateral aspect of the thigh or into the upper outer quadrant of the gluteal region if the amounts are large.

(*b*) *Technique of injection*

A simple and efficient method of preparing the site for injection is to rub the part with swabs soaked in methylated spirit, and then paint with iodine.

(i) *Intradermal injection*

The operator stretches the skin by holding the forearm tightly in his left hand, and slowly inserts the needle, with the bevel upwards, for about 2 mm. into the superficial layers of the dermis almost parallel with the surface. A special short needle with a short bevel is used ; this can usually be seen faintly through the epidermis during injection. A raised blanched bleb is a sign that the injection is satisfactory and has not been made too deeply.

(ii) *Subcutaneous injection*

The patient is instructed to place his hand on his hip. The upper arm is steadied with the operator's left hand, the skin being made taut with the thumb. Then, holding the syringe in the right hand, the operator passes the needle at an acute angle well into the subcutaneous tissue. On completion of the injection the needle is withdrawn and the skin again swabbed.

Care must be taken to avoid aspirating blood or tissue fluid into the syringe. *On no account will a needle be used again without re-sterilization.* (*See* Section IV.)

34. General precautions

(*a*) The operator and all assistants must wash their hands thoroughly with soap and warm water and dry them on a clean towel before commencing work and at intervals during prolonged operations. As an extra precaution during mass inoculations, or if there is reason to think that the operator's hands are infected, the hands may be steeped in some suitable disinfectant. All staff should wear white gowns or coats.

(*b*) *Needles* should be handled only with sterile forceps, *syringes* with *dry* washed hands, taking care to touch only the outside of the barrel and the handle of the piston. There must be no talking, coughing or sneezing over a sterile syringe.

(*c*) In order to avoid nausea and fainting, men must not be kept waiting for long periods in extremes of climate. Queues of men in the actual room where inoculations are taking place must also be avoided. Aromatic spirits of ammonia and liq. adrenaline, 1 in 1,000, should be kept available for treatment.

(*d*) Not more than two injections should normally be given at one session to any one person, except in cases of urgency. Programmes should be so organized that men do not receive further inoculations while they have sore arms or are otherwise suffering from a previous injection (*see* Section XVIII) ; for example, it is permissible to vaccinate against smallpox and inoculate with T.A.B. in different arms at the same session, but it is bad practice to give T.A.B. to men who have been vaccinated a few days before and who may now be feeling its effect.

(*e*) *It is important* that before performing any vaccination or inoculation, the M.O. should satisfy himself that the individual is in good health and that there is no history of recent exposure to such diseases as measles, scarlatina, diphtheria or erysipelas. In the event of contact with a case of smallpox however, it may be necessary to carry out the vaccination of individuals who have been exposed to infection with diseases such as those mentioned above.

(*f*) Only one dose will be taken into each syringe at a time. This will be completely expelled into the patient. The needle will be withdrawn and sterilized by holding in hot oil or boiling water while the piston is firmly held against the base of the barrel. This procedure will always be carried out unless and until an efficient valve is made available for introduction between the needle and the syringe, so obviating the risk of reflux infection. Before recharging the syringe the needle must be cooled by dipping in sterile normal saline if live vaccines are being used.

(*g*) In the event of poliomyelitis becoming extraordinarily prevalent in any locality, the use of diphtheria antigens will be temporarily suspended (*see* also para. 52).

SECTION VI

MASS INOCULATIONS

35. When performing mass inoculation it is advisable to have a staff of at least four, consisting of a medical officer to give the injections, an N.C.O. to fill the syringes and re-sterilize the needles, an orderly to marshall the personnel and swab their arms, and a clerk.

At least four 2 ml. syringes, a dozen needles, apparatus for hot oil sterilization and a pair of sterile forceps are required. If the syringes and needles have not been previously sterilized by hot air or autoclaving, a shallow sterilizer will also be required. These syringes are loaded with one dose each, the fourth is kept sterile in reserve.

After injecting one dose the medical officer sterilizes the needle in hot oil, or if this is not available, boiling water *see* para. 34 (*f*). He then hands the syringe to the N.C.O. for reloading and picks up a loaded syringe for the next injection. The N.C.O. takes up only one dose into the empty syringe handed to him and then places it in a sterile test tube in a convenient position. Where indicated he changes the needle with sterile forceps.

When more than one type of inoculation is to be given at one time, the number of syringes and needles should be increased, and an extra assistant employed to help fill the syringes and see that the vaccines are not mixed up.

Under no circumstances will anyone other than a medical officer be allowed either to give an injection or to vaccinate against smallpox without the authority of the D.G.A.M.S.

For precautions, *see* para. 34.

PART III

TECHNICAL INSTRUCTIONS FOR CARRYING OUT VARIOUS ACTIVE AND PASSIVE IMMUNOLOGICAL PROCEDURES

SECTION VII

ACTIVE IMMUNIZATION AGAINST THE ENTERIC GROUP OF FEVERS (AND TETANUS)

36. General

Immunity is conferred against typhoid, paratyphoid A and paratyphoid B fevers and tetanus by innoculation with TABT combined prophylactic. TABT is prepared in two dilutions ; that for the second dose of primary immunization (TABT II) has twice the TAB content of the other (TAB I). The TAB element of the combined prophylactic is heat killed, phenol preserved TABT vaccine, dilute, for children is also available.

37. Dosage (Adults TABT I & II)

All doses will be 1.0 ml. . . Primary immunization will be by three doses, the second 4-6 weeks after the first and the third 6-12 months after the second. Immunity will be maintained by annual re-inoculation while at risk. For all injections except the second dose at primary immunization (*see* above) the preparation containing the smaller amount of TAB will be used (TABT I).

38. Duration of Immunity

A *detectable* level of antibody to the Enteric Group is said to exist for about five years after a routine primary immunization, but a *protective* level is achieved for a much shorter period, say one to three years in different individuals.

Immunity to tetanus lasts for five years.

39. Re-inoculations

(*a*) As long as the individual is at risk annual boosting doses must be given. All others require a single boosting dose every three years or on leaving the United Kingdom if more than six months has elapsed since primary or boosting inoculation.

(*b*) *Re-immunization.*—If after primary immunization, three or more years elapse without re-inoculation, primary immunization must be repeated, as a single boosting dose alone will not stimulate a sufficient rise in the level of circulating antibody to give complete protection.

40. Reactions

In a large proportion of cases there is little or no reaction, while in others there may be transient pyrexia and discomfort. Redness and swelling may

occur at the site of the inoculation ; this is often the result of injecting the vaccine too near the elbow, but need give no cause for anxiety. In rare cases there may be some pyrexia associated with pallor, sweating and even collapse. Enquiry will then often elicit the fact that the patient has not rested. The condition improves rapidly with rest, warmth and hot drinks.

41. Special Precautions

The inoculation should be made at as late an hour as possible so that the worst of any reaction is over by the morning. Personnel must be warned not to take any alcoholic drink. They should be excused duty for 36 hours after the inoculation and forbidden to leave barracks.

Other causes of severe reactions are :—

(*a*) failure to shake the bottle of vaccine before use ;
(*b*) using the dregs of an old bottle ; and
(*c*) inaccurate dosage, particularly from using a syringe with indistinct markings or of larger volume than 2·0 ml.

SECTION VIII

ACTIVE IMMUNIZATION AGAINST TETANUS

42. General

Immunity is conferred by the injection of tetanus toxoid (T.T.) which consists of tetanus toxin rendered atoxic with formalin.

This is now available combined with T.A.B. Vaccine—*see* paragraphs 36-41.

The combined prophylactic will normally be used.

43. Dosage

For *primary immunization* against tetanus alone, 1·0 ml. of tetanus toxoid is injected subcutaneously at intervals as shown below :—

1st Injection	*2nd Injection*	*3rd Injection*
1·0 ml.	1·0 ml. not less than six or more than twelve weeks after the first injection.	1·0 ml. six to twelve months after the second injection.

The doses given above may be given to personnel of all ages and of either sex.

44. Duration of Immunity

The immunity conferred by these injections lasts for five years.

45. Reinforcement of Immunity

Under peace conditions

A reinforcing dose of 1·0 ml. will normally be given every five years.

On Active Service

Unless documentary evidence of immunisation within the preceding two months can be produced a reinforcing dose will be given before departure on active service. Reinforcing doses will continue to be given at yearly intervals throughout the period of active service.

46. Reactions

Reactions to tetanus toxoid are rare and usually mild. People with a history of asthma or hayfever may be more liable than others to an allergic reaction. Such cases should be given a reduced dose, *e.g.*, 0·1 ml. followed some hours later or on the next day by the ordinary dose of 1·0 ml. if no symptoms have occurred.

SECTION IX

THE SCHICK TEST AND ACTIVE IMMUNIZATION AGAINST DIPHTHERIA

(A) THE SCHICK TEST

47. General

This is a biological test which depends on the neutralization of the Schick-test fluid (Schick toxin) by the subject's diphtheria antitoxin. It is used both to detect those who are susceptible to diphtheria and require immunization, and to confirm a useful degree of immunity after immunization.

The test is carried out by the intradermal injection into the flexor surface of the left forearm of an amount of Schick toxin equivalent in terms of "combining power" to 1/1000 unit of antitoxin. The resulting reaction is compared with that produced by a similar dose of heated (inactivated) toxin given into the right forearm.

48. Technique

The skin over the flexor surfaces of both forearms is cleaned with spirit and allowed to dry. 0·2 ml. of Schick test toxin is injected strictly intradermally into the cleaned area of the left arm using a sterile 1 ml. syringe reserved for the purpose. The needle must be of a type suitable for intradermal injection and must fit the nozzle closely so that there is no leakage.

With a separate, similar syringe, 0·2 ml. of Schick control fluid (heated toxin) is injected intradermally into the right forearm. The injections should raise a white wheal 5 to 10 mm. in diameter. Results are read 5 days later. Syringes used for Schick control fluid should be readily identifiable from those kept for Schick toxin ; a good plan is to place indiarubber bands around the barrels of the control syringes.

