A MANUAL OF IMMUNOLOGY

Pertaining to Communicable Diseases Commonly Encountered in Georgia

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PREFACE

Current literature, both popular and medical, has been replete with accounts and reports of new adventures in the field of immunology. This is as it should be. Nevertheless, the busy practitioner or health officer who has time to read only briefs and summaries is apt to be confused and led astray from basic principles. This publication is designed to bridge the gap between exhaustive studies and incomplete summaries.

In this manual the authors have attempted to incorporate the most reliable procedures of preventive and therapeutic immunology available, together with such new information as has been found to be worth while by conservative and experienced authors. It is obvious that, in view of the rapid strides now being made in the field of immunology, such a manual of procedure must be subject to frequent revision. This first edition was prepared by the medical staff of the Georgia Department of Public Health, and approved by the public health committee of the Georgia Pediatric Society.

CONTENTS

SMALLPOX
(Variola)

A. TESTS FOR SUSCEPTIBILITY: None, other than reaction to vaccination, which varies with the degree of susceptibility to cow pox (and by inference, to smallpox). Reactions to smallpox vaccination may be briefly described as follows:

1. PRIMARY REACTION. (Also known as "vaccinia" or "take".) This is seen in persons never previously vaccinated, or whose immunity from previous vaccinations or from the disease has disappeared. A small papule appears on the third to fifth day with a vesicle gradually enlarging to the typical lesion; with a pustule by the seventh day; with a crust by the twelfth to fourteenth day; and with gradual subsidence during the third week. An individual with such a reaction may be assumed to have been susceptible to smallpox, as well as to vaccine virus.
2. ACCELERATED REACTION. (Also known as "partial" or "vaccinoid" reaction.) This is encountered in persons retaining partial immunity from previous vaccination or from prior attack of the disease. The papule appears on the third to the fifth day, and always goes through the vesicle stage, usually pustulation also; the height of the reaction is usually reached by the sixth or seventh day, and rapidly subsides. The reaction may range anywhere between primary reaction and "immune" reaction. It indicates varying degrees of partial immunity.
3. IMMEDIATE REACTION. (Also known as "immune" reaction.) This is seen in persons possessing very active immunity from recent vaccination or from a prior attack of the disease. A papule appears in the first two days, and except for an occasional tiny vesicle at its summit, it remains the same until it gradually subsides over a period of two weeks or more.

Regardless of the type of reaction encountered, a safe degree of immunity is conferred on the susceptible, and protection is added or prolonged for the non-susceptible. If no type of reaction results, no conclusion can be drawn, inasmuch as this is likely the result of impotent virus or faulty technique.

B. ACTIVE IMMUNITY

1. INHERENT: None
2. NATURALLY ACQUIRED: Immunity (usually permanent) results from an attack of smallpox (either frank or unrecognized).

3. Artificially Acquired: By vaccination with vaccine virus (cow pox virus). This immunity, like others, is relative. Usually a fairly safe degree of protection lasts from 5 to 7 years.

   Technique: The washed skin (soap and water) should be cleansed with alcohol, ether or acetone. Time must be allowed for complete evaporation to avoid killing the virus. Preparations of iodine, or any chemical disinfectant not completely volatile should *not* be used.

   (a) The Multiple Pressure Method is a recommended procedure. Place a drop of vaccine on the prepared skin; hold a sterile needle practically parallel to the skin surface, its point within the drop; press 10 to 20 times over an area not exceeding one-eighth inch in diameter, to break the epidermis without causing bleeding. A single puncture of this sort frequently fails and is not recommended.

   (b) The Single Scratch Method is a recommended procedure. A small drop of vaccine is placed on the prepared skin, and a sterile needle held at a 45° angle to the skin surface, its point within the drop. A superficial scratch is made for a distance of from one-eighth to one-fourth inch, to break the epidermis without causing bleeding. The vaccine should be gently and momentarily rubbed in with the shaft of the needle.

   (c) Intradermal Injection (0. 1 c. c., half and half vaccine and sterile saline) has been recommended by some, but is not widely used.

   (d) Scarification with a cutting edge, and

   (e) Cross-hatching by multiple scratches

   are mentioned only to be condemned.

