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

Memorandum on Immunological Procedures

Ministry of Defence

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

Amendments Nos 1 entered. May 1972

London: Her Majesty's Stationery Office 1968

Price 12s 6d. net

Memorandum on Immunological Procedures

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

Ministry of Defence **J.S.P. 311**

First Published 1952
Fourth Edition 1968

London: Her Majesty's Stationery Office 1968

Contents

List of Tables

List of Abbreviations

A.P.T.	Alum Precipitated Toxoid (diphtheria).
A.T.G.	Anti-Tetanic Globulin (human).
A.T.S.	Anti-Tetanus Serum (equine).
A.T.T.	Adsorbed Tetanus Toxoid.
B.C.G.	Bacille Calmette-Guerin (attenuated strain of *M. tuberculosis*).
D.T.	Diphtheria-Tetanus prophylactic.
D.T.P.	Diphtheria-Tetanus-Pertussis prophylactic.
F.T.	Formol Toxoid (diphtheria).
g.	Gramme.
I.D.	Intradermal.
I.N.A.H.	Isonicotinic acid hydrazide.
I.M.	Intramuscular.
mg.	Milligramme.
ml.	Millilitre.
P.A.S.	Sodium para-amino salicylic acid.
P.P.D.	Purified protein derivative (*M. tuberculosis*).
P. Vacc.	Primary vaccination.
S.C.	Subcutaneous.
T.A.B. dilute	Typhoid, Paratyphoid A and B prophylactic for children.
T.A.B. intradermal	Typhoid, Paratyphoid A and B prophylactic.
T.A.B.T. intradermal	Typhoid, Paratyphoid A and B, and Tetanus prophylactic.
T.A.B.T.D.	Typhoid, Paratyphoid A and B, Tetanus and Diphtheria prophylactic.
T.A.F.	Toxoid-Antitoxin Floccules (diphtheria).
T.T.	Tetanus Toxoid.
Y.F.	Yellow Fever vaccine.

Introduction

A new edition of this memorandum has become necessary owing to the introduction of new vaccines and the modification of others, and on account of the adoption of changes in technique and in vaccination schedules, since the publication of the third edition in 1961.

Although the presentation and form are similar to those of earlier editions, advantage has been taken of this opportunity to modernize the book completely and to rewrite some of the sections. It is presented in loose leaf form in order that future amendments and additions, which will be many and extensive if past experience is any guide, may take the form of page replacement or addition.

At the end of this edition a new section has been added which includes recent advances in immunological agents and techniques. So far as is possible the present position as regards their acceptance and availability in the Services is stated. It is intended to keep this section under constant review in order to amend and add to it as new vaccines and techniques become available to the Services.

The Tuberculin Tine Test and the Linear Scratch Technique are described in detail and have been included in the sections on Tuberculosis and Smallpox respectively.

Earlier editions of the Memorandum have been exclusively an Army production although it has been extensively used by the other Services and civilians. This edition is a departure from that practice and it is now written as an Inter Service publication, the fullest co-operation having been freely given by both the Royal Navy and the Royal Air Force during its preparation. Small administrative differences occur between the three Services, but if this edition is kept in its proper context as mainly intended for professional and technical guidance and due regard is paid to currently operating Queen's Regulations, Admiralty Instructions, Defence Council Instructions, etc, no administrative difficulties should be encountered.

The editor wishes to acknowledge gratefully the advice and assistance afforded by the Army Pathology Advisory Committee* in general, and to those members of that Committee in particular, who have given much of their time to detailed draft reading. Furthermore we are grateful to Professor F. R. G. Heaf CMG, MD, FRCP, for his advice and help with Section 11 'Active Immunization Against Tuberculosis'.

Editorial Committee

Major-General M. H. P. Sayers OBE, QHP, MD, FCPATH, L/RAMC,
Director of Army Pathology, Ministry of Defence (*Chairman*).

Air Vice-Marshal W. P. Stamm CBE, QHS, FRCP, FCPATH, RAF,
Senior Consultant in Pathology and Tropical Medicine, Royal Air Force.

Surgeon Captain P. S. Fuller MD, DPH, FCPATH, RN,
Adviser in Pathology to Medical Director-General (*Naval*).

Lieutenant-Colonel J. E. Noble MCPATH, MRCS, LRCP, DTM& H, RAMC,
Officer Commanding, David Bruce Laboratories (*Editor*).

Lieutenant-Colonel D. E. Worsley MB, DPH, DTM&H, RAMC,
Ministry of Defence.

Squadron Leader A. W. McCracken MB, ChB, MCPATH, DCP, DTM&H, RAF,
Pathologist, RAF *Institute of Pathology and Tropical Medicine* (*Assistant Editor*).

***Army Pathology Advisory Committee**

Brigadier (Retd) Sir John Boyd OBE, FRS, MD, FRCP, DPH
Scientific Consultant, The Wellcome Trust.

Colonel J. A. Dudgeon MC, TD, FCPATH,
Consultant Virologist to Hospital for Sick Children, Great Ormond Street.

Professor D. G. Evans, DSc, PhD, FCPATH, FRS,
Professor of Bacteriology, London School of Hygiene and Tropical Medicine.

Surgeon Captain P. S. Fuller MD, DPH, FCPATH, RN,
Adviser in Pathology to Medical Director-General (*Naval*).

Professor B. W. Lacey MD, BSc, FCPATH
Hon. Consultant Pathologist to the Army.

Major-General R. J. G. Morrison CBE, QHP, MD, FRCP, L/RAMC,
Director of Medicine and Consulting Physician to the Army.

Major-General A. Sachs (Retd) CB, CBE, MD, MSc, FRCP, FCPATH,
Consultant Pathologist, Queen Victoria Hospital, East Grinstead.

Major-General M. H. P. Sayers OBE, QHP, MD, FCPATH, L/RAMC,
Director of Army Pathology, Ministry of Defence (*Chairman*).

Professor R. W. Scarff CBE, MD, FCPATH, DPH,
Consultant Pathologist, Middlesex Hospital.

Brigadier R. A. Smart CBE, MB, MRCP, DPH, L/RAMC,
Director of Army Health, Ministry of Defence.

Air Vice-Marshal W. P. Stamm, CBE, QHS, FRCP, FCPATH, RAF,
Senior Consultant in Pathology and Tropical Medicine, Royal Air Force.

Surgeon Captain J. Travers-Morgan LMSSA, DPH, RN,
Department of Medical Director-General (*Naval*).

Sir Graham Wilson MD, FRCP, DPH,
London School of Hygiene and Tropical Medicine.

Air Commodore R. O. Yerbury CBE, MB, BS, DPH, MRCS, LRCP, RAF,
Director of Health and Research, Royal Air Force.

Lieutenant-Colonel J. C. Crook MD, MCPATH, DTM&H, RAMC,
Assistant Director-General, Ministry of Defence (*Secretary*).

Administrative instructions

Vaccinations required
Documentation and maintenance of records
International certificates

Section 1 Vaccinations required by Service personnel and their families

1 General

The different immunizing procedures (vaccinations and tests for susceptibility to infection) 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 are given in Section 2 and for certification in Section 3.

*Volumes of doses of vaccines are liable to change following technical advances in their production which lead to enhanced potency. Dose volumes given in this Section should therefore be verified by checking against the instructions on labels, containers, etc.

2 Service Vaccination Centres

In general vaccinations are carried out at Service Vaccination Centres all of which are located at Service medical centres. Some may be performed by civilian doctors (para 37).

3 Importance of Protection

Although acceptance of vaccinations is voluntary, officers, other ranks and families must be made to understand that conditions of Service life, particularly overseas, expose the individual to risks of acquiring certain infectious diseases greater than those normally incurred by civilians in the United Kingdom. The vaccinations recommended are therefore necessary to safeguard the person's own health as well as to protect the Services from epidemics which might seriously interfere with their efficiency. Further, protection against one or more of the diseases with which the International Sanitary Regulations are concerned may be required by the countries to or through which Service personnel and their families may travel. *Since nobody will be excused or prevented from going overseas because he has refused a vaccination*, non-acceptance of such an international requirement may result in detention in quarantine up to the full incubation period of the disease concerned, or in other forms of delay or inconvenience. There are certain restrictions which must be observed in the use of smallpox or yellow fever vaccines during pregnancy or in infancy (paras 9 and 15).

4 Travel by Air

Travellers by air are particularly liable to be called upon to produce evidence of having complied with the appropriate International Regulations on prophylactic immunizations. Requirements vary according to the countries traversed and should be investigated well in advance before taking a journey. All officers and Ministry of Defence sponsored civilians who are liable to travel by air at short notice should arrange to be vaccinated against yellow fever and should maintain their state of immunity by being revaccinated within successive periods of ten years, to avoid the likelihood of delay in departure. Similar action should be taken as regards *primary* vaccination against smallpox. Regular revaccination against this disease is advisable to avoid the possibility of an incapacitating reaction while travelling, or after completion of the outward journey.

5 Travel by Sea

Ordinarily, travellers by sea are required to be protected against smallpox only. Under the special circumstances mentioned in para 15, vaccination against yellow fever is also required.

Responsibility regarding Vaccinations

6 Royal Navy

In the Royal Navy these responsibilities are set forth in Queen's Regulations for the Royal Navy, Articles 4209, 4264 and 4265 and in B.R. 1991 *Instructions for the Royal Naval Medical Service*, Chapter 4, Section 1.

7 Army

Commanding officers and medical officers are responsible as follows:

(a) Commanding officers are responsible for:

(1) maintaining a vaccination record for all ranks so that the vaccination state may be readily available at any time;
(2) warning all those who refuse vaccination of the possible consequences to themselves and their comrades (para 3) and publishing such refusals in Part II/III Orders;
(3) publishing in unit Orders quarterly the names of those due for vaccinations in the coming quarter, notifying in these Orders a suitable time for those named to report to the medical centre and arranging that each will be available at the stated time;
(4) arranging for all personnel warned for movement overseas to be given the appropriate vaccinations in due time, and checking that they are in possession of the necessary international certificates, where applicable, before departure;
(5) arranging that any special precautions recommended by the medical officer are observed.

(b) Medical officers are responsible for:

(1) advising unit commanders on all matters dealing with immunological procedures;

(2) vaccinating, or arranging for the vaccination of, all such individuals who present themselves at times arranged by their commanding officers;
(3) recording immunological procedures as laid down in Sections 2 and 3;
(4) rendering such returns as may be called for by higher authority.

8 Royal Air Force

The responsibilities of commanding officers and medical officers in the Royal Air Force are similar and are dealt with in Queen's Regulations for the Royal Air Force (4th Ed.), para 1409.

Individual Vaccines

9 Smallpox (see section 15)

(a) *New entrants.* All new entrants, whatever their history of immunization against smallpox, will be vaccinated on enlistment. The vaccination site will be inspected on or about the third day and reinspected on the seventh to the tenth day after vaccination for evidence of success. Positive results will be recorded, as primary vaccination or revaccination as the case may be, as laid down in section 15. If at the second inspection there is no visible specific reaction the vaccination will be repeated at once, followed by inspections, as after the first attempt, and recording of the result. In the event of a second failure a third and final attempt will be made, inspected and recorded as before.

(b) *Revaccination*

(1) *General.* Revaccinations will be performed every three years or at shorter intervals if demanded by local statute. The result will be inspected and recorded as described above.
(2) *Special Circumstances.* In the presence of an epidemic or of an unusually high incidence of smallpox, revaccination may be ordered by the local commander on the advice of his senior medical officer. As a guide to offering such advice, senior medical officers should bear in mind that an individual will very rarely contract smallpox up to one year after successful vaccination or revaccination. When more than one year has elapsed, protection, while considerable for up to three years or longer, is not always absolute and overt infection may occur following exposure, though for several years the disease, if acquired, is likely to be in an attenuated form.

(c) *Before proceeding overseas.* All service personnel *and their families* proceeding overseas from the United Kingdom should be vaccinated not less than 14 days before departure unless already vaccinated within the previous three years.

(d) *Restrictions.* The above rules are, however, subject to the following restrictions:

(1) *Pregnant women.* Under normal circumstances vaccination of pregnant women against smallpox will not be carried out (para 156).
(2) *Infants.* Infants should not normally be vaccinated during the first year of life unless there is a special risk of smallpox or a need to satisfy international certification and then preferably not within the first three months.

(3) *Children.* Children with active, or a history of, infantile eczema should not be vaccinated. Special precautions must also be taken to keep such children well away from contact with recently vaccinated subjects, especially their siblings.
(4) *Vaccination during treatment.* Vaccination should not be carried out in a person undergoing treatment with cortisone or other corticosteroid drug.

(e) *When vaccinating against smallpox and against yellow fever are both required*

(1) *Adults and children more than one year old.* Yellow fever vaccine should be given first. Vaccination or revaccination against smallpox may then follow after an interval of *not less than four days.* If for any reason primary vaccination against smallpox, or revaccination which is followed by a primary type of response, has been carried out first, yellow fever vaccine *must not be given* until twenty-one days have elapsed.
(2) *Infants under one year old.* Infants less than one year old should not normally be vaccinated against yellow fever (para 15(c)). If, however, this becomes necessary in particular circumstances there must be an interval of at least twenty-one days between vaccination against smallpox and vaccination against yellow fever no matter which is given first (para 189).

10 Diphtheria (see section 10)

(a) Owing to the prevalence of diphtheria in certain overseas theatres, all officers and other ranks of the Army and R.A.F. will, on joining, be tested for susceptibility to this disease and if necessary be immunized against it. Children should be fully immunized, particularly when proceeding outside the United Kingdom.

(b) *Procedure*

(1) *Adults.* On joining the Services a Schick test of suceptibility will be done. The test sites will be examined on the second or third day afterwards and again on the fifth to the seventh day. The earlier reading is necessary to *detect pseudo-reactors* who may react badly if given diphtheria prophylactics and should not be immunized. *Those found positive and without a pseudo-reaction* will be immunized by two injections of Formol Toxoid (F.T.) at not less than four weeks interval. A third injection will normally be required six to twelve months later.
(2) *Children.* Children will generally be immunized against diphtheria, tetanus and pertussis, at the same time, by the use of the combined vaccine Diphtheria-Tetanus-Pertussis prophylactic (D.T.P.). The first of four doses of this vaccine should be given at the age of six months. Maintenance doses will be with Diphtheria-Tetanus prophylactic (D.T.) and are required at school entry and at eight years of age. Immunization of children up to twelve years of age may be started *without preliminary Schick testing.*

11 Tuberculosis (see section 11)

(a) *Vaccination*

(1) All entrants to the Army and R.A.F., personnel of Gurkha units and their families, St. John and the British Red Cross Society Service Hospital Welfare Officers, S.S.A.F.A. Sisters, medical and nursing ancillaries and others who will be working with patients are to be tuberculin tested and negative reactors vaccinated against tuberculosis.
(2) Service personnel or members of their families who are known contacts of

tuberculous cases will be tuberculin tested and the negative reactors will be vaccinated against tuberculosis.

(3) Tuberculin testing and B.C.G. vaccination may be extended to other groups, especially children, in special circumstances or at request. It is particularly recommended for all families going to overseas stations where tuberculosis is likely to be prevalent in local populations.

(4) The Royal Navy procedure is given in current D.C.Is (Royal Navy).

(b) *Procedure.* For new entrants a Heaf test will be carried out during the period of initial training. Negative reactors will receive B.C.G. vaccine forthwith unless the individual has incurred a risk of contact with a known source of tuberculous infection within the three months before the test. In the latter event the person concerned will be removed from such contact (if that has not already been done) and a second Heaf test will be done six weeks after the first or six weeks after removal from exposure whichever is the later. If this second test is also negative B.C.G. vaccine will be given at once.

(c) *A Heaf test for conversion,* when required to comply with para 106(b), will be carried out eight weeks after vaccination. Maintenance of immunity will be controlled by the Heaf test which will be carried out every five years. Negative reactors to tests for conversion or maintenance will be revaccinated.

12 Enteric (Typhoid and Paratyphoid A and B) Fevers (see section 7)

(a) *Vaccination*

(1) Service men and women should be vaccinated against the enteric group of fevers, as should families proceeding anywhere outside the United Kingdom. For adults and children over twelve years old primary vaccination against these diseases is generally combined with protection against tetanus by the intradermal injection of a combined prophylactic 'Typhoid-Paratyphoid vaccine in Tetanus Toxoid for intradermal use (T.A.B.T. Intradermal)'.

(2) Children of twelve years and under are normally immunized against tetanus in infancy. Those under one year of age *will not be vaccinated against enteric fevers.* Those from one to twelve years inclusive who need immunization against enteric fevers are vaccinated with 'Diluted T.A.B. for children' given subcutaneously.

(3) For all those who require vaccination against enteric fevers because they are going overseas, at least the first two doses for primary vaccination should have been given before their arrival at the port of embarkation or air trooping centre.

(b) *Procedure*

(1) *Primary vaccination* of adults and older children consists of three doses, each of 0·1 ml. 'T.A.B.T. intradermal', injected into the skin. The second dose is given four to six weeks after the first and the third dose normally follows six to twelve months later. If, however, an individual is about to proceed or has proceeded on active service before his primary course is finished i.e. the third dose given, he should receive his third dose as soon after three months from his second as possible.

(2) For children aged one to twelve inclusive who require it, primary vaccination is carried out by three subcutaneous injections of the diluted T.A.B. vaccine. For those of normal weight a first dose of 0·2 ml. is followed after four to six weeks by a second of 0·4 ml. The third dose of 0·2 ml. follows six months after the second.

The dose should be reduced for under-weight children, or for subsequent doses if an undue reaction follows an earlier one.

(c) *New entrants.* Vaccination against enteric fevers will be started before the completion of primary training of all new entrants.

(d) *Maintenance of Immunity.* Following primary vaccination, immunity will be maintained by further injections of T.A.B.T. vaccine (paras 67 and 69) *until the individual is thirty-five years old,* as follows:

(1) A single reinforcing dose will be given every three years. From the age of thirteen upwards 0·1 ml. of T.A.B.T. will be given intradermally, but younger children will receive 0·2 ml. of diluted T.A.B. vaccine subcutaneously for each maintenance dose. In epidemics or when the local senior medical officer considers the individual at special risk, the interval may be shortened to one year in which case T.A.B. may be given in place of T.A.B.T.
(2) Those over thirty-five years old whose immunity has been established and maintained up to that age, as defined above, will not be given further maintenance doses. They should however, be given a reinforcing dose in the circumstances considered in (e) below. If immunity has not been established and maintained it is advisable to offer the full course of primary vaccination to persons over thirty-five years old should they become liable to the risk of incurring enteric fevers.

(e) *Reinforcement of immunity in the presence of an epidemic of typhoid fever or other major risk of infection*

(1) When an epidemic of typhoid or paratyphoid arises among service personnel, their families or the civilian population, a reinforcing dose of T.A.B. vaccine should be given to service personnel and families proceeding to these areas.
(2) Persons receiving this dose should include those over thirty-five years of age whose routine maintenance of immunity has been discontinued in accordance with (d)(2) above.
(3) Similar action should be taken in the area involved and for those proceeding to it, should a serious breakdown of the public or military sanitary services occur in a locality where typhoid fever is endemic.

(f) *Primary vaccination in the presence of an epidemic of typhoid fever or other major risk of infection*

(1) Primary vaccination of those who have not been previously immunized is contra-indicated only if the individual has been in immediate contact with a known case of enteric fever. In this event the vaccine would be unlikely to establish a useful degree of immunity in time to combat the risk of infection and its administration might be a cause of added danger to an individual already incubating the disease.
(2) Similar considerations may be applied at times of seriously increased liability to *paratyphoid* infection. However, such a risk, if unassociated with a similar risk of typhoid fever, will not usually cause so urgent a need to consider reinforcement of immunity, in view of the generally milder nature of the disease.

13 Tetanus (see sections 7, 8 and 10)

(a) All Service personnel will be protected against tetanus by active immunization.

Similar protection is recommended for families whether proceeding outside the United Kingdom or not.

(b) *Procedure*

(1) *Primary vaccination* is normally carried out by the use of combined prophylactics: T.A.B.T. for adults (para 12) and D.T.P. for children (para 10). If the third dose of tetanus toxoid, either as T.A.B.T. or as T.T., has not been given before one year following the second dose, vaccination must be repeated from the beginning with T.A.B.T. or T.T.

(2) *Maintenance.* A maintenance dose of 0·1 ml. 'T.A.B.T. intradermal' will normally be given every three years. After the age of thirty-five, T.T. will be given alone in subcutaneous doses of 0·5 ml. at five year intervals. For children, however, D.T. will usually be given for the first two maintenance doses (paras 10 and 97(d)).

(c) *Special Provisions before and during Active Service*

(1) When primary immunization has not been completed, i.e. the third dose not given, the third dose of the vaccine will be given as soon after three months from the second as possible.

(2) Further reinforcing doses of 0·5 ml. T.T. alone will be given subcutaneously on wounding: otherwise maintenance doses of 'T.A.B.T. intradermal' will be given at the normal interval of three years.

14 Poliomyelitis (see section 9)

(a) *Primary Vaccination*

(1) *New entrants—unimmunized.* Vaccination of new entrants who have not already been vaccinated against poliomyelitis will be started during initial training. Vaccination will consist of three doses, each of three drops, of *Sabin* type oral live vaccine at intervals of four to eight weeks. If the vaccine is regurgitated a dose may be repeated. The interval between the second and third doses may be extended in exceptional circumstances (see also sections 19 and 20).

(2) *New entrants—previously immunized*

(*a*) New entrants who have received two doses of *oral live vaccine* prior to enlistment will have the course completed as in (1) above provided that the interval between their last dose and enlistment is less than one year. When the period is greater than one year the new entrants will be treated as unimmunized and the full course given.

(*b*) Those who have had one dose only prior to enlistment will receive a full course as in (1) above.

(*c*) Those who have had one dose of *Salk type killed vaccine* not more than one year prior to enlistment may have poliomyelitis vaccination completed with *oral live vaccine* provided that two doses, each of three drops, are given at an interval of four to eight weeks.

(3) *Families.* Families, including children over six months old, should be vaccinated against poliomyelitis with live oral vaccine as described in (1) above.

(b) *Reinforcing Doses.* Reinforcing doses should be offered to:

(1) immunized children joining school;

(2) immunized persons at special risk of contracting poliomyelitis (paras 84 and 85).

(c) *Restrictions.* Vaccination with live oral vaccine *should not be undertaken*

(1) In children under six months.
(2) In the first four months of pregnancy.
(3) In close family contacts of a case of poliomyelitis.
(4) In individuals with pyrexia, undiagnosed illness, intercurrent infections, or in indifferent health.
(5) In individuals with diarrhoea or other intestinal dysfunction.
(6) During therapy with cortisone or other corticosteroid drug, unless agreed in consultation with the physician in charge of the patient.
(7) In known cases of penicillin hypersensitivity.

(d) *A past history of poliomyelitis is not a contraindication to vaccination against the disease as different strains occur.*

15 Yellow Fever (see section 16)

(a) *When vaccination required*

(1) All serving personnel, except QARANC and WRAC servicewomen, of PULHEEMS Employment Standard FE, LE and BE should be vaccinated.
(2) In addition all personnel travelling from the United Kingdom to countries in the Yellow Fever Endemic Zones are advised to be vaccinated for their own protection.
(3) International Certificates of Vaccination are not required as a condition of entry from the United Kingdom, but passengers are advised to carry such certificates, which may be required if travelling from one country to another within these zones.
(4) The Yellow Fever Endemic Zones are:
The continent of Africa between latitudes 15° North and 10° South.
The continent of South America north of latitude 15° South.
Panama (excluding the Panama Canal Zone).
The regulations for individual countries within these zones vary from time to time, and intending travellers should therefore make appropriate enquiries at least three weeks before the date of departure.

(b) *Restrictions on the use of yellow fever vaccine*

(1) *Pregnant women and children under one year of age* should never receive yellow fever vaccination except in circumstances in which they are liable to contract the disease, when the risks of vaccination are outweighed by the risk of contracting yellow fever. Pregnant women and children under one year of age should receive a medical certificate in the form shown in para 29. The majority of countries which require persons arriving from infected areas to possess international certificates of vaccination against yellow fever exempt children *under one year old* from this requirement.
(2) Action when vaccination against yellow fever and against smallpox are both required is described in para 9(*e*).
(3) Yellow fever vaccine should not be administered to persons who are 'egg' sensitive.

(c) Apart from possible neurological sequelae in the young infant or in a foetus *in utero* which constitute the reason for the ban referred to above, yellow fever vaccine is not followed by any reaction and only one attendance is necessary.

16 Typhus (see section 14)

(a) *When vaccination required.* In special areas as notified from time to time.

(b) *Primary vaccination* consists of a course of three subcutaneous injections of 1·0 ml. at intervals of seven to fourteen days.

(c) *Maintenance.* In endemic areas maintenance doses are given annually. In the presence of an epidemic a reinforcing dose will be given when three months have elapsed since primary vaccination or a maintenance dose. Reinforcing doses will be repeated at intervals of three months while the individual remains at epidemic risk.

(d) *Restriction. Infants under one year old* will not be vaccinated against typhus.

17 Plague (see section 13)

(a) *When vaccination required.* In special circumstances only.

(b) *Primary vaccination* is with two subcutaneous injections at an interval of ten to twenty-eight days.

(c) *Maintenance doses* are given every six months while at risk.

(d) *Dosage.* The size of doses for both primary vaccination and maintenance of immunity varies according to the age of the subject (para 134).

(e) *Restriction. Infants under one year old* will not be vaccinated against plague.

18. Cholera (see section 12)

(a) *When vaccination required.* Travellers by air to the Far East via India and Pakistan must be vaccinated against cholera and hold a valid international certificate of such vaccination. Immunization against cholera may also be needed in circumstances involving risk of infection and all personnel proceeding to the Far East are advised to be vaccinated for their own protection.

(b) *Primary vaccination* is with one *subcutaneous* injection of 0·5 ml. *or* one *intradermal* injection of 0·1 ml. of cholera vaccine. The single dose meets the normal requirement for travel.