49. Results

(*a*) A *negative* result should show no reaction in either arm. Rarely a mild transient erythema due to trauma is observed.

(*b*) A *positive* result shows a flush on the left arm appearing generally after 24 to 36 hours and reaching its maximum development on the fourth to

seventh day. At this time there is an area of oedema 50 to 30 mm. in diameter, which may be slightly raised above the surface of the skin. The erythema fades in the second week, leaving an area of brown pigmentation and superficial desquamation. The right arm shows no reaction.

(*c*) *Pseudo reading*

In some individuals who are susceptible to the foreign proteins contained in the test and control fluids, both arms will show reactions which are usually less sharply circumscribed than a typical positive reaction. These flushes develop during the first 24 hours and have almost completely faded as a general rule by the fifth day.

In a negative-and-pseudo reactor, the reactions on both arms are equal or nearly equal.

In a positive-and-pseudo, or "combined" reactor, the control arm will show a pseudo-reaction which fades as already described, whilst the reaction in the test arm continues to develop. By the fourth day the difference in the two arms is usually distinctive.

The correct interpretation of some pseudo reactions calls for considerable experience and more than one inspection of the arms. It is worthy of note that well-marked pseudo reactors almost always have very high titres of circulating antitoxin and are therefore immune to diphtheria.

The four types of reaction may be tabulated as follows :—

Schick reading	*Left Arm (Test)*	*Right Arm (Control)*
Negative	—	—
Positive	+	—
Negative-and-Pseudo	pseudo	pseudo
Positive-and-Pseudo (Combined) ..	+ and pseudo	pseudo

(B) ACTIVE IMMUNIZATION AGAINST DIPHTHERIA

50. General

All ranks are Schick tested on enlistment and those proving to be positive are immunized against diphtheria before completion of their primary training. (*See* para. 52.)

The agent used is Alum Precipitated Toxoid (A.P.T.).

51. Dosage

(*a*) *Adults*

Two intramuscular injections are given. The first dose is 0·2 ml. and the second, 28 days later, is 0·5 ml.

Personnel who show the combined reaction (Schick positive-and-pseudo), although presumably susceptible to diphtheria, are *NOT* immunized owing to the risk of severe local and general reactions. In practice these individuals may be partly immunized already, and may become completely immune in the months following, without any further artificial immunization.

If necessary, Diphtheria Prophylactic T.A.F. (Toxoid-Antitoxin Floccules) can be given with less likelihood of trouble from reactions. This agent requires three doses of 1·0 ml., four weeks being the usual interval between injections. It is not used as a routine in the Army.

(*b*) *Children*

It is usual to immunize children during the first year of life, giving them boosting doses of 0·5 ml. at 2 and 5 years of age. Children under the age of 8 can safely be immunized without being Schick tested but this test must *always* be performed before immunizing anyone over that age owing to the risk of troublesome reactions in those who may have become Schick pseudo-reactors. *Combined Diphtheria-Pertussis Prophylactic* is also available for children of from 4 months to 5 years of age. (*See* Section X.)

52. Special Precautions

Recent research work has shown that there may possibly be some relationship between inoculation and the occurrence and site of paralysis in poliomyelitis. It would appear that although in the United Kingdom combined diphtheria-pertussis antigens (containing alum)* may have been more liable to cause trouble than others, diphtheria antigens alone have also been involved in a number of cases.

In the event of *poliomyelitis* becoming exceptionally prevalent in any locality the use of diphtheria antigens, including those containing pertussis antigens, will be temporarily suspended. Further, in view of the seasonal incidence of poliomyelitis it may be advisable to restrict mass diphtheria immunization as far as possible to non-epidemic periods of the year.

A full inoculation history will in future be recorded on the in-patient case sheet of cases diagnosed as poliomyelitis.

No restrictions will be placed on carrying out the routine Schick test, but susceptibles will only be immunized when poliomyelitis is not prevalent. If, however, exceptional prevalence of poliomyelitis occurs simultaneously with an outbreak of diphtheria in the same locality, immunization will be carried out by the subcutaneous inoculation of purified formol toxoid.

Any orders in this connection altering the routine immunization laid down in para. 50 will be issued by the D.M.S./D.D.M.S. concerned.

* Such prophylactics are no longer used in the United Kingdom.

SECTION X

COMBINED ACTIVE IMMUNIZATION AGAINST DIPHTHERIA AND PERTUSSIS

53. General

Combined Diphtheria-Pertussis Prophylactic and *Diphtheria-Tetanus-Pertussis Prophylactic* are available for children from 4 months to 5 years of age.

54. Dosage

(*a*) *Diphtheria-Pertussis Prophylactic*

Three doses, each of 1·0 ml. are given deep subcutaneously or intramuscularly at intervals of 4 to 6 weeks for primary immunization, preferably between the 3rd and 6th months. A boosting dose may be given at one year and before the child starts to attend school. The first dose should be given about 3 weeks after smallpox vaccination.

(*b*) *Diphtheria-Tetanus-Pertussis Prophylactic*

Three doses, each of 1·0 ml. are given deep subcutaneously or intramuscularly at intervals of 4 weeks beginning at the 3rd or 4th month. The first dose should be given about 3 weeks after smallpox vaccination. A boosting dose may be given at one year and before the child starts to attend school.

55. **Special Precautions** (*See* para. 52)

SECTION XI

TUBERCULIN TESTS AND ACTIVE IMMUNIZATION AGAINST TUBERCULOSIS

(A) TUBERCULIN SENSITIVITY—THE MANTOUX AND HEAF TESTS

56. General

The graded intradermal or Mantoux test is suitable for military personnel. but should not be performed within 14 days of vaccination against smallpox. A single test with 10 I.T.U. of Old Tuberculin or a Heaf Test is performed in connection with the Army B.C.G. Scheme.

57. The Graded Mantoux Test

(*a*) An area of skin over the upper third of the flexor surface of the forearm is cleaned with spirit and allowed to dry.

(*b*) 0·1 ml. of a dilution of Old Tuberculin is then injected strictly intradermally to produce a wheal about 5 mm. in diameter.

(*c*) The complete test is done in two stages.

(i) The *first* test consists of the intradermal injection of 0·1 ml. of a 1/10,000 dilution of tuberculin, equivalent to a dose of one unit, International Standard.

The arm is examined after 72 hours and the areas of oedema and erythema are each measured in millimetres.

A *positive* result consists of a "raised" area of oedema of not less than 6 millimetres in diameter. *Simple erythema* is not regarded as a positive reaction.

(ii) If the test is negative it is repeated immediately using 0·1 ml. of a 1/100 dilution of Old Tuberculin equivalent to a dose of 100 units, International Standard. The result is examined and measured as before.

Notes

1. The World Health Organization has defined the unit of tuberculin (1951) as the activity contained in 0·00001 ml. of the International Standard preparation at present in use.

2. Separate syringes and needles must be kept for each dilution used. They are preferably dry sterilized and must never be used for any other purpose.

3. The results will be recorded in A.B. 439, A.B. 64 (Pt. 1) and other relevant documents.

4. The area of oedema in positive reactors will be noted thus :—

Date Mantoux 1 unit Positive 10 mm.

or

Date Mantoux 100 units Positive 10 mm.

Non-reactors and doubtful reactors to 1/100 dilution (100 units) will be recorded as " Mantoux—Negative ".

5. No Mantoux negative reactor will be employed in or about tuberculosis hospitals or wards.

58. The Heaf Multiple Puncture Test

This is carried out with the Heaf multiple puncture instrument. Either pure O.T. (adrenalised with 0·1 ml. of 1 per cent. adrenalin solution per ml. undiluted O.T.) or P.P.D. 2·0 mg. per ml. is used. No adrenalin is added to the latter.

Technique

(*a*) *Apparatus required*

A spirit lamp.
A fine glass rod or platinum loop 2 mm. diameter.
Multiple puncture apparatus.
O.T. or P.P.D.
Methylated spirit. Petri dish.

(*b*) *Method*

A small amount of spirit is put into the Petri dish. The multiple puncture apparatus is sterilized by just touching the surface of the spirit with the end plate of the apparatus and then passing it through the flame. The apparatus is then placed so that the needles do not become contaminated.

A suitable site is usually about a hand's breadth below the bend of the elbow on the anterior aspect of the forearm. Care must be taken to avoid superficial veins.

The skin is cleaned with spirit and a small amount of tuberculin is spread with a sterile platinum loop or glass rod as an even film over about 1 sq. cm. of skin and the loop or rod is re-sterilized for the next test.

The end of the apparatus is then pressed firmly over the film and the six needles released by the spring action. For adults and children over 1 year 2 mm. penetration is the general rule ; for children under 1 year old needles with a penetration of 1 mm. are used.

The apparatus is then sterilized as before in readiness for the next test.

The arm is allowed to dry for about half-a-minute and no dressing is necessary.

By following the drill about 120 persons can be tested per hour without difficulty.

(*c*) *Reading*

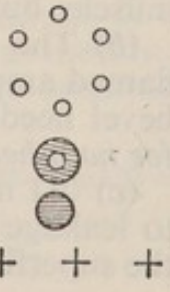
The result can be read from 72 hours to 7 days after the test.

A Positive result of the *first* degree is recorded when there are four or more indurated papules which can be felt.

A Positive of the *second* degree is recorded when the papules have coalesced to form a ring.

A Positive of the *third* degree is recorded when there is a large plateau of induration.

Anything greater than this is *fourth* degree.



The occasional third and fourth degree results should be treated with mepyramin cream.

Note :—Results are recorded by degree of reaction in accordance with the above.

(B) ACTIVE IMMUNIZATION AGAINST TUBERCULOSIS— B.C.G. VACCINATION

59. General

(*a*) Immunization against tuberculosis is based on the assumption that the acquisition of tuberculin sensitivity is accompanied by a degree of immunity.