   In all instances the vaccine should be allowed to dry on the arm. Shields or occlusive dressings should not be placed over the site. If there develops much soreness or the pustule ruptures, it is permissible to use a *thin* gauze dressing to diminish friction from clothing.

4. When to Vaccinate: Each individual should be vaccinated against smallpox prior to the age of six months, and every five years thereafter; also whenever exposed.

   Contraindications: *None* for contacts or in areas of prevalence. For purposes of routine immunization, skin diseases are indications for postponement until the lesions subside.

C. PASSIVE IMMUNITY

1. Inherent: None
2. Acquired: None

D. IMMUNOLOGIC THERAPY

1. For Cases: None

2. For Contacts: Immediate vaccination. Immunity probably begins about the eighth day following vaccination and reaches its height at the fourteenth day. The sooner after exposure successful vaccination is secured, the greater the likelihood and degree of protection. If done immediately, it usually will prevent; and if done within seven or eight days, it can be expected either to prevent or attenuate the infection. With further delay, results are variable.

CHICKEN POX
(Varicella)

A. TESTS FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. Inherent: None
2. Naturally Acquired: One attack usually confers life-long immunity. Second attacks are rare (not to be confused with an atypical prolonged case with apparent remissions).
3. Artificially Acquired: Varying degrees of immunity can be secured by inoculation with vesicle fluid from a case of chicken pox. This is of little practical value and carries the risk of transmitting syphilis or unrecognized smallpox. Some authorities recommend its use in institutions.

C. PASSIVE IMMUNITY

1. Inherent: Immunity of varying degree and duration may exist in infants under six months of age.
2. Acquired: Some authorities report transient passive immunity, of a few weeks duration, from intramuscular injection of 5 to 10 c. c. of serum from Wasserman negative recent convalescents. This is not generally employed.

D. IMMUNOLOGIC THERAPY

1. For cases: Treatment with recent convalescent serum has been recommended, but its value is not proven.
2. For contacts: None, except for special indications (debilitating disease, etc.) when convalescent serum may be tried (C-2).

MUMPS
(Epidemic Parotitis)

A. TEST FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. Inherent: None known

2. NATURALLY ACQUIRED: One attack usually confers lasting immunity. Second attacks are rare.
3. ARTIFICIALLY ACQUIRED: None

C. PASSIVE IMMUNITY
1. INHERENT: Most infants are born with some immunity which disappears within a year. The disease is uncommon in the first year.
2. ARTIFICIALLY ACQUIRED: Intramuscular injection of 6 to 10 c. c. of serum (10 to 15 c. c. whole blood) obtained from a recent convalescent (syphilis free) is believed to confer some temporary protection. The value of this has not been proven to the point of general acceptance.

D. IMMUNOLOGIC THERAPY
1. CASES: Intramuscular injections of 50 to 100 c.c. of convalescent serum have been advised to prevent complications. Proof of its value is lacking.
2. EXPOSURES: None is advised ordinarily. For special indications (other illness during epidemic periods) convalescent serum may be tried (C-2).

MEASLES
(Morbilli, Rubeola)

A. TESTS FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY
1. INHERENT: None
2. NATURALLY ACQUIRED: Immunity which is almost invariably permanent results from an attack of measles, either typical or modified.
3. ARTIFICIALLY ACQUIRED: None generally accepted

C. PASSIVE IMMUNITY
1. INHERENT: None, with the exception that infants born of mothers who have had measles are usually immune for some four to six months after birth.
2. ACQUIRED: Immunity lasting from two to five weeks may be induced by intramuscular injection of specific antiserum. For this purpose the following may be used:
   (a) Serum or whole blood from a recent convalescent (best results if obtained between the tenth to the thirtieth day of convalescence). Dosage varies, averaging about 10 c. c. of the serum. If whole blood is used, the dosage should be at least twice this amount.
   (b) Serum or whole blood obtained from individuals who have had measles. Here again dosage varies, but the average

is from 15 to 20 c.c. of serum, and at least double these amounts for whole blood.

Any of the above should be secured only from syphilis-free individuals.

Specific serum or blood, if given prior to the fifth day following exposure, is likely to protect completely against the disease. Children under three, and other children, if frail, should receive complete protection.