(c) *The international certificate* is valid for six months starting six days after vaccination, after which a further single dose is required before it can be renewed. If revaccination takes place *within* the six months the revaccination certificate is valid at once. If revaccination has not taken place within the six months a period of six days must elapse before the certificate is again valid. It should be noted that the international certificate becomes valid six days after the administration of the first inoculation.

(d) *Persons proceeding to a cholera endemic or epidemic area* should receive two *subcutaneous* injections of 0·5 ml. and 1·0 ml. of cholera vaccine at an interval of seven to twenty-eight days *or* two *intradermal* injections of 0·1 ml. at a similar interval.

(e) *Maintenance doses.* These are given every six months while at risk.

(f) *Restriction.* Infants under one year old will not be vaccinated against cholera.

19 Personnel transferred from one overseas command to another or on a temporary visit to the United Kingdom from overseas

Commands overseas will ensure that the requisite vaccinations have been given to those concerned before they leave for another overseas command. This applies to British Forces in N.W. Europe in respect of personnel being despatched to the United Kingdom for onward transmission to other overseas stations. Unit commanders overseas must ensure that any serving officer, soldier or family member proceeding to the United Kingdom on leave or temporary duty will be re-vaccinated before their departure if any International Certificate of Vaccination becomes invalid within six weeks of their arrival in the United Kingdom.

20
21 } Reserved.
22

Section 2 Documentation and Maintenance of Records

23 The method of documentation and maintenance of records for personnel in all three Services is similar. Such minor variations as occur are published from time to time in current QRs and DCIs.

24 Personal and unit records

(a) Medical officers are responsible for the correct entry of all vaccinations and tests of immunity in the appropriate sections of F.Med.4.

(b) Commanding Officers are responsible for ensuring that arrangements are adequate for maintaining an up-to-date record of the vaccination state of their units.

25 Method of recording

In recording procedures the following details will always be given and the entry will be initialled by the vaccinator:

(a) *Vaccine records*

(1) Type of vaccine given—accepted abbreviations, as given in the relevant paragraphs of this Memorandum, may be used.
(2) Dosage (where applicable, i.e. for injected vaccines).
(3) Route of administration (for injected vaccines, i.e. intradermal (ID), subcutaneous (SC), or intramuscular (IM)) and site.
(4) Date of vaccination (month by name not number).

(5) Batch number of vaccine and name of manufacturer.
(6) *Smallpox vaccination only*, the result and whether it was primary vaccination or revaccination will be recorded (see section 15).
(7) *Tuberculosis*. Vaccination against tuberculosis will be recorded in red ink.

The following are examples of how to record vaccinations in the appropriate sections of F.Med. 4:

Table 7 Smallpox vaccinations

7 Dec 60	BMH Iserlohn	Lister Batch 7500	14 Dec 60	R.V.(S)	A.B. Capt.

Table 8 Other vaccinations

3 Aug 60	BMH Iserlohn	TABT DBL Batch 5	0·1 ml (ID)	PQ Surg. Lt.

Table 10 Yellow Fever vaccinations

1 Dec 60	RAF Wegberg	Wellcome Batch 300	0·5 ml SC	XY Flt. Lt.

(b) *Records of tests of immunity*. These will show the result as well as the date and the initials of the medical officer who made the test. *For tuberculin* tests the *site* will also be given (see section 11). The following are examples of how to record tests of immunity:

Table 11 Heaf Test

2 Nov 60	BMH Rinteln	neg L arm	A.B. Capt.

Table 12 Schick Test

10 Sep 60	Cambridge MH	pos and pseudo	A.B. Capt.

Refusal of a vaccination by Army Personnel

(a) A refusal to be vaccinated will be published in Part II/III Orders (for officers as a Section 'A' occurrence).

(b) The refusal will also be entered in A.F.B. 199A or A.F. B. 200.

27 Vaccination after previous refusal by Army Personnel

(a) Acceptance of vaccination after a previous refusal will be published in Part II/III Orders and recorded in A.F. B. 199A or A.F. B. 200.

(b) The vaccination will be recorded in the normal way as described in para 25 above.

28 Refusal of a vaccination and vaccination after previous refusal by Royal Navy and Royal Air Force Personnel

The relevant procedures are laid down in the following regulations:

(a) For the Royal Navy: in Queen's Regulations, Articles 4209, 4264 and 4265 and in B.R. 1991 *Instructions for the Royal Naval Medical Services*, Chapter 4, Section 1.

(b) For the Royal Air Force: in Queen's Regulations para. 1409.

29 Medical Certificates

Certain vaccination procedures are contraindicated in pregnant women, and in very young children for other reasons. When such vaccination is refused, the Medical Officer will provide the patient with a medical certificate in the form set out as follows:

MEDICAL-IN-CONFIDENCE

Medical Certificate of Exemption from Vaccination

This is to certify that:

....

Forename(s) Surname (in block capitals)

Date of birth:..... Sex:.....

has *NOT* been vaccinated by me against the following disease(s) for the reason(s) indicated:

Vaccination*	Reason for not Vaccinating*
Smallpox†	Eczema Pregnancy (Other reasons—specify)
Yellow Fever	Pregnancy Under one year of age (Other reasons—specify)
Cholera	Under one year of age

* delete all inapplicable data

† also complete second part of certificate below

....

(doctor's signature) (medical qualifications) (date)

Vaccination Centre Stamp

I also certify that, to the best of my knowledge, the above-named person has not been in contact with a case of smallpox.

....

(doctor's signature) (medical qualifications) (date)

Vaccination Centre Stamp

30
31 } Reserved
32

Section 3 International certificates of vaccination

33 International certificates, which must be on the officially recognized form (duplicated or typescript substitutes may not be used), will always be provided for those vaccinated against smallpox, yellow fever or cholera, since they afford the only universally accepted evidence of protection.

34 International certificate forms are issued by the Department of Health and Social Security and will be indented for through the usual channels. The duration of validity of each is as follows:

(a) *Smallpox*. These are valid for three years beginning eight days after the date of successful primary vaccination or on the date of revaccination.

(b) *Cholera*. These are valid for six months beginning six days after the date of the first dose, or on the date of a revaccination performed within six months of primary vaccination or of a previous revaccination.

(c) *Yellow Fever*. These are valid for ten years beginning ten days after the date of vaccination, or on the date of a revaccination carried out within ten years of an earlier dose. The vaccine must be of an approved type and the vaccination has been performed by an authorised representative from a recognised yellow fever vaccination centre.

35 The certificate forms provide spaces for the entries of revaccinations. In the case of yellow fever, and to a lesser degree cholera, it is important that they be used for this purpose rather than that a fresh certificate be issued, since only thus is the necessary evidence provided of the immediate validity of a revaccination, unless the earlier certificate is retained as well for production during the early days after the revaccination, paras 4 and 15(a).

36 International certificates will bear the stamp of the appropriate United Kingdom Government Vaccination Centre or of the yellow fever vaccination centre from which an authorised representative carried out the vaccination. They must be completed and signed by the medical officer who has carried out the vaccination. Abbreviations will not be used on them and the date will be recorded in the sequence day, month, year—the month being written in letters not figures. During movements overseas these international certificates will be carried by the individual or by draft conducting officers or N.C.Os, as appropriate. In the Army international certificates enclosed in B Med 27 (Rev) will be kept in the F.Med.4. In the R.N. and R.A.F. the safe keeping of vaccination certificates is the responsibility of each individual.

37 Families

Families may, when convenient, be vaccinated by civilian doctors. The vaccination against smallpox, yellow fever and cholera will also be recorded on the appropriate International Certificate of Vaccination. These certificates are to be kept in B Med 27 or B Med 27 (Rev) in accordance with current instructions. The documents are forwarded by the Ministry of Defence Family Passages Section. They must be completed and signed by the doctor concerned and authenticated by the Office of the Medical Officer of Health of the local authority, or by the town, urban or rural district council for the area in which the doctor lives. Yellow fever vaccination must be performed at a recognised civilian or Service centre or by an authorised representative from such a centre.

38 Medical Certificates

Certain vaccination procedures are contraindicated in pregnant women, very young children and others. When such vaccinations are not performed for any reason a medical certificate in the form described in para 29 must be provided by the medical officer.

39
40 } Reserved.
41

Instructions for the care, maintenance and sterilization of syringes
Mass immunization procedure
Injection technique

Section 4 The choice, care, maintenance and sterilization of syringes used for immunological procedures

42 The Choice of Syringes and Needles

(a) *Syringes for use once only.* The most suitable type of syringe which is available to all Service Vaccination Centres is the disposable plastic syringe, supplied sterile by the makers. This type of syringe is used *once* and discarded (para 54).

(b) *Syringes for re-use.* Glass syringes for the injection of vaccines or of sensitivity test antigens should be of the all-glass type or all-glass except for a metal needle mount which is attached to the barrel either without the use of cement or with a heat resistant cement in accordance with British Standards. Glass syringes with a metal piston should not be used: they cannot be sterilized when assembled, are more liable to break on heating and are slow to cool after sterilization by heat.

(c) *Needles.* Disposable needles, supplied sterile by the manufacturers, used once only and discarded immediately after use are the most suitable. A needle for intradermal injection should be short (half-inch), of narrow gauge and have a short bevel in accordance with British Standards. For subcutaneous or intramuscular injection a longer needle with a long bevel is preferable.

43 Segregation of Syringes

(a) When disposable syringes are not available, it is essential that syringes used for injecting vaccines or sensitivity test antigens should be kept separate at all times from those used for aspirating infected or potentially infected fluids.

(b) Syringes used in experiments or tests on animals must not be obtained from, or sent to, Central Sterile Syringe Supply Services, but should be cleaned and sterilized under separate arrangements (usually at the laboratory concerned). No syringe which has ever been used for injection of animals will be used on a human being.

(c) Syringes used for Schick testing will not be used for other purposes and separate syringes must be kept for the test and control fluids (para 92). In particular Schick test syringes must not be used for performing the Mantoux test. The latter test has, in general, been superseded in the Services by the Heaf test (paras 103 to 105) but, if the use of it is requested, separate syringes and needles must be provided and these should not be used for any other purpose.

44 Central Sterile Syringe Supply Service

It is most desirable that syringes for re-use should be supplied sterilized in suitable containers from a Central Sterile Supply Service. The instructions given hereunder are applicable to the preparation of syringes issued from such a central service for carrying out immunological procedures. Simpler methods which may be used for the local preparation of syringes, when necessary, are also described.

45 Cleaning and Preparation for Sterilization

(a) *Cleaning of Syringes*

(1) Since syringes used for immunological purposes must at all times be kept separate from those used for aspirations (para 43), those used for vaccinating and sensitivity testing will not become soiled with more than traces of blood or other protein material. The more elaborate cleansing methods used and proposed for the removal of such matter are not therefore needed; the syringes merely require washing out just after use with tap water, followed later by thorough washing in de-ionized or distilled water, draining and drying in a warm oven.

(2) Syringes used for administering serum for passive immunization should also be washed out repeatedly with tap water after use. They should later be soaked for an hour or more in a warm solution of soft soap, or a suitable detergent in de-ionized or distilled water, drained, rinsed thoroughly in de-ionized or distilled water, drained again and dried.

(b) *Cleaning of Needles*

(1) The needle hub should first be cleaned out with a swab, which must be frequently changed when a large number of needles are being treated. This is followed by squirting a solution of soap or a detergent, clean water, distilled or de-ionized water and air—in that order—through the needle, which is then dried. In large units these operations can be carried out more quickly by attaching the wool swabs for cleaning the hubs to a dental burr and by attaching the needles for further treatment to multiple nozzles on a tube into which the washing solution, rinsing water and air are pumped in turn.

(2) After cleaning, the point of the needle should be inspected under a lens. It should be sharp and straight. Deflection of the stream of fluid when the needle is being washed may give earlier indication of a damaged point, as may preliminary testing by plunging the washed needle through a rubber diaphragm and then withdrawing it. No needle should be accepted for use without direct visual examination, after which the tip should be preserved by a guard or by inserting it in a suitable porous pad, of a type from which filaments will not become detached and enter or adhere to it, when not protected by a guard.

46 Containers

(a) The best container to use depends on whether the syringe is for local use only or for distribution, and on the nature of the sterilizing equipment.

(b) For local use, and for treatment in a sterilizer which is not provided with a high vacuum pump, wrapping in kraft paper is probably best, or two layers of closely woven fabric secured with tape may be used.

(c) Syringes for issue to other units may be placed in glass tubes plugged with cotton wool; the tube and contents should not be wrapped in cellophane. *A metal container* will not be used.

47 Assembly

Syringes should be packed separately for sterilization as follows:

(a) *For dry-heat sterilization*, which is the treatment of choice, the syringes are assembled. The needle is preferably also attached and protected, if necessary, by covering the shaft with a longer piece of tubing. Each syringe is placed in a heat resistant container which is then, according to its type, closed with its cap or sealed. Tubes should be sealed with metal foil caps using the appropriate apparatus for applying them. Wrapping the tubes wholly or partially in kraft paper or cellophane tends to limit the sterilizing temperature.

(b) *Sterlization by steam under pressure.* When adequate equipment for dry-heat treatment is not available, syringes are sterilized assembled, as this avoids the risk of contaminating them when putting them together later. If steam treatment of an assembled syringe is to be effective, the syringe must not only be free from a water-repellent lubricant, as should all articles to be sterilized by steam, but must also be *assembled wet*. This precaution is necessary in view of the difficulty of ensuring access of steam between plunger and barrel.

48 Prevention of breakages

If the syringe does not fit a rigid container closely, packing with absorbent cotton wool or fitting the syringe with rings of elastomeric silicone ('silicone rubber') may be necessary.

49 The Sterilization of Syringes in Containers

(a) *Dry Heat* (*this is the method of choice*)

(1) The most commonly used apparatus for dry heat treatment is a hot air oven. This should be electrically heated, thermostatically controlled and provided with a fan and a thermometer. *Tight packing must be avoided*, and any baskets used as secondary containers must be wide meshed, so that circulation of hot air is not impeded. Treatment should be for one hour at 160°C, timed from when that temperature is shown on the thermometer.

(2) The oven may be loaded cold or hot, but even when loaded hot (by which time is saved) there is a drop in temperature after loading and the sterilizing period is reckoned from the time when the effective temperature is regained.

(3) As a partial check on sterilization Browne's Tube No. 3 may be used. It should be placed in a container similar to that used for the syringes, in the midst of the syringe containers. Sterilization should be regarded as inadequate if the colour does not change to green. On the other hand a change to green is not in itself proof that every item in the load is sterile.

(b) *Steam under pressure*

(1) Syringes for steam sterilization must be assembled wet. High vacuum dressing sterilizers or any efficient type of pressure steam sterilizer, including those of

domestic pressure-cooker type, may be used. In any autoclave in which the air is displaced by steam and not removed by a high vacuum pump, glass tubes used as primary syringe containers must be placed on their sides, or be inverted, and any secondary container used must be pervious to steam. Sterilization should be checked by the use of Browne's Tube No. 2.

(2) 'Pressure cookers' are suitable for small units. Treatment in them should be at 15 lb. pressure for fifteen minutes. Sterlization should be checked by the use of Browne's Tube No. 1. Overloading must be avoided. Some difficulties may arise in drying syringes after treatment in these small sterilizers. This may be minimized by reducing the pressure as quickly as possible after sterilization by immediately removing the pressure weights with a long hook or fork. The remaining water is then emptied out and the syringes dried in the cooker for a short time over a low heat.

(c) *Boiling*. Boiling water cannot be relied upon to sterilize in an acceptable time and resort to boiling for first treatment of an unsterile syringe should not be necessary in Service medical units. For *resterilization* in the course of a vaccination session see para 55. If, in an emergency, reliance has to be placed on boiling, this must be for *at least ten minutes*, and must be preceded by meticulous cleaning of the syringe.

50
51 } Reserved.
52

Section 5 Mass immunization

53 The provision of a separate syringe and needle for each individual when large numbers are being vaccinated, which is essential to avoid the risk of transference of infection, may present a special problem in the absence of large numbers of disposable syringes, since speed of operation is also necessary. The danger of using one syringe and several needles is the transference of serum hepatitis by the reflux of tissue fluid which occurs on changing the needles. This problem may in time be overcome when needleless injectors, at present under trial, become available for general distribution.

54 Separate Syringes

The ideal solution of this problem is the provision of a disposable sterile syringe for each person. Supplies of these are now available at Service medical units. The alternative of issuing a separate sterile syringe for each person from a central syringe supply service is feasible when numbers required do not exceed the resources of the centre: numbers should rarely be excessive under normal peacetime conditions.

55 Rapid Sterilization between Injections

Under emergency conditions, however, when larger numbers are involved, recourse may be necessary to resterilization between injections. For this purpose, since the

syringes used will have been originally supplied sterile, the only organisms requiring destruction should be those derived from a person in the course of vaccination. Of these, the viruses of hepatitis are among the most important and most heat-resistant. For the destruction of such contaminants the temperatures and durations of exposure needed to kill bacterial spores are not essential.

(a) *Complete Resterilization*

(1) Ideally the whole syringe should be treated and for this purpose may be boiled for *not less than ten minutes*. To ensure 'sterilization' within this time each syringe must be boiled separately or a number started at the same time, because introduction of other syringes into the boiler once the ten-minute period of boiling has begun may recontaminate those syringes already in it. The sterilizing period for all the articles in the boiler must be reckoned from the time the last article is put in.

(2) When more than a few persons are to be vaccinated, the syringes must be sterilized in batches. At least two boilers with lids must be provided.

(3) The syringes are rinsed out with sterile water after use; when a batch has been collected, all are immediately placed, assembled wet, in the boiler and the lid closed. Using a timer, the period of sterilization is reckoned from the time the contents of the boiler reach boiling point. Time must be allowed for this and for the syringes to cool after sterilization.

(4) One medical officer with three assistants is, on average, able to vaccinate six persons per minute. Sixty syringes will therefore be used during the sterilizing period.

(5) Approximately one third of the syringes in use must be collected to make up the first batch for resterilization which, therefore, cannot start until about six minutes after the session begins. Thus, to avoid delay, not less than one hundred syringes should be provided sterile for the vaccinator so that he has enough to work with until the first resterilized batch is ready for use. Proportionately fewer syringes will be needed if a slower rate of vaccination is accepted or if extra boilers are used.

(b) *Resterilization of the needle only—for use in emergency*. Resterilization of the needle only is acceptable provided that reflux of potentially infected tissue fluid into the syringe does not take place. Then, only the needle can become contaminated with an infective agent from an individual in the course of giving him an injection and resterilization of the whole syringe becomes unnecessary. The needle must be resterilized, however, *while still attached to the syringe*, since removing it before sterilization transfers its possibly infected contents to the tip of the syringe. A method of treating needles based on the above is as follows:

(1) After each injection the vaccinator himself dips the needle half-way up the butt for ten seconds into a bath of oil maintained at 150°C to 160°C. The temperature is shown by a thermometer dipping into the oil. Medicinal liquid paraffin is considered suitable for this purpose. *The piston must be firmly held against the base of the barrel of the syringe from the time of completion of the injection until the needle is removed from the oil.*

(2) Several syringes in rotation should be used in order to allow the needle to cool before re-charging with a dose of vaccine.

(3) This method has been used in the Services for some time and remains acceptable provided that the technique of sterilization described above is strictly adhered to *and that at no time, from the moment the needle is inserted into the skin before an injection until its completion, is any backward movement of the piston allowed.* This second proviso, which is essential to ensure fulfilment of the assumption on which the method is based, is not an easy one with which to comply.

(4) Minor disadvantages of the method are that one operator is unlikely to vaccinate more than three persons a minute if it is properly carried out, and that the *piston must not be withdrawn before making an injection.* However, though this is a useful way of ensuring that a vein has not been entered, it is not essential before making an intradermal or a subcutaneous injection, when such an accident should be avoidable by exercising reasonable care.

(5) Sterilization of the needle only—in hot oil between injections as described above—should therefore be reserved for circumstances in which resources are not available for providing a sterile syringe for each person in any of the other ways mentioned.

56 Other Methods of Vaccination

There are two possible methods of by-passing the difficulties of sterilization which arise when a needle and syringe are used.

(a) *Needleless injection.* Needleless injectors, which deliver a dose of vaccine as a high velocity jet, are in use for subcutaneous vaccination. Intradermal injection by this method is under trial and once a satisfactory instrument has been perfected it may become available for mass vaccinations in the Services.

(b) *Oral vaccination.* The development of attenuated strain vaccines for oral administration, such as the poliomyelitis vaccine used at present, avoids all the difficulties of sterilization of syringes described above. This method may also be extended to other diseases in the future as new vaccines become available.

57 Contraindications

In the Armed Forces mass immunization should rarely be called for provided the requisite vaccination state is maintained. The main objection to mass immunization is that it is impossible to carry out the precautions outlined in para 63a, with the result that a number of persons will be vaccinated who ought not to be, resulting in the ocurrence of cases of illness and of adverse reactions that ought not to occur.

58
59 } Reserved.

Section 6 Injection technique

60 Vaccine Containers: Filling of Syringes

(a) *Ampoules*

(1) Once an ampoule has been opened the whole of the contents must be used at one session, or the unused portion must be discarded. Material in opened ampoules must not be reserved for future use.

(2) Before opening an ampoule of vaccine the label should be checked, the ampoule shaken and any liquid in its neck dislodged. If not already present, a file mark should be made on the neck of the ampoule which should then be swabbed with alcohol and broken off with sterile forceps or with the fingers covered with a sterile gauze swab. The ampoule is then held on a slant, the sterilized needle inserted and the syringe charged with a dose of vaccine.

(b) *Rubber Capped Bottles*

(1) The label of the bottle should be checked. If the bottle contains suspended antigen it should be shaken thoroughly to ensure a uniform vaccine. The rubber cap is then treated by thorough wiping with a sterile swab dipped in 70–75 per cent v/v alcohol.
(2) An air inlet in the form of a sterile needle, adequately plugged with sterile cotton-wool to act as a filter, may be inserted through the rubber cap before the vaccine is withdrawn. This allows the easy removal of the vaccine without producing a negative pressure which could be a cause of later contamination. Vaccine is then taken up into the syringe by passing the needle vertically through the cap, inverting the bottle and withdrawing the quantity required into the syringe.
(3) An alternative method of avoiding a vacuum and assisting removal of the vaccine is to inject a volume of air from the syringe into the bottle before withdrawing vaccine. To render this procedure itself safe, however, this air must be sterile. This may be achieved by withdrawing air from the container in which the syringe has been sterilized, when removing the syringe therefrom. Before making an injection any air which has entered or remains in the syringe should be expelled. Too frequent punctures of the cap may lead to contamination of the contents, and bottles with caps in bad condition should be discarded, as should any container which is nearly empty at the end of a vaccination session. Ideally the contents of a bottle should be finished in one session, otherwise the bottles should be replaced in their cartons and placed in a refrigerator.

61 Site of Injecting Vaccine

(a) *Intradermal Injection*

(1) For intradermal T.A.B., T.A.B.T. or Cholera vaccine the site of election is behind the posterior border of the distal portion of the deltoid muscle.
(2) For B.C.G. the injection must be made over the insertion of the deltoid or up to half-way between the insertion and origin of the muscle. With this vaccine injection higher up the arm toward the point of the shoulder may involve the cervical glands or lead to unsightly keloid scarring (see para 116 (d)).
(3) For sensitivity tests, intradermal injections are usually given in the middle of the front of the forearm. *This site should not be used for injecting vaccines.*

(b) *Subcutaneous Injection.* Subcutaneous injections should be made in a location where the skin is loose, the tissues yielding and the veins scarce. The site of election for the subcutaneous injection of most vaccines is the same as that given for the intradermal injection of T.A.B. or T.A.B.T.

(c) *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 if the amounts are large. In using the deltoid care must be taken to avoid the circumflex nerve. With these injections there is some risk of the needle entering a vein. The piston should therefore be withdrawn before making the injection and hence between such injections sterilization of the needle only is *not* acceptable (para 55 (b)).

(d) *Choice of arm.* In left-handed people the right arm should be used.

62 Technique of Injection

The site of injection should be clean and should be treated with acetone, 75 per cent alcohol or surgical spirit. The skin should be allowed to dry before the puncture is made.

(a) *Intradermal Injection.* The operator stretches the skin by holding the part tightly in one hand and with the other slowly inserts the needle with the bevel upwards for about 2 mm. into the superficial layers of the dermis almost parallel with the surface. The needle should be short with a short bevel which can usually be seen faintly through the epidermis during insertion. A raised, blanched bleb showing the pits of the hair follicles is a sign that the injection has not been made too deeply, and its diameter gives a useful indication of the amount which has been injected. A bleb of 7 mm. diameter is approximately equivalent to 0·1 ml.

(b) *Subcutaneous Injection.* The subject is instructed to place his hand on his hip. The operator steadies the arm with one hand, picking up a fold of skin between forefinger and thumb or drawing the skin taut with the thumb. Holding the syringe in the other hand he then 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.

63 General Precautions

(a) Before performing any vaccination the medical officer should satisfy himself that the individual is in good health; that there is no history of recent exposure to infectious disease or previous severe reactions to vaccination; that the individual is not undergoing radiotherapy or treatment with corticosteroids; and that the appropriate time interval after any previous immunization has elapsed. It is also important to ascertain whether a woman is pregnant or not. When vaccinating with a live vaccine further precautions may have to be taken (paras 156, 266 . . .).

(b) The vaccinator and all assistants must wash their hands thoroughly before commencing work and at intervals during prolonged sessions. All the staff should wear clean gowns or coats.

(c) Syringes should only be handled with dry, washed hands, taking care only to touch the outside of the barrel and the handle of the piston. When not in actual use they should be replaced in the sterile containers in which they were sterilized or in a sterile test tube placed in a horizontal or slightly inclined position.

(d) There must be no talking, coughing or sneezing over a sterile syringe. Needles, if not already attached to the syringe, must be handled only with sterile forceps.

(e) In order to avoid nausea and fainting, persons to be vaccinated must not be kept waiting for long periods in extremes of climate, and queues in the actual room where the vaccinations are taking place should be avoided. A solution of 1:1000 adrenaline, which on rare occasions may be needed urgently, should be kept available.