(*b*) Vaccination with B.C.G. (*Bacille Calmette-Guérin*) is of value only to tuberculin negative reactors. Healthy subjects who are tuberculin positive have already been infected and are relatively immune. In the Army, B.C.G. vaccination is at present offered as a routine to tuberculin negative reactors in the following categories :—

(i) All soldiers who enlist on regular engagements in the R.A.M.C. All R.A.M.C. personnel whether regular or otherwise who are sleected for training or employment as laboratory technicians, radiographers and operating theatre technicians.
(ii) All other ranks of the R.A.D.C.
(iii) All other ranks of the Q.A.R.A.N.C.
(iv) Those serving in Gurkha, Seychellois or Fijian units.
(v) The St. John and British Red Cross Society Service hospital welfare officers.
(vi) Civilian physiotherapists employed in military hospitals.

No member of the R.A.M.C., either officer or other rank, who specially requests this immunization will, however, be refused.

(*c*) The *Bacille Calmette-Guérin* is a bovine type of tubercle bacillus possessing a low virulence which has been achieved by frequent subculture on a special medium. The B.C.G. vaccine when prepared for injection consists of living organisms and must be used within 14 days of the date of manufacture. Unused vaccine *must* be destroyed.

The vaccine is best kept at a temperature of 3° to 6° C. which prevents it from freezing or multiplying. The active life of the material is progressively curtailed by increase in temperature and it is quickly destroyed by ultra-violet light and exposure to direct sunlight.

(*d*) Before use the ampoule should be well shaken and the vaccine carefully examined. The preparation which is at present available to the Army is for intradermal use. This should be only very faintly hazy, but if there is more than this haziness, or an unusual colour, or if the presence of clumps is observed in the shaken suspension, then the ampoule must be rejected.

60. Technique of vaccination with suspension prepared for intradermal use

(*a*) The site of inoculation is usually over the insertion of the left deltoid muscle, but the antero-lateral surface of the thigh can be used.

(*b*) The skin is cleaned with spirit and the vaccine drawn up from the flamed ampoule into a sterile glass tuberculin type syringe fitted with a short bevel needle. *Both syringe and needle should be reserved for this and used for no other purpose.*

(*c*) 0·1 ml. of the vaccine is injected strictly intradermally without loss due to leakage from the needle track. Care must be taken to ensure that only the superficial layer of the skin is injected. A satisfactory vaccination should

produce a white wheal 5 mm. in diameter. For children under 5 years of age two doses of 0·05 ml. are injected separately over the insertion of one deltoid.

(*d*) In successful cases a local reaction develops at the site in from 3 to 6 weeks. It begins as a small papule which slowly increases in size and may in some cases break down into a shallow painless ulcer. Healing commences after about 8 weeks leaving a tiny scar.

61. Follow-up and recording of results

(*a*) Six weeks after the date of vaccination the lesion is inspected and described as follows :—

size of induration in mm.
„ „ papule in mm.
„ „ macule in mm.
„ „ vesicle in mm.
„ „ ulcer in mm.
presence of glandular enlargement, if any.
„ „ an abscess if any.

(*b*) At the same time either a Heaf multipuncture test or a Mantoux test, using 1/1000 (10 I.T.U.) of Old Turbeculin or P.P.D. is performed as a conversion test.

Should the tuberculin conversion test be negative, it must be repeated six weeks later, *i.e.*, 12 weeks after the original date of vaccination. If it is still negative the patient should be revaccinated if fluid B.C.G. vaccine has been employed. If dried vaccine has been given, a third tuberculin test for conversion will be made after a further six weeks, *i.e.*, 18 weeks after vaccination, before resorting to revaccination.

62. Precautions

(*a*) All personnel who receive B.C.G. vaccination should be isolated from all known sources of tuberculosis for six weeks before and six weeks after vaccination.

(*b*) In new born infants (*i.e.*, infants up to 4 weeks of age) with tuberculous mothers, tuberculin testing before segregation is not necessary as tests will inevitable be negative. A single test after segregation will be carried out as above, and B.C.G. vaccination performed at once if it be negative. In general, segregation of children and infants for six weeks both before and after B.C.G. must be supervised, but need not be in hospital. New born infants, however, must be segregated in hospital, as it is impossible otherwise to guarantee complete separation of an infant from its mother both before and after vaccination.

(*c*) A full plate chest X-ray must be taken before vaccination.

63. Annual examination of immunized personnel.

All immunized personnel must be tuberculin tested annually to ensure that reversion has not taken place. Whenever possible an annual X-ray examination of the chest will also be carried out at the same time as the annual tuberculin test. Personnel who have reverted will be offered re-immunization.

NOTE:—The Mantoux test will be carried out with 1/1000 (10 units) Old Tuberculin or P.P.D.

SECTION XII

ACTIVE IMMUNIZATION AGAINST CHOLERA

64. General

Cholera vaccine is a heat-killed, phenol-preserved vaccine, each ml. containing 8,000 million organisms.

65. Primary Immunization

For primary immunization, two doses of vaccine are injected subcutaneously at an interval of 7 to 14 days. The dosage is as follows :—

	1st Dose	*2nd Dose*
Adults and children over 5 years ..	0·5 ml.	1·0 ml.
Children aged 1 to 5 years	0.25 ml.	0·5 ml.

Children under 1 year are not immunized.

66. Duration of Immunity

Immunity is short lived, not exceeding six months.

67. Re-immunization

A single re-immunizing dose of vaccine must be given every six months as long as the individual is at risk. Adults and children over five receive 0·5 ml., and children aged one to five years receive 0·25 ml. of the vaccine.

68. Reactions

Reactions are negligible.

SECTION XIII

ACTIVE IMMUNIZATION AGAINST PLAGUE

69. General

Plague vaccine consists of a suspension of an avirulent strain of the organism, which has been killed with formalin and preserved with phenol.

70. Primary Immunization

For primary immunization, two doses of vaccine are injected subcutaneously at an interval of 10 to 14 days. The dosage is as follows :—

	1st Dose	*2nd Dose*
Adults and children over 12 years ..	0·5 ml.	1·0 ml.
Children aged 5 to 12 years	0·25 ml.	0·5 ml.
Children aged 1 to 5 years	0·1 ml.	0·2 ml.

Children under 1 year are not immunized.

71. Duration of Immunity

Immunity is short lived.

72. Re-immunization

A single re-immunizing dose of vaccine must be given every six months while the individual is at risk, or when there is a risk of an epidemic. The re-immunizing dose for adults is 0·5 ml., for children aged five to twelve 0·25 ml., and for children one to five 0·1 ml. of vaccine.

73. Reactions

Inoculation is sometimes followed by severe local and general reactions.

SECTION XIV

ACTIVE IMMUNIZATION AGAINST TYPHUS FEVER

74. General

Typhus vaccine is prepared from suspensions of rickettsiae grown in the yolk sac of developing chick embryos. The vaccine at present in use is prepared at the Connaught Medical Research Laboratories, Toronto. A similar type of vaccine which was used in the war was prepared by the Lederle Laboratories, New York, by the method of Cox. These vaccines afford protection against both the louse borne and flea borne types of typhus. No vaccine is available which will give protection against scrub typhus.

75. Dosage

Primary immunization is achieved with three subcutaneous injections of 1·0 ml. of vaccine given at weekly intervals. This dosage can be given to children but infants under one year should not be immunized.

76. Duration of Immunity

Immunity is short lived.

77. Reinforcement of Immunity

A " booster " dose of 1·0 ml. must be given every three months after primary immunization while the individual is at risk during an epidemic. In endemic areas a single dose of 1·0 ml. should be given annually to maintain immunity.

78. Reactions

Local discomfort at the site of innoculation is common but general reactions are rare.

SECTION XV

VACCINE LYMPH AND VACCINATION

79. Supply

Other than in overseas commands where local supply of vaccine lymph is established the vaccine lymph for the Army is supplied by the Lister Institute and distributed from the David Bruce Laboratories, East Everleigh, Near

Marlborough, Wilts. Indents on AFI 1209 from units in U.K. will be addressed DIRECT to the O.C. David Bruce Laboratories, stating the amount required in each of the following packs :—

(*a*) 25 doses pack (Dried lymph with diluent)
(*b*) 100 doses pack (,, ,, ,, ,,)

In the case of overseas commands where there is no satisfactory local source of supply of glycerinated or dried vaccine lymph consolidated demands will be sent direct to War Office A.M.D.3b under arrangements to be made by DMS/DDMS/ADMS concerned.

80. Storage

(*a*) Dried Vaccine Lymph should be kept in a refrigerator if possible. Its life without refrigeration is at least 6 months in temperate and one month in tropical climates.

(*b*) Glycerinated lymph maintained at a temperature of minus 10° C. will last 12 months from the notified date of manufacture. (This requires a special refrigerator, which should be available at all Medical Equipment Depots.) For use vaccine lymph should be obtained fresh as and when required and used immediately. If this is impracticable, the lymph must be stored in an icebox or refrigerator at a temperature between 0° and 10° C. Lymph maintained between these temperatures should be used within 14 days (and preferably within 7 days) of issue. Maintained in a cool dark place, vaccine lymph should not be used after 7 days from the date of issue. Once a capillary tube is opened, the contents must be used immediately. Any surplus will be discarded and not kept for subsequent use.

81. Object

The immediate object of vaccination is to introduce vaccinia virus into the deeper layers of the epidermis where multiplication takes place most easily. Probably the best method of doing this is by the multiple pressure technique which has several advantages over other methods; *e.g.*, it is almost completely painless, involves a minimum of trauma, is less likely to be associated with unduly severe local reactions or septic complications, and ensures a higher proportion of " takes ".

82. Preparation of the skin and reconstitution of vaccine

(*a*) The area to be vaccinated will be well cleansed with soap and water and thoroughly dried with a sterile gauze pad before vaccination. The area may be swabbed gently with acetone if available, but care should be taken not to rub so vigorously as to damage the epidermis and encourage the development of secondary vesicles. Methylated spirit, alcohol, or similar agents will *not* be applied. However, the application of a highly volatile agent such as ether is said to facilitate the penetration of vaccinia virus into the skin, as well as to have an antiseptic action on the skin site.