Other children, especially those in robust health, are probably best protected by a partial immunity sufficient to modify, but not entirely prevent the disease. In such case the attack is mild with less likelihood of complications, but at the same time allows the individual to develop permanent active immunity. If serum or blood be given after the fifth day of exposure and prior to the onset of symptoms, such modification can usually be secured. The degree to which the disease is modified varies with the potency of the serum, the dosage, and how soon after the fifth day of exposure it is administered. Given with or immediately prior to the onset of symptoms, little effect can be expected. In all instances better results are to be expected if the child be isolated following use of antiserum, to prevent continued exposure.

(c) McKhann and others have secured similar results in preventing and modifying measles with globulin placental extracts. Such products are on the market. If satisfactory antiserum or blood is not available, 2 to 4 c. c. of this extract may be employed.

D. IMMUNOLOGIC THERAPY

1. CASES: No specific treatment commonly accepted.
2. CONTACTS: Prevention or modification as noted above.

SCARLET FEVER

A. TEST FOR SUSCEPTIBILITY: Dick test: 0. 1 c. c. of "Dick" test toxin given intradermally (not subcutaneously). Read 18 to 24 hours later. A red area ½ cm. or more in diameter is a positive test and indicates susceptibility. Otherwise the test is considered negative and is ordinarily indicative of immunity. Negative reactors have been known to develop the disease.

B. ACTIVE IMMUNITY

1. INHERENT: None
2. NATURALLY ACQUIRED: One attack usually confers immunity for life, but second attacks are recorded. Active immunity is also conferred by mild attacks unrecognized, and from repeated subclinical exposures. Many adults have negative Dick tests but deny having had the disease.
3. ARTIFICIALLY ACQUIRED: Scarlet fever streptococcus toxin is

used to immunize susceptible individuals and will reverse a positive Dick test. Average dose: Scarlet Fever toxin, beginning with 500 units, then at weekly intervals increasing to 800, 2,000, 8,000, and 80,000 units subcutaneously. As a result of reactions, both local and constitutional, many have not accepted this procedure as a routine measure. Others feel that more general use is advisable. Age for immunization: preferably 18 to 24 months; not advisable under one year.

C. PASSIVE IMMUNITY

1. INHERENT: Usually present during the first year of life.
2. ACQUIRED: Immunity of a few weeks' duration may be obtained by:
   (a) Intramuscular injection of convalescent or adult serum (10 to 20 c. c.) or whole blood (20 to 30 c. c.).
   (b) Scarlet fever antitoxin (2.5 to 5 c. c.) given intramuscularly. Because of alarming reactions frequently encountered, this procedure is not recommended as a routine.

D. IMMUNOLOGIC TREATMENT:

1. CASES:
   (a) *Scarlet fever antitoxin* is usually limited to those cases exhibiting marked toxemia. Dosage: One to two ampoules —6,000 to 12,000 antitoxin units—should be used as early as possible. Severe reactions are common, and caution should be exercised in the use of this therapeutic agent.
   (b) *Convalescent serum*—30 to 60 c. c.—intramuscularly is probably of equal value. Reactions are minimal, and it is the treatment of choice. Whole blood from a recent convalescent is useful but the amount should be twice that of the serum.
   (c) *Adult whole blood* (sero-negative) may also be used, but large amounts (100 to 200 c. c.) are required. It should preferably be obtained from persons who have had the disease, although most adults are immune. Administer intramuscularly or if cross-matched, by transfusion.
2. CONTACTS: Immunization is not advised unless there is a special indication. The short incubation period necessitates immediate use of preventive measures. For this purpose, the following may be employed:
   (a) *Convalescent serum* (10 *to* 20 *c. c.*) *or convalescent whole blood* (20 *to* 40 *c. c.*)
   (b) *Adult whole blood* (60 *to* 100 *c. c.*)
   (c) *Antitoxin* (2 *to* 5 *c. c.*). Use with caution. Undesirable reactions are common.

DIPHTHERIA

A. TEST FOR SUSCEPTIBILITY: Schick Tests: 0.1 c. c. Schick test material (containing 1/50 minimum lethal dose of diphtheria

toxin for a 250 gm. guinea pig) is injected *into* and not under the skin of the left forearm. For a control a similar amount of the material (heated to 75° for 5 min.) is injected into the skin of the right forearm.