(f) Only one dose of vaccine will be taken into each syringe at a time. Multiple doses in a syringe are not permissible.

64 Types of Reaction

The more serious types of reaction which may follow the administration of vaccines are:

(a) *Local Reaction.* Some local discomfort, swelling and redness may be expected, but occasionally this may be more severe and progress to local necrosis, ulceration and scarring. Sixteen severe local reactions have been reported in the Army during the last five years.

(b) *Pyrexial Reaction.* A pyrexia may occur which lasts 24 to 48 hours in most cases. This may be associated with malaise, headache, vomiting and rigor. A temperature above 101°F is unusual.

(c) *Neurological Reaction.* This may consist of the very occasional occurrence of blindness due to optic neuritis which may be transient or permanent.
Encephalopathy is more common, which may be transient with convulsions or permanent due to encephalitis. Ascending myelitis, transverse myelitis and peripheral neuritis have all been reported. It is not known whether these neurological reactions result from undue sensitivity of the patient or from some material in the vaccine, but they are generally regarded as allergic manifestations.

(d) *Dermatological Reaction.* This may consist of local or generalized urticaria, non-specific rashes, eczema or a generalized infection such as vaccinia.

(e) *Anaphylaxis.* Although severe anaphylactic shock is rare following vaccination, minor degrees are not uncommon. Delayed allergic reactions are not uncommon following certain immunizations eg tetanus toxoid and diphtheria toxoid.

(f) *Severe generalized reaction.* Vaccination may be associated with a local or generalized lymphadenopathy and with splenic and/or hepatic enlargement. Generalized arthropathy has also been reported. Very occasionally collapse and death a few hours after vaccination has been reported, especially with T.A.B. vaccine. This is presumably due to a direct cardio-vascular reaction.

(g) *Provocation disease.* In certain cases a vaccination may precipitate an attack of the specific disease or of unrelated disease. Owing to the risk of provocation, vaccination of those unimmunized by injection should be avoided in an explosive epidemic.

(h) Although not a clinical reaction is should also be noted that false positive cardiolipin tests may occur after vaccination.

65
66 } Reserved.

Technical information regarding:

Immunizing antigens
Immunological test reagents
Passive immunization*

Section 7 Simple and combined vaccines against the enteric group of fevers

67 General

(a) The enteric group of fevers consists of typhoid, paratyphoid A and paratyphoid B.

(b) For adults and older children of thirteen years and upwards primary vaccination against the enteric fevers is generally combined in the Services with vaccination against tetanus. Vaccination will be by the intradermal injection of 'Typhoid-Paratyphoid Vaccine in Tetanus Toxoid for intradermal use (T.A.B.T. Intradermal)'.

(c) Infants under one year old will not be vaccinated against enteric fevers.

(d) Children from one to twelve years of age inclusive will be vaccinated subcutaneously with 'Diluted Typhoid-Paratyphoid Vaccine (diluted T.A.B.)'.

(e) Maintenance or reinforcing doses will be carried out with the appropriate vaccine mentioned above. See also paras 12(e) and 12(f) for the indications for the use of 'Typhoid-Paratyphoid Vaccine for intradermal use (T.A.B. Intradermal)', i.e. without tetanus toxoid, in the presence of a major risk.

*Volumes given for doses of vaccines and of antisera should be verified by reference to the instructions on labels, containers, etc., since the volume in which a dose is contained is liable to change following improvements in production techniques. The maker's instructions should therefore be noted and followed.

68 Vaccines: constitution, dosage and site of injection

(a) *T.A.B.T. Intradermal*

(1) The vaccine contains 5,000 million killed enteric organisms and approximately 20 Lf doses of tetanus toxoid per ml.

The numbers per ml. of enteric organisms are as follows:

Salm. typhi	2,000 million
Salm. paratyphi A	1,500 million
Salm. paratyphi B	1,500 million

(2) The dose for each injection is 0·1 ml. This dose cannot be increased more than twofold either in volume or concentration of organisms without a risk of central necrosis of the injected skin.

(3) The intervals between doses are given in para 12.

(4) The site of election for injection is into the skin of the outer aspect of the arm behind the posterior border of the distal portion of the deltoid muscle. Usually the left arm in a right-handed person is used unless contraindicated (paras 117(b) and (c)).

(5) *Vaccines should not be injected* into the skin of the forearm, though that is the site of choice for administering certain immunological test reagents (paras 61 and 92).

(6) While strictly intradermal injection is desirable in order to avoid reactions, which is the chief advantage of this route, there is evidence to suggest that injection of the same dose subcutaneously, or partly subcutaneously, will produce an immunological response similar to that following a strictly intradermal injection, though reactions are then liable to be more severe.

(b) *T.A.B. Intradermal*

(1) This vaccine has the same content and proportions of killed organisms as has T.A.B.T. Intradermal, but does not contain tetanus toxoid.

(2) All doses, whether primary (when applicable), maintenance or reinforcing, are also 0·1 ml.

(3) The site of election for the injections is as for T.A.B.T. Intradermal and the intervals between doses in different circumstances are given in para 12.

(c) *T.A.B. Dilute*

(1) This vaccine is intended for children from one to twelve years old and contains 1,000 million killed enteric organisms per ml. It is given subcutaneously.

The numbers per ml. of enteric organisms are as follows:	
Salm. typhi	400 million
Salm. paratyphi A	300 million
Salm paratyphi B	300 million

(2) Intradermal injection of children is not easy and the advisability of using that route for them depends on a future assessment of the degree of liability to skin sensitization by it.

(3) The first and third doses for primary vaccination and all subsequent doses are 0·2 ml. The second dose for primary vaccination will generally be 0·4 ml. though for undersized children, or following anything more than a mild reaction to the first dose, the second dose also should not be greater than 0·2 ml.

(4) The intervals between doses under varying conditions are given in para 12.

(5) The site of election for subcutaneous injection is deep to that given above for intradermal injection, that is to say *under* the skin of the outer aspect of the arm behind the posterior border of the distal portion of the deltoid muscle. Care must be taken to avoid entry into a vein.

(d) *Avoidance of intramuscular injection.* None of the above vaccines should be injected intramuscularly.

69 Degree, duration and maintenance of immunity

(a) Vaccination does not give full protection against enteric fevers, and though case incidence should be lessened, overt infections may still occur in those who are vaccinated. When this happens the severity of the disease is not likely to be mitigated by the vaccination. In the absence of direct evidence it is hard to assess the duration of immunity following injections of T.A.B. vaccine. However, on the basis of accepting the partial validity of tests for residual antibodies, *protection* is assumed to be maintained for at least one year and *basal immunity* to exist for three years after primary immunization or a maintenance dose. Those at risk, therefore, are given annual doses to preserve protection and those not at risk are given doses every three years to maintain basal immunity (para 12(d)).

(b) It is further considered that Service personnel who have reached the age of thirty-five should have received a sufficient number of injections of T.A.B. vaccines to produce some permanent basal immunity; moreover reactions to injections of the vaccine may tend to become more troublesome in such older people. Hence maintenance doses, both in the absence of risk and under normal conditions of overseas service, may be discontinued after that age. There is no reliable evidence in support of the idea that susceptibility to enteric fevers falls in middle life. Hence, in the face of a liability to special risk, those over thirty-five years old will be given the reinforcing doses advocated in such circumstances (para 12(e)).

70 Reactions

Severe reactions, both local and general (see para 64), can and do occur particularly if vaccine intended for intradermal use is given subcutaneously. Reactions following intradermal vaccine given correctly are generally considerably less than those following subcutaneous injections.

71 Precautions

(a) Although reactions to intradermal injection of vaccines containing T.A.B. are generally much less than those which follow subcutaneous vaccination, it remains advisable, where feasible, to vaccinate as late in the day as possible, to excuse those vaccinated from duty for thirty-six hours and to keep them in barracks.

(b) The bottle of vaccine must be shaken before use, and the dregs of old bottles discarded, to avoid over-dosage which, as pointed out above (para 68(a)), may cause a small area of skin necrosis.

72
73 } Reserved.
74

Section 8 Active immunization against tetanus

75 Primary vaccination

(a) Primary vaccination against tetanus is generally combined with vaccination against the enteric fevers in adults (paras 12, 13 and 67). In children it is usually combined with vaccination against diphtheria (paras 10, 13(b) and 97). In exceptional circumstances, however, it may be carried out separately by injecting tetanus toxoid (T.T.) subcutaneously (paras 76(c), 199(f) and 203).

(b) *Tetanus Toxoid.* This is tetanus toxin rendered non-toxic by treatment with formalin. It contains 20 Lf. doses per ml. and is usually used in the following dosage irrespective of age or sex.

(c) *Dosage.* Unless otherwise indicated on the label or container, primary vaccination with tetanus toxoid will consist of three injections of 0·5 ml. The second injection will be given six to twelve *weeks* after the first injection and a third injection will be given six to twelve *months* after the second injection.

76 Maintenance of immunity

T.T. subcutaneously will be used (paras 13(c), 199(f) and 203).

(b) T.A.B.T. is given intradermally in 0·1 ml. doses at three-year intervals for maintenance of immunity.

(c) For the maintenance of immunity after the age of thirty-five, T.T. will be given alone in subcutaneous doses of 0·5 ml. at five-year intervals. Reinforcement subcutaneous doses of 0·5 ml. will also be given on wounding or injury (para 199).

77 Reactions

Reactions to tetanus toxoid are rare and usually mild. People with a history of allergic conditions may be more liable than others to reactions of an allergic type. Such persons should first be given a subcutaneous 'trial dose' (para 221) of 0·1 ml. followed not less than half an hour later by the ordinary subcutaneous dose of 0·5 ml. if no symptoms have occurred. Within the present scheme the repeated injection of tetanus toxoid may, in a few persons, result in a progressively increasing local induration of a transient nature.

78
79 } Reserved.
80

Section 9 Active immunization against poliomyelitis

81 General

(a) Owing to the prevalence of poliomyelitis in certain overseas stations it is particularly important that Service men and women and their families should be protected by at least three doses of *Sabin type oral live vaccine* before proceeding to such stations. Details of dosage and intervals between doses, with particular reference to this requirement and to certain restrictions on the use of this vaccine, are given in para 14.

(b) *Inactivated vaccine*. Formalin-inactivated (killed) (Salk type) poliomyelitis vaccine was formerly used by the Services. It was administered in four doses of 1·0 ml. injected intramuscularly. This vaccine is not now recommended in the Services. The dosage of live oral vaccine required by persons who have not completed courses of 'Salk' vaccine are described below and in para 14(a).

82 The nature of living attenuated oral poliomyelitis vaccine

(a) This vaccine is for routine vaccination against poliomyelitis and contains living attenuated poliomyelitis viruses of types 1, 2 and 3. It has been prepared from the Sabin strains and is offered in such strength that a human dose is contained in three drops. Before any batch of vaccine is released for use, it will have been subjected to tests for safety with results satisfactory to the Medical Research Council.

(b) *Dosage*. A course consists of three doses, each of three drops, given at intervals of four to eight weeks. The interval between second and third doses may be extended in exceptional conditions. If the vaccine is regurgitated a dose may be repeated. The vaccine can be administered on a lump of sugar or in syrup (B.P.). For babies a dropping pipette may be used.

(c) *Mode of action*. The administration is usually followed by multiplication of the viruses in the wall of the intestine, by their excretion in the faeces, and by the development of poliovirus antibodies.

83 Reactions

The vaccine is not known to cause reactions either local or general.
Occasional cases of poliomyelitis have been reported 10–14 days after vaccination. Whether this is coincidental or not is not known.

84 Use of Vaccine

(a) A full course of oral vaccine consisting of three doses as defined above may be administered as a means of routine immunization to persons who have not previously received vaccination against poliomyelitis by any method.

(b) Where persons have had one or two doses of 'Salk' type killed vaccine, not more than one year earlier, they may have poliomyelitis vaccination completed with not less than two doses each of three drops of oral live vaccine at an interval of four to eight weeks. For those that have been partially immunized with oral vaccine, see para 14(a).

(c) Maintenance doses for those who have previously received three doses of 'Salk' type killed vaccine should be with oral vaccine.

(d) All immunized children joining school should be offered a reinforcing dose of vaccine. The interval between the reinforcing dose and the last previous dose should not be less than four weeks.

(e) A reinforcing dose of vaccine should be offered to immunized persons at special risk, regardless of age group, who have not had poliomyelitis vaccine within the preceding three years. Examples of such persons at special risk are medical, dental and nursing officers and medical ancillary personnel in contact with cases; families in contact with cases; persons proceeding outside Europe or North America.

85 Notes on Restrictions

(a) The restrictions on the use of oral poliomyelitis are enumerated in para 14(c).

(b) *Seasonal poliomyelitis.* Routine use of the oral vaccine may be undertaken in any season and is not contraindicated during periods of high poliomyelitis prevalence.

(c) *Pregnancy.* There is no evidence that pregnancy is a contraindication, but women known to be pregnant should preferably not be given oral vaccine earlier than the fourth month of their pregnancy.

(d) *Killed Vaccines.* Oral poliomyelitis vaccine may be given at the same time as any killed vaccine.

(e) *Tonsillectomy.* Whereas no restriction is necessary in the United Kingdom, tonsillectomy should be postponed until the course of oral vaccine has been completed in countries overseas where poliomyelitis is endemic.

(f) *Use of one type vaccine in epidemics.* Where one dose of oral vaccine is to be used in epidemics to protect those who have not been previously vaccinated, the relevant type to that present in the epidemic will be used; this monovalent poliomyelitis vaccine can be obtained on a special demand.

86 Presentation, Distribution and Storage of Vaccine

(a) *Presentation.* Poliomyelitis vaccine will be supplied to the Services either in pliable dropper bottles made of polythene or in glass vials with separate droppers.

(b) *Transport.* When the transport from the supplier to the holder (Medical Store) is estimated to take not more than thirty-six hours, cartons containing the vaccine will be placed in carbon-dioxide snow in insulated containers which will retain the vaccine in a frozen state. When the holder receives the cartons he should place them in storage at 0° to 4°C to maintain the vaccine until it is issued for use.

(c) *Storage*: See Table 1

Table 1 Storage of oral poliomyelitis vaccine

Source	*Storage conditions*	*Life*
Supplier (e.g. drug house)	Deep-frozen vaccine at minus 10°C or below	2 years from date of manufacture.
Holder (e.g. A.M.E.D. and Base Medical Stores)	Unfrozen vaccine at up to 4°C	Maximum of 1 year from date of issue from deep freeze or expiry date, whichever is earlier.
User (e.g. Hospitals and Medical Centres)	Thawed vaccine at 4–10°C	6 months.
	Thawed vaccine in a cool dark place (i.e. not over 15°C)	14 days.

(1) *Unfrozen oral poliomyelitis vaccine* may be held at Base Medical Stores in the refrigerator at up to 4°C, for a maximum period of one year from the date of receipt from the supplier, or up to the manufacturer's expiry date, whichever is earlier.

(2) *Thawed oral poliomyelitis vaccine* has a life of six months from the date of issue from the holder if it is stored at refrigerator temperatures, but it should not be used after the expiry date on the container. When thawed vaccine in pliable dropper bottles or glass vials has been removed from the refrigerator for use, it must be kept in a cool place away from direct sunlight and preferably should be used the same day. Any vaccine kept out of the refrigerator under these conditions for a total of more than fourteen days should be destroyed in its container by boiling.

(d) *Distribution of vaccine to user*. When vaccine is issued by the holder for use, the required number of individual packages, containing pliable dropper bottles or glass vials, should be removed from the appropriate storage shown in (c) above and the labels checked. If these are not marked with an expiry date by the manufacturer, they should be so marked, using an indelible pencil or suitable rubber stamp, to indicate expiry six months from the date of issue when stored at refrigerator temperature. Delivery to the user should not take more than twenty-four hours.

(e) *Deterioration of the vaccine*. Vaccine which has become turbid or which is time-expired in relation to the various stages of storage, distribution and administration indicated above, should not be used, but should be destroyed in its container by boiling.

87
88 } Reserved.
89

Section 10 Active immunization against diphtheria

90 Susceptibility to diphtheria

In the United Kingdom unimmunized children under twelve will usually be susceptible to diphtheria and are unlikely to suffer from severe reactions to the vaccines. No test for susceptibility is therefore necessary for them. For adults and children over twelve, however, the following considerations apply:

(a) Owing to the great reduction in the incidence of diphtheria in the United Kingdom, acquirement of natural immunity as a result of sub-clinical or mild infection is now unlikely. Such a natural immunity is, however, a possibility in individuals over twelve years of age and these persons do not need vaccination. A proportion of them would suffer more or less severe local or general reactions if vaccinated.

(b) Conversely, individuals who have been immunized in early childhood, but who have not been given maintenance doses, will show an increasing tendency for their immunity to wane as adult life approaches. Hence from twelve years old onwards a test of susceptibility should be carried out before vaccination against diphtheria.

Susceptibility test

91 The Schick Test

(a) This is a biological test to determine whether a person has already developed his or her own diphtheria antitoxin and is therefore no longer susceptible to the disease.

(b) The test consists of the intradermal injection of Schick toxin. This is a toxic filtrate of a culture of *Corynebacterium diphtheriae* diluted with a buffer solution. The dose is 0·2 ml. and the strength of the diluted toxin such that this amount is rendered ineffective by mixing with 1/750 unit of antitoxin, but still causes a reaction when mixed with 1/1250 unit, if such mixtures are tested in the skin of a guinea-pig. In man, the average amount of antitoxin in the blood to neutralize the test dose is 1/200 unit per ml.

(c) Since certain individuals may react to constituents of the test fluid other than the toxin, a control test is also made by injecting, at a different site, a similar dose of the fluid which has been treated by heat to destroy the toxin in it.

92 Technique

The skin of the middle of the flexor surface of both forearms is cleaned with spirit and allowed to dry. 0·2 ml. of toxin is then injected intradermally, as described in para 62, into the cleansed site on the left arm and 0·2 ml. of control fluid is injected

into the prepared site on the right arm. Correct injection should raise a weal 8 to 10 mm. in diameter. *Separate syringes must be kept for the two fluids;* that for the toxin should bear some means of identification.

93 Reading and Interpretation of Results

(a) Results of the tests may be *negative*, indicating circulating antitoxin and immunity; or *positive*, when there is little or no circulating antitoxin and hence a susceptibility to diphtheria. Combined with either, however, there may be a *pseudo* reaction due to sensitivity to constituents of the test fluid other than the toxin. Hence a pseudo reaction is recognized by occurring at both sites of injection.

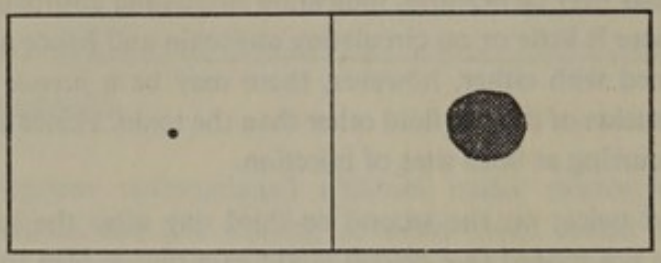
(b) Results are read twice; on the second or third day after the injection—so that pseudo reactors are not missed (*see* below), and again on the fifth to the seventh day to detect late reactors and check the earlier reading.

(c) Interpretation is summarised in table 2 and is based on the following characteristics :

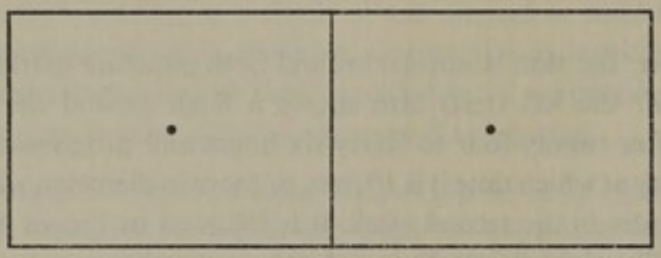
(1) *Negative reaction:* the skin is normal around both puncture marks.
(2) *Positive reaction:* the left (test) arm shows a flush around the puncture which usually starts after twenty-four to thirty-six hours and progresses until the fourth to the seventh day at which time it is 10 mm. or more in diameter, with some oedema. The erythema fades in the second week. It is followed by brown pigmentation and desquamation. The right (control) arm shows no reaction.
(3) *Pseudo reaction* ('Negative-and-pseudo'): *both* arms show a flush around the puncture. It occurs early, is at its maximum in twenty-four to seventy-two hours and has faded by the fifth or sixth day.
(4) *Positive-and-pseudo reaction*:* a flush on both arms; that on the left side being much larger, more persistent, and followed by staining and desquamation. The difference between the two sides is usually clear on the fourth day, but with a marked pseudo reaction on the right (control) arm interpretation may be difficult.

Table 2 Shick test for susceptibility to Diphtheria. Erythema on the third day.

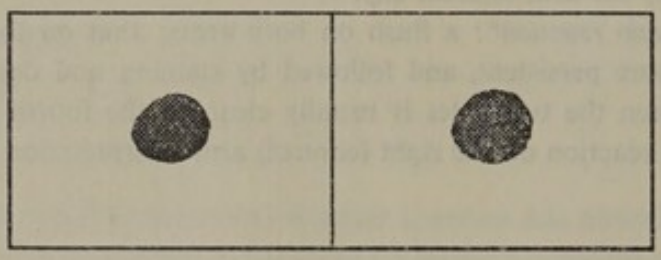
Right arm (control) | Left arm (test)



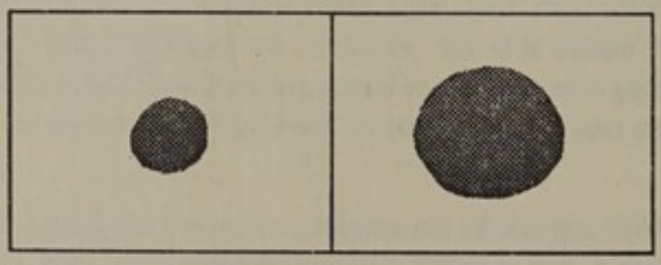
Positive reaction i.e. susceptible



Negative reaction i.e. immune



Pseudo reaction i.e. immune
(Negative-and-Pseudo reaction)



Positive-and-Pseudo reaction i.e. susceptible*

*See para 94 (b) below.

Vaccination

94 Vaccination

(a) Vaccination of Service personnel and their families against diphtheria is necessary in order to maintain the reduced incidence of the disease in the United Kingdom and

also because there is a high incidence of diphtheria in certain overseas theatres. All ranks are therefore Schick tested soon after joining the Services and those giving a *positive reaction*, as defined above, are vaccinated. The course should start during their preliminary training.

(b) *Positive reactors who also show a pseudo reaction must not be immunized* since the response to the control fluid may presage severe local and general reactions to immunization. Interpretation may be difficult and, even when the Schick reaction is also positive as shown by the greater response on the test arm, well marked pseudo reactors have been found to have circulating antitoxin.

Types of vaccine for adults

95 (a) The prophylactic issued is Formol Toxoid (F.T.).

(b) Combined prophylactics for adults, such as T.A.B.T.D., are not recommended in view of the lack of necessity and possible undesirability of vaccinating those already immune (para 90), and the possibility that those already immunized against diphtheria in childhood will show a preponderant response to the diphtheria component, and an inadequate response to the other components, of such a combined vaccine.

(c) Formerly Alum Precipitated Toxoid (A.P.T.) was the vaccine of choice in the Services owing to its high potency. Due to the severity of reactions to A.P.T., Formol Toxoid is now preferred for general use. A.P.T. is, however, recommended in special circumstances (paras 211–216).

(d) Toxoid-Antitoxin Floccules (T.A.F.) are not recommended. This is a prophylactic which, by sensitizing to horse proteins, may prejudice the subsequent use of horse antitoxins of any type (e.g., tetanus antitoxin) that may be required for treatment.

96 Formol toxoid

(a) *Dosage*

(1) Two doses, each of 0·5 ml. will be given at an interval of six weeks.
(2) Normally this will be followed by a third dose of 0·5 ml. six to twelve months later.
(3) A third dose will, however, only be given without a preceding Schick test if vaccination was primary and if no undue reaction has been caused by the earlier doses.
(4) In a known case of revaccination owing to lost immunity, or when an undue reaction has followed an earlier dose, a Schick test will replace the third dose and a further dose will only be given if the test is positive, as defined in para 93(c). When that is so, a reduced dose of 0·25 ml. is advisable.
(5) It is possible that some previously vaccinated, but no longer immune, persons may react unduly to the *first* revaccination dose. In such a case a Schick test should replace the second dose, further action depending on the result, as at (4) above.

(b) *Method of administration.* The toxoid should be injected *deep* into the subcutaneous tissue behind the posterior border of the distal portion of the deltoid muscle, or intramuscularly into the deltoid muscle.

Types of vaccine for children and infants

97 (a) *Type of vaccine*

(1) Diphtheria Tetanus prophylactic (D.T.) *or* Diphtheria-Tetanus-Pertussis prophylactic (D.T.P.—'Triple prophylactic') *or* Formol Toxoid (F.T.) may be used in children over one year old. D.T.P. is the vaccine of choice for children up to the age of five years. D.T. is the vaccine of choice for school children.

(2) Primary immunization against whooping cough after the age of five years is not usually considered advisable because the peak danger period has been passed and there is also a high incidence of reactions to pertussis vaccine in the older child.

(3) D.T. is preferred to F.T. owing to the increasing appreciation of the desirability of general immunization of the population against tetanus. This is much more likely to be achieved with the use of a combined prophylactic than if F.T. and tetanus toxoid are offered separately.

(b) *Dosage, and age of administration*

(1) D.T.P. is given in three doses, starting between six months and one year of age Each dose is that stated by the manufacturers and is given at intervals of four to six weeks. A further dose may be given about one year later.

(2) D.T. is given in three doses, each of the volume stated by the manufacturers, at intervals of four to six weeks. This primary course is administered to unimmunized children at school entry. For older children of twelve years and over, a preliminary Schick test is essential in order to obviate the untoward consequences of injecting diphtheria prophylactic into Schick pseudo-reactors (para 94).