(*b*) *Reconstitution of the Vaccine*

The 25-dose ampoules are those which will normally be used and the reconstituting fluid for these is issued in a double-ended ampoule so that the fluid can be transferred to the dried vaccine without using sterilized hypodermic syringes and needles ; thus the risk of accidental contamination in the hands of semi-skilled personnel is much reduced. The 100-dose ampoules are only likely to be used for mass vaccination in an emergency or for exceptionally large groups of people ; owing to the greater volume of

reconstituting fluid required this is issued in an ordinary glass ampoule. A sterilized syringe must be used for the transfer of fluid to the dried material. In common with other products dried from the frozen state resuspension of the vaccine is almost immediate after a slight shake.

After the material has been resuspended in fluid it has a strictly limited life and any surplus vaccine should be discarded and not kept for subsequent use unless it can be stored in a refrigerator at a temperature below 10° C., when the potency will be maintained for a week.

83. Technique of Multiple Pressure Vaccination

A small drop of vaccine lymph covering an area of about one-eighth of an inch in diameter is placed on the skin at the prepared site, usually in the region of the deltoid insertion on the left arm. A flat-sided needle, which should be of relatively large size, in good condition, sharp and sterile, is held parallel or tangential to the arm with the forefinger and middle finger above and the thumb below. The side of the needle point is then pressed firmly and rapidly into the drop 30 times as a routine, taking about ten seconds. The number of "pressures" to be employed in making the insertion varies according to the vaccination history of the individual being vaccinated (*see* below). In making the pressures, the needle is lifted clear of the skin each time.

This rapid up and down motion of the needle is in a plane perpendicular to the surface of the skin. The needle point is *not* driven into the skin, but at each pressure the elasticity of the skin pulls a little of the epidermis over the point of the needle so that the virus-bearing lymph is carried into the deeper epidermal layers. If the skin has not been unduly irritated by a preliminary cleansing procedure and the needle has been properly aligned, no pain or bleeding should occur and within a few hours there will be no evidence of trauma.

The excess vaccine lymph should be gently wiped off the arm with cotton wool as soon as the pressures have been completed and the remainder should be allowed to dry.

84. Use of a dressing

Many authorities consider the immediate application of a dressing unnecessary. Vaccine lymph, however, is highly infective, and patients may carry infection from the arm to other parts of the body or to other persons. Therefore, after the lymph has been allowed to dry, the vaccination site will be covered with sterile, but not antiseptic, lint or gauze, kept in place by adhesive strapping. The upper arm should not be washed until the crusts have separated—the less interference there is with the normal development of the lesions the better. At the stage of maximum reaction, the dressing of the arm may well be replaced by a piece of sterile gauze attached to the inner surface of the garment in contact with the lesion. The vaccinated arm should be rested as far as possible, preferably in a sling when the reaction is at all severe.

85. Types of vaccination

(*a*) *First vaccination* after enlistment will be carried out by means of a single insertion about one-eighth of an inch in diameter. If there is a definite scar of previous vaccination *thirty pressures* will be employed in making this insertion ; if there is no evidence of previous vaccination *ten pressures* only will be employed. Reading will be made on the eighth day after vaccination,

and, if there is no evidence of vesicle formation at that time, a repeat vaccination will immediately be carried out with one insertion, but employing 30 pressures in all cases.

(*b*) *Routine re-vaccination* will be by a single insertion with 30 pressures. If there is no vesicle formation on inspection, a further attempt will be made immediately by means of two insertions with 30 pressures each. The first insertion will be one inch from the site of the previous unsuccessful vaccination, while the second will be on the opposite arm.

(*c*) When *re-vaccination* is undertaken in the presence of an epidemic or of undue prevalence of smallpox, there will be at least two separate areas of insertion with 30 pressures in each.

(*d*) *Primary vaccination of infants.*—A single insertion by the multiple pressure technique using 30 pressures will be employed, as young babies are less prone to reaction than adults. The best age for vaccination in a thriving infant is from 3 to 4 months.

86. **Reading of results**

(*a*) *Practical considerations*

Accurate reading of the result of vaccination depends mainly on the period of time after insertion at which the maximum local reaction occurs but also depends on the *degree* of reaction. Maximum reaction may occur at any time within 2 to 10 days after vaccination. Ideally, there should be frequent inspection of the arm until the maximum local reaction is observed. Frequent inspection is not practicable. Provided a *reasonably* accurate assessment of the nature of " takes " (which indicates only the degree of immunity at the time of vaccination) can be made, this is all that is required. The results which may be anticipated are shown in the following table* :—

	Papule	Vesicle	Pustule	Scab	Scab off
Primary ..	4 days	5 days	8 days	11 days	21 days
Vaccinoid or Accelerated	2 days	3 days	4 days	5 days	8 days
Immediate or Immune	Papule under 1 day. (Usually no vesicle. Fades within 3 days.)				

N.B.—The times given are subject to considerable variation.

(*b*) *The Interpretation and Reading of Results*

Inspection will be made on the eighth day after vaccination, and action taken as follows :—

(i) *When vesicle or pustule formation has occurred.*

(1) if the subject *has not been* previously vaccinated, the result will be recorded as PRIMARY VACCINATION (SUCCESSFUL)—P.V.(S).

(2) if the subject *has been* previously vaccinated, the result will be recorded as REVACCINATION (SUCCESSFUL)—R.V.(S).

* The above table has been taken from " Antisera, Toxoids, Vaccines and Tuberculosis " 3rd Edition, by Dr. H. J. Parish, published by E. & S. Livingstone, Ltd.

(ii) *When vesicle or pustule formation has not occurred :*

The subject will be re-vaccinated immediately and inspections carried out between 8 and 14 days after re-vaccination.

(1) *When vesicle or pustule formation occurs* the result will be recorded in accordance with para. 86 (*b*)(*i*) above.

(2) *When vesicle or pustule formation is still not produced* the result will be recorded as " Insusceptible to vaccination " (I.T.V.) in military documents, but this term will not be used on international certificates (*see* para. 89).

This insusceptibility will *not* be considered a final life-long categorisation; re-vaccination will be carried out at the usual intervals (*see* para. 7(*b*) and 88).

Note : A *local reaction occurs* which reaches maximum size on the second or third day and is accompanied by elevation and itching of the site but without vesicle formation ; this was previously recorded on international certificates as " Reaction of immunity."

Certain authorities do not however agree with this interpretation and consider that the local or immediate reaction is a sensitivity reaction and is not necessarily indicative of immunity.

87. **Precautions with regard to simultaneous use of other immunizing agents**

Whenever possible, yellow fever inoculation should precede *primary* vaccination against smallpox. There should be an interval of at least four days between yellow fever inoculation (when given first) and primary vaccination against smallpox (when given subsequently). If *primary* vaccination against smallpox is done first, there should be an interval of 21 days from the date of vaccination before the yellow fever inoculation is given. Where there is evidence of previous successful vaccination against smallpox, yellow fever immunization and re-vaccination may be carried out at the same sessions, but, if time permits, yellow fever immunization should always precede re-vaccination by at least four days.

Other inoculations may be given at the same time as vaccination but in the opposite arm. [*See* also para. 34(*e*)].

When infants under the age of nine months are to be vaccinated against both yellow fever and smallpox, there should be an interval of 21 days between the two, no matter which is performed first.

88. **Intervals between re-vaccination**

(*a*) *Forces on home service or serving in North West Europe :*

Re-vaccination will be carried out every three years.

(*b*) *Forces serving overseas other than North West Europe :*

Re-vaccination will be carried out every two years or at such shorter intervals as may be rendered necessary by local ordinances. Information regarding such special cases will be notified to those concerned as it becomes necessary.

All troops and their families *proceeding* overseas other than to North West Europe (from the United Kingdom or from North West Europe) will be vaccinated not less than 14 days previously, unless they have been vaccinated within the previous two years.

(*c*) *Epidemics :*

In the presence of an epidemic or undue prevalence of smallpox, appropriate vaccination procedure may be ordered by the local commander on the advice of his senior medical officer.

89. Certification

An international certificate of vaccination must be issued to the individual and *must* be on F.Med.101 supplied through the Command Publication and Stationery Sections R.A.O.C. In order to avoid unnecessary complications for travellers, with effect from 1-10-52 when completing the certificate, it will *only* be recorded whether the vaccination is primary or a re-vaccination, and if primary whether successful. The term insusceptible to vaccination will not be used. In all cases the usual record will be made in A.B.64 (Part I) or A.B.439. (*See* para. 18.)

SECTION XVI

ACTIVE IMMUNIZATION AGAINST YELLOW FEVER

90. General

A living attenuated strain of pantropic virus (17D) is used to produce active immunity in persons likely to be exposed to yellow-fever infection. It is grown in chick embryo, from which a ground-up vaccine is prepared. This is frozen and dried *in vacuo*.

91. Dosage

The vaccine is reconstituted with *cold* sterile normal saline immediately before use, and is injected subcutaneously. The volume is generally arranged to contain one dose in 0·5 ml., and any solution which is not used within half an hour should be discarded. Only one injection is necessary. There is no lower age limit ; inoculation may if necessary be given in the first week of life at full dosage, but should be avoided in infants under nine months of age.

92. Duration of immunity

Immunity is probably complete in most cases by the tenth day and persists for six years. (From 1-10-52, an International Certificate of vaccination against Yellow Fever (F.Med.103) is valid for six years.)

93. Re-immunizing dosage

The re-immunizing dose of yellow fever vaccine is 0·5 ml. for persons of all ages and of either sex, irrespective of the date of the last inoculation against yellow fever.

94. Reactions

Neither local nor general reactions occur in the vast majority of cases. Allergic symptoms may be observed in subjects hypersensitive to egg or chicken protein, and are as a rule readily controlled by the injection of adrenaline, or an antihistaminic.

To avoid reactions associated with combined administration of yellow fever and smallpox vaccines the precautions given in paragraph 87 must be carefully observed.

To avoid the risk of encephalitis in young infants the inoculation should be avoided if possible during the first nine months of life.