THE TEST SHOULD BE READ ON THE FOURTH OR FIFTH DAY; EARLIER READINGS MAY GIVE FALSE OR PSEUDO-POSITVE REACTIONS.

1. A POSITIVE REACTION revealed by redness and slight induration from 1 to 2 cm. in diameter indicates that there is less than 1/50 unit of diphtheria antitoxin per c. c. of blood serum of the individual. Such individuals are considered susceptible to diphtheria.
2. A NEGATIVE REACTION is indicated by the absence of redness at the site of the injection, as the toxin introduced is neutralized by antitoxin in the blood of the immune individual.
3. A PSEUDO-REACTION is usually the anaphylactic response to the protein in the material used and is produced by the Schick and control material alike. It appears early (6 to 18 hours) and is usually gone by the fourth day. This reaction rarely occurs in infants; it is most likely to occur in older children and adults.

Negative reactions may be obtained in non-immune individuals due to faulty material or technique. Schick-negative individuals may develop the disease. In such cases its course is usually light.

4. PRACTICAL APPLICATION OF SCHICK TEST:
   (a) To determine whether or not a given individual needs to be immunized. Due to the fact that naturally acquired immunity is so frequently present in older children and adults, it is advisable to "pre-Schick" those over 5 years of age before giving an immunizing agent. The same may be done with younger children, the majority of whom are susceptible, but as a general rule, "pre-Schicking" is not employed.
   (b) To determine presumptively whether an individual has been successfully immunized. Where possible, "post-Schicking" should be done six months after administration of toxoid. A positive reaction is an indication for repeating the toxoid.

B. ACTIVE IMMUNITY

1. INHERENT: None known
2. NATURALLY ACQUIRED: One attack usually confers immunity, although second and third attacks occur. "Post-Schick" testing is recommended after diphtheria in younger children. Subclinical infections confer immunity, and account for most instances of natural immunity.
3. ARTIFICIALLY ACQUIRED: Usually occurs after the administration of alum precipitated toxoid, plain toxoid, or toxin-anti-

toxin. Recent studies have shown that these agents in the order of their effectiveness in antibody production are as follows:

(a) Two doses of A. P. toxoid at three-week intervals
(b) Three doses of plain toxoid at three-week intervals
(c) One dose of A.P. toxid
(d) Two doses of plain toxoid at three-week intervals
(e) One dose of plain toxoid

Toxin-antitoxin is not recommended for young children. Each child should be Schick tested four to six months after immunization is completed. An inherent immunity is practically gone by the end of the first year; the ideal time to give toxoid is at about six months of age. Babies have very little, if any, reaction to A.P. toxoid, whereas the reaction tends to increase in severity in children over five years of age. *Never give toxoid in amounts larger than the dose recommended in directions accompanying the product.*

C. PASSIVE IMMUNITY

1. INHERENT: Usually present at birth, disappearing during the first year of life. Therefore active immunization should be given at about six months of age.
2. ACQUIRED: By the administration of diphtheria antitoxin. The usual dose for temporary prophylaxis is 1000 units. This immunity lasts from two to three weeks after which time the person should be actively immunized (toxoid). The routine use of antitoxin prophylatically for exposures is not recommended (particularly during an epidemic). The protected period is too short, and there is definite risk of producing serum sensitivity sufficient to interfere with serum therapy if the individual should contract diphtheria.

D. IMMUNOLOGIC TREATMENT

1. CASES: The bulk in which the dosage of diphtheria antitoxin is contained is now so small that it need not be considered. It is no longer necessary to remember the dosage by age, weight, etc. The important thing is to know how long the patient has been ill and to appreciate the severity of the disease. If it is mild or moderately severe, from 20,000 units to 40,000 units of antitoxin are given intramuscularly. If the patient is seriously ill, from 40,000 units to 80,000 units of antitoxin may be given intravenously or intramuscularly. If the blood pressure has fallen, the antitoxin should be given intravenously. If the case is one of diphtheria gravis, from 80,000 units to 200,000 units may be necessary. Watch for immediate, accelerated and late serum reactions.
2. CONTACTS: Should be placed under close observation and at the first sign of disease should be treated as a case. (See also B-2 and C-2.)

PERTUSSIS
(Whooping Cough)

A. TEST FOR SUSCEPTIBILITY: None applicable to general use. (Opsonic index and complement fixation tests are being studied experimentally.)