(c) *Method of administration.* Both prophylactics are given by deep subcutaneous or intramuscular injection.

(d) *Maintenance of immunity.* D.T. will be the vaccine used to maintain immunity both for children immunized with D.T. and for those immunized with D.T.P. When F.T. has been used as the immunizing prophylactic its use will be continued for maintaining immunity. The first maintenance dose (of D.T. or F.T. as indicated) will be given at school entry. The second will be given at eight years of age.

98 Reactions

The acute systemic pyrexial reaction (see para 64) may occur in Schick negative children, who are given vaccine of the A.P.T. type. Schick negative adults may show similar reaction even if given F.T.

99 Precautions against severe reactions

See para 63e.

100
101 } Reserved.

Section 11 Active immunization against tuberculosis

102 Susceptibility to tuberculosis

Vaccination against tuberculosis is only needed by those who have been shown, by a negative tuberculin test, to be highly susceptible to the disease. Persons to be so tested may be divided into six categories:

(a) All those entrants to the Regular Forces who have not recently been, and are not while serving expected to be, subject to a risk of infection beyond that incidental to normal Service life in any part of the world.

(b) Similarly situated personnel of Gurkha units and their families. In regard to their children see paras 120 and 121.

(c) Those who, by reason of their employment or otherwise, have been in recent contact with known sources of tuberculous infection, but for whom future risk should not be greater than that incurred by those in category (a) above. These will include contacts of known cases from whom they are now separated.

(d) Those who, though not previously at special risk, will, in the course of future duty or otherwise, be exposed to infection, e.g. medical and nursing ancillaries and others who will be working with patients.

(e) Those who have been and will remain exposed to infection, e.g. Medical and Nursing Officers, many of whom will have been tested, and vaccinated if necessary, before joining the Services.

(f) Families of Service men or women: these should be tested, and vaccinated if necessary, before proceeding overseas to stations where tuberculosis is prevalent (paras 120 and 121).
Note. The differences in immediate and follow-up procedures in respect of persons in these categories are referred to in para 11(b) and summarized below (para 106).

Susceptibility tests

103 The Heaf Test

(a) *General.* The routine tuberculin test for susceptibility to tuberculosis used in the Services is the Heaf test. Like all tuberculin tests, it is a test for sensitization indicating the presence of tuberculo-protein most likely due to past or present infection by the tubercle bacillus. See also para 107. For certain purposes the Army may find that the Disk-Tine Tuberculin test is more convenient (para 108). In a *healthy person* such sensitivity is usually associated with some degree of immunity to further infection and hence it is the negative reactor who is specially liable to contract tuberculosis.

(b) *Heaf gun.* The test is carried out with the Heaf multiple puncture instrument (Heaf gun). This should be of a pattern in which the needles are exposed for a great part of

their length and not housed in, so that they can be heat-sterilized by the method to be described, without over-heating the instrument.

(c) *P.P.D.* The tuberculin used is Purified Protein Derivative (P.P.D.) in a solution containing 2·0 mg., i.e. 100,000 tuberculin units (T.U.) per ml. It has been estimated that the test dose given is then of the order of 50 to 60 T.U.

(d) *Keeping properties of P.P.D.* The strong solution referred to above will keep at refrigerator temperature for one year; P.P.D. in the dried state keeps for several years; more dilute solutions are unstable unless specially treated and even then their usefulness is limited to a few weeks. (See Table 24 at para 242(d)).

104 Technique of Heaf Testing

(a) *Sterilization of the Heaf gun.* The end plate of the gun is dipped in acetone, spirit or absolute alcohol in a suitable container (e.g. a petri dish) to a depth of about 2–3 mm. to ensure that the effective parts of the tips of the needles are immersed. It is then withdrawn and the acetone or alcohol is set alight by momentary contact with a spirit flame, or other burner, from which it is at once removed on ignition, and the acetone or alcohol is allowed to burn until the flame goes out. The end of the apparatus is then placed so that the needles will not become contaminated (e.g. in a sterile tube lying on its side) and allowed to cool. Cooling takes about thirty seconds. If two instruments are in use, one can always be cooling.

(b) *Site.* A site about a hand's breadth below the bend of the elbow on the front of the forearm is cleaned with acetone or spirit and allowed to dry.

(c) *P.P.D. application.* The P.P.D. solution is next applied to the prepared area of skin with a sterile loop, glass rod, or special applicator, and spread as an even film over an area of about 1 sq. cm.

(d) *Application of the gun.* The apparatus is placed vertically to the skin surface, the end plate is firmly applied to the tuberculin-coated skin and the needles are released. For all persons needles with a penetration of 2 mm. are now used. The needles must all be sharp in order that reactions may be correctly graded (para 105). After the puncture the arm is allowed to dry. No dressing is needed.

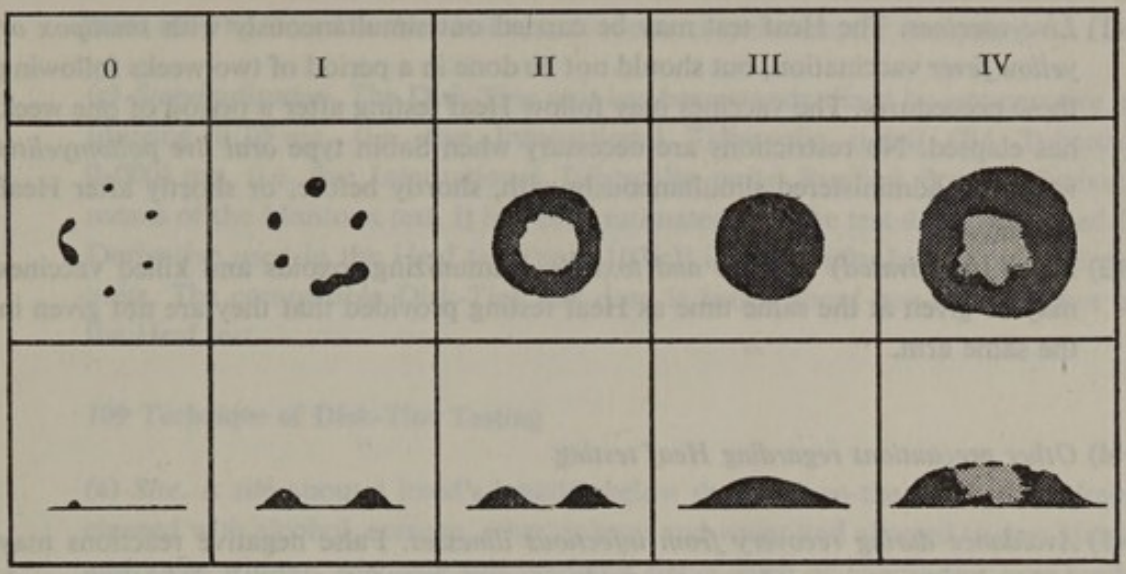
(e) *Re-sterilization.* The end plate and distal parts of the needles are sterilized as in (a) above and allowed to cool before further use.

105 Reading of Results

The result may be read from ninety-six hours to seven days after the test, the optimum time being between four and five days. Gradings are as follows:

(a) *Negative*	
Grade 0:	No reaction; or any local reaction consisting of *less than four* indurated papules. Three such papules, even if they coalesce, do not constitute a positive reaction.
(b) *Positive*	
Grade I:	Four or more *palpable* papules. *Induration which can be felt* is an essential feature of all positive results.
Grade II:	The papules have coalesced to form a ring.
Grade III:	A plateau of induration.
Grade IV:	A large area of induration with blistering, ulceration or necrosis.

Table 3 Heaf test grades—readings at four days.



106 Indications and Contraindications for Heaf Testing

(a) *Definitions*

(1) *Conversion* occurs when a person previously Tuberculin test negative becomes Tuberculin test positive as a consequence of vaccination with B.C.G. vaccine or actually experiencing some form of tuberculous infection. This tuberculous infection may be so slight as to have been sub-clinical and may have passed unnoticed by both the person and his or her medical attendant.

(2) *Reversion* occurs when a person who has previously been Tuberculin test positive as a result of B.C.G. vaccination is found on later Tuberculin testing to be Tuberculin test negative due to waning of his of her active immunity (para 103(a)).

(b) *Heaf tests required before and after vaccination with B.C.G. are summarised in Table* 4.

Table 4 Heaf Tests before and after B.C.G.

Recent-past and future liability to infection	Tests before vaccination	Tests for tuberculin conversion.
Normal both for pre-Service and for future Service life (paras 102(a) and (b))	One (negative)	Nil.
Normal for pre-Service life but *enhanced* risk during Service (para 102(d))	One (negative)	Yes, eight weeks after vaccination.
Recent contact but future liability *normal* for Service life (para 102(c))	Two (negative) (second test six weeks after first negative, or six weeks after removal from source of risk, whichever is later)	Nil.
Recent-past and future-expected exposure to enhanced risk (paras 102(d) and (e))	Two (negative) (second test six weeks after first negative, or six weeks after removal from source of risk, whichever is later)	Yes, eight weeks after vaccination.

(c) *Intervals to be observed between Heaf testing and unrelated vaccinations*

(1) *Live vaccines.* The Heaf test may be carried out simultaneously with *smallpox or yellow fever* vaccination, but should not be done in a period of two weeks following these procedures. The vaccines may follow Heaf testing after a period of one week has elapsed. No restrictions are necessary when Sabin type *oral live poliomyelitis vaccine* is administered simultaneously with, shortly before, or shortly after Heaf testing.

(2) *Killed (inactivated) vaccines and toxoids.* Immunizing toxoids and killed vaccines may be given at the same time as Heaf testing provided that they are not given in the same arm.

(d) *Other precautions regarding Heaf testing*

(1) *Avoidance during recovery from infectious illnesses.* False negative reactions may occur during periods of pyrexia or during recovery from certain infections, such as measles and influenza, hence testing should be avoided at such times. Tuberculin sensitivity may also be lowered in certain other conditions, e.g. in the puerperium, in patients with one of the reticuloses, and in those undergoing treatment with corticosteroids.

(2) *Site for tests of reversion.* When testing for negative reversion after B.C.G. vaccination the test should be carried out on the other arm to that used for the initial (or last previous) Heaf test, the site of which should have been recorded (para 25), as local changes in sensitivity may affect the result.

107 Action Regarding Tuberculin Positive Reactors

A positive Heaf test should be correlated with the individual's Mass Miniature Radiography film to determine whether the sensititivity is due to past or current infection (para 103(a)). The latter may be suspected when a Grade III or Grade IV reaction has occurred. In particular those at special risk (paras 102(c), (d) and (e)) with such a reaction and *all* naturally tuberculin positive *children* who show a Grade II, III or IV reaction, should be sent for a full plate X-ray of the chest. Furthermore persons in frequent contact with cases of tuberculosis or tuberculous material should have an X-ray once every six months (but not more frequently) and those in occasional contact should be X-rayed annually.

108 The Disk-Tine Tuberculin Test

(a) Like the Heaf test, the Disk-Tine Tuberculin test (Tine test; Tine Rosenthal test) is a skin test for indicating sensitization to tuberculo-protein in an individual, by a multipuncture method (para 103(a)).

(b) *The Disk-Tine unit.* Each unit consists of a stainless steel disc, with four tines each 2 mm. long, attached to a plastic handle. The tines have been dip-dried with Old Tuberculin. The entire unit has been sterilized with ethylene oxide gas and twenty-five

such units are each clipped into a separate compartment of a twenty-five unit block. Each unit will remain sterile until it is removed from its individual holder. Unused units may be stored in their holders, at room temperature, for two years.

(c) *Standardization.* The Disk-Tine unit has been standardized by comparative studies, utilizing 0·05 mg. (i.e. five International Tuberculin units) Old Tuberculin or 0·0001 mg. (i.e. five International Tuberculin units) Purified Protein Derivative by means of the Mantoux test. It has been estimated that the test dose of Purified Protein Derivative used in the Heaf test (para 103(c)) is about fifty International Tuberculin units. The comparable Disk-Tine test dose is hence about one-tenth of that used in the Heaf test.

109 Technique of Disk-Tine Testing

(a) *Site.* A site about a hand's breadth below the bend on the front of the forearm is cleaned with alcohol, acetone, ether or soap and water and allowed to dry. Hairy areas and areas without adequate subcutaneous tissue, such as concavities over tendons or bone, should be avoided.

(b) *Method of application.* Remove a Disk-Tine unit from the twenty-five unit block by leverage or snapping the handle from the container base. Care must be taken not to bend the container base or more than one unit may be released. The left hand is placed at the dorsal aspect of the patient's arm, encircling it in such a way that the skin of the ventral surface can be evenly stretched at the selected, cleaned test site. Apply the Disk-Tine unit firmly for one second with the right hand, using such pressure that in addition to the four puncture sites there is a circular depression of the skin caused by the plastic base. A momentary stinging sensation occurs which may cause the patient to 'jump' and withdraw the arm, with resultant scratching if the operator is not prepared for it and is not holding the arm firmly enough.

(c) *Dressing.* No dressing or after care of the test site is needed.

(d) *Disposal of the unit.* The Disk-Tine test unit should never be re-used. The unit is disposable and should be dropped into a discard unit such as a beaker or foot-operated waste-bin, so that there is no chance of its accidental re-use.

110 Reading of results

The results may be read from forty-eight to seventy-two hours. Gradings are as follows:

(a) *Negative*	
Grade O:	No reaction—needle marks only.
(b) *Positive*	
Grade I:	One or more *palpable* papules of 2 mm. or more in diameter.
Grade II:	Four *palpable* papules of 4 mm. in diameter, more or less coalescing.
Grade III:	A plateau of induration with erythema.
Grade IV:	A more extensive area of induration with blistering, ulceration or necrosis.

111 Intervals to be Observed Between the Disk-Tine Test and Unrelated Vaccinations

These are as for the Heaf test, para 106(d).

112 Comparison of the Disk-Tine Test to the Heaf Test

It has been shown in comparative studies between the Disk-Tine test and the Heaf test that a discrepancy of some 15 per cent occurs between the two. All these cases are in the direction of Heaf positive–Disk-Tine negative and are considered to be due to the fact that the Heaf test represents a much 'stronger' test (approximately fifty Tuberculin units). It has been suggested by the W.H.O. that the 'weaker' test using five Tuberculin units is a more appropriate strength for routine epidemiological work.

113
114 } Reserved.
115

Vaccination

116 Vaccination

(a) *The vaccine.* The vaccine used in the Services is British freeze dried B.C.G. (Bacille Calmette-Guerin) a living culture of an attenuated strain of *Mycobacterium tuberculosis.* The dried material is reconstituted just before use with the diluent supplied with it. As the dried vaccine is highly sensitive to sunlight, it will be stored at refrigerator temperature *in the dark*, where it will keep for twelve months. Similar conditions while in transit are desirable, but the vaccine will withstand transportation at tropical temperatures for seven days provided it is always protected from sunlight.

(b) *Method of administration.* In the Services B.C.G. is given by intradermal injection, *and it is of the utmost importance* that the vaccine be given strictly intradermally and none of it *be injected under the skin* since if that occurs abscess formation at the injection site is more likely. In the opinion of some authorities, break-down of the lymph glands draining that site is also more likely. Hence B.C.G. vaccination should only be done by those skilled in giving intradermal injections. The multiple puncture method of vaccination, although giving encouraging results, is still in the experimental stage.

(c) *Dosage.* The dose in all persons over one year of age is 0·1 ml. of the reconstituted vaccine. For infants under one year of age 0·05 ml. should be given.

(d) *Site of injection.* The site of the injection is over the insertion of the left deltoid or up to half way between the insertion and origin of the muscle; *the injection should not be given at the point of the shoulder.* Injection higher than the recommended sites is liable to involve the lymph drainage area of the cervical rather than the axillary glands and may be followed by break-down of the former (see (b) above). The vaccination site should be cleaned and allowed to dry before an injection is made.

117 Intervals to be Observed Between B.C.G. and Other Vaccinations

(a) *Living vaccines*

(1) With the exception of poliomyelitis vaccine, there should be an interval of ten days between vaccination with B.C.G. and previous or later vaccination with all other *live vaccines.*
(2) Poliomyelitis vaccine may be given at the same time as B.C.G.

(3) In special circumstances smallpox vaccine may be given in one arm and B.C.G. vaccine in the other, at the same time; but it should be remembered that this procedure may commit both arms to healing ulcers for a period of about three weeks, and no other vaccination procedure will be possible during that time.

(b) *Killed vaccines and toxoids.* B.C.G. may follow killed vaccines or toxoids a week after they have been given. B.C.G. should not be followed by such vaccines, owing to the reactions caused by some of them, until after ten days; in an emergency a single other dead vaccine or toxoid may be given at the same time as, or soon after, B.C.G. *provided the other arm is used.*

(c) *Other precautions regarding B.C.G. vaccination*

(1) The individual must be in good health at the time of vaccination and free from infectious disease, local septic conditions, etc.

(2) B.C.G. vaccination should not be given to persons with extensive chronic skin lesions, e.g. psoriasis, dry scaly eczema, etc.

(3) B.C.G. vaccination should only be carried out by those who have acquired the proper technique.

(4) The arm which has been vaccinated with B.C.G. should not normally be used for further vaccinations for three months, since such use might set up regional lymphadenitis.

118 Treatment of severe reactions

The normal reaction to B.C.G. vaccination consists of an area of induration, 6–12 mm. in diameter, which is usually at its maximum at 3–6 weeks. A shallow ulcer may develop, but regional adenitis is minimal.

(a) *Ulcers.* Local ulceration or discharging lesions are best treated with sodium para-amino salicylic acid (P.A.S.) powder or Isonicotinic acid hydrazide (Isoniazid, I.N.A.H.) powder.

(b) *Abcesses.* Fluctuant swellings may be aspirated with streptomycin replacement. For infants with marked glandular involvement, P.A.S. and isoniazid may be given for four to six weeks. General health is not affected in such cases.

(c) *Refractory lesions.* Refractory types of lesions usually respond to local ultra-violet light treatment.

(d) Generalised infections with the B.C.G. tubercle bacillus several months after vaccination have been reported but are rare. Treatment with the anti-tuberculosis drugs is indicated.

Table 5 Summary of reactions to B.C.G. and treatment

Local Reactions	Regional Lymph Gland Involvement	Remote Lymph Gland Involvement	Treatment
Normal 6–12 mm induration ± ulcer	Usually slight	No	Nil.
Ulceration and/or discharge	Usually moderate or marked	No	Local PAS or INAH powder. U.V. Light.
Severe*	Abscess formation	No	Aspiration with Streptomycin replacement. U.V. Light.
Severe*	Marked ± abscess formation	Yes	Systemic PAS and INAH. U.V. Light.

* These reactions are rare and should be referred to hospital for treatment.

(e) A lupoid reaction or keloid is occasionally seen 1–2 years later at the local site, particularly if it has been chosen too high on the shoulder.

119 Post-Vaccination Care

(a) *General.* For those not liable to future special risk (paras 102(a), (b) and (c)) no test for conversion to tuberculin positive is required (para 106(b)). No special post-vaccination segregation is needed.

(b) *Those to be at risk*

(1) Individuals whose future occupation or circumstances will involve definite risk of infection (paras 102(d) and (e)) will be given a test for conversion to tuberculin positive eight weeks after B.C.G. vaccination (para 106(b)). If this test is negative they will be revaccinated.
(2) Until a positive tuberculin reaction has been obtained they will be kept from any known or likely source of infection (such as personal contact with cases, or duties involving contact with potentially infected material). In particular no medical, dental, nursing officer or auxiliary, laboratory technician or other individual whose normal duties involve contact with patients or tuberculous material, will be employed in wards in which tuberculous patients are being treated, or be allowed near such patients or tuberculous material, unless he or she is naturally tuberculin positive or has been rendered so artificially.

120 B.C.G. Vaccination of Children in Contact with Tuberculosis

(a) *Newborn infants of mothers with active or recently quiescent tuberculosis*

(1) A newborn infant of a mother with active or recently quiescent tuberculosis should be removed from its mother at birth. No Heaf or tuberculin test is needed, and the infant should be vaccinated with B.C.G. on the fourth or fifth day after birth. The risk of abscess formation must be accepted in these circumstances (see para 121 (1)(1).
(2) The baby should remain in hospital segregated from the mother until a definite local reaction at the vaccination site has developed. When this occurs the child may be returned to the mother provided that any active disease is receiving treatment, the mother has been told how to protect the baby from infection and she remains under supervision so long as her tuberculosis is active.
(3) If no local reaction develops in eight weeks, revaccination in the other arm should be done, using a fresh batch of vaccine. Separation from the mother is continued until a local lesion develops. The child is then returned to the mother. If there is no local reaction after four weeks following the second vaccination, the child is tuberculin tested and if negative revaccinated once again. In the rare event of no lesion developing after the third vaccination the child may be returned to the mother, but kept under observation.

(b) *Contact between child and mother with arrested or recovered tuberculosis.* The child should be tuberculin tested and if negative given B.C.G. forthwith. No special action need be taken.

(c) *Older children who are contacts of cases.* Action required is as for infants who have been in contact with mothers or other persons with active tuberculosis.

121 B.C.G. Vaccination of Children NOT known to be contacts of cases of tuberculosis

The Heaf test may be carried out at any age; but the most suitable age, and that at which vaccination of negative reactors is required, depend upon prevailing circumstances as follows:

(a) *Under general Service conditions*

(1) Vaccination during infancy is best avoided because, particularly in early infancy, the incidence of regional adenitis with abscess formation is very much higher. For this reason very early testing and vaccination (eg from birth to three years old) is not indicated *except perhaps in the case of Gurkha infants* for whom para 121(3)(b) applies.

(2) Heaf or tuberculin testing should usually be deferred until the child is ten to fifteen years old; at this time negative reactors are to be vaccinated. When, however, it is known that the tuberculin positive rate in children by the age of ten years, in a locality, is high (20 per cent or more) children of Service men or women in such a locality may be Heaf tested as soon as possible after other immunological procedures have been completed, between three and five years of age and be vaccinated forthwith if tuberculin negative.

(3) On the other hand when the tuberculin positive rate among children under five is very low, B.C.G. vaccination is not at once necessary even if the Heaf test has been carried out at this earlier age and is negative. Vaccination interferes with the future *diagnostic* value of tuberculin tests and may well be deferred until the child is ten years old when of course B.C.G. must still *not be given without a repetition of the Heaf test*, with a negative result.

(b) *Residence overseas.* Tuberculosis is very prevalent in most overseas stations and it is inadvisable that any tuberculin negative member of a Service family should be exposed to such conditions. Hence it is strongly recommended that children of Service men or women who are liable to be sent overseas, whatever their age, should be Heaf tested, and the negative reactors be vaccinated before they go.

122
123 } Reserved.
124

Section 12 Active immunization against cholera

125 The vaccine

Cholera vaccine is a heat-killed, phenol-preserved suspension of *Vibrio cholerae*. It consists of equal proportions of three types of Vibrio cholerae—Inaba, Ogawa and El Tor, to give a total of 8,000 million vibrios in each ml. of vaccine.

126 Primary vaccination

(a) Primary vaccination for adults and children over five years of age is with *one intradermal* injection of 0·1 ml. or *one subcutaneous* injection of 0·5 ml. of cholera vaccine.

(b) Primary vaccination for children of one to five years of age inclusive is with one 0·25 ml. *subcutaneous* injection of cholera vaccine.

(c) The single dose meets the normal requirement for travel.

(d) Children less than one year old are not vaccinated with cholera vaccine.

127 Persons proceeding to a cholera epidemic or endemic area

(a) Adults and children over five years of age proceeding to a cholera epidemic or endemic area should be given *two subcutaneous* injections of 0·5 and 1·0 ml. of cholera vaccine at an interval of ten to twenty-eight days *or two intradermal* injections of 0·1 ml. at a similar interval.

(b) Children of one to five years inclusive should be given *two subcutaneous* injections of 0·25 ml. and 0·5 ml. respectively at a similar interval.

(c) Cholera vaccine dosage is summarized in Table 6.

Table 6 Cholera vaccine: dosage

	Subcutaneous		Intradermal	
	1st dose	2nd dose	1st dose	2nd dose
Adults and children over five years	0·5 ml.	1·0 ml.	0·1 ml.	0·1 ml.
Children of one to five years	0·25 ml.	0·5 ml.	Not recommended	

128 Duration and Maintenance of Immunity

Immunity is short lived and maintenance doses are needed every six months for those at risk. The dose required is that for primary vaccination and is as follows: adults and children over five years of age, 0·5 ml. given subcuteneously *or* 0·1 ml. given intradermally; children under five years of age, 0·25 ml. given subcutaneously.

129 International Certificate

The requirements and validity of International Certification for cholera vaccine are detailed in para 18.

130 Reactions

Reactions after cholera vaccine tend to be mild and the use of intradermal vaccine produces less severe reaction than subcutaneous vaccination. Mild local, pyrexial and dermatological reactions have been reported (see para 64).

131
132 } Reserved.

Section 13 Active immunization against plague

133 The Vaccine

Plague vaccines prepared in the United Kingdom are generally suspensions of cultures of avirulent strains of *Pasteurella pestis* grown on solid media at 37°C, which are preserved with phenol after having been killed by treatment with formalin. Each ml. of vaccine contains 2,000 million organisms. It is possible that more potent vaccines may be forthcoming in the future.

134 Primary Vaccination

For primary immunization two doses of vaccine are injected subcutaneously at an interval of ten to twenty-eight days, the dosage is given in Table 7.

Table 7 Plague vaccination dosage

	1st dose	2nd dose
Adults and children over 12 years	0·5 ml.	1·0 ml.
Children 5 to 12 years old	0·25 ml.	0·5 ml.
Children 1 to 5 years old	0·1 ml.	0·2 ml.

Children under 1 year are not vaccinated.

135 Duration and Maintenance of Immunity

Immunity is short lived and maintenance doses, equal to the *first* primary vaccination dose for the appropriate age, are needed every six months for those at risk.

136 Reactions

Moderately severe local and general reactions may follow injections of plague vaccine.