SECTION XVII

ACTIVE IMMUNIZATION AGAINST RABIES

95. General

The vaccine usually supplied to the Army is that prepared by the Lister Institute, Elstree, and is a sterile suspension of killed rabies virus in 0·5 per cent. phenolized saline. It contains a 4 per cent. suspension of the brain and medulla of rabbits that have died from rabies after inoculation with "fixed" rabies virus.

The vaccine contains a flocculent precipitate which settles out on standing. The bottle should therefore be thoroughly shaken to ensure an even distribution of the contents before withdrawing each dose.

Stations in the Far East are supplied with vaccine manufactured by The Pasteur Institute, Kasauli, and by the civil laboratories at Kuala Lumpur and Hong Kong, whose instructions may differ from those given here ; the maker's recommendations should obviously be followed.

96. Administration of the Vaccine

The usual aseptic precautions must be carefully observed.

The vaccine should be injected subcutaneously into the areolar tissue on the side of the abdomen about two inches below the margin of the ribs. As the inoculations are given daily, it is not advisable to inject into the same spot every day but to vary the site of inoculation with each succeeding dose.

97. Care of patient

Patients undergoing anti-rabies treatment should live under as healthy conditions as possible. A liberal diet is recommended. Constipation should be avoided and the use of alcoholic beverages should be forbidden. Patients undergoing treatment are able ordinarily to attend to their work, but they should avoid fatigue, chills, long walks, and violent exercise. This advice should be followed for ten days after the completion of treatment, and it is then exceptional for general reactions to occur. Some local soreness, together with erythema about the site of inoculation, may be experienced, and slight malaise may be felt. The exceptional cases are probably very susceptible to the inoculation of a foreign protein.

98. Lines of treatment

In determining the duration and intensity of treatment for any particular patient, the following points should be taken into consideration :—the number of bites, the depth and severity of the bites, the position of the bites, whether on the head, face, neck, or on the exposed skin of any other part of the body ; whether through clothing, whether the wound was treated with an antiseptic and, if so, how soon after infliction ; the evidence as to whether the animal which inflicted the bites suffered from rabies ; and lastly, the time that had elapsed before the patient reported for treatment.

Bites through the clothing are less dangerous than those through the exposed skin, unless the animal has held on and bitten savagely. Patients with bites or scratches on the head, face or neck, or the fingers, must be regarded as severe cases and treated accordingly. Patients coming late (after 4-5 days) require longer treatment than those who come early.

The skin must be broken before infection can take place, but infection is possible through an uninjured mucous membrane.

The saliva of a dog is infective for a few days before the animal shows any outward symptoms of rabies ; it may be infective for as long as 5 days, and in a few cases it has been found to be infective for 6-7 days ; these points should be borne in mind in the giving or refusing of treatment to persons bitten, or licked on scratches or abrasions, by dogs apparently healthy at the time, but which have later developed symptoms of rabies, usually within ten days.

All cases of multiple and severe bites through the exposed skin or through clothing should receive *intensive* treatment. Light bites (single or through clothing) require *medium* treatment. Licks on abrasions or doubtful cases of infection should receive *light* treatment.

99. Dosage

Schemes of dosage are given by the makers for light, medium and intensive treatments. Patients over 12 years of age receive such doses while patients under 12 years of age are given one-half to three-quarters of these amounts.

SECTION XVIII

100. Reports

In the event of any untoward results following the use of any immunological procedures, *e.g.*, local sepsis, generalised vaccinia, severe pyrexia, nervous symptoms, etc., a full report will at once be made to :—

The Director of Pathology,
The War Office (A.M.D.8),
London, S.W.1.

The following details will be included :—

The full personal particulars of patient ;
Batch number of immunizing agent used and other identification particulars ;
The source of the immunizing agent ;
Date of receipt of immunizing agent ;
Date of administration ;
Date of onset of symptoms ; and a complete clinical description of the case.

SECTION XIX

101. SUMMARY OF ACTIVE IMMUNOLOGICAL PROCEDURES

(A) ADULT MALES

Disease	Agent used	Primary immunizing dosage	Interval between doses	Boosting dose	Interval after primary immunization and between boosting doses	Remarks	Reference to section in text
Enteric fever Tetanus	T.A.B.T. I and T.A.B.T. II (2nd dose only).	(i) 1·0 ml. (T.A.B.T. I) (ii) 1·0 ml. (T.A.B.T.II) (iii) 1·0 ml. (T.A.B.T. I)	4 to 6 weeks 6 months To 12 months	1·0 ml.	Every 12 months or sooner in the case of an outbreak.	Routine for all personnel.	Section VII.
Diphtheria ..	Alum precipitated toxoid (A.P.T.).	(i) 0·2 ml. (ii) 0·5 ml.	28 days	—	—	Routine for all Schick positive recruits, except in the presence of an outbreak of poliomyelitis.	Section IX.
Smallpox ..	Vaccine lymph ..	10 pressures	—	30 pressures.	Home and N.W. Europe — every 5 years. Elsewhere – every 2 years. Also when specially ordered.	Routine for all personnel.	Section XV.
Tuberculosis ..	B.C.G. vaccine ..	0·1 ml.	—	—	—	Certain personnel of R.A.M.C. and Q.A.R.A.N.C. only.	Section XI.
Cholera ..	Cholera vaccine ..	(i) 0·5 ml. (ii) 1·0 ml.	7 to 14 days	0·5 ml.	Every 6 months ..	When specially ordered.	Section XII.
Plague ..	Plague vaccine ..	(i) 0·5 ml. (ii) 1·0 ml.	10 to 14 days	0·5 ml.	Every 6 months ..	When specially ordered.	Section XIII.
Typhus ..	Typhus vaccine (epidemic and murine).	(i) 1·0 ml. (ii) 1·0 ml. (iii) 1·0 ml.	7 days .. 7 days.	1·0 ml.	Every 3 months ..	When specially ordered.	Section XIV.
Yellow Fever ..	Yellow Fever vaccine.	0·5 ml.	—	0·5 ml.	Every 6 years ..	When specially ordered.	Section XVI.

(B) WOMEN AND CHILDREN OVER 12

Women and children over twelve years of age receive the same dosages of the same vaccines as adult men, with the proviso that dosages may be proportionately reduced for those who are obviously underweight.

(C) CHILDREN UNDER TWELVE YEARS OF AGE

Disease	Agent used	Age	Primary immunizing dosage	Interval between doses	Boosting dose	Interval after primary immunization and between "boosting" doses	Remarks	Reference to section in text
Enteric Fever	Dilute T.A.B.T. for Children.	6 to 12 years	(i) 1 ml.* (ii) 1 ml.* (iii) 1 ml.*	}	ml. ml.	Every 12 months ..	When exposed to risk and when necessary for travel.	Section VII.
	do.	1 to 5 years	(i) 1 ml.* (ii) 1 ml.* (iii) 1 ml.*	}	ml.	Every 12 months ..	When exposed to risk and when necessary for travel and providing the weight is normal.	Section VII. Section VII.
	* Dilute T.A.B.T. I for Under 1 yr.		(i), (iii) and subsequent doses		—Dilute T.	A.B.T. II for (ii)		
			Children under one year are not immunized.					
Tetanus ..	Tetanus Toxoid or T.A.B.T.	All ages.	Children of all ages receive the same dosage as adults.				When exposed to risk.	Section VIII. (Section VII)
Diphtheria ..	Alum Precipitated Toxoid (A.P.T.)	All ages, usually first year.	(i) 0·2 ml. (ii) 0·5 ml.	} 28 days ..	1.0 ml.	At 2 years of age and again at 5 years.	When requested by the parents.	Section IX.
	Combined Diphtheria—Pertussis Prophylactic.	6 months to 8 years.	(i) 1.0 ml. (ii) 1.0 ml. (iii) 1.0 ml.	} 4 to 6 weeks. } 4 to 6 weeks.	—	—	When requested by the parents.	Section X.
Smallpox ..	Vaccine lymph ..	No lower age limit, preferably 3 to 4 months	30 pressures	—	30 pressures.	As for adults ..	When requested by the parents when exposed to risk and when necessary for travel.	Section XV.

(C) CHILDREN UNDER TWELVE YEARS OF AGE—*continued*

Disease	Agent used	Age	Primary immunizing dosage	Interval between doses	Boosting dose	Interval after primary immunization and between "boosting" doses	Remarks	Reference to section in text
Tuberculosis..	B.C.G. vaccine ..	Any age	As for adults	B.C.G. vaccination will not normally be undertaken from Army resources, but will be carried out in civilian clinics.			Mantoux or Heaf test negative reactors only. *Not* when suffering from measles, whooping cough, eczema or furunculosis.	Section XI.
Cholera ..	Cholera vaccine	Over 5 years	(i) 0·5 ml. (ii) 1.0 ml.	7 to 14 days	0·5 ml.	Every 6 months ..	When exposed to risk and when necessary for travel.	Section XII.
		1 to 5 years	(i) 0·25 ml. (ii) 0·5 ml.	7 to 14 days	0·25 ml.	Every 6 months ..	When exposed to risk and when necessary for travel.	Section XII.
		Under 1 year	Children under 1 year are not immunized.					Section XII.
Plague ..	Plague vaccine ..	6 to 12 years	(i) 0·25 ml. (ii) 0·5 ml.	10 to 14 dys.	0·25 ml.	Every 6 months ..	When exposed to risk and when necessary for travel.	Section XIII
		2 to 5 years	(i) 0·1 ml. (ii) 0·2 ml.	10 to 14 dys.	0·1 ml.	Every 6 months ..		
		Under 1 year	Children under 1 year are not immunized.					
Typhus ..	Typhus vaccine ..	Over 1 year	Children over 1 year of age receive the same dosage as adults.				When exposed to risk and when necessary for travel.	Section XIV
		Under 1 year	Children under 1 year of age are not immunized.					
Yellow Fever	Yellow fever vaccine.	All ages ..	Children of all ages receive the same dosage as adults.				When exposed to risk and when necessary for travel.	Section XVI

SECTION XX

102. SUGGESTED PROGRAMME OF INOCULATION PROCEDURES

(a) Scheme for Recruits

Week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1st	1	2	3	4	5 T.A.B.T. (I) Vaccinate —Small-pox	6 Rest	7 Rest
2nd	8	9	10	11	12	13 Inspect vacc. Re-vacc. if necessary. Schick test	14
3rd	15	16	17	18 Read Schick 1st A.P.T. ifnecessary	19	20	21
4th	22 Final inspect. of re-vacc. if necessary	23	24	25	26	27	28
5th	29	30	31	32	33 T.A.B.T. (II)	34 Rest	35 Rest
6th	36 1st Mantoux* or Heaf	37	38 Read Mantoux* or Heaf 2nd Mantoux* if necessary	39	40 Read 2nd Mantoux* Give B.C.G.* ifnecessary	41	42
7th	43	44	45	46 2nd A.P.T. where necessary	47	48	49
8th	50	51	52	53	54	55	56
9th	57	58	59	60	61 Inspect B.C.G.* and record	62	63

(Continued on next page)

(*a*) *Scheme for Recruits*—continued.