B. ACTIVE IMMUNITY

1. INHERENT: None
2. NATURALLY ACQUIRED: From previous attack of disease; such immunity is neither absolute nor life long. Second attacks, though not common, do occur.
3. ARTIFICALLY ACQUIRED: Vaccine does not afford absolute protection, but increasing evidence indicates that it is of value if given well in advance of exposure. Due to the high mortality of the disease in infants and young children, and severity of the reaction from immunization in older children, the procedure is ordinarily limited to preschool children (infants in particular). The optimum age is from three to six months.
   The question of products and interval between injections is at present in a very unsettled state. The general trend is toward increasing dosage. The more concentrated vaccine appears to have greater immunizing value. Pertussis toxoid has appeared on the market but its value is as yet unknown.

C. PASSIVE IMMUNITY

1. INHERENT: None
2. ARTIFICIALLY ACQUIRED: Convalescent serum appears to immunize passively in some instances, prior to the onset of symptoms. It is probably of little value once symptoms have developed.

D. IMMUNOLOGIC THERAPY

1. CASES: Vaccines, convalescent sera, etc., are used in the treatment of pertussis but evidence of their value, once symptoms have appeard, is inconclusive.
2. CONTACTS: Convalescent sera, vaccines, etc., if administered immediately following exposure, many either prevent the disease or mitigate its severity. Such procedures, however, cannot be relied upon.

PNEUMOCOCCUS PNEUMONIA

FOREWORD

Since there are no less than 30 distinct immunologic types of the pneumococcus, it must be borne in mind that immunity, either active or passive as herein discussed, is homologous for each type. For example, specific immunity to Type 1 affords no protection

against any other type. One may acquire immunity to more than one type, but each system of immunity is specific.

A. TESTS FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. INHERENT: None
2. NATURALLY ACQUIRED: Type specific immunity of variable degree and duration usually follows an attack of pneumococcus pneumonia. Also constant exposure to pneumococci normally harbored in the upper respiratory tract, as well as minor focal infections, are no doubt important factors in the acquisition of immunity.

   The threshold of naturally acquired resistance to pneumococcus pneumonia may be lowered by such precursive infections as colds, influenza and measles.
3. ARTIFICIALLY ACQUIRED: Prophylactic vaccination with bacterins and with carbohydrate extracts of pneumococci have been tried experimentally, but satisfactory evidence of its value is yet to be determined.

C. PASSIVE IMMUNITY

1. INHERENT: None, except that the newborn infants of immune mothers are temporarily protected.
2. ACQUIRED: Passive immunity can be produced with pneumococcic serum. This has no practical application, however, except therapeutically. (See below.)

D. IMMUNOLOGIC THERAPY

1. CASES: Intravenous administration of antipneumococcic serum of a type homologous to that causing the infection. Since there are 30 immunologically distinct types, it is essential that the type be identified by appropriate laboratory tests before the serum is selected. For typing, the most accurate and rapid method is the Neufeld test, provided it is done by well trained and experienced technicians.

   The success of serum therapy depends on early administration —the sooner after onset the better. After the fourth or fifth day it is of very little value.

   Detailed instructions accompanying the package should be followed closely, including due precautions against untoward serum reactions.
2. CONTACTS: None