137
138 } Reserved.
139

Section 14 Active immunization against typhus fever

140 The Vaccine

The typhus vaccine used in the Services is a killed suspension of rickettsiae grown in the yolk sacs of developing chick embryos. It affords a good measure of protection against epidemic (louse-borne) and murine (flea-borne) typhus, but not against scrub (mite-borne) or tick typhus.

141 Primary Vaccination

For primary immunization three doses, each of 1·0 ml. with intervals of seven to fourteen days between them, are injected subcutaneously. Dosage is the same for children as for adults, but children under one year are not vaccinated.

142 Duration and Maintenance of Immunity

Immunity is short lived and maintenance or reinforcing doses are needed as follows:

(a) *In endemic areas* a single dose of 1·0 ml. annually.

(b) *During an epidemic* a dose of 1·0 ml. every three months while at risk.

143 Reactions

Local discomfort at the site of injection is common: general reactions are rare.

144
145 } Reserved.
146

Section 15 Immunization against smallpox

147 The Vaccine

(a) *Freeze-dried vaccine*

(1) The smallpox vaccine used in the Services is usually a freeze-dried, vacuum-sealed preparation of living vaccinia virus which is reconstituted just before use with the diluent provided with it. It is supplied in twenty-five dose and one hundred dose packs. Containers of less than twenty-five doses cannot be economically produced. To avoid waste it is therefore desirable that, as far as possible, vaccination against smallpox should be performed on groups of several persons at a time, and not on single individuals. The diluent for the twenty-five dose container is issued in a double-ended ampoule from which transfer to the dried vaccine can be made without the use of a syringe. The diluent for the one hundred dose container is issued in an ordinary glass ampoule and a sterile syringe must be used to add the fluid to the dried vaccine. On addition of the fluid and a slight shake, resuspension of the vaccine takes place almost at once.

(2) The dried vaccine lasts indefinitely at 'refrigerator temperature' (2°C to 10°C); for a year when kept in a cool dark place (not over 15°C); or for one month at tropical temperatures (see Table 20 at para 242(a)). The reconstituted vaccine should be used at once, but will retain potency for one week if kept in the refrigerator.

(b) *Glycerinated lymph*

(1) Glycerinated lymph may be supplied. It is issued in glass or polythene capillary tubes containing single or multiple doses. It will keep for a year at *minus* 20°C. Once issued it deteriorates gradually, but remains potent for up to fourteen days in a refrigerator and up to seven days in a 'cool dark place'. Opened tubes cannot be stored and any lymph remaining after use must be discarded.

(2) *Glycerinated lymph issued in glass capillary tubes should only be expelled by means of a lymph expeller.* The average amount of lymph required is enough to cover an area of skin one-eighth of an inch in diameter.

(3) Lymph contained in polythene capillary tubes can be expressed after snipping the end of the plastic tube with scissors. Contamination of the scissors is inevitable and appropriate precautions are necessary. It may be wise to keep a special pair of scissors solely for this purpose. The scissors should preferably be boiled after use or else wiped with a swab thoroughly soaked in surgical spirit; but alcohol should not be allowed in contact with smallpox vaccine. It may be more convenient to

pierce one end of the tube with a sterile disposable hypodermic needle. If the needle is introduced into the lumen of the plastic tube it will contain enough vaccine when withdrawn to enable it to be used for a successful vaccination by either scarification or multiple pressure.

148 Methods of Vaccination

(a) *The multiple pressure method.* This is used in all the Services (para 149).

(b) *The linear scratch method.* This method is preferred as an alternative to the multiple pressure technique in the Royal Air Force (para 151).

149 The Multiple Pressure Method

The technique is as follows:

(a) *Site of vaccination.* The area of choice for vaccination is over the insertion of the left deltoid muscle. It is well washed with soap and water and then thoroughly dried. This area should then be cleaned by swabbing with acetone or ether. Spirit or alcohol or any non-volatile antiseptic must not be applied.

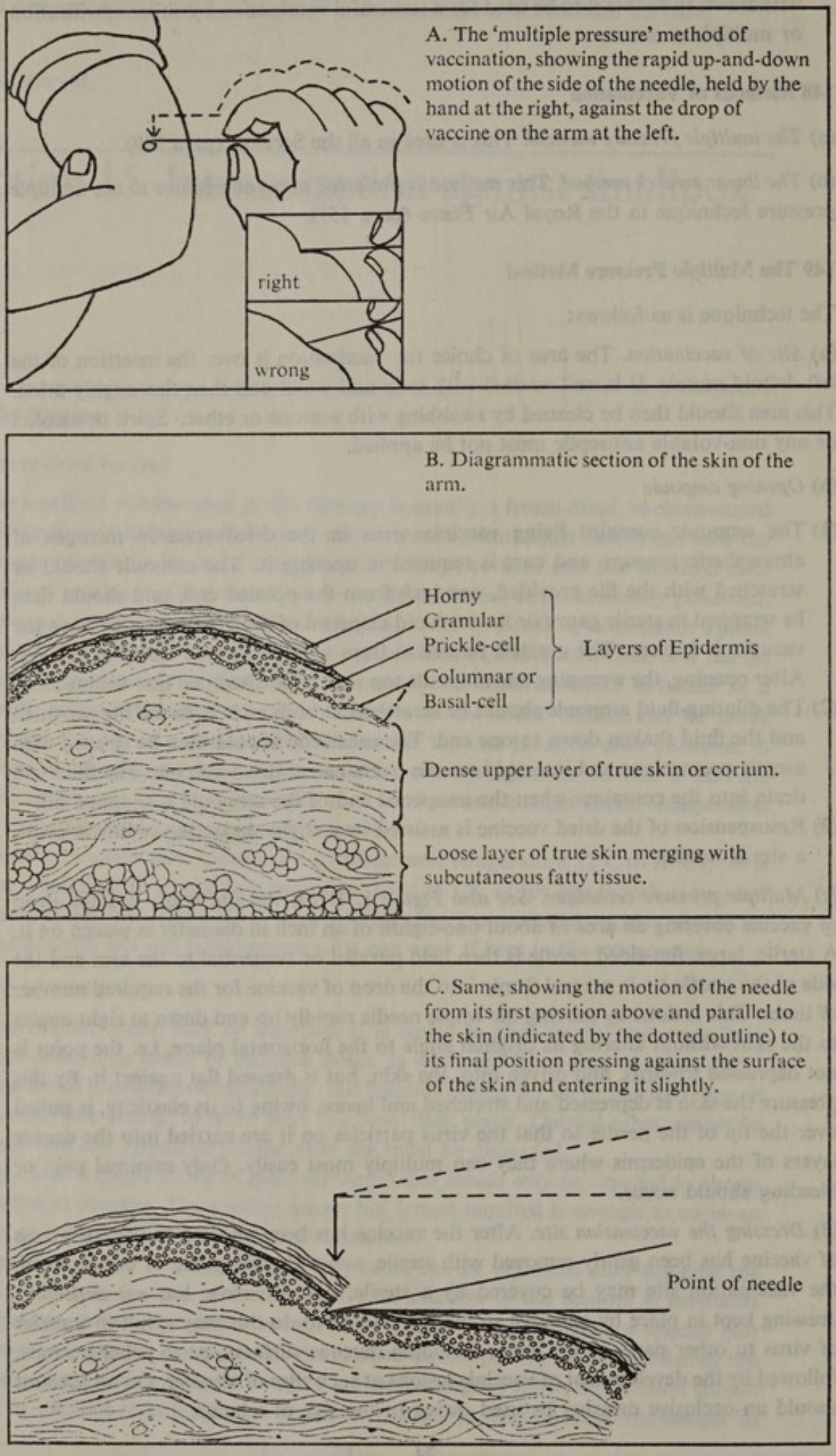
(b) *Opening ampoule*

(1) The ampoule contains living vaccinia virus in the dried state in nitrogen at atmospheric pressure and care is required in opening it. The ampoule should be scratched with the file provided, one inch from the pointed end, and should then be wrapped in sterile gauze or lint to avoid dispersal of the dried material when the vacuum is broken. The greatest hazard is from vaccine powder entering the eye. After opening, the wrapping and ampoule top should be discarded into disinfectant.
(2) The diluting-fluid ampoule should be scratched at both ends with the file provided and the fluid shaken down to one end. The other end should then be opened with aseptic precautions and inserted into the container of dried vaccine. The fluid will drain into the container when the unopened end of the ampoule is snapped off.
(3) Resuspension of the dried vaccine is assisted by a slight shake, tap or stirring with a sterile needle.

(c) *Multiple pressure technique. See also Figure* 1. When the site is dry a small drop of vaccine covering an area of about one-eighth of an inch in diameter is placed on it. A sterile, large, flat-sided needle is then held parallel or tangential to the arm and the side of the needle tip is pressed firmly into the drop of vaccine for the required number of times. This is done by moving the whole needle rapidly up and down at right angles to the skin without altering its original angle to the horizontal plane, i.e. the point is not depressed towards, and driven into, the skin, but is pressed flat against it. By this pressure the skin is depressed and stretched and hence, owing to its elasticity, is pulled over the tip of the needle so that the virus particles on it are carried into the deeper layers of the epidermis where they can multiply most easily. Only minimal pain or bleeding should occur.

(d) *Dressing the vaccination site.* After the vaccine has been allowed to dry, or excess of vaccine has been gently removed with sterile, *non-antiseptic* gauze or cotton wool, the vaccination site may be covered by a sterile, non-occlusive, but *not antiseptic*, dressing kept in place by adhesive strapping. Failure to do this may result in transfer of virus to other parts of the body, including mucous surfaces, or to other persons, followed by the development of vaccinia lesions at such sites of transfer. On no account should an occlusive dressing be used owing to the risk of tetanus.

Figure 1 The Multiple Pressure Technique



A. The 'multiple pressure' method of vaccination, showing the rapid up-and-down motion of the side of the needle, held by the hand at the right, against the drop of vaccine on the arm at the left.

B. Diagrammatic section of the skin of the arm.

Dense upper layer of true skin or corium.

Loose layer of true skin merging with subcutaneous fatty tissue.

C. Same, showing the motion of the needle from its first position above and parallel to the skin (indicated by the dotted outline) to its final position pressing against the surface of the skin and entering it slightly.

150 Dosage using multiple pressure method

The number of pressures to be made depends on whether the vaccination is primary or a revaccination (and if the latter after how long an interval), on the age of the subject, on whether it is a repeat following an immediate previous failure and on the imminence of risk, as shown in Table 8.

Table 8 Multiple pressure method: dosage

Adult or child	Degree of risk	Nature of vaccination	Number of drops of vaccine	Number of pressures per drop	Remarks
Adult	Normal	Primary	1	10	—
		Repeat Primary (after failure)	1	30	To be carried out at once after failure of first attempt.
		Revaccination (*first after child vaccination*)	1	10	Primary response likely.
		Revaccination (*after later primary vaccination or previous revaccination*)	1	30	—
		Repeat Revaccination (after failure)	2	30	To be carried out at once after failure of first attempt. One drop an inch from the site of that failure, the other drop on the opposite arm.
	Epidemic or undue prevalence of smallpox	Primary or Revaccination	2 or 3	30	Drops on two or three separate areas an inch apart. (When there is immediate risk and the need to establish immunity quickly, a larger local reaction outweighs the general desirability of keeping such reactions small.)
Child	Normal	Primary	1	30	—
	Epidemic or undue prevalence of smallpox	Primary	2 or 3	30	Drops on two or three separate areas an inch apart.

151 The Linear Scratch Method

(a) The area to be vaccinated is prepared as described in para 149(a).

(b) The vaccine is reconstituted as is described in para 149(b).

(c) *Linear scratch technique.* A sterile Hagedorn needle at least three inches long is recommended. Lymph is applied to the skin separately when using glycerinated lymph and by dipping the sterile needle into the ampoule when using freeze dried vaccine. The needle should be held with the forefinger along the shaft. The technique is as follows:

(1) Place the thumb or forefinger of the other hand above the site chosen and tense the skin at the vaccination site by pulling slightly upwards towards the shoulder.

(2) Make a light scratch one-quarter of an inch long holding the needle almost parallel to the skin. The object of this light scratch is to determine the texture of the skin which is subject to considerable variation.

(3) After determining the texture of the skin, increase the angle of the needle to the skin and make a further one-quarter inch scratch along the course of the initial light scratch. Increasing the angle of the needle to the skin increases the cutting power of the needle and up to four scratches may be made along the line of the original light scratch until the correct depth of scratch is obtained, after which the vaccine is rubbed into the scratch by using the flat side of the needle. If there is no congestion the amount of bleeding is negligible.

(d) *Dressing the vaccination site.* The vaccine is allowed to dry and the site is dressed as described in para 149(d).

152 Dosage Using Linear Scratch Method

(a) The dosage for primary vaccination in children and adults, for repeat vaccination in children and for revaccination in adults is a single linear scratch; the dosage for repeat vaccination in adults is two linear scratches.

(b) When one scratch is made in a repeat vaccination it should be at least one inch from the failed site.

(c) When two scratches are made in repeat vaccinations, one should be at least one inch from the failed site, the second should be on the other arm.

153 Reading, Interpretation and Recording of Results

Dependent upon the nature of the response, maximum reaction at the site may occur at any time from two to ten days after vaccination (see Table 9 below). Daily inspection is therefore desirable, but on grounds of practicability the number of inspections may be reduced to not less than two, which should then be made on the third or fourth, and on the sixth, seventh or eighth days after vaccination (see Tables 15 to 17 at paras 190 to 192).

Table 9 Response to vaccination*

	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)				
	The times given may vary considerably.				

*This table is reproduced by courtesy of the authors from 'Antisera, Toxoids, Vaccines and Tuberculins', 5th Edition, by H. J. Parish and D. A. Cannon, published by E. & S. Livingstone Ltd.

154 The effects observed are interpreted and recorded as follows:

(a) *When a vesicle or pustule has formed*

(1) If the subject has never been vaccinated before, the result will be recorded as '*Primary Vaccination* (*Successful*)'; this may be abbreviated as 'P.V.(S)' on Service documentation. On International certificates (para 36), the appropriate spaces are marked with an 'X'.
(2) If the subject has been vaccinated successfully before, the result will be recorded as 'Revaccination (Successful)'; this may be abbreviated as 'R.V.(S)' on Service documents. Success or otherwise of revaccination need not be recorded on International certificates.
(3) It should be noted that a fresh attempt at primary vaccination after failure is not a revaccination but a '*Repeat Vaccination*'.

(b) *When no vesicle or pustule is observed.* The subject is at once vaccinated again as described in para 150 and Tables 15 to 17 at paras 190 to 192; but more frequent inspection over a longer period is desirable. Then:
(1) On the occurrence of a vesicle or pustule the result will be recorded as shown at (a) above.
(2) If no vesicle or pustule is produced there may be a papule with itching of the site. This may be an indication of immunity; on the other hand it may merely be due to non-specific sensitivity and the first interpretation is not acceptable until a third attempt at vaccination has been made and inspected. If this also fails the individual may be shown as '*Insusceptible to Vaccination*', or 'I.T.V.', on Service documents only. Such 'insusceptibility' will not be considered as permanent, however, and future revaccination will be carried out as usually required (para 9(b)).

155 Protection Afforded by Vaccination

(a) Immunity acquired from vaccination is variable: revaccination with potent vaccine one year after a successful primary vaccination will yield a certain number of takes.

(b) Assuming correct technique and a potent vaccine, a satisfactory 'take' can be obtained in all non-immunes up to the first two to three days of incubation of an attack of smallpox. Once the rash appears less than 10 per cent can be vaccinated successfully.

(c) Successful vaccination with a vaccine of reduced potency will not confer protection in under three weeks unless the vesicle produced is more than one-half inch in diameter.

(d) International certificates of successful *primary* vaccination are valid on the eighth day for three years.

(e) International certificates of *revaccination* are valid at once for three years.

(f) International certificates of *failed primary* vaccination are valid for three years on conclusion of three consecutive attempts at vaccination.

156 Contraindications and Restrictions to Vaccination against Smallpox

(a) *Pregnant women*

(1) Under normal circumstances vaccination of pregnant women against smallpox is not to be carried out owing to the risk of foetal malformations. Under exceptional circumstances, such as contact with an actual case of smallpox, vaccination should be performed, but the patient should receive gamma globulin by intramuscular injection at the same time (para 233).

(2) *Under no circumstances* will pregnant women be vaccinated under cover of methisazone (Marboran), as this drug is contraindicated during pregnancy.

(b) *Infants.* Infants should not normally be vaccinated during the first year of life because at this time there is always a certain number of infants with an unstable nervous system who may die advertitiously after vaccination. If, however, there is a special risk of smallpox or a need to satisfy international certification it should be carried out, but then preferably not within the first three months.

(c) *Illness or poor health.* Vaccination should be postponed in individuals who are ill or in poor health or recovering from a febrile illness except in circumstances described in para 233.

(d) *Eczema*

(1) *If any individual, particularly an infant, has or has had atopic eczema, vaccination against smallpox will not be performed because of the risk of a generalised eczema reaction.*
(2) An eczematous person who has been in contact with smallpox should be protected by the administration of methisazone (Marboran) by mouth, or by post-vaccinial gamma globulin by intramuscular injection (para 157).
(3) Great care must be taken to ensure that an infant suffering from atopic eczema is not allowed contact with a vaccination performed on another person.

(e) *Local skin sepsis or allergy.* Vaccination against smallpox should be avoided or delayed in individuals who are suffering from local skin sepsis of the arm or an allergic illness until those conditions have been adequately treated.

(f) Vaccination against smallpox is contraindicated in persons who have a history of *convulsions*, or who are suffering from *leukaemia* or *hypogammaglobulinaemia*, or who are undergoing *cortiscosteroid therapy*.

(g) Precautions regarding the simultaneous use of smallpox vaccine and other vaccines are described in para 160.

157 Immunization of Contacts

(a) All persons, with the exception of those in para 156, who are known to have been in contact with a case of smallpox should be vaccinated or revaccinated at once.

(b) Those who have never been vaccinated before, or whose *vaccination history is considered unsatisfactory* (para 156), should also be given post-vaccinial gamma globulin by intramuscular injection or, except in pregnancy, methisazone (Marboran) by mouth.

158 Post-vaccinial gamma globulin

(a) Post-vaccinial gamma globulin is obtained from the plasma of recently vaccinated individuals and contains antibodies to vaccinia virus. The best dose has not yet been determined. In general 1·0 to 1·5 grammes may be given to adults and to children alike, but doses of 2·0 grammes or more may be desirable for unvaccinated close contacts. Limiting factors to increased dosage are availability and the large volume of liquid needed to dissolve big doses.

(b) Vaccination should, when practicable, precede injection of the gamma globulin by twelve to forty-eight hours: then interference with active immunization by the injected antibodies is unlikely and the vaccination should be successful; if it is not, vaccination should be repeated.

(c) When supplies of post-vaccinial gamma globulin to treat a group of susceptible contacts are limited, preference should be given to pregnant women, to infants under one year, to the previously unvaccinated and to those whose last successful vaccination was the least recent, in that order (para 233).

159 Methisazone (Marboran)

(a) The recommended dosage schedule by mouth is a loading dose of 200 mg/Kg followed by 400 mg/Kg given in divided doses over a period of 48 hours.

(b) The principle side-effect of the drug is vomiting which should be controlled by an anti-emetic drug.

(c) Methisazone may be used in the prophylaxis of vaccinia infections (para 157(b)) and in the protection of eczematous persons who have been in contact with smallpox (para 156(d)(2)). *Under no circumstances* are pregnant women to be vaccinated under cover of methisazone as this drug is contraindicated in pregnancy.

(d) The drug is indicated in the treatment of eczema vaccinatum and vaccinia gangrenosa. The prognosis of vaccinia gangrenosa is grave and the general condition of the patient must be maintained carefully to avoid disturbances in electrolytic balance and intercurrent bacterial infection.

160 Precautions Regarding the Simultaneous Use of Smallpox Vaccine and Other Vaccines

(a) *Yellow fever*

(1) When vaccination against smallpox and against yellow fever are both needed yellow fever vaccine should be given first. Vaccination or revaccination against smallpox may then follow after an interval of *not less than four days.*

(2) If, for any reason, primary vaccination against smallpox or revaccination which is followed by a primary type of response has been carried out first, yellow fever *will not be given* until twenty-one days have elapsed. When an individual has been vaccinated against smallpox first and a vaccinoid (accelerated) or immediate (immune) response has already occurred (para 153), yellow fever may be given without further delay.

(3) In an *emergency* smallpox revaccination of an individual showing evidence of previous successful vaccination may be carried out at the same time as yellow fever vaccination.

(b) *B.C.G. vaccination*

(1) There will be an interval of *ten days* between smallpox vaccination and B.C.G. vaccination, *irrespective of which is given first.*

(2) In special circumstances smallpox vaccination may be given at the same time as B.C.G. vaccination *provided the other arm is used* (para 117(1)).

(c) *Oral poliomyelitis vaccine.* Oral poliomyelitis vaccination can be given at the same time as smallpox vaccination in adults, but an interval of *seven days* should elapse between these vaccinations in children, whichever is given first.

(d) *All dead vaccines and toxoids.* An interval of *seven days* should elapse between smallpox vaccination and all dead vaccines and toxoids, except in an emergency, when one dead vaccine or toxoid may be administered at the same time as smallpox vaccination provided that the other arm is used.

(e) *Measles vaccine.* An interval of 4 weeks should elapse between smallpox and measles vaccination.

161 Reactions and Complications

Smallpox vaccination is liable to be followed by more complications than any other known vaccination. These affect particularly the skin, the eye and the central nervous system. Among the skin complications are generalised vaccinia, autogenous vaccinia, eczema vaccinatum and chronic progressive vaccinia or vaccinia gangrenosa. Vaccinial infections of the eye may be characterised by conjunctivitis, keratitis and blepharitis. Among the neurological complications, the most characteristic is the so-called post-vaccinial encephalitis.

162
163 } Reserved.

Section 16 Active immunization against yellow fever

164 The Vaccine

The vaccine used in the Services is a freeze-dried preparation of the attenuated 17D strain of yellow fever virus grown in chick embryos. The vaccine is reconstituted with cold sterile isotonic saline. Since it is very thermolabile this must be done immediately before use and any of the suspension which is not used within half an hour must be discarded. The vaccine is highly susceptible to heat even in the dried state and must be stored at 4°C or less, preferably at minus 10°C, when it remains effective for one year or such other period as may be notified by the manufacturer. When kept in a cool dark place, not over 15°C, it lasts for one month (para 242(a)). It must be transported under cold storage conditions.

165 Method of Vaccination

The vaccine is given by subcutaneous injection, the volume of saline added to the dried vaccine usually being such that the dose is contained in 0·5 ml. Only one injection is necessary.

166 Maintenance of Immunity and Restrictions on Vaccination against Yellow Fever

Immunity is considered to be established in ten days and lasts for at least ten years. Maintenance of immunity is described in para 15(a) and contraindications to vaccination in para 15(c).

167 Precautions Regarding the Simultaneous Use of Yellow Fever Vaccine and other Vaccines

The intervals normally to be observed between yellow fever vaccination and other immunological procedures carried out before or after it are given in para 189.

(a) *Smallpox vaccine.* Action when vaccination against yellow fever and against smallpox are both needed is described in paras 9(e) and 160(a).

(b) *Oral poliomyelitis vaccine.* Yellow fever vaccine and oral poliomyelitis vaccine may be administered at the same time.

(c) *B.C.G. vaccine.* An interval of ten days should elapse between the administration of yellow fever vaccine and B.C.G. vaccine, irrespective of which is given first.

(d) *Dead vaccines and toxoids.* A single dead vaccine or toxoid may be administered at the same time as yellow fever vaccine provided that the opposite arm is used.

168 Restrictions

Restrictions on the use of yellow fever vaccine are given in para 15(b).

169
170 } Reserved.

Section 17 Immunization against rabies

171 General

(a) In general immunization against rabies in man implies the prophylactic treatment of persons bitten by animals either manifestly rabid or suspected of being rabid, or persons otherwise directly exposed to the risk of infection with the virus of rabies.

(b) Individuals who have been bitten in the United Kingdom, Australia, Hong Kong or Singapore (or in Austria, the Netherlands, Norway, Portugal, Sweden or Switzerland), all of which have been free from rabies for some time, should only be given such treatment when there is incontrovertible evidence that the biting animal was suffering from rabies. Hence, normally, immunization against rabies is only necessary in the above-mentioned territories for recent arrivals who have been bitten elsewhere by an animal subsequently diagnosed as rabid. In those cases the time factor is most important and must be investigated, since if the dog remains normal for ten days or more (Table 10 at para 177) after inflicting the bite or licking a fresh break in the skin, or a mucous membrane, it can be accepted that it was not infective at the time and immunization of the person concerned is not required. The same conclusions can be drawn without precise knowledge of the daily health of the animal if it was still alive more than two weeks after any dangerous contact with the patient.

(c) In all cases it is most important that the biting animal be caught if possible and *held alive* for observation. It must not be killed as in most cases the need or otherwise for commencing immunization, or the indications for stopping it, are determined by the well-being or illness of the dog (para 177).

(d) All bite wounds, especially when there is a risk of rabies, should receive immediate local treatment consisting of thorough cleaning with soap, and flushing of the wound. When there is a risk of rabies this may be followed, where the site permits, by sponging the wound dry and carefully applying concentrated nitric acid into the depths of puncture wounds with a suitable applicator—such as a capillary pipette. This application may be followed by treatment with a solution of sodium bicarbonate. Where it can be avoided the bite wounds should not be immediately sutured.

(e) *In all cases of dog bites the additional risk of tetanus should be remembered* and appropriate action taken (para 202(c)).

(f) Vaccine treatment consists of a long course of daily injections of a rabies vaccine which in itself carries some risk (see below). While receiving a course the subject should live under as healthy conditions as possible. The avoidance of constipation, fatigue, violent exercise and alcohol is strongly recommended during and for ten days after such a course. In cases of more severe exposure to risk, vaccine treatment should be preceded by the injection of hyperimmune antirabies serum (paras 173, 176 and 177).