Week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
10th	64	65	66	67	68	69	70
11th	71	72	73	74	75	76	77
12th	78	79	80 Mantoux* conversion	81	82 Read Mantoux* conversion	83	84

* Mantoux testing and B.C.G. immunization apply mainly to certain R.A.M.C. and Q.A.R.A.N.C. personnel.

(*b*) *Scheme for the complete protection of Travellers :*

Day 1	..	Cholera 1†	and	Yellow fever.†
Day 5	..	Vaccination†	and	T.A.B.T.
Day 11	..	Cholera 2.		
Day 13	..	Read vaccination.††		

Between the 13th and 27th days, Plague 1 and 2 *OR* Typhus 1, 2 and 3 may be given when convenient, if required.

Note.—The time intervals given above are, for some inoculations, less than those given elsewhere in this memorandum. This is to enable travellers to receive all the necessary inoculations in the minimum time compatible with satisfactory protection, but **longer intervals will always be used when the time available permits.** Travellers will not necessarily require all the procedures mentioned above.

† Require international certificates.
†† If the first vaccination does not "take", re-vaccinate immediately and read 8 days later, *i.e.*, on the 21st day.

SECTION XXI

PASSIVE IMMUNIZATION AGAINST TETANUS

103. General

Tetanus antitoxin (anti-tetanus serum or A.T.S.) is prepared by immunizing horses with a preliminary course of injections of tetanus toxoid, followed many months later by injections of crude toxin. The horses are then bled, and the serum obtained is purified and concentrated. When issued, it contains, 1,500 international units per ml.§

§ The units mentioned are those adopted in 1950, and are equivalent to the old units and to the U.S.A. units as follows :—
1,500 I.U. (1950) = 3,000 I.U. (1928) = 1,500 units (U.S.A.).

104. Dosage

(*a*) *Immune personnel* (*i.e.*, those actively immunized with Tetanus Toxoid).

Immune personnel are given a reinforcing dose of Tetanus Toxoid on wounding.

In addition, prophylactic A.T.S. 1,500 I.U. intramuscularly will be administered in the following circumstances :—

(i) where there has been undue delay between wounding and surgical attention, and

(ii) when the wounds are multiple.

(*b*) *Non-immune personnel* (including those partially immunized and those whose immunity has lapsed).

These should receive the initial dose of 1,500 I.U. followed by two more similar doses at weekly intervals if the surgeon in charge of the case considers this necessary.

Children may be given the same dosage as adults.

105. Duration of Immunity

One intramuscular injection of A.T.S. confers protection which is maximal in two or three days but which declines as the antitoxin is " thrown out ", becoming slight in less than three weeks.

106. Treatment

A.T.S. neutralizes circulating toxin, and has little effect on toxin already fixed in the central nervous system. Hence it has a prophylactic effect rather than a therapeutic action. (For details of the therapeutic dosage, *see* " A Field Surgery Pocket Book " (Revised : 1950).)

107. Reactions (*See Section XXVIII*)

Since A.T.S. is a foreign protein preparation, acute anaphylactic reactions may occur following its use. Such reactions are more likely in specially sensitive subjects who give a history of asthma, etc. In these cases 0·2 ml. of a 1 in 10 (or even 1 in 100) dilution of the serum should be injected subcutaneously as a trial dose. If there is no general reaction in half an hour, the full injection may be given slowly ; the patient should be kept warm and adrenaline should be immediately available. (*See* para. 138 on intravenous sera).

SECTION XXII

PASSIVE IMMUNIZATION AGAINST THE GAS GANGRENE GROUPS OF ORGANISMS

108. General

Antitoxic serum for use against an organism of the clostridial group is usually prepared by injecting horses with the toxoids and toxins of the appropriate organism. The antiserum is concentrated and purified and issued as the specific antitoxin—Gas Gangrene Antitoxin (*perfringens*, *septicum* or *oedematiens*) or Gas Gangrene Antitoxin (*polyvalent*). The latter contains a mixture of the antitoxins of *Cl. welchii* (*Cl. perfringens*), *Cl. septicum* and *Cl. oedematiens*.

109. Dosage

The prophylactic dose of Gas Gangrene Antitoxin (polyvalent) recommended for the passive immunization of wounded personnel contains 10,000 units of Cl. perfringens antitoxin, 5,000 units of Cl. septicum antitoxin, and 10,000 units of Cl. oedematiens antitoxin. This dose must be given intramuscularly as soon as possible after the injuries are received ; a quicker response follows intravenous administration.

110. Duration of Immunity

Immunity conferred by passive means using antiserum is always short lived—a matter of about three weeks at the outside.

111. Treatment

For use in treatment, Gas Gangrene Antitoxin (polyvalent) should be given in doses at least three times larger than those used for prophylaxis, and the dose should be repeated at intervals of 4-6 hours, according to the condition of the patient. Larger doses may be required for serious cases.

112. Reactions

Anaphylactic reactions can occur with gas gangrene antitoxin as with any other antiserum.

SECTION XXIII

PASSIVE IMMUNIZATION AGAINST DIPHTHERIA

113. General

Diphtheria antitoxin is mainly used in the treatment of diphtheria, but when it is advisable to establish immunity rapidly in a susceptible contact, 500 to 2,000 units may be given intramuscularly. This confers protection for only two or three weeks, on the average.

A more lasting immunity follows combined active and passive immunization, 500 units of antitoxin being given intramuscularly into one arm and 0·5 ml. of Diphtheria Prophylactic, A.P.T. into the other arm. One further injection of 0·5 ml. of A.P.T. is given six weeks later. The development of active immunity is somewhat retarded by injecting antitoxin at the same time as the first dose, but a useful level of antitoxin should be attained eventually.

In certain circumstances it may be better to immunize persons actively with diphtheria prophylactic and to watch carefully for signs of diphtheria, antitoxin being injected only when a sore throat develops.

Special precautions may be necessary when injecting persons who are sensitive to serum. (*See* Section XXVIII).

PART IV

PRECAUTIONS TO BE TAKEN FOR THE STORAGE OF BIOLOGICAL PRODUCTS TO ENSURE THAT THEY ARE SUITABLE FOR USE AND FULLY POTENT

(Instructions for the care of Biological Test Products and Blood Transfusion Products are included in this section)

SECTION XXIV

THE STORAGE AND STABILITY OF BIOLOGICAL PRODUCTS

114. General

To ensure that full protection is given, it is essential that only fully potent immunizing agents are used. The potency of biological products is dependent on the conditions of storage and the time that has elapsed since the date of manufacture.

115. Maintenance of stocks

Biological products (sera, toxoids, vaccines, tuberculins, etc.), have a limited life. Stocks held by user units should therefore be kept to an absolute minimum compatible with anticipated demands in order that the item can be used before date of expiry. Where stocks are maintained they will be stored in batches according to date of expiry, and it is the responsibility of officers commanding distributing depots and user units, to ensure that the vaccines and sera with the earliest dates of expiry are issued first. The life of biological products depends on satisfactory storage conditions as noted below.

116. Conditions of storage

(1) *Distributing depots*

Officers commanding distributing depots will ensure that under no circumstances is there any departure from the conditions of storage laid down in this paragraph.

(*a*) *Products requiring special storage*—living virus and bacterial vaccines.

(i) *Vaccine lymph*

Whenever possible not more than one distributing depot should intervene between the manufacturer and the user. Vaccine lymph should be obtained from the manufacturer packed in ice (at a temperature of 0° C. to minus 20° C., but not lower) and immediately stored in a refrigerator at a temperature of minus 10° to minus 20° C. When maintained at this temperature of minus 10° C. it will keep for twelve months. This requires a special refrigerator, which is available at all medical equipment depots where the lymph is stored.

(ii) *Dried Smallpox Vaccine*

This may be maintained at Room temperature for one month at tropical temperatures or six months in temperate climates. Refrigeration is desirable as the vaccine remains potent for two years at the temperature of an ordinary domestic refrigerator and if maintained at a temperature below 0° centigrade it should remain potent for at least five years.

(iii) *Yellow fever vaccine*

Yellow fever vaccine at present supplied from the United Kingdom or South Africa must be maintained at a temperature at or below 4° C. (preferably at minus 10° C.).

(iv) *Dried B.C.G. vaccine*

Dried B.C.G. vaccine is a freeze dried product which must be stored at or below 4° C. It should remain potent for six months.

(v) *Fluid B.C.G. vaccine*

Fluid B.C.G. vaccine must be kept at a temperature of 3-6° C. and must not be exposed to light. The vaccine must be used within ten days of manufacture.

(*b*) *Products requiring normal storage*

Normal storage of biological products is at refrigerator temperatures of 2° C. to 10° C. The under-mentioned products must be stored at this temperature :—

(i) *Toxoids.*—(These should be stored in the dark but not at a temperature lower than 2° C. where they might freeze.)

(ii) *Bacterial vaccines.*—(Particular care is necessary with alcohol treated T.A.B. vaccine. This should never be stored at temperatures above 10° C. or below 2° C.)

(iii) *Rabies vaccine.*—(The required storage temperature is as near 2° to 4° C. as possible, but not lower where it might freeze. Although not so labile as other vaccines, it should not be left outside the refrigerator for long periods.)