TUBERCULOSIS

A. TESTS:

1. FOR SUSCEPTIBILITY: None; human susceptibility is universal, though varying in degree.

2. For diagnostic aid: Tuberculin test.
The intradermal (Mantoux) method is by far the best.
(a) Two types of test material are commonly used: Old Tuberculin and Purified Protein Derivative of tuberculin. In the case of each, two dilutions are employed, the weaker being invariably used first. *The stronger concentration should never be injected until there has been a negative reaction to the weaker.* Old Tuberculin dilutions contain 0.01 mg. and 1.0 mg. of tuberculin to each 0.1 c. c. respectively as "first" and "second" test doses. The Purified Protein Derivative is supplied as "first" and "second" strength tablets with diluent and instructions for making test solutions.
(b) *Into* the skin (not under it) of the alcohol-cleansed forearm is injected 0.1 c.c. of the "first test strength" (weaker) using a tuberculin syringe for accuracy.
(c) The test is read in 48 to 72 hours. A "1 plus" reaction is indicated by an area of edema, or a wheal, from 5 to 10 mm. in diameter, which may or may not be surrounded by a red area. If the wheal is larger it is read as a "two" or "three plus" and, if any tendency to sloughing, as a "four plus."
(d) If there is no edematous area of 5 mm. or larger within 48 to 72 hours, a similar intradermal injection of 0.1 c. c. of "second test strength" (stronger) is given. This should be "read" similarly in 48 to 72 hours.
(e) If there is no edema of 5 mm. in diameter, or larger, by that time, the test is negative.
3. A positive tuberculin test indicates that the individual is or has been infected with tubercle bacilli. It does not prove the presence of tuberculous disease. Neither does the degree of reaction have any diagnostic or prognostic import. It is believed that the more recent the infection, the more severe the tuberculin reaction is likely to be.
A negative test does not disprove past or present infection, but active tuberculosis is rarely present when the test is repeatedly negative.

B. ACTIVE IMMUNITY

1. Inherent: Not measurable but present in varying degrees.
2. Naturally acquired: The tendency to healing of tuberculous lesions, and the obvious ability of the body to develop resistance to the disease are well known. How much of this resistance is specific immunity is problematical. Certainly a large part is phagocytic, cellular, and mechanical. An individual is most apt to develop increased resistance to his own disease, but often is less likely to exhibit immunity to reinfections. Whether strain specificity is a factor is uncertain. It may be said that

variable immunity may follow recovery from infection, either clinical or sub-clinical.

3. ARTIFICIALLY ACQUIRED: The use of vaccine is in an experimental stage. It cannot be recommended on the basis of results to date.

C. PASSIVE IMMUNITY

1. INHERENT: None
2. ARTIFICIALLY ACQUIRED: None

D. IMMUNOLOGIC THERAPY

1. CASES: None has proven generally effective.
2. EXPOSURES: None

TYPHOID FEVER

A. TEST FOR SUSCEPTIBILITY: None.

B. ACTIVE IMMUNITY

1. INHERENT: None.
2. NATURALLY ACQUIRED: One attack of typhoid usually protects against subsequent attacks. Second and third attacks in the same individual have been reported.
3. ARTIFICIALLY ACQUIRED: An artificial immunity to typhoid fever may be established by the subcutaneous administration of killed typhoid bacilli suspended in normal saline.

   (a) For the initial immunization, the vaccine is administered at intervals of one week. The first dose is one-half minim per ten pounds of body weight and the two succeeding doses, 1 minim for ten pounds of body weight with a maximum dosage of ½ c.c., 1 c.c. and 1 c.c. respectively.

   (b) Vaccine for oral administration has been introduced, but there is insufficient evidence of efficacy to warrant its general acceptance.

   (c) Maximum immunity develops in from three to four weeks after the first dose is given and in a few months begins to diminish. Immunity thus acquired may be lost entirely in about two years. It is recommended that one dose of 0.5 c. c. of the vaccine be administered annually after the initial course, in order to maintain immunity. If more than two years' time is allowed to elapse, three doses as for initial immunization should be given.

   (d) Since typhoid fever may occur in those of any age, the vaccine may be administered to young and old alike. In routine mass immunization programs, the vaccine should be given to all above one year of age. The presence of any febrile illness is considered to be a contraindication to giving typhoid vaccine. In familial or near-neighbor contact, in epidemics, and in areas

where typhoid is endemic, all persons should be given the vaccine.

Immunity produced by typhoid vaccine is relative and not absolute, and a massive infection of a vaccinated individual may produce the disease. Vaccinated persons should rigidly observe all rules of sanitation and hygiene.

C. PASSIVE IMMUNITY

1. INHERENT: None.
2. ACQUIRED: None.

D. IMMUNOLOGIC THERAPY

1. CASES: None that is practical or generally accepted.
2. EXPOSURES: Immediate vaccination.

PARATYPHOID FEVER

The same principles of immunization against typhoid fever are likewise considered applicable to paratyphoid fever.

Until quite recently it was customary to employ a mixed vaccine—that is, one containing a major component of killed typhoid organisms and lesser components of paratyphoid A and paratyphoid B organisms. This practice has been largely discontinued for the following reasons:

1. Paratyphoid fever is a relatively rare disease.
2. The mixed vaccine causes more severe local and systemic reactions than does a plain typhoid vaccine.