(g) The value of different types of vaccine, modified dosage schedules and methods of re-establishing immunity, should that become necessary, are subjects of current study and hence the recommendations that follow may later need some modification because of conclusions arising from such investigations.

172 Rabies Vaccines

(a) *Killed vaccines*

(1) *Semple type vaccines.* Killed vaccines of the Semple type consist of a killed phenolized suspension of fixed rabies virus in infected animal central nervous tissue usually prepared from rabbit brain and medulla. The vaccine may also be made from infected sheep or goat brain. Vaccines from different sources of production may have been prepared by methods which vary in detail; there may be differences in concentration of nervous tissue in them, and no wholly acceptable measure of standardization of potency of different vaccines has yet been achieved. Hence, in respect of certain vaccines of this type issued to stations overseas, the makers' instructions for use may differ to a slight extent from those given below. When that is so the manufacturers' recommendations should normally be followed.

(2) *Duck embryo vaccine.* A different type of vaccine has recently been developed. It consists of a killed suspension of fixed virus in infected duck embryos. Use of this vaccine may diminish the risk of nervous complications of treatment—the 'neuro-paralytic accidents'—which occasionally follow injections of Semple type vaccines and which are attributed to constituents of the nervous tissue present in them, and not to the killed rabies virus. Evidence is not as yet complete that duck embryo vaccine is as effective as nerve tissue vaccine. Hence, though both of these vaccines are available items of supply for the Services, duck embryo vaccine will, for the present, only be used in Service practice in the circumstances indicated in para 174 and in the note to Table 10 at para 177.

(b) *Attenuated vaccines.* The original Pasteur antirabies vaccine was a living attenuated virus in nervous tissue, where attenuation was effected by slow drying of the infected cords of rabbits. Attenuated vaccines are now, however, represented by chick embryo vaccines. These have been shown to be of value for immunizing animals and one of them—H.E.P. (high egg passage) Flury vaccine (a freeze-dried suspension of living modified rabies virus cultivated in chicken embryos)—has been tested in man. It has the advantage of being given in small doses by the intradermal route and in animals appears not to provoke neuro-paralytic accidents. It appears to be no better a protective antigen than killed vaccines, but is more variable in antigenicity. Live attenuated vaccines are not recommended and are not available in the Services.

173 Hyperimmune Antirabies Serum

Antirabies serum is usually produced by the hyperimmunization of horses, though serum has also been prepared from donkeys, mules and rabbits. Gamma globulin has been obtained as well from antirabies horse serum. An acceptable serum should contain 80 International units per ml. or more. Some refined concentrated sera contain as much as 200 units per ml. The serum normally used in the Services is refined and concentrated horse serum. As with all other antisera derived from the horse, *subcutaneous trial doses* with subsequent appropriate action as described in para 221 will always be carried out before full doses of antirabies serum are given.

174 Choice of Vaccine

(a) *Semple type vaccine*

(1) Semple type vaccine will generally be used for a first course of treatment with antirabies vaccine. Supplementary doses to the first course which are needed when such a course is combined with serum treatment will be with duck embryo vaccine (footnote to Table 10 and para 177).
(2) Local and general reactions to Semple type vaccine may occur and necessitate a change to duck embryo vaccine (see (b) below). Local reactions including some degree of redness, swelling, pain and pruritis may occur (para 175), but such signs and symptoms only indicate a need to change the type of vaccine if they are marked. Similarly headache, fever, general malaise, nausea or tingling sensations may herald the onset of nervous system sensitivity; treatment with nervous tissue vaccine should be stopped at once, if such reactions occur, and duck embryo vaccine be used for any further doses necessary to complete immunization.

(b) *Duck embryo vaccine*. Duck embryo vaccine will be reserved for use in the following circumstances:
(1) For the supplementary doses of vaccine given ten and twenty days after the last dose of the first course of injections, which are required when serum has also been given.
(2) When the patient is known or suspected to be sensitive to central nervous tissue vaccine.
(3) For all cases of revaccination of those who have received previous treatment with central nervous tissue vaccine, namely Semple type vaccine.
(4) When the patient appears to be developing local or central nervous system sensitivity to central nervous tissue vaccine (see (a) above).
(5) When treatment is being given for cases of only minor exposure such as licks on the recently abraded skin or on mucous membranes.
(6) Duck embryo vaccine should not be given to persons who are known to be sensitive to duck egg protein, except in cases of necessity, and then with special precautions.

175 Administration and Dosage of Vaccine

(a) Killed Semple type vaccine is normally injected into the subcutaneous tissue of the abdominal wall in daily doses for fourteen days. Care must be taken not to inject the vaccine into a vein. The volume of each dose is that recommended by the manufacturer and is commonly 2 ml. Patients under twelve years of age are normally given doses of one-half to three-quarters of the adult dose. The vaccine container must be thoroughly shaken to ensure an even distribution of the contents before withdrawing each dose.

(b) It is usual to give the first injection subcutaneously into the abdominal wall on one side over the rectus muscle about two inches below the margin of the ribs. Further injections are then given on alternate sides progressing down the abdomen.

(c) Since injections are given daily and local redness, swelling and pain may occur, it is inadvisable to repeat injections into the same spot. If the local reaction in the abdominal wall becomes uncomfortably severe, as may occur in thin persons, or persons wearing tight clothing, the vaccine may be injected subcutaneously into the arms, at

the insertion of the deltoid muscle or into the legs, at the junction of the upper and middle thirds on the outer aspect of the thigh.

(d) When serum is given concurrently with vaccine it is important to continue injections of vaccine until at least the fourteenth day in order to avoid interference by the serum with the production of active immunity. For the same reason it is equally important to administer the serum early and to give a full dose in the course of one day. Further doses of serum should *not* be given at a later date.

(e) Courses of treatment will be terminated before the full number of injections have been given if the subsequent history of the biting animal shows that it was not rabid at the time the subject was bitten (Table 10).

176 Dosage and Route of Administration of Serum

(a) When serum treatment is indicated to supplement vaccination, it must be given as early as possible (Table 10). If the interval between infliction of the bites and serum treatment is longer than twenty-four hours, larger doses, up to two or three times as great as those indicated below, have been recommended.

(b) When possible not less than 5 ml. should be infiltrated under and around the bite wounds. In sites such as the hand or face only a much smaller local dose can be tolerated.

(c) General serum treatment should also be given, consisting of the intramuscular or subcutaneous injection of not less than 40 International units per kg. (=25 I.U. per lb.) body weight. If the volume is likely to cause discomfort the dose may be divided and parts of it be injected at different sites. The total dosage must be given in as short a time as possible. This period of time must be less than twenty-four hours. Divided doses must *not* be separated by any considerable time interval as this may interfere with the response to concurrent vaccination (para 174).

(d) The first dose of vaccine should follow the administration of serum without delay, unless otherwise indicated, under appropriate circumstances, in para 177.

177 Indications for the Use of Rabies Vaccine and Antirabies Serum

(a) Table 10 which follows is based on that given in the World Health Organization Technical Report No. 321, 1966, by the Expert Committee on Rabies.

(b) Serum is recommended after *all* bites by dogs which are other than apparently healthy. Distinction in treatment between severe and relatively trivial bites is only retained for those inflicted by apparently healthy dogs, when serum is advised for severe bites but not for trivial ones. The table also contains a distinction not made in the World Health Organization Report: namely, that when a person has been licked by a rabid animal on pre-existing cuts or abrasions, treatment is only needed if such wounds are fresh, open, or raw. When pre-existing cuts and abrasions are known to have been protected by a scab, or were more than twenty-four hours old at the time, their having been licked does not necessitate immunization against rabies. When treatment for licks is needed, the vaccine used should preferably be duck embryo vaccine (para 174(b)).

Table 10 Guide for specific post-exposure treatment of rabies

Nature of exposure	Status of Biting animal		Recommended specific treatment
	At time of exposure	During observation period of 10 days	
I No lesion			
Indirect contact	Rabid	—	None.
II Licks			
(1) Unabraded skin; pre-existing cuts or abrasions over 24 hours old or covered by a scab	Rabid	—	None.
(2) Fresh, raw, or open pre-existing wounds or abrasions of skin; abraded or unabraded mucosa	(a) Healthy	Clinical signs of rabies or proven rabid (laboratory)	Start vaccine at first signs of rabies in the animal.
	(b) Signs suggestive of rabies	Healthy	Start vaccine immediately; stop treatment if animal normal on fifth day after exposure.
	(c) Rabid, escaped, killed or unknown	—	Start vaccine immediately.
III Bites	(a) Healthy	Clinical signs of rabies or proven rabid (laboratory)	If bites are severe (multiple or face, head, finger or neck bites) give serum immediately; this is not necessary for trivial bites. In *all* cases start vaccine at first sign of rabies in the biting animal.*
	(b) Signs suggestive of rabies	Healthy	Serum immediately; followed by vaccine; vaccine may be stopped if animal is normal on fifth day after exposure.
	(c) Rabid, escaped, killed or unknown (d) Wild (wolf, jackal, fox, bat or other wild animal)	—	Serum immediately; followed by vaccine.*

* Course of vaccine given after serum treatment should be followed by supplementary doses of vaccine, which should if possible be duck embryo vaccine (para 174), ten and twenty days after the last usual dose.

178 Re-establishment of Immunity

When an individual is exposed to the risk of rabies infection for a second time, having had a course of vaccine previously in connection with an earlier exposure, there is, in most cases, an adequate response to one or two reinforcing doses of vaccine. However, a small proportion of cases show little or no response, and it is not, therefore,

entirely safe to rely upon one or two doses for reinforcement of immunity. A full second course is thus indicated. On the other hand if Semple type vaccine was used for the first course the risk of a neuro-paralytic accident if it is used again would seem to be increased. Duck embryo vaccine should therefore be used for such cases (para 174(b)).

179 Reactions and Complications

Local reactions are given in para 174(a)(2). Neuro-paralytic reactions of varying severity are comparatively common after anti-rabies vaccination. Unlike smallpox vaccine, which may give rise to encephalitis, rabies vaccine tends to affect the spinal cord, giving rise to dorso-lumbar myelitis, acute ascending myelitis of the Landry type, encephalo-myelitis and peripheral neuritis (see paras 174(a)(2) and 64).

180
181 } Reserved.

Section 18 Notification of untoward effects of vaccinations, or of other immunological procedures

182 Definition

The following are to be considered untoward effects after any immunological procedure: local sepsis, skin necrosis or ulceration, generalised vaccinia, eczema vaccinatum or vaccinia gangrenosa, severe pyrexia, neurological symptoms, or any reaction attributable to the preceding vaccination, inoculation, or skin test which requires the admission of the subject to hospital or causes him to be unfit for full duty for longer than forty-eight hours.

183 Procedure

(a) When any of the above-mentioned conditions arise following a vaccination or other immunological procedure, a full report will be made at once to the appropriate addressee ((b) below) in accordance with the proforma at Table 11.

Table 11 Specimen form for reporting untoward effects

Note—This report will be completed in duplicate.
One copy is for the appropriate Service Directorate.
One copy for F Med 9.

MEDICAL-IN-CONFIDENCE

Reports: Immunological Procedures

Ref. Section 18

'Memorandum on Immunological Procedures (J.S.P. 311)'

A report on the u/m is submitted

No. ..... Rank ..... Name .....

Age ..... Unit.....

(a) Immunizing Agent .....

(b) Manufacturers or original distributors.....

(c) Batch No. or other identification details.....

(d) Date of receipt of the agent.....

(e) Conditions of storage after receipt.....

(f) Date of Administration .....

(g) Date of onset of symptoms .....

(h) History of other recent vaccinations if relevant.....

.....

(i) Clinical description of the case.

(j) Number vaccinated or re-vaccinated.

Date.....

.....
Signature of Medical Officer

(b) *Appropriate addressees* to whom reports should be sent are:

Addressee	*Route*
Royal Navy	
Medical Director General (Naval), Ministry of Defence, Empress State Building, London, SW6	Direct.
or *Army*	
The Director of Army Pathology, Ministry of Defence (AMD 7), London, SW1	Through D.D.P. or A.D.P. ..... Command.
or *Royal Air Force*	
Ministry of Defence MA4 (RAF), Tavistock Square, London, WC1	Direct.

184
185 } Reserved.
186

Section 19 Summary of vaccinations

The following abbreviations are used in the tables:

ID	intradermal
SC	subcutaneous
IM	intramuscular
P.Vacc.	primary vaccination
Maint.	maintenance

187 Table 12 Adults and children of thirteen years and over

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Enteric Fever	T.A.B.T. (ID)	3 doses each of 0·1 ml.	(*a*) Between 1st and 2nd: 4 to 6 weeks (*b*) Between 2nd and 3rd: 6 to 12 months	ID	T.A.B.T. (ID) T.A.B. (1D)	0·1 ml.	3 years except when at special risk, then 1 or 2 years.	ID	(1) Routine for Servicemen and Servicewomen. (2) Maint. continued until age 35 (not needed for families not at risk)	12 and 67–71
Tetanus (under 35 years of age)	As for Enteric Fever				As for Enteric Fever				As for Enteric Fever	13 and 75–77
Tetanus (over 35 years of age)	Not applicable generally				T.T.	0·5 ml.	5 years	SC	After the age of 35 years, protection and maintenance will be by T.T.	76

Adults and Children of thirteen years and over—*continued*

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Poliomyelitis	Oral poliomyelitis 'Sabin' type vaccine.	3 doses each of 3 drops	4 to 8 weeks	Oral	See paragraphs 14(b), 84(d) and (e)				(1) Routine for Servicemen and Servicewomen. (2) For procedure in respect of those already partially immunized with 'Salk' vaccine (para 14(a))	14 and 81–86
Diphtheria	FT	3 doses each of 0·5 ml.	(a) Between 1st and 2nd: 6 weeks (b) Between 2nd and 3rd: 6 to 12 months	SC or IM					(1) Routine for all Schick positive new entrants *if not pseudo reactors* (paras 10(b) and 94). (2) A further Schick test will precede the 3rd dose of vaccine unless the vaccination is truly primary and no undue reaction has followed the first or second dose (para 96(a))	10 and 90–98
Tuberculosis	Freeze-dried B.C.G.	1 dose of 0·1 ml.		ID	Revaccination as indicated by reversion to tuberculin negative on periodic testing				(1) Routine for all tuberculin negative new entrants. (2) Heaf test for reversion, after vaccination conversion, every 5 years under normal service conditions (para 106(c))	11 and 102–121

Adults and Children of thirteen years and over—*continued*

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Smallpox	Freeze-dried vaccine *or* Glycerinated lymph	1 insertion of 10 pressures *or* 1 scratch ¼″ long		Multiple pressure *or* Linear scratch	Revaccination with one insertion of 30 pressures every 3 years *or* Revaccination with 1 scratch ¼″ long every 3 years				(1) In the face of special risk: (*a*) Increased number of insertions and/or pressures or scratches are needed (para 150). (*b*) Special revaccination may be ordered (para 9(b)) (2) If P.Vacc. fails it is repeated using 30 pressures or 2 linear scratches (para 150). (3) Vaccination of pregnant women (other than those at special risk) will not be undertaken (para 156)	9 and 147–160
Cholera	Cholera vaccine	1 dose of 0·5 ml. *or* 1 dose of 0·1 ml.		SC *or* ID	Cholera vaccine	0·5 ml. *or* 0·1 ml.	Every 6 months while at risk	SC *or* ID	(1) Travellers to Far East via India and Pakistan: otherwise when specially ordered. (2) 2 doses of 0·5 ml. and 1·0 ml. subcutaneously *or* 2 doses of 0·1 ml. intradermally at an interval of 7–28 days is advised when proceeding to a country where cholera is epidemic	18 and 125–129

Adults and children of thirteen years and over—*continued*

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Plague	Killed avirulent plague vaccine	2 doses: 1st 0·5 ml. 2nd 1·0 ml.	10 to 28 days	SC	Killed avirulent plague vaccine	0·5 ml.	Every 6 months while at risk	SC	When specially ordered	17 and 133–136
Typhus	Killed typhus vaccine (epidemic and murine)	3 doses each of 1·0 ml.	7 to 14 days between 1st and 2nd and between 2nd and 3rd doses	SC	Killed typhus vaccine (epidemic and murine)	1·0 ml.	(*a*) *In endemic areas:* annually (*b*) *During epidemic:* every 3 months	SC	When specially ordered	16 and 140–143
Yellow Fever	Yellow fever vaccine (chick embryo 17D)	Usually 0·5 ml. after reconstitution		SC	YF vaccine (chick embryo 17D)	0·5 ml.	Every 10 years	SC	(1) Persons proceeding through, entering, residing in, or leaving yellow fever endemic areas. (2) Pregnant women and children under one year of age should not normally be vaccinated (para 15(c))	15 and 164–167

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Enteric Fever	T.A.B. (dilute)	3 doses: 1st 0·2 ml. 2nd 0·4 ml. 3rd 0·2 ml.	(*a*) Between 1st and 2nd: 4 to 6 weeks (*b*) Between 2nd and 3rd: 6 months or on arrival overseas, whichever is sooner	SC	Still under 13: T.A.B. (dilute) *or* 13 and over: T.A.B. (ID)	0·2 ml. *or* 0·1 ml.	Annually while at risk	SC *or* ID	(1) Only needed when at risk. (2) Reduced doses for underweight children or following an undue reaction to an earlier injection. (3) No Maint. when not at risk. (4) Infants under 1 year not vaccinated	12 and 67–71
Tetanus	DT	3 doses each of 0·5 ml. (or as on label)	(*a*) Between 1st and 2nd: 4 weeks (*b*) Between 2nd and 3rd: 6 months	SC or IM	DT	1st: 0·5 ml. 2nd: 0·5ml.	At school entry At age 8 or 9	SC or IM	(1) If DT used, 1st dose at 10 months old: Pertussis vaccine separately and earlier. (2) If D.T.P. used, 1st dose at 6 months old. (3) Maint. doses may be reduced to 0·1 ml. if sensitivity suspected. (4) Older children already immunized against diphtheria, and others to whom combined prophylactics are not given, may be immunized against tetanus alone by use of TT as for adults (*see* remarks column in para 187)	13, 90, 98 and 75, 77
	or D.T.P.	4 doses each of 0·5 ml. (or as on label)	*or* (*a*) Between 1st and 2nd and between 2nd and 3rd: 4 to 6 weeks (*b*) Between 3rd and 4th: One year	*or* SC or IM	TT	3rd and later doses: 0·5 ml.	5 years after last DT and every 5 years thereafter.	SC		

Children under thirteen—*continued*

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Diphtheria	DT or D.T.P.	As against tetanus (above)							(1) FT may be used to immunize against diphtheria alone, if indicated. P.Vacc., as for adults; Maint. doses, also of FT, at school entry and at 8–9 years (full or reduced dose; note (3) tetanus). (2) Up to age 12 years Schick test may be omitted in U.K. before P.Vacc. against diphtheria	10 and 90–98
Poliomyelitis	Oral poliomyelitis vaccine	3 doses each of 3 drops	4 to 8 weeks	Oral	*See* para 84	At school entry and when at special risk		Oral	See paras 14 and 84	14, 81–86
Tuberculosis	Freeze-dried B.C.G.	1 dose of 0·1 ml.		ID	Revaccination as indicated by reversion to tuberculin negative on periodic testing				(1) Tuberculin negative reactors only. (2) Indications for B.C.G. vaccination of children under varying circumstances *see* paras 120–121	11 and 102–121

Children under thirteen—*continued*

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Smallpox	Freeze-dried vaccine *or* Glycerinated lymph	1 insertion of 30 pressures *or* 1 scratch ¼″ long		Multiple pressure *or* Linear scratch	Revaccination with one insertion of 30 pressures every 3 years *or* Revaccination with 1 scratch ¼″ long every 3 years				(1) P.Vacc. never before 3 months, normally in 2nd year (para 9(*d*)). (2) In face of special risk after 3 months old use 2 or 3 insertions of 30 pressures each	9 and 147–160
Cholera	Cholera vaccine	1 dose *Age 1 to 5:* 0·25 ml. *5 years and over:* 0·5 ml. *or* *Over 5 years:* 0·1 ml.		SC *or* ID	Cholera vaccine	0·5 ml. *or* 0·1 ml.	Every 6 months while at risk	SC *or* ID	(1) Under 5 years ID not recommended. (2) When exposed to risk and when necessary for travel. (3) Generally infants under 1 year are not vaccinated, but doses as for those aged 1 to 5 may be given if desired. (4) 2 doses of 0·5 ml. and 1·0 ml. subcutaneously *or* 2 doses of 0·1 ml. intradermally, at an interval of 7–28 days, is advised when proceeding to a country where cholera is prevalent	18 and 125–129

Children under thirteen—*continued*

Disease	Primary vaccination				Maintenance or reinforcement				Remarks	Paragraphs giving detailed information
	Vaccine	Dose	Interval between doses	Route of administration	Vaccine	Dose	Interval between doses	Route of administration		
Plague	Killed avirulent plague vaccine	2 doses: *Age 1 to 5:* 1st 0·1 ml. 2nd 0·2 ml. *Over 5 years:* 1st 0·25 ml. 2nd 0·5 ml.	10 to 28 days	SC	Killed avirulent plague vaccine	As 1st P.Vacc. dose for age	Every 6 months while at risk	SC	(1) When exposed to risk. (2) Infants under 1 year are not vaccinated	17 and 133–136
Typhus	Killed typhus vaccine (epidemic and murine)	*Age over 1 year:* 3 doses each of 1·0 ml.	7 to 14 days between 1st and 2nd and between 2nd and 3rd doses	SC	Killed typhus vaccine (epidemic and murine)	1·0 ml.	(*a*) *In endemic areas:* annually. (*b*) *During epidemic:* every 3 months	SC	(1) When exposed to risk. (2) Infants under 1 year are not vaccinated	16 and 140–143
Yellow Fever	Yellow fever vaccine (chick-embryo 17D)	*Age over 1 year:* Usually 0·5 ml. after reconstitution		SC	Yellow fever vaccine (chick-embryo 17D)	0·5 ml.	Every 10 years.	SC	(1) Needed for travel purposes—older children as for adults. (2) Only in very exceptional circumstances will infants under 1 year and *more particularly those under 2 months* be vaccinated. Vaccination is *not* generally required for travel purposes for those under 1 year old	15 and 164–167

Measles

Section 20 Immunization time-tables

189 Table 14 Intervals between the administration of different antigens

Where antigen given first is	Interval which should elapse before giving						
	Yellow fever vaccine	Smallpox vaccine	B.C.G.	Oral Poliomyelitis vaccine	Measles vaccine	Dead vaccine or toxoid	P.P.D. (Heaf Test)
Yellow fever vaccine	—	4 days (infants under 1 year—21 days)	10 days	None	4 weeks	None‡	14 days§
Smallpox vaccine	21 days*	—	10 days†	7 days‖	4 weeks¶	7 days†	14 days§
B.C.G.	10 days	10 days‡	—	None	4 weeks	None‡	—
Oral Poliomyelitis vaccine	None	7 days‖	None	—	None	None	None
Measles vaccine¶	4 weeks	4 weeks	4 weeks	None	—	14 days	4 weeks
Dead vaccine or toxoid	None‡	7 days†	None‡	None	14 days	—	None‡
P.P.D. (Heaf Test)	7 days§	7 days§	—	None	4 weeks	None‡	—

* Unavoidable when the smallpox vaccination was primary. If that is not known—or if it was a revaccination after a long interval so that a primary type of response is likely—time must be allowed for the nature of the response to become apparent. A primary response will then show that the full 21 days interval is necessary; a more rapid one, that (when the matter is urgent) the yellow fever vaccine may be given without further delay (para 160(a)). In an emergency revaccination against smallpox and vaccination or revaccination against yellow fever may be given at the same time.

† In rare circumstances smallpox vaccine may be given at the same time provided the other arm is used.

‡ Use the other arm.

§ May be given at the same time in certain circumstances.

‖ May be given at the same time in adults.

¶ Measles vaccination should precede smallpox vaccination.

190 Table 15 A ten week immunization programme including yellow fever vaccination for Service personnel

Week	Monday	Friday
1		Smallpox vaccination* Schick Test. Oral Poliomyelitis I.
2	Inspect smallpox vaccination. Read Schick Test.	Repeat smallpox vaccination if necessary. Re-read Schick Test.
3	Inspect repeated vaccination, if necessary.	Re-inspect repeated vaccination, if necessary.
4		Heaf Test. FT I if necessary.
5		Read Heaf Test. T.A.B.T. I. Oral Poliomyelitis II.
6		B.C.G. if required. Cholera*: other arm.
7		—
8		Yellow fever*.
9		FT II if necessary.
10		T.A.B.T. II. Oral Poliomyelitis III.

* International Certificates required.
FT refers to diphtheria formol toxoid.

191 Table 16 A seven week immunization programme excluding yellow fever vaccination for Service personnel

Week	Monday	Friday
1		Smallpox vaccination*. T.A.B.T. I: other arm. Schick Test. Oral Poliomyelitis I.
2	Inspect smallpox vaccination. Read Schick Test.	Repeat smallpox vaccination if necessary. Re-read Schick Test. FT I if necessary.
3	Inspect repeated vaccination, if necessary.	Re-inspect repeated vaccination, if necessary. Oral Poliomyelitis II.
4		Heaf Test. T.A.B.T. II: other arm.
5		Read Heaf Test.
6		B.C.G. if required. Cholera*: other arm.
7		FT II if necessary. Oral Poliomyelitis III.

* International Certificates required.
FT refers to diphtheria formol toxoid.

192 Table 17 Alternative schemes for rapid primary immunization of travellers

Day	Yellow fever given before smallpox	Smallpox given before yellow fever.
1	Yellow fever* and Oral Poliomyelitis I.	Smallpox* and T.A.B.T. I: opposite arms.
8	Smallpox* and T.A.B.T. I: opposite arms.	Oral Poliomyelitis I. Inspect smallpox vaccination and repeat *if necessary*.
15	Cholera*. Inspect smallpox vaccination and repeat *if necessary*.	—
22	—	Yellow fever* and Cholera*: opposite arms.
29	T.A.B.T. II and Oral Poliomyelitis II.	T.A.B.T. II and Oral Poliomyelitis II.