(iv) *All types of antisera.*

(v) *Diagnostic sera and bacterial diagnostic suspensions.*

(2) *User units with refrigeration*

The normal conditions of storage will be at refrigerator temperatures. All products referred to in para. (1) above will be stored at this temperature with the following provisos :—

(*a*) *Vaccine lymph* will not normally be stocked by user units, it will be obtained fresh as and when required, and used immediately. When it is necessary to maintain stocks for short periods vaccine lymph stored at refrigerator temperatures up to a maximum of 10°C. will keep for 14 days, and must be used within this period. A suitable temperature is provided by the ordinary domestic refrigerator.

(*b*) *Yellow fever vaccine* is issued only to specially selected inoculating centres, a list of which is available in the office of the D.D.M.S. or A.D.M.S.

Yellow fever vaccine must be maintained at a temperature at or below 4° C. (preferably at minus 10° C.) during storage. During transit (usually by air outside U.K.) vaccine is in ice in vacuum containers. The date of expiry is one year from the date of manufacture. In view of the short life of this vaccine, it will normally be obtained by user units direct from the manufacturer or distributing centre as and when required, and used immediately.

Under no circumstances will yellow fever vaccine be stored other than at a temperature of 4° *C., or less, preferably at minus* 10° *C.*

(3) *User units without refrigeration*

It is possible that in certain isolated units and in some Medical Centres refrigeration is not available. In these units only sufficient quantities of biological products will be maintained for routine use, and will be stored in a cool dark place, preferably in an ice box. *When vaccine lymph is maintained in a cool dark place (not at refrigerator temperature) it may not be used after 7 days.*

Note 1.—Once a capillary tube of vaccine lymph has been opened the contents must be used immediately. Any surplus must be discarded and not kept for subsequent use.

Note 2.—When yellow fever vaccine has been reconstituted any solution which is not used within 30 minutes must be discarded.

Note 3.—Special care must be taken in packing to ensure that the labels do not become detached from the containers of vaccines, antisera, etc.

117. Care in transit

Care in the transport, collection and distribution of vaccines and sera is of the utmost importance, particularly in warm climates. Any deterioration resulting from undue exposure is irreparable. Potency, once lost, cannot be restored by subsequent cold storage. Special care is required during transit of the following :—

(*a*) *Vaccine lymph*—should be packed in ice at a temperature of 0° C. to minus 20° C. but not lower during transit and on receipt immediately stored at minus 10° to minus 20° C.

(*b*) *Yellow fever vaccine*—should be packed in ice in vacuum containers during transit and on receipt immediately stored at 4° C. or less, preferably at minus 10° C.

(*c*) *Rabies vaccine*—should be packed in ice and transported at temperatures as near to 2 to 4° C. as possible, but not lower where it might freeze.

(*d*) *Schick test toxin*

(i) *United Kingdom*

Providing the toxin will arrive at its destination within 24 hours ordinary packing and transportation will suffice.

(ii) *Overseas—ex United Kingdom*

The toxin will be sent in a vacuum container packed in ice at a temperature of 0° C. The ice should be replaced at intervals of 24 to 48 hours.

(*e*) *Other biological products*—when despatched should be stored during transit in as cool a place as possible*, and sent by the most expeditious route. Care should be taken to ensure that these products do not remain in the sun while awaiting transportation, and they should be carefully labelled to indicate their perishable nature.

118. The Life of biological products

(*a*) The life of biological products is dependent on the conditions of storage given in para. 116 above. The life given in the table that follows is correlated

---

* With the exception of T.A.B. vaccine, which must be maintained at refrigerator temperature during transit (*see* para. 123).

with the conditions of storage. It will be noted that in this table only optimum conditions of storage are considered. Where these are not available in user units it is assumed that only sufficient quantities of biological products will be maintained for routine use, since owing to inadequate storage facilities, deterioration and a consequent loss of potency is certain to occur.

(*b*) All biological products are kept in the dark. This direction is of special importance in the case of materials containing thiomersalate, since preservation may become less effective if the products are exposed unnecessarily to light.

(*c*) The limits between which immunizing agents are transported and stored are reasonable and can be achieved under present day arrangements so that medical officers may confidently assume that the life of these products, as given in Section XXV is reliable.

SECTION XXV

TABLE CORRELATING STORAGE CONDITIONS WITH THE LIFE OF BIOLOGICAL PRODUCTS

Note.—Refrigerator Temperature Range is 2° *C.* to 10° *C.*

Name and Description of Products	Storage Temperature	Life
119 (*a*) **Vaccine lymph**	(i) Minus 10° to minus 20°C. (ii) Refrigerator temperature. (iii) Cool dark place.	(i) 12 months from notified date of manufacture. (ii) Fourteen days from date of issue. (iii) Not more than seven days from date of issue.
(*b*) **Dried Smallpox Vaccine**	(i) Minus 10° to minus 20°C. (ii) Refrigerator temperature. (iii) Unrefrigerated— (*a*) Temperate. (*b*) Tropical.	(i) 5 years. (ii) 2 years. (iii) (*a*) 6 months. (*b*) 1 month.
120. **Yellow fever Vaccine**	4°C. or less, preferably at minus 10°C.	(*a*) Wellcome. 12 months from notified date of manufacture. (*b*) S.A.I.M.R. as notified by manufacturer.
121. **Toxins** (*a*) Schick test toxin.	Refrigerator temperature but not at lower temperature where it might freeze.	(*a*) 6 months from notified date of manufacture.
(*b*) Dick test toxin.	Do.	(*b*) 3 months from notified date of manufacture.

Note.—In no circumstances is it permissible to increase the life of these products.

LIFE OF BIOLOGICAL PRODUCTS—*continued*

Name and Description of Products	Storage Temperature	Life
122. Toxoids		
(*a*) A.P.T.* (Preserved with thiomersalate)		
(i) Rubber capped and stoppered.	Refrigerator temperature but not at lower temperature where it might freeze.	(*a*) (i) 2 years from notified date of manufacture.
(ii) Sealed glass ampoules.	Do.	(ii) 2½ years from notified date of manufacture.
(*b*) T.A.F.* (Preserved with phenol)	Do.	(*b*) 2½ years from notified date of manufacture.
(*c*) Tetanus Toxoid* (Preserved with phenol)	Do.	(*c*) 3 years from the notified date of manufacture (given on the carton), or 6 months beyond the notified expiry date (on label of bottle).
(*d*) (i) Staphylococcus toxoid (1 in 10).	Do.	(*d*) (i) 3 months.
(ii) Staphylococcus toxoid (undiluted)*.	Do.	(ii) 1 year from the date of manufacture.
123. Vaccines		
(*a*) T.A.B. (Alcoholized) (or T.A.B.C. Alcoholized)	Refrigerator temperature but not at lower temperature where it might freeze.	(*a*) 12 months from notified date of manufacture.
(*b*) T.A.B. (Phenolized) (or T.A.B.C. Phenolized & T.A.B.T.)	Do.	(*b*) Do.
(*c*) (i) Dried B.C.G. vaccine.	At or below 4°C.	(*c*) (i) 6 months from date of manufacture.
(ii) Fluid B.C.G. vaccine.	3 to 6°C.	(ii) 10 days from date of manufacture.
(*d*) Other bacterial vaccines (Cholera, Plague, etc.).	Do.	(*d*) 18 months from notified date of manufacture.
124. Typhus vaccine	Do.	18 months from notified date of manufacture.
125. Influenza vaccine (Virus vaccines).	Do.	2 years from date of manufacture.
126. Rabies vaccine		
(*a*) Lister Institute vaccine.	Refrigerator temperature as near 2°C. to 4°C. as possible, but not at lower temperatures where it might freeze.	(*a*) 6 months from date of manufacture.
(*b*) Other preparations.	Do.	(*b*) 3 months unless notified otherwise by the manufacturer.
127. Tuberculin (Old)		
(*a*) Undiluted.	Refrigerator temperature.	(*a*) 5 years.
(*b*) Diluted.	Do.	(*b*) 3 months from the date of manufacture.

* *Note.*—When refrigerator temperature is impracticable store in a cool dark place. The life of A.P.T., T.A.F., tetanus toxoid, and staphylococcus toxoid (undiluted) is then six months.

Name and Description of Products	Storage Temperature	Life
128. Antitoxic Sera		
(*a*) Enzyme refined antitoxic sera—		
(i) Sealed glass ampoules.	Do.	(*a*) (i) 5 years from date of manufacture.
(ii) Rubber closures.	Do.	(*a*) (ii) 2½ years from date of manufacture.
(*b*) Concentrated.	Do.	(*b*) 2½ years from date of manufacture.
(*c*) Unconcentrated.	Do.	(*c*) 2½ years from date of manufacture.
	(For deterioration at other temperatures *see* Section XXVI).	
129. Other biological products		
(*a*) Concentrated bacterial suspensions for agglutination tests.	(*a*) Refrigerator temperature but not at temperatures where they might freeze.	(*a*) 1 year except Proteus OXK which is 6 to 9 months from date of *receipt* in medical equipment depot.
(*b*) Diluted suspensions.	(*b*) Do.	(*b*) 2 years from date of *receipt* in medical equipment depot
(*c*) Diagnostic sera.	(*c*) (i) Do.	(*c*) (i) 2 years from date of *receipt* in medical equipment depot.
	(ii) Ice box or cool place.	(*c*) (ii) 12 months from date of *receipt*.
(*d*) Wassermann and Kahn antigens, etc. (Products containing cholesterol).	(*d*) Cool dark place — *NOT* refrigerator.	(*d*) As notified on the labels.
130. Blood transfusion products		
(*a*) Preserved whole blood.	4° to 6°C. MUST NOT BE FROZEN. Do not place by the ice container in domestic refrigerator.	(i) Trisodium citrate anticoagulant : Max. of 7 days from date of collection. (ii) Disodium citrate glucose anticoagulant : 21 days from date of collection (Blood older than this may be used in emergencies, but only on the advise of a pathologist). In both (i) and (ii) there must be a clear-cut line of demarcation between cells and supernatant plasma and no visible evidence of deterioration.