CEREBROSPINAL FEVER

(Epidemic Meningococcus Meningitis)

A. TEST FOR SUSCEPTIBILITY: None that has been generally used

B. ACTIVE IMMUNITY

1. INHERENT: Not known
2. NATURALLY ACQUIRED: Some immunity of unknown duration is present in those who have recovered from the disease, and is likewise present in carriers.
3. ARTIFICIALLY ACQUIRED: Data recently collected indicates that immunity may possibly be produced by administration of small doses of meningococcus toxin. Further information is needed to confirm this.

C. PASSIVE IMMUNITY

1. INHERENT: Not known
2. ARTIFICIALLY ACQUIRED: It is believed that the administration of anti-meningococcic serum or of meningococcic antitoxin will confer some passive immunity. The degree and duration, how-

ever, are difficult to estimate, and the procedure is not recommended for prophylaxis.

D. IMMUNOLOGIC THERAPY

1. For Cases: There are two forms of antisera commonly employed in therapy:
   (a) Antimeningococcic serum, which supposedly is both antitoxic and antibacterial; and
   (b) Meningococcus antitoxin, which is a serum product supposedly antitoxic only. Results generally seem to be good with both.

   There are 3 routes for the administration of either of the above two products: Intramuscular, intravenous, and intraspinal. The amount of total dosage in a given case varies so greatly that there can hardly be said to be an average. It is felt that such treatment will accomplish all that can be expected of it within 4 days, and that the first 48 hours should be the period during which most of the serum or antitoxin is to be used. Most opinion is to the effect that intraspinal plus intravenous or intramuscular injections is more effective than either of these routes alone. Certainly where a high degree of bacteremia is evident (many petechiae, etc.) prompt administration of at least one intravenous dose is indicated.
2. For Exposures: Except for special indications, prophylactic doses of serum or antitoxin had best not be given. With the very frail child this may be tried. In usual cases, however, close observation with intensive therapy at the first sign of the disease is recommended.

ANTERIOR POLIOMYELITIS
(Infantile Paralysis)

A. TEST FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. Inherent: It is not known whether there is any active inherent immunity or not.
2. Naturally Acquired: In all probability, immunity results from subclinical infections; in this respect the disease seems comparable to diphtheria. Epidemiologically, it appears that a large part of the population is immune to this disease.
3. Artificially Acquired: None

C. PASSIVE IMMUNITY

1. Inherent: Unknown
2. Artificially Acquired: Convalescent serum has been used; practically, however, this procedure has not proven to be of any benefit.

D. IMMUNOLOGIC THERAPY

1. CASES: None
2. EXPOSURES: None

NOTE: Several nasal sprays have been advocated and at least some of these have prevented monkeys from contracting the disease. Where controlled experiments in human beings have been tried, the results did not appear to show any significant difference between the sprayed and unsprayed groups. It has been pointed out that the anatomical structure of the human nasal passages presents a difficult problem in the application of the spray.

ERYSIPELAS

NOTE: Most opinion is now to the effect that this disease can be caused by any of the 27 or more types of hemolytic streptococci in that group of human origin referred to as "Streptococcus pyogenes." From neither the bacterial nor the toxic point of view, therefore, does Erysipelas seem to be limited to a single strain of the hemolytic streptococcus.

A. TEST FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. INHERENT: None known
2. NATURALLY ACQUIRED: One attack does *not* seem to confer immunity. (There may be some natural antitoxic immunity that is highly strain-specific, thus failing to protect against new attacks of different strains.)
3. ARTIFICIALLY ACQUIRED: Although vaccines have been developed, there is no satisfactory evidence of their value.

C. PASSIVE IMMUNITY

1. INHERENT: None that is demonstrable
2. ARTIFICIALLY ACQUIRED: Erysipelas antitoxin has been recommended, but its value is very much open to doubt. It is not recommended for prophylaxis. Neither does convalescent serum seem to be of practical value.