* International Certificates required.

193 Table 18 Emergency immunization programme for travellers

Day 1	Yellow Fever*. Cholera*.
Day 5	Smallpox*.

* International Certificates required.

Malarial prophylaxis

The need for malarial prophylaxis in many subtropical and tropical countries *must not be overlooked.*

194 Table 19 Dates for vaccination from infancy to school-leaving age

(A) Strongly recommended for all children

Age	Vaccine	Route of Administration	Interval
6 months	Diphtheria-Tetanus-Pertussis	IM or SC	4–6 weeks between each of 3 doses.
	Oral Poliomyelitis	Oral	4–8 weeks between each of 3 doses.
2 years	Measles*	SC	—
2 years (after third month in cases of risk or for international certification)	Smallpox†	MP or Linear Scratch	—
School Entry or at 5 years	Diphtheria-Tetanus (if primary)	IM or SC	4–8 weeks between each of 3 doses.
	Diphtheria-Tetanus (if revaccination)	IM or SC	1st at School Entry. 2nd at 8–10 years.
	Smallpox	MP or Linear Scratch	—
	Poliomyelitis	Oral	—
Girls 11–14 years	Rubella	SC	One dose only.
School Leaving or at age 15–19 years	Poliomyelitis Tetanus Toxoid Smallpox	Oral SC MP or Linear Scratch	— —

(B) Additional Vaccination for special circumstances including travelling and residence outside the United Kingdom

Minimum age	Vaccine	Note
1 week after birth	BCG	When necessary.
12 months (between 3 and 12 months only in cases of risk or for international certification)	Yellow fever†	When necessary.
12 months	TAB (Dilute)	When necessary.
12 months	Cholera†	When necessary.
12 months	Plague	When necessary.

* Measles vaccination should precede smallpox vaccination by at least four weeks.
† International Certificates required.

195 Notes on Immunization Tables

(a) The suggested immunization programmes set out above follow so tight a time-table that vaccination against Plague or Typhus cannot be included. If immunization against Plague and/or Typhus is also needed to safeguard the individual, courses of these vaccines should follow after completion of the recommended schedules.

(b) The time intervals given above are in some instances shorter than those prescribed in para 189. They are thus not fully satisfactory from the immunological standpoint and longer intervals complying with that table will always be used when time permits.

(c) Every traveller will not need all the vaccinations mentioned in the foregoing time-tables and medical officers concerned will adjust the programme as necessary to comply with each individual's requirements.

(d) In order to avoid, as far as possible, the need to apply immunologically unsatisfactory foreshortened schemes, steps should be taken by the persons concerned, and by their medical officers, to ensure that the immunization state of all those individuals (Service personnel and Ministry of Defence sponsored civilians) who are liable to travel at short notice, is always kept up to date. This applies particularly to vaccinations necessary to satisfy International Travel Regulations (paras 4 and 33–38).

196
197 } Reserved.
198

Section 21 Prevention of tetanus

Introduction

199 Policy

The policy of Service Medical Directorates concerning the treatment of wounds and abrasions potentially infected with tetanus is as follows:

(a) Active immunization is the only measure which affords reliable protection against tetanus. *Universal active immunization should be the ultimate goal* (sections 7, 8 and 10).

(b) The treatment of an individual will always be decided by the doctor in clinical charge of the patient.

(c) Tetanus antitoxin *should not be used to protect those who already have an established basic immunity against tetanus*, as they can secure adequate reinforcement by a single injection of tetanus toxoid.

(d) If the patient has *no* established basic immunity against tetanus, the use of tetanus antitoxin will need to be considered. There are known to be hazards in the use of, as well as in the withholding of, antitoxin.

(e) Where there is reason to believe that surgical toilet cannot be, or has not been complete, or where there has been delay in treatment, the use of tetanus antitoxin should certainly be considered.

(f) When thorough wound treatment is possible without delay, reliance should be placed on wound toilet and the use of antibiotics. An injection of a combined short- and long-lasting penicillin should be given at once, and penicillin treatment continued until the wound is healed. An oral tetracycline should be used if the patient is sensitive to penicillin. If such antibiotic treatment is given, specific prophylaxis should be confined to giving tetanus toxoid in all cases and the course completed where necessary. Responsible medical opinion would certainly accept this as a reasonable course, and it is recommended.

(g) When antitoxin is given, it is desirable to *initiate active immunization at the same time*, by the injection of *adsorbed tetanus toxoid* (as opposed to the standard fluid tetanus toxoid). Every effort should be made to encourage the patient subsequently to complete the course of active immunization by further injections of toxoid (which may be either adsorbed or standard fluid tetanus toxoid, preferably the latter). This is important for those who may be involved in later accidents (para 207). A patient who has been sensitized to horse serum may derive little protection from subsequent injections of equine tetanus antitoxin (section 23).

(h) In cases where tetanus antitoxin is indicated, a horse serum preparation will almost always be appropriate, but if available, human anti-tetanic gamma-globulin (ATG) should be used.

200 Inconspicuous lesions

It is recognised that the tetanus bacillus can infect and multiply in inconspicuous lesions. Although any prick or surface abrasion, however insignificant, might ultimately prove to be a source of tetanus infection, the Service Medical Directorates consider that it is not reasonable to require that every person who has received trivial pricks and abrasions should be given either antitoxin, antibiotics or tetanus toxoid.

Tetanus antitoxin

201 Tetanus antitoxin (equine)

Tetanus antitoxin (anti-tetanus serum or A.T.S.) is prepared by immunizing horses with tetanus toxoid followed by tetanus toxin. The plasma or serum collected from these animals is refined and concentrated.

202 Indications for prophylactic use of tetanus antitoxin

(a) Tetanus antitoxin should be given to prevent tetanus developing following wounds or injuries *when the patient is non-immune and the injury is such as to give rise to the risk of tetanus*. When the injury is of that nature, but the patient is immune, vaccination against tetanus having been carried out and maintained as described in para 13 and sections 7, 8 and 10, tetanus antitoxin *will not normally* be given. The patient will generally receive a further reinforcing dose of tetanus toxoid.

(b) Only when the injury is associated with *severe and prolonged shock*, as a result of which response to a special reinforcing dose of toxoid may be poor, should the use of antitoxin as well be considered *for those immune cases whose level of circulating antibody may have waned.* Such lowered immediate protection need only be anticipated as likely more than six months after the first two doses of toxoid or more than three years after the third. The problem should therefore not arise in the field, since special provisions have been made to avoid it by advancing the times of giving the third and fourth doses before active service—while retaining the further reinforcing dose on wounding (para 13(c)).

(c) A definition of 'non-immune', and guidance concerning types of injury associated with a risk of tetanus, follow:

(1) *The non-immune patient.* In considering the need for passive prophylaxis against tetanus those whose immunity is incomplete or has lapsed will be treated as non-immune. Those who have never been vaccinated against tetanus and those who have only had two doses of tetanus toxoid are so defined.

(2) *The injury is associated with a risk of tetanus.* Wounds more than three or four hours old, especially if they are already infected with pyogenic organisms and fresh wounds, however small, when they are deep or penetrating and may have been contaminated with manure or road dirt, or contain a foreign body; when they are deep and cannot be closed properly; when they are associated with devitalization of adjacent tissue such as crush injuries, and cases of dog bites (para 171), may all be associated with a risk of tetanus.

(3) *Tetanus terrain.* Wounds acquired in areas where tetanus is encountered.

(4) *Surgery involving old wounds.* The possibility should also be borne in mind that surgical intervention involving previously injured tissue may carry a risk of tetanus, due to latent spores in that tissue, to those subjected to such treatment who are non-immune.

203 Cases for which tetanus antitoxin is usually not needed

Fresh superficial wounds and abrasions should not give rise to a risk of tetanus if adequately cleaned and dressed. The local incidence of tetanus should, however, be considered (para 202(c)) and risk of tetanus may supervene, indicating a need for tetanus antitoxin.

204 Dosage of tetanus antitoxin and precautions against reactions

Non-immune persons, as defined in para 202(c)(1), suffering from such injuries described in para 202(c)(2, 3 and 4), should be given a dose of 1,500 International units of tetanus antitoxin by intramuscular or subcutaneous injection. *Precautions against untoward reactions must be taken as described in section* 23. Except in the case of an individual who has had previous injections of serum, including serum-vaccine preparations such as Diphtheria T.A.F., when the dose may be raised to 10,000 units (para 225), the dose of 1,500 International units should generally suffice. However, similar doses may be given at weekly intervals if considered necessary, in the light of clinical progress, by the surgeon in charge.

205 Duration of effect of tetanus antitoxin: after-treatment

The protective effect of an injection of tetanus antitoxin is generally at its height in two or three days. It may be adequate for about two weeks, but has become slight before three weeks have passed. Since one treatment with antitoxin is liable to render the future use of antitoxin of less value (para 225), the last dose of it given on such a first occasion must be accompanied by adsorbed tetanus toxoid (para 207) or must be followed after six to eight weeks by the first dose of a course of active immunization against tetanus by either T.A.B.T. or tetanus toxoid.

206 Human anti-tetanic globulin

Human anti-tetanic globulin (A.T.G.) may be increasingly available and should then be used instead of equine anti-tetanus serum (A.T.S.), in doses of 250 to 500 units.

Adsorbed tetanus toxoid

207 Adsorbed tetanus toxoid

(a) *The reason for using adsorbed tetanus toxoid.* The protective effect of tetanus antitoxin is comparatively short-lived (para 205). It is therefore necessary to commence active immunization against tetanus as soon as possible. The active response to tetanus toxoid (para 13 and paras 75 to 77) is interfered with by the administration of tetanus antitoxin and this prophylactic must be delayed *at least* six weeks after an injection of tetanus antitoxin. The active response to *adsorbed tetanus toxoid* is not impaired by the presence of circulating tetanus antiserum and can hence be given simultaneously *without the six weeks delay.*

(b) *Adsorbed tetanus toxoid* is ordinary fluid tetanus toxoid adsorbed on aluminium hydroxide and is satisfactory in that it is not eliminated rapidly, but acts over a much longer period of time.

(c) *The advantages of adsorbed tetanus toxoid* lie entirely in its superiority for the *first injection which may be given simultaneously with tetanus antitoxin.* While there is little to choose between adsorbed tetanus toxoid and ordinary fluid tetanus toxoid, the latter is preferred for primary vaccination and reinforcement injections as there is a tendency for the adsorbed preparation to give a slightly higher incidence of local reactions.

(d) *Subsequent immunization.* Second and third injections, following *simultaneous A.T.S.* and *adsorbed tetanus toxoid* injections may be of either adsorbed or fluid tetanus toxoid, but the latter is to be preferred for the reason stated in sub-para (c) above.

(e) *Dosage.* The dose of adsorbed tetanus toxoid is 0·5 ml. administered subcutaneously. For primary immunization, two doses at an interval of six to twelve weeks are required. A third injection should follow one year later.

208
209 } Reserved.
210

Section 22 Combined active and passive immunization against diphtheria in the event of an outbreak

211 Indications

(a) The policy in the Services is active immunization against diphtheria of all dependent children, together with all adults and children over twelve years of age who give a *positive* reaction to the Schick test (see section 10). The likelihood of an outbreak of diphtheria in a susceptible group in the Services such as a school, hospital or similar institution is therefore remote.

(b) Active and passive immunization against diphtheria may be required in the following circumstances:
(1) For contacts of cases of diphtheria unless such contacts are known to be immune.
(2) For persons who are not known to be immune and who are at risk during explosive outbreaks of diphtheria.

(c) When, in such circumstances, the susceptibility of an adult or child over twelve years of age to diphtheria is unknown, it may be *inadvisable* to incur the delay involved in awaiting the result of a preliminary Schick test (paras 90 to 93) to determine the degree of risk, before concomitantly giving prophylactic antitoxin and adsorbed diphtheria toxoid.

212 Combined active and passive immunization

(a) This method is of particular value when a case of diphtheria develops in a group of susceptible individuals in a school, hospital or other institution where the extent and distribution of the infective agent is unknown, or when further introduction of infection is to be anticipated.

(b) In these circumstances passive immunization alone, which wears off in two to three weeks, may be followed by the appearance of diphtheria cases due to infection from healthy carriers.

(c) Combined active and passive immunization consists of giving simultaneous injections *into opposite arms* of diphtheria antitoxin and *adsorbed* diphtheria toxoid followed two to four weeks later by a second dose of *adsorbed* diphtheria toxoid, thus stimulating active immunity under cover of a passive immunity.

213 Dosage

(a) The prophylactic dosage of refined serum diphtheria antitoxin is 500 units given intramuscularly.

(b) Alum-precipitated (adsorbed) diphtheria toxoid (A.P.T.) is administered deep subcutaneously or intramuscularly in two doses of 0·5 ml. at an interval of two to four weeks.

214 Bacteriological control of the outbreak and isolation of carriers

The combined active and passive immunization results in only a transitory protection of exposed individuals until the second dose of A.P.T. has been administered. There is an intermediate period of relative susceptibility between the wearing off of the passive and the development of the active immunity, and it is therefore necessary to take throat swabs from the entire population at risk and to segregate all carriers from whom virulent organisms are isolated. This isolation should continue until fourteen days after the completion of the *second* dose of A.P.T. By this time active immunity in the remainder of the community will have developed to such an extent that the risk of further cases occurring would be remote. If, of course, the carriers have become negative under treatment within this time, they can be allowed to return to the community.

215 Summary of action

(a) Swab the entire community.

(b) Active and passive immunization of all contacts without evidence of previous immunization.

(c) Segregate all carriers of virulent diphtheria organisms.

(d) Complete active immunization by second dose two to four weeks after the first.

(e) Two weeks after completion of active immunization programme release carriers from isolation.

216 Note. The advantage of this procedure is that when the programme is strictly adhered to there is no need to close the school, hospital or institution in which the outbreak of diphtheria has occurred.

217
218 } Reserved.
219

Section 23 Serum reactions and serum sensitivity tests

220 Types of reactions

The more serious types of reaction which may follow the administration of serum are:

(a) *Anaphylactic shock*. A rare and dangerous condition which comes on typically within a few minutes of a serum injection, but may start with less intensity up to two hours later. Death may occur rapidly if treatment is not prompt and adequate. The symptoms are dyspnoea, pallor and collapse. The blood pressure falls and the pulse may become imperceptible. Sometimes there is oedema or a rash. Many subjects of anaphylactic shock have a history of major allergy such as asthma or infantile

eczema rather than one of previous serum treatment, and the shock is liable to occur in such individuals following a *first* injection of serum.

(b) *Serum sickness.* A syndrome of rashes, pyrexia, oedema and joint pains of late onset of which two types occur. There is a 'delayed' type occurring seven to twelve days after a serum injection and an 'accelerated' type which tends to occur in those who have previously had serum and begins three or four days after the injection.

(c) *Thermal reaction.* A rare reaction consisting of sudden pyrexia with rigors following soon after an intravenous injection of serum; probably due to pyrogens produced in the batch of serum during processing.

(d) *Local reaction without constitutional disturbance.* Localised erythema or urticaria, which occurs seven to ten days after the injection. It lasts about two days and though the lesions may be very irritating, the reaction as a whole is not dangerous.

(e) *Local hypersensitivity.* A very rare reaction, analogous to the Arthus phenomenon in animals, which may follow repeated injections of serum or vaccine. It consists of swelling and marked induration, leading to sloughing of the skin, subcutaneous tissue and even muscle.

221 Serum sensitivity tests

(a) Intradermal, conjunctival, and scratch tests for sensitivity are unreliable and can be misleading since skin sensitivity may be a local phenomenon the presence or absence of which does not necessarily reflect the existence or otherwise of general sensitivity. Thus, fatal shock has followed the administration of serum after a negative intradermal test, while conversely, in a number of cases no general reaction followed full doses of serum to persons who had shown a strongly positive intradermal reaction a few hours earlier. Such tests are therefore not recommended.

(b) Instead a *subcutaneous* '*trial dose*', consisting of a small volume, usually 0·2 ml., of serum is given at least half an hour before a larger dose which may then follow if the trial dose has caused no ill effect. Depending on the patient's history, this trial dose of serum may be administered undiluted or may need to be diluted before being used. The larger dose referred to may be a further trial or full dose in accordance with the indications set out in para 222 below.

(c) This small preliminary dose should show whether the subject is liable to an immediate general (anaphylactic) allergic reaction and, at the same time should limit such a reaction, should it occur, to a relatively mild attack responding rapidly to treatment. In deciding upon the degree of necessity for a trial dose, and on its nature, the personal and family history of the patient are most important and must therefore be obtained. He should be questioned as to whether he has ever suffered from asthma, from infantile eczema or from other allergic conditions; whether there is a history of any allergic manifestations in his family; and whether he has ever received an injection of *serum* as opposed to *vaccines*, but including *Diphtheria T.A.F.*, which contains a small quantity of serum.

222 Precautions

In accordance with the conditions cited in para 221 above appropriate precautions will be taken as follows:

(a) *No allergy: no previous serum* (including Diphtheria T.A.F.). *A subcutaneous trial dose* of 0·2 ml. undiluted serum is still desirable if time permits *and will be used* if the serum to be injected is unrefined. Unrefined serum should now rarely be used. If there are no symptoms or signs after a period of half an hour the full dose may be administered subcutaneously or intramuscularly without further delay.

(b) *No allergy: previous serum. A subcutaneous trial dose* of 0·2 ml. undiluted serum will be given, followed by the full dose subcutaneously or intramuscularly after the lapse of at least half an hour without ill effect.

(c) *Minor or doubtful allergy: no previous serum.* When the patient is subject to minor allergic conditions, such as hay fever, food sensitivity or adult eczema, a trial dose, usually of undiluted serum, is necessary. A history of severe and frequent attacks may indicate the advisability of starting with a trial dose at 1:10 dilution and following this with one of pure serum, as described below under 'Major allergy', before the main dose is given.

(d) *Major allergy such as asthma or infantile eczema.* It is necessary to ask about the severity and frequency of the attacks and about any other allergic conditions in the patient or his family. Persons suffering from major allergy should only be given serum when absolutely necessary and the main dose should be preceded by at least two or preferably three trial doses of falling dilutions of serum as follows: 0·2 ml. of a 1:100 dilution of serum may be given as a first trial dose; this is followed after half an hour or more without reaction by a second trial dose of 0·2 ml. of a 1:10 dilution which, if accepted without ill effect, is again followed half an hour or more later by the final trial dose of 0·2 ml. undiluted serum. This procedure, while very safe is tedious, so to avoid undesirable delay, the first trial dose may be omitted and a start be made with the 1:10 dilution.

223 Treatment of serum reactions

A syringe containing 1·0 ml. of 1/1000 solution of adrenaline and fitted with a needle ready for *immediate* use, together with a further supply of the adrenaline solution for further doses if necessary, will always be kept at hand when serum is injected. *The patient must remain under direct medical observation for half an hour at least after a serum injection.*

(a) *Anaphylactic shock*

(1) *Adrenaline.* On the onset of anaphylactic shock consisting of dyspnoea, pallor and collapse, an intramuscular injection of adrenaline should be given at once; even momentary delay may prove fatal. The dose is 1·0 ml. of the 1/1000 solution for adults; 0·5 ml. for children. In either case, further doses of 0·5 ml. should be repeated if recovery is not rapid—for example, if the systolic blood pressure in an adult remains below 100 mm. of mercury.

(2) *Antihistamines.* While adrenaline is the first and essential requirement, a potent antihistamine drug should also be given by mouth as soon as possible. Its use may be continued for ten days or so with a view to limiting later allergic manifestations. This is especially so when it is necessary to repeat attempts at passive immunization (para 224).

(3) *Cortico-steroids.* Further benefit, enhancing and prolonging the response to adrenaline and antihistamine treatment, may be conferred by the use of a cortico-steroid preparation in cases where adrenaline is slow to act. To this end an intravenous injection of 100 mg. hydrocortisone hemisuccinate sodium may follow the injection of adrenaline in addition to the oral use of an antihistamine. The effect of the antihistamine may be prolonged, particularly when passive immunization has been resumed, by further oral administration of a suitable corticoid such as prednisone or prednisolone. Intravenous hydrocortisone hemisuccinate sodium is particularly indicated when the response to adrenaline is poor and the blood pressure remains subnormal for some hours. When cortico-steroids are contraindicated (*see* below) such cases should be treated in hospital by a slow intravenous drip of diluted noradrenaline. Where this procedure is necessary blood pressure readings must be taken frequently in order to avoid an unduly elevated pressure.

(4) *Cortico-steroid therapy is contraindicated* in cases of peptic ulcer, diabetes and tuberculosis; in patients suffering from *any infection which is not under effective antibacterial control* and before an operation or anaesthetic. These last mentioned restrictions are liable to limit greatly the cortico-steroid treatment of acute serum reactions—for example, of those following tetanus antitoxin or diphtheria antitoxin. Tetanus antitoxin may be given to persons with infected wounds—which may also require operative treatment. Diphtheria antitoxin is almost exclusively used for treatment of active infection with *Corynebacterium diphtheriae.*

(b) *Serum sickness.* Antihistamines are given by mouth. If symptoms are not controlled by this treatment corticoids such as prednisone or prednisolone in doses of 5 mg., six-hourly for adults, may be given for some days by mouth *provided their use is not contraindicated* (*see* above). Skin irritation should be treated with soothing lotions until it subsides.

(c) *Thermal reactions.* In general no treatment, other than keeping the patient comfortable, is needed and the reaction usually subsides in fifteen to twenty minutes. If the pulse is weak, suggesting some associated anaphylaxis, an injection of adrenaline should be given.

224 Completion of passive prophylaxis after a general reaction (anaphylaxis) to a trial dose

(a) Treatment described in para 223, of a general reaction to a trial dose as required in paras 221 and 222, should be followed by the return of the blood pressure to normal, and disappearance of all symptoms and rashes. This usually occurs in three or four hours, but may take as long as twelve hours.

(b) When such full recovery has taken place, sensitivity is *normally* in temporary abeyance and there need be no further delay in resuming necessary serum treatment. Waiting, if prolonged beyond two days, is undesirable as it may allow the patient to become sensitive again.

(c) Normally, resumption of treatment will start with a further trial dose of undiluted serum, to be followed, if no general reaction occurs in half an hour, by the main dose. This trial dose is advised as a precautionary measure even though a general reaction is very unlikely.

(d) The main dose will generally be given intramuscularly, but, in circumstances of extreme urgency, the bulk of it should be injected intravenously *after a preliminary intramuscular injection has been tolerated for at least half an hour*, but preferably for two hours. When serum is given under the above circumstances the patient should not suffer from anaphylaxis, but may still develop an accelerated type of serum sickness which will call for treatment. Hence, if he has been allowed to leave the medical unit after the serum has been given, he must be warned of this possibility and instructed to report its occurrence at once.

225 Rapid elimination of immune serum by persons with a history of serum injections

(a) Patients with a past history of injections of serum, including serum-vaccine preparations, such as Diphtheria T.A.F., may have developed antibodies (precipitins) to the serum itself which will cause future doses of any immune serum to be rapidly eliminated from the body. This is because most immune sera are obtained from the horse. In certain cases most of the antibody introduced may have disappeared after two days.

(b) It is unlikely that this type of sensitivity will invariably be revealed by reaction to a trial dose, but its existence may cause passive immunization to fail and in some cases with a fatal result. When, therefore, an antitoxin is necessary for a person who is known to have been given serum before, it is desirable to give a much larger dose than the normal one, in the hope that this larger dose will help to counteract any accelerated removal.

(c) Rapid repetition of small doses of serum is not recommended in these circumstances as it seems possible that this might stimulate its rapid elimination in cases not as yet sensitized, or enhance the rate of elimination in those who are.

(d) Owing to the variable protection resulting from second or subsequent doses of serum in persons who develop precipitins, the need for commencing a course of *adsorbed toxoid immediately* (para 205) or *fluid toxoid six to eight weeks after* the last injection of serum is again stressed. Active immunization obviates the use of serum in the event of further tetanus-prone injury or in suspected diphtheria.

226 Intravenous injections of serum

Intravenous injections of serum are generally not needed for prophylaxis. When they are required for treatment, or in the circumstances discussed in para 224, they should always be preceded by an intramuscular injection which is itself preceded if necessary by a trial dose or doses. The intravenous injection can follow, preferably two hours and certainly not sooner than half an hour afterwards, if during the interval the intramuscular dose has been tolerated by the patient. The serum to be injected must be at room temperature and the injection must be given *very slowly* with a careful watch for signs of distress. If such signs occur, injection must stop at once. The patient must be kept warm and recumbent during the injection and for an hour afterwards, during which time he is kept under constant medical observation.

227
228 } Reserved.
229

Section 24 Human immunoglobulin Prophylactic use

230 Normal human immunoglobulin

(a) Normal human immunoglobulin is a sterile preparation of proteins of human plasma and contains, several times concentrated, the antibodies of normal adults. It is prepared from pooled human plasma and the final preparation is derived from at least one thousand donations of blood.

(b) Normal human immunoglobulin is used to protect susceptible contacts of measles, rubella, infectious hepatitis and, occasionally, poliomyelitis. It is doubtful whether it is of any value for preventing or treating mumps, chickenpox or whooping cough.

231 Route and time of administration and duration of effect

(a) Human immunoglobulin is given intramuscularly or subcutaneously, but should not be given intravenously.

(b) Human immunoglobulin should be given as soon as possible after exposure. It will not protect in all cases and, when it does, its effect will wane. If exposure occurs again more than three weeks after a prophylactic injection of human immunoglobulin consideration should be given to repeating the dose.

232 Indications for prophylactic use and dosage

(a) *Measles*

(1) The main value of human immunoglobulin is for attenuating or preventing the disease in young or debilitated children. Human immunoglobulin has also been used to help control outbreaks of the disease in hospitals and institutions, but reliance should mainly be put on isolation and other measures. It is of no value for treatment.

(2) *Dose:*	*Attenuation*	All ages	0·25 g.
	Prevention	Under 1 year	0·25 g.
		1–2 years	0·50 g.
		3 years and over	0·75 g.