Note.—Constancy of storage temperature of preserved whole blood is of the greatest importance. Bottles may be removed from the refrigerator for a maximum period of 30 minutes for the performance of compatibility tests. Partly used bottles of blood, or bottles which have been removed from the refrigerator for more than 30 minutes should be discarded. When transported, a temperature of 4° to 6°C. should be maintained by using a suitable insulated container.

(*b*) Fluid plasma.	Room temperature (not above 22°C.) in the dark. Should not be refrigerated.	May be used providing it is crystal clear and there is no deposit.

Name and Description of Products	Storage Temperature	Life
c) Dried plasma.	Room temperature (not above 22°C.) in the dark.	Indefinite, providing adequately dried and sealed to exclude air and moisture (in tropical and sub-tropical climates product is canned). Only practical criterion of fitness for use is rapid (*i.e.*, within 10 mins.) and complete solution on reconstitution. Incomplete solution or gel formation indicates unfitness for use.
(*d*) Dextran.	Preferably not above room temperature.	Probably 5 years. Must be crystal clear and without deposit.
(*e*) Crystalloid solutions.	Room temperature (not above 22°C.).	Indefinite, providing sealing is efficient. Must be crystal clear and without deposit.
(*f*) Haemagglutinating sera.		
Anti A and anti B sera.		
Control tests performed with known cells whenever these sera are used can alone show that the sera are potent and not giving false positive or negative readings. The lives given below are approximate and may not be attained by some sera and may be exceeded by others.		
(i) Dried.	Room temperature (not above 22°C.).	Usually indefinite, providing adequately dried and hermetically sealed.
(ii) Liquid.	Ideally at minus 22°C.	Several years, possibly indefinite.
	Ordinary refrigerator temperature.	12 – 18 months, providing sterility is maintained.
	Room temperature.	Not more than 2 weeks, providing sterility is maintained. This may be increased if preservative (*e.g.*, chloroform) has been added.
Note.—Blood grouping serum (*liquid*) which does not contain a bacteriostatic should be kept frozen solid preferably at a temperature below minus 22°C. and should be used with precautions against bacterial contamination and deterioration.		
Anti-Rh sera :		
Control tests performed with known cells whenever these sera are used can alone show that the sera are potent and not giving false positive or negative readings. The lives given below are approximate and may not be attained by some sera and may be exceeded by others.		
i) Dried.	Room temperature (not above 22°C.).	Usually indefinite, providing adequately dried and hermetically sealed.
(ii) Liquid.	Ideally at minus 22°C.	2 years.
	Ordinary refrigerator temperature.	Up to 4 weeks, providing sterility is maintained.
	Room temperature.	Few days only, providing sterility is maintained.

Notes.

(1) In some cases the date of preparation and not the date of manufacture is given on the labels. For practical purposes these terms are to be regarded as the same.

(2) When the expiry date of the product *only* is given by the manufacturer, no extension beyond this date is permissible.

(3) When *both* the date of manufacture and the expiry date are given, the life of the product will be calculated from the date of manufacture in accordance with the instructions given in the table above.

(4) Representative samples of diagnostic suspensions and sera referred to in para. 129 should be periodically tested during storage for potency.

SECTION XXVI

131. **Antitoxic sera—deterioration at different temperatures**

(*a*) The rate of deterioration in the case of enzyme refined and concentrated sera stored at different temperatures is given in the table below :—

Type of Serum	Stored at ° C.	Deterioration per annum
Enzyme refined.	0 to 5	Negligible (up to 5 years).
	5 to 15	Not more than 3%.
	20	Not more than 5%.
	37	10 to 20%.
Concentrated.	0 to 5	Negligible.
	5	Not more than 5%.
	15	10%.
	20	20%.
	37	25 to 50%.

(*b*) *Enzyme refined sera* (*i.e.*, the majority of antitoxic sera, *e.g.*, diphtheria tetanus, staphylococcal, gas gangrene) can generally be used at least up to 5 years from the date of manufacture.

Provided these antitoxic sera have been filled in sealed glass ampoules and stored in distributing centres at temperatures not exceeding 10° C. during the whole period of storage, the life may be extended a further two years, *i.e.*, to seven years from the date of manufacture. Such enzyme treated antitoxic sera received in user units from distributing centres which have already had a life in excess of five years, will be used within six months from the date of issue and any antisera not used during this period will be destroyed. *Except in a grave emergency where more recent sera are not obtainable, these sera will not be used beyond 7 years from the date of manufacture.* When the life of a serum has to be extended, the dosage should be increased to allow for possible deterioration.

(*c*) *Sulphate precipitated sera, i.e.*, the concentrated sera, have a life of 2½ years from the date of manufacture and will not be used beyond their date of expiry except in a serious emergency, when allowance must be made for loss of unitage.

132. **Biological test products—turn over**

(*a*) Biological test products should be turned over quickly and it should not be necessary to keep diagnostic sera in medical equipment depots for longer than 12 months. Diagnostic sera should, however, retain their potency under refrigerator conditions in medical equipment depots for a period up to 2 years from the date of receipt, and they should not be disposed of before that time has elapsed unless there is definite evidence, supported where possible by the recommendations of the D.D.P. or A.D.P. concerned, that the sera have, in fact, deteriorated.

(*b*) In the case of diagnostic suspensions every effort should be made to turn over stocks every 6 months, and, except in the case of diluted suspensions, these should not be issued after more than 9 months have elapsed from the date of receipt in medical equipment depots, or other distributing units.

SECTION XXVII

133. **Assay of biological products**

When reduction of potency of any biological product is suspected, representative samples should be sent for assay as under :—

(*a*) Antitoxic sera and products not included in (*b*) and (*c*) below—to the War Office (A.M.D.3).

(*b*) Vaccines and biological test products prepared by the David Bruce Laboratories—to the David Bruce Laboratories, Everleigh, Nr. Marlborough, Wiltshire.

(*c*) Kahn and Wassermann Antigens—to the Serology Laboratory, Pathology Department, R.A.M.C. College, Millbank, London, S.W.1.

Note.—A representative sample will consist of the bottle containing the remainder of the biological product under suspicion (if available) together with two other unopened bottles bearing the same batch number. (A minimum of 10 ml. of the antiserum or 50 ml. of tetanus toxoid will be required.)

SECTION XXVIII

SERUM REACTIONS AND SERUM SENSITIVITY TESTS

134. **Types of Reactions**

The following are the more serious types of reactions which may follow the administration of serum :—

(1) *Anaphylactic Shock.*—A rare and dangerous condition appearing within a few minutes of injection, or with less intensity up to two hours later.

(2) *Serum Sickness.*—A syndrome of rashes, pyrexia and joint pains, of late onset. (" Delayed " type after 7-12 days : " accelerated " type after 3-4 days in persons who have previously had serum.) Case incidence is now about 5 per cent. and the symptoms mostly mild and transient.

(3) *Thermal Reaction.*—Sudden pyrexia with rigors following intravenous injection and due to pyrogenic substances produced in certain batches during serum processing.

135. **Treatment**

A small sterile syringe and needle and a 1 : 1000 solution of adrenaline should always be available when serum is injected. THE PATIENT MUST ALWAYS BE KEPT WARM AND UNDER OBSERVATION FOR AT LEAST 30 MINUTES AFTER RECEIVING SERUM BY ANY ROUTE.

Anaphylactic Shock (dyspnoea, pallor and collapse) should be treated with an immediate injection of 0·5-1·0 ml. of Adrenaline (1 : 1000), either intramuscularly or subcutaneously. Anti-histamine drugs are also very useful and are indicated particularly when urticaria or oedema develops (*see* para. 137.)

Serum Sickness.—Anti-histamine drugs are also indicated in the treatment of this condition. Soothing lotions such as calamine, may be applied to the skin.

Thermal Reactions.—These usually subside within 15-20 minutes. The patient should be kept warm and given an injection of adrenaline if there is any weakness of the pulse.

136. **Serum Sensitivity Tests**

Intradermal conjunctival and scratch serum sensitivity tests are unreliable and are not recommended. The use of the " trial dose " of 0·2 ml. of serum subcutaneously as a preliminary to the main injection is preferable. If a general reaction (anaphylaxis) should develop it is likely to be mild and to respond readily to the usual treatment viz. : warmth, recumbency and injections of adrenaline and an antihistaminic drug.

The patient's previous history of :—

(*a*) allergic conditions especially asthma and infantile eczema, and

(*b*) injections of serum,

should always be obtained. The information received (*see* below) will determine the procedure to be adopted.

(1) *No allergy : no previous serum.*—Give main dose of serum intramuscularly (if time, give " trial dose " of undiluted serum).

(2) *Previous serum.*—Give a " trial dose " first. Then if no general symptoms, the main dose subcutaneously.

(3) *Allergy.*—A " trial dose " of 1 : 10 dilution subcutaneously followed in the absence of general symptoms, by a " trial dose " of undiluted serum subcutaneously. The main dose should be given intramuscularly.

(4) *Doubtful allergy.*—As for methods 2 or 3 above, depending on the urgency of the case.

137. **Note on the use of anti-histamine drugs.** (*See* paragraph 135 above).

The injection of an anti-histamine drug together with adrenaline has been recommended for the treatment of severe anaphylaxis. Anti-histamine drugs should not replace adrenaline and great care must be exercised when administering them parenterally.

Promezathin is given by deep intramuscular injection and Mepyramin subcutaneously in doses of not more than 50 mgm.

When suitable preparations of these drugs for parenteral use are not available oral administration is recommended. The drug selected should be given by mouth at the same time as the adrenaline is injected—its action commences within half an hour and re-enforces the action of the adrenaline. This combination of adrenaline and anti-histamine drug has been tested and found satisfactory.

138. **Intravenous Injections of Serum**

In all severe cases, when intravenous injections of serum may be indicated, serum should not be given unless an intramuscular injection given half an hour previously, has been tolerated. The serum, which must be at room temperature, *must* be given very slowly and the patient kept warm and recumbent during the injection and for at least 30 minutes and preferably one hour afterwards.

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