(b) *Rubella*

(1) Although there is controversy as to the value of immunoglobulin in preventing rubella, it is still offered to pregnant women who are not known to have had the disease previously who have not been vaccinated against rubella and who have been in definite close contact with infection in the first four months of pregnancy. It is of no value in treatment.

(2) In order that a false sense of security is not engendered in medical officers looking after patients the following scheme should be adopted:

(*a*) Venepuncture should be performed and a specimen of serum sent for examination for rubella antibodies, the request form being marked 'URGENT'.

(*b*) Immunoglobulin 1500 mg. will be administered.

(*c*) If the report on the serum is POSITIVE, the woman can be reassured and no further action is required.

(*d*) If the report is NEGATIVE, a further specimen of serum will be sent three weeks after the first.

(*e*) If the report on this second specimen is NEGATIVE, rubella infection has not occurred, and the woman can be reassured (vaccination against rubella should be offered in the POST-PARTUM period (see para 269b(1)(b)).

(*f*) If the report is POSITIVE, rubella infection has occurred and the obstetrician in charge of the patient should consider what further action is required.

(3) Dose: 1·50 g.

(c) *Infective hepatitis*

(1) Normal human immunoglobulin is used to prevent infective hepatitis in contacts in whom an unmodified attack would be considered dangerous. It has also been used to control outbreaks of the disease in hospitals and institutions, but owing to the shortage of supply, reliance should mainly be put on other measures. It is of no value for treatment.

(2) *Dose:*	Under 10 years	0·25 g.
	10 years and over	0·50 g.

(d) *Poliomyelitis*

(1) The increasingly widespread use of poliomyelitis vaccines, which produce an active immunity, has almost entirely eliminated the need to use human immunoglobulin as a prophylactic agent against poliomyelitis. It has been given to protect those who are to be closely associated with the care of early cases and who have not been actively immunized against the disease. It may also be given to protect infants exposed to the disease shortly after birth and unimmunized children in a hospital ward where a case occurs. It is of no value for treatment.

(2) *Dose:*	Under 1 year	0·5 g.
	1–6 years	1·0 g.
	7 years and over	1·5 g.

233 Anti-vaccinal human immunoglobulin

Anti-vaccinal human immunoglobulin is a sterile preparation of the proteins of human plasma separated from the blood of individuals recently vaccinated against smallpox. It is used for the treatment of generalized vaccinia, eczema vaccinatum, and accidental infections endangering the eye. It is also used for protecting unvaccinated smallpox contacts, for example, when evidence of recent successful vaccination is lacking or when there is insufficient time for vaccination to confer protection. The decision to use anti-vaccinal immunoglobulin for protecting smallpox contacts must depend upon the circumstances of each case (para 157).

(a) *Generalised vaccinia and eczema vaccinatum*

	At once	*2 days later if not recovering*
Dose: Under 1 year	0·5 g.	0·5 g.
1–6 years	1·0 g.	1·0 g.
7–14 years	1·5 g.	1·5 g.
15 years and over	2·0 g.	2·0 g.

(b) *Ophthalmia vaccination*

For patients with lesions involving the eye, frequent instillation of anti-vaccinial immunoglobulin in 10 per cent solution is said to be useful.

(c) *Prevention of smallpox in unvaccinated contacts*

Dose: Under 1 year	0·5 g.
1–6 years	1·0 g.
7 years and over	1·5 g.

234 Convalescent human immunoglobulin.

(a) Convalescent immunoglobulin is a sterile preparation of the proteins of human plasma separated from the blood of individuals who have recently recovered from one or other of certain infectious diseases.

(b) For obvious reasons only small amounts of convalescent immunoglobulin can occasionally be prepared. There is no evidence concerning the value of convalescent measles immunoglobulin, nor does there appear to be a need for a product more potent against measles than normal human immunoglobulin.

(c) Likewise there is little evidence to suggest that convalescent rubella immunoglobulin gives better results than normal human immunoglobulin in preventing rubella in those exposed to the disease. Convalescent mumps immunoglobulin might be of value in preventing complications in adults suffering from mumps, but this has not been demonstrated.

Therapeutic Use

235 Normal human immunoglobulin.

Normal humar immunoglobulin is used for treating the congenital and acquired forms of the rare disorder, hypogammaglobulinaemia. Injections are given at regular intervals to raise and maintain the plasma immunoglobulin concentration. The recommended dosage is 0·1 gram per kilogram body-weight at four weekly intervals.

236
237 } Reserved.
238

Storage of vaccines and antisera
Duration of potency

Section 25 General principles
Stocks
Transportation

239 General

Biological products (vaccines, sera, etc.) have a limited life. They are normally given an expiry date related to the date of manufacture, which may also be stated on the label or container, but which also depends on correct storage for its validity. Correct storage generally involves some degree of refrigeration, but not freezing, usually at 'refrigerator temperature', i.e. 2°C to 10°C, and the exclusion of light. Details in respect of individual products are tabulated in para 242.

240 Maintenance of stocks

In view of the perishable nature of these products, stocks held both by distributing depots and by user units should be as small as is compatible with their respective anticipated needs, so that items can be used before they become time expired. For the same reason containers of each type of product should be grouped together in batches characterized by date of expiry and those soonest due to become time expired be issued and used first.

241 Care in transit

The following items require special care while in transit:

(a) *Poliomyelitis vaccine, oral*

(1) In temperate climates the vaccine should be dispatched at normal ambient temperature, and on receipt should be placed in an ordinary refrigerator and maintained in the unfrozen state at a temperature not exceeding 10°C, at which temperature it will have a life of six months. Vaccine removed from the refrigerator should not be exposed to direct sunlight or to room temperature over 15°C.

(2) Any partially used containers are to be returned to the refrigerator immediately and marked to show the date of initial opening. This vaccine can subsequently be used within fourteen days, and material not used during this period should be destroyed. Any opened bottles of vaccine which are not used during this period should be destroyed.

(3) Any unopened vaccine kept out of the refrigerator at room temperature up to 15°C for accumulative periods of more than fourteen days should be destroyed in its container by boiling. Should any vaccine become turbid in less than fourteen days it is to be destroyed in the same way.
(4) For transit in tropical climates the vaccine should be suitably protected to ensure that the temperature does not rise above 15°C.

(b) *B.C.G. vaccine.* Dried B.C.G. vaccine should preferably be transported, as it must be stored, at 2°C to 10°C in the dark. Unrefrigerated transport is permissible in temperate climates provided that the vaccine will arrive at its destination within forty-eight hours. For transit in tropical climates air transport should be used and the material kept as cool as possible and stored at 2°C to 10°C on landing. If air transport is not available the vaccine should be packed in ice in a vacuum container, the ice being replaced as necessary.

(c) *Yellow fever vaccine.* Yellow fever vaccine is best transported, as stored, at a temperature below freezing point. However, a somewhat higher temperature, as provided by packing in ice in vacuum containers, with replacement of the ice as required, is acceptable during transit.

(d) *Rabies vaccine.* Rabies vaccine should be transported as nearly as possible within the temperature range 2°C to 4°C. It must not be frozen and vaccine which has inadvertently been frozen should be discarded. For practical purposes packing in ice, replaced as necessary, in vacuum containers, as for yellow fever vaccine, is satisfactory while in transit.

(e) *Cholera vaccine.* Ideally cholera vaccine should be stored at 2°C to 10°C. It may, however, be stored in a cool dark place at 15°C provided it is always protected from light. Under no circumstances will cholera vaccine be stored near or in the freezing chamber of a refrigerator as the suspension becomes mucoid and no longer readily dispersible on shaking. This leads to a white flaky deposit and vaccines seen, after vigorous shaking, to contain such a deposit should be discarded. Unrefrigerated transport is permissible provided the temperature does not rise above 15°C.

(f) *Schick test toxin.* Unrefrigerated transport of Schick test toxin is permissible in the United Kingdom provided it will arrive at its destination within forty-eight hours. When being sent overseas it should be packed in ice in a vacuum container, the ice being replaced as necessary.

(g) *Other biological products.* Other products should be stored during transit at a temperature above freezing point, but otherwise in as cool a place as possible. They should be sent by the quickest route, should not be allowed to remain exposed to the sun or other sources of heat while awaiting transportation or collection and should be labelled to show their perishable nature.

Section 26 Tables correlating storage conditions with 'life' (duration of effective potency) of biological products

(Note Refrigerator Temperature Range is 2°C to 10°C)

242 (a) *Living vaccines*

Table 20 Storage of living vaccines

Product	Storage temperature	'Life'
Dried Smallpox vaccine	(i) Refrigerator temperature or lower.	Keeps indefinitely.
	(ii) Unrefrigerated:	
	(a) In a cool dark place (i.e. not over 15°C)	1 year.
	(b) Tropical temperature	1 month.
Smallpox: Glycerinated Lymph	(i) At minus 10°C	1 year from the date of manufacture or as notified by the manufacturer.
	(ii) Refrigerator temperature, 4°C or less	14 days or as directed by the manufacturer.
Yellow Fever vaccine	(i) 4°C or less, *preferably at minus* 10°C	1 year } From date of manufacture (or as notified by the manufacturer).
	(ii) In a cool, dark place (i.e. not over 15°C)	1 month }
Oral Poliomyelitis vaccine	(i) Frozen vaccine at minus 10°C or below	2 years from date of manufacture.
	(ii) Unfrozen vaccine at up to 4°C	Maximum of 1 year from date of issue from deep freeze.
	(iii) Thawed vaccine at 4–10°C	6 months.
	(iv) Thawed vaccine in a cool, dark place (i.e. not over 15°C)	14 days.
Tuberculosis vaccine: Dried B.C.G.	Refrigerator temperature *in the dark*	1 year.

242 (b) *Dead vaccines*

Table 21 Storage of dead vaccines

Product	Storage temperature	'Life'
Rabies Vaccine: (a) Semple type	Between 2°C and 4°C in the dark, *not* frozen	3 to 6 months } or as notified by the manufacturer.
(b) Dried Duck Embryo	Between 2°C and 4°C in the dark	14 to 18 months } or as notified by the manufacturer.
Enteric vaccines: (T.A.B.T., T.A.B. or T.A.B. diluted for children)	(i) Refrigerator temperature, *not* frozen	2 years } from date of manufacture.
	(ii) In a cool, dark place (i.e. not over 15°C)	6 months } from date of manufacture.
Cholera vaccine	In a cool, dark place (i.e. not over 15°C) *not* refrigerated	18 months } from date of manufacture.
Others	Refrigerator temperature, *not* frozen	18 months } from date of manufacture.

242 (c) *Toxoids*

Table 22 Storage of toxoids

Product	Storage temperature	'Life'
Diphtheria vaccine FT Combined Diphtheria and Tetanus vaccine	(i) Refrigerator temperature, *not* frozen	1 year or as notified by the manufacturer.
	(ii) In a cool, dark place (i.e. not over 15°C)	6 months.
Tetanus vaccine T.T	(i) Refrigerator temperature, *not* frozen	3 years.
	(ii) In a cool, dark place (i.e. not over 15°C)	2 years.
Combined Diphtheria, Tetanus and Pertussis vaccine D.T.P.	Refrigerator temperature, *not* frozen.	2 years.

242 (d) *Sensitivity test reagents*

Table 23 Storage of sensitivity test reagents

Product	Storage temperature	'Life'
Schick Test Toxin	Refrigerator temperature, *not* frozen	6 months from date of manufacture.
Dick Test Toxin	Refrigerator temperature, *not* frozen	3 months from date of manufacture.

Table 23 Storage of sensitivity test reagents—contd.

Product	Storage temperature	'Life'
Tuberculin P.P.D.		
(a) Dried	Refrigerator temperature	Indefinitely.
(b) Strong solution (2.0 mg. per ml.)	Refrigerator temperature	1 year.
(c) Dilute solutions	Not applicable	No life: discard after use.
Tuberculin Tine Test	Room temperature	2 years from date of manufacture.

242 (e) *Antitoxic sera**

Table 24 Storage of antitoxic sera

Product	Storage temperature	'Life'
(a) Enzyme refined		
(i) In sealed glass ampoules	(i) Refrigerator temperature	5 years
	(ii) In a cool, dark place (i.e. not over 15°C)	3 years
(ii) In containers with rubber closures	Refrigerator temperature	2½ years
(b) Unconcentrated	Refrigerator temperature	2½ years
		from date of manufacture.
Dried Human Post-vaccinial Gamma Globulin	In a cool, dark, dry place at 10°C to 20°C	4 years from date of preparation.

*Sera should on no account be frozen.

243 *Expiry Date*

When only one expiry date for a product, and not its date of manufacture, is stated on the label or container, *no extension of* '*biological life*' beyond that date is permitted. Of those products which have reached their expiry date, dead vaccines and test reagents should be discarded and living vaccines should be destroyed by boiling before disposal.

244 *Extension of life of enzyme refined antitoxic sera*

(a) Enzyme refined antitoxic sera in sealed glass ampoules have a life of five years in the refrigerator (*see* Table 24). However, provided they are kept at 2°C to 10°C deterioration per annum does not exceed 3 per cent—though it may reach 20 per cent at 37°C. Hence sealed ampoules of such sera which have reached their five-year expiry date while refrigerated in distributing centres may have their life extended for a further two years, i.e. to seven years from date of manufacture.

(b) Ampoules with such an extended life which have been issued to user units will, however, be used within six months of issue even if that falls short of the new expiry date. *Except in grave emergency where no more recent sera are obtainable these sera will not be used beyond seven years from the date of manufacture or after being held for six months of extended life in a user unit, whichever is the earlier.* When the life of a serum has to be extended the dosage should be increased to allow for possible deterioration.

245 Assay of biological products

When reduction of potency of a biological product is suspected, representative samples may be sent for assay as under:

(a) Antitoxic sera—to the appropriate Service Directorate of the Ministry of Defence (para 183(b)).

(b) Vaccines and test products prepared by the David Bruce Laboratories—to the Officer Commanding David Bruce Laboratories, East Everleigh, Marlborough, Wiltshire.

246
247 } Reserved.
248

Other vaccination procedures

Section 27 General

249 General

From time to time Service Medical Officers receive enquiries about, or requests for, vaccines other than those described in detail in earlier sections; as a consequence it has been decided to include a section containing notes on other vaccines about which enquiries have most frequently been made, and wherever possible to state the policy regarding their use in the Services at the time of writing.

250 Vaccines

Anthrax, Influenza, Measles and Rubella vaccines are dealt with separately in ensuing paragraphs. In recent years a large number of viruses and other agents capable of causing disease in man have been isolated. The position in regard to vaccines for some of these is shown in Table 25 below.

Table 25 Recent vaccines—the position in 1971

Disease or Virus	Vaccines produced: Inactivated	Vaccines produced: Live attenuated	Availability	Remarks
Mumps	Yes	Yes	Inactivated vaccine only available	Limited use in adult males. Army trials in Gurkha Recruits.
Adenovirus	Yes	Yes	Not available	Polyvalent vaccine of types 3, 4 and 7 used in clinical trials in American Servicemen.
Primary Atypical Pneumonia	Yes	No	Not available	Early trials only.
Respiratory Syncytial Virus	Yes	No	Not available	Vaccine containing types 1 and 2 being developed.

Table 25 Recent vaccines—the position in 1971—contd.

Disease or Virus	Vaccines produced: Inactivated	Vaccines produced: Live attenuated	Availability	Remarks
Para-influenza	Yes	No	Not available	Vaccine containing types 1, 2 and 3 being developed.
Rhino-viruses	Yes	Yes	Not available	Early trials with vaccines to HGP and PK strains of rhinovirus and to Echo 28.
Louping ill	Yes	No	No general requirement	For laboratory workers handling this virus.
Q-Fever	Yes	No	No general requirement	For special risk workers in laboratories and abattoirs.
Infective Hepatitis	No	No	Nil	Isolation of virus not confirmed.

Anthrax

251 General

Persons at risk from anthrax work in a relatively small number of industrial processes including those concerned with animal hides and by-products. Selective immunization within these industries is hence the best approach to the prevention of anthrax.

252 Anthrax vaccine

(a) Anthrax vaccine is an alum precipitate of the antigen found in sterile filtrates of *Bacillus anthracis*. It should be stored at refrigerator temperature, but *not* allowed to freeze.

(b) Three intramuscular injections each of 0·5 ml. administered at intervals of three weeks, followed by a fourth dose given at six months after the third. Reinforcing doses of 0·5 ml. administered intramuscularly should be given at yearly intervals to persons continuing at risk.

253 Reactions

Reactions to anthrax vaccination are extremely rare.

254 Contraindications to anthrax vaccination

No contraindications to anthrax vaccination have been published as it is normally only administered to healthy persons at risk in specialized industries which demand a high standard of fitness in their employees.

255 Reserved.

Influenza

256 General

(a) Influenza A viruses have been isolated from most of the big epidemics of the disease and it has been found that every few years these epidemic influenza viruses undergo major and minor antigenic changes. Similar, but less pronounced, changes have occurred with the influenza B virus.

(b) The occurrence of different types of influenza virus which give no cross-immunity to each other, means that the composition of an influenza vaccine must be based on the virus types which are most prevalent in the population at risk at the time or on the type causing a pandemic.

257 Influenza vaccines

(a) The viruses can be readily cultivated in fertile hens' eggs and the allantoic fluid from these is rich in antigen suitable for vaccine manufacture.

(b) Two types of vaccine have been prepared and are designated 'inactivated influenza virus vaccine (formolized)' and '(live) attenuated influenza virus vaccine'.

(c) Attenuated vaccine given intranasally will cause infection and stimulate antibody production with only minor illness. However, since antibody protection is less than that from killed vaccine, this type of vaccine is not recommended.

258 Inactivated influenza virus vaccines

(a) These vaccines are prepared from virus which has been separated from hen's egg allantoic fluid and formolized. The virus may be suspended in saline or an adjuvant emulsion such as liquid paraffin, Arlacel or Drakeol. These vaccines should be stored at refrigerator temperature, but should *not* be allowed to freeze.

(b) Saline vaccines are administered *subcutaneously* in two doses of 1 ml. at an interval of four weeks. Mild local and general toxic effects occur in a small proportion of persons receiving saline vaccines.

(c) Adjuvant vaccines are given in one *intramuscular* dose of 1 ml. Whilst immediate reactions are fewer, a small persistent nodule at the vaccination site may be encountered.

(d) Revaccination is necessary annually before the 'influenza season' or when an outbreak of influenza occurs in which the responsible virus is of a different serotype to those contained in the vaccine.

259 Indications for influenza vaccination

Vaccination against influenza, using a vaccine containing the appropriate serotype, is indicated only in persons at special risk:

(a) Routine vaccination is recommended for patients suffering from chronic diseases which may be aggravated by influenza. These include chronic pulmonary disease, chronic heart disease, chronic renal disease, diabetes and endocrine disorders.

(b) Vaccination may also be considered for certain categories of persons, such as nurses, medical officers and workers in essential services when a locality or country is threatened by a large epidemic of influenza.

260 Contraindications to influenza vaccination

Vaccination with influenza vaccine is contraindicated in persons who have a history of allergy, particularly to feathers or egg protein.

261 Reserved.

Measles

262 General

(a) Measles vaccination is now available to all children aged one to fifteen years, who have not previously had the disease. Once initial vaccination of all children up to the age of fifteen years has been completed, vaccination should be offered as a routine procedure to children shortly after the first birthday.

(b) Vaccination is particularly recommended for those children likely to develop serious complications should they acquire measles, e.g. congenital heart disease.

263 Measles vaccine

The vaccine (Mevilin-L) consists of a freeze-dried preparation of living attenuated measles vaccine of the Schwartz strain made by Glaxo or an American vaccine (Dow's Chemicals) distributed by Glaxo. It is supplied in one dose or five dose vials with the appropriate number of vials of 0·5 ml. Water for Injection, BP for reconstitution. When ordering quote BJSC 6505–99–211–1788 Measles Vaccine, Freeze-dried 1 (or 5) dose vial with 0·5 ml. (or 3·0 ml.) ampoule Water for Injection, BP.

264 Vaccination against measles

(a) *To prepare the vaccine.* Withdraw the Water for Injection, BP from the ampoule supplied with a sterile disposable syringe, add it to the vial of vaccine and let it stand for about a minute. Mix by drawing the suspension into the syringe and expelling at once. Withdraw 0·5 ml. of the reconstituted vaccine for each dose and inject as soon as possible. Injections may be given *intramuscularly* or *subcutaneously*.

(b) *Vaccination*

(1) Attenuated measles virus is quickly killed by ether, alcohol and detergents. Care is needed to avoid contact with these substances when sterilising the skin prior to immunisation.
(2) The vaccine from Dow's Chemicals (U.S.A.) may vary in appearance from colourless to pale straw on reconstitution, and on standing the colour slowly changes to pink. This colour development is of no consequence and does not indicate loss of potency.

265 Reactions

(a) Reactions to vaccination usually appear after about eight days. The symptoms are mild and include pyrexia and symptoms of subclinical measles which is not infectious to susceptible contacts. Occasional febrile convulsions, without any sequelae, have been reported. Some vaccines, with insufficiently attenuated virus, have caused, particularly in infants, a measles encephalitis indistinguishable from the natural disease.

(b) In young or debilitated children it may be considered desirable to administer a dose of normal human immunoglobulin (250–750 mg. according to age) by injection into the opposite arm in order to lessen the severity of reactions (para 230 and 232).

266 Contraindications to Measles Vaccination

Live attenuated measles vaccine should not be given to:

(a) Infants under one year of age.

(b) Children suffering from any intercurrent infection.

(c) Debilitated children or those with a history or family history of convulsions.

(d) Children with a history of allergy, particularly those sensitive to hen's eggs.

(e) Cases of leukaemia, Hodgkin's disease or other malignant conditions.

(f) Cases of hypogammaglobulinaemia.

(g) Cases undergoing cortico-steroid or immuno-suppressive treatment.

(h) Children who have received smallpox vaccination within the previous four weeks.

267 Relation to other immunising procedures

An interval of at least four weeks should be allowed to elapse between measles vaccination and any other immunological procedure, particularly smallpox vaccination.

268 Storage

Vials of measles vaccine should be protected from light and stored in a refrigerator at 2–10°C (36–50°F). Reconstituted vaccine should be used within one hour of preparation. Each vial bears an expiry date.

Rubella

269 General

(a) The relationship between maternal rubella and infection of the foetus with death and malformation, is now fully established. Immunoglobulin is no longer considered by many to be of value in preventing German measles in pregnant women exposed to infection and active vaccination should be offered as the only effective method of immunoprophylaxis.

(b) Rubella vaccine is available for the following:

(1) Girls between the ages of 11 and 14 years, without preliminary antibody screening.
(2) Adult females *who are sero-negative for rubella antibodies.* In order to minimise the need to carry out venepuncture for testing, and to screen widely, this category may be divided into two groups:

(*a*) Non pregnant women who request vaccination. Any women so vaccinated should be personally warned by her doctor that pregnancy should not take place during the two months following vaccination.

(*b*) Those attending antenatal clinics. Screening for rubella antibodies should be incorporated into routine antenatal examination and those sero-negative should be offered vaccination IN THE POST-PARTUM PERIOD, again with a personal warning by her doctor that there should not be a further pregnancy within two months after vaccination.

(*c*) Screening for rubella antibodies is performed by the Virology Laboratory of the Department of Pathology, Royal Army Medical College. A 5 ml. specimen of sterile serum is required.

270 Rubella vaccine

The vaccine available ("Cendevax", Smith, Kline and French Laboratories) is a live, attenuated, freeze-dried preparation of the Cendehill strain of rubella virus supplied as a single dose vial together with an ampoule containing 0·5 ml. sterile reconstituting fluid.

271 Vaccination against rubella

(a) *To prepare the injection.* Withdraw the reconstituting fluid into a sterile disposable syringe, add it to the vial of vaccine, leave for one minute, and mix by drawing the suspension into the syringe and expelling at once.

(b) *Vaccination*

(1) Attenuated virus vaccines are quickly killed by ether, alcohol and detergents. Care is needed to avoid contact with these substances when disinfecting the skin prior to immunisation.
(2) The dose of 0·5 ml. reconstituted vaccine should be administered by the subcutaneous route only.

272 Reactions

(a) Reactions are infrequent and usually of a mild nature. Slight fever, sore throat and slight enlargement of the posterior cervical glands have been reported about the second week after vaccination.

(b) Reactions such as mild arthralgia and arthritis have been observed, almost exclusively in adult women during the third to fourth week after vaccination. No permanent sequelae have been reported.

273 Contraindications to rubella vaccination

Live attenuated rubella vaccine should not be given to:

(a) Anyone who could be pregnant, or could become pregant within the following 2 months.

(b) Those suffering from acute febrile illness or chronic debilitating disease.

(c) Those suffering from malignant conditions such as leukemia or Hodgkin's disease.

(d) Those with hypogammaglobulinaemia or other immunological deficiency states.

(e) Those undergoing cortico-steroid or immuno-suppressive treatment.

(f) Those who have received smallpox vaccination or other live vaccine other than oral poliovaccine within the previous 4 weeks.

274 Storage

The freeze-dried vaccine and diluent fluid should be stored at temperatures between 2–8°C (35–46°F) and protected from light; lower temperatures will not harm the vaccine, but may damage the diluent fluid. Reconstituted vaccine should be used within one hour of preparation.

275 Relation to other immunological procedures

An interval of at least four weeks should be allowed to elapse between rubella vaccination and another live vaccine excluding oral poliomyelitis vaccine.

Index

(96645) Dd. 134808 K 93 7/68 Hw.

Printed and published by
Her Majesty's Stationery Office

To be purchased from
49 High Holborn, London WC1
423 Oxford Street, London W1
13A Castle Street, Edinburgh 2
109 St Mary Street, Cardiff CF11JW
Brazennose Street, Manchester 2
50 Fairfax Street, Bristol 1
258 Broadstreet, Birmingham 1
7 Linenhall Street, Belfast BT2 8AY
or through any bookseller

Printed in England

SO Code No. 57-631-0-68