D. IMMUNOLOGIC THERAPY

1. CASES: Treatment with antitoxin, or with convalescent serum, has not been shown conclusively to be of value. There seems to be no specific strain of streptococcus or toxin associated with Erysipelas. If antitoxin is to be used, any erythrogenic (such as Scarlatina) antitoxin would seem to be as rational as another. There is no evidence of any antibacterial effect, and antitoxic results are extremely variable.
2. EXPOSURES: None of proven value

NOTE: On the basis of confirmed results, chemo-therapy

(sulphanilamide) seems to be of definite value in treatment, far superior to any claims for immuno-therapy.

STAPHYLOCOCCUS INFECTIONS

A. TEST FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. INHERENT: Unknown
2. NATURALLY ACQUIRED: There is a tendency for the antitoxin level of the blood to increase during childhood. Chronic staphylococcic infections may increase the antitoxin level of the blood.
3. ARTIFICIALLY ACQUIRED: Staphylococcus toxoid is said to be useful in producing active immunity. Its effectiveness remains yet to be determined. Toxoid is usually limited to chronic local infections. It is not advised for use in systemic infections.

C. PASSIVE IMMUNITY

1. INHERENT: Unknown
2. ARTIFICIALLY ACQUIRED: (See below)

D. IMMUNOLOGIC THERAPY

1. CASES: The value of staphylococcus antitoxin is limited. It does not prevent complications and is not bactericidal. It may serve to relieve symptoms resulting from toxemia. The local inflammatory process is not affected by its use. Its use is usually restricted to acute systemic infections.

TETANUS
(Lockjaw)

A. TEST FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. INHERENT: None known
2. NATURALLY ACQUIRED: None proven. (Previous evidence that an intestinal carrier state results in natural acquisition of immunity has not been substantiated.)
3. ARTIFICIALLY ACQUIRED: Active immunity can be produced by the administration of tetanus toxoid (either plain or alum precipitated). The production of antitoxin following toxoid injection is slow, reaching a maximum in 3 to 5 months. Therefore it is unsuitable as a prophylactic against tetanus from an existing wound.

   NOTE: Tetanus toxoid has been used for too short a time and in too few instances for final conclusions. The following represents conservative opinion upon the subject as of the present.

Active immunity once established varies considerably as to degree, the average antitoxin level in the blood being about that following the usual prophylactic dose of antitoxin. Such immunity apparently lasts 12 to 18 months, gradually declining thereafter.

Re-injection following previous immunization with toxoid usually results in a rapid rise of immunity (7 to 15 days) usually to a much higher level than the first response.

(a) Routine use of this measure is hardly indicated except for specific groups subject to frequent exposures such as: Agricultural and stock raising workers, military personnel, etc.

(b) Dosage of tetanus toxoid. Plain: Three 1 c. c. doses at 3 to 4 week intervals. Alum precipitated: Two 1 c. c. doses at 3 to 4 week intervals.

(c) To keep a fairly high level of resistance, a single re-injection should be given every 12 to 18 months.

(d) At time of injury, individuals previously immunized should receive a single injection of toxoid.

(e) Toxoid is worthless as a substitute for antitoxin at the time of injury for those not previously immunized.

(f) Tetanus toxoid is entirely worthless for therapeutic purposes.

C. PASSIVE IMMUNITY

1. INHERENT: Unknown

2. ARTIFICIALLY ACQUIRED: By administration of prophylactic dosage of tetanus antitoxin.

(a) The dose varies from 500 to 3,000 American units, depending upon the character and severity of the wound. The average standard dose is 1,500 units. Larger doses are indicated where there is extensive tissue damage (including compound fractures). It should be given as soon after injury as possible, but may be effective when given later.

(b) Antitoxin is gradually eliminated, so that little immunity remains at the end of two weeks. Therefore in severe wounds not healing satisfactorily, a second dose should be given about one week later. The immunity is anti-toxic rather than anti-bacterial and does not destroy or prevent development of tetanus bacilli in the wound. Secondary operations for removal of foreign bodies, etc., should be preceded by a second prophylactic dose.

(c) Due precautions against serum sensitivity always should be taken, particularly since there is ample time for administering fractional de-sensitizing doses if necessary. (Also bovine serum may be substituted for horse serum.)

(d) There is no absolute rule as to which injuries indicate tetanus antitoxin and which do not; nor is there any test

that can be applied. However, antitoxin is definitely indicated in compound fractures, fireworks, gunshot and penetrating wounds; deep cuts, punctures, severe burns, and ragged wounds, especially where clothing, dirt, and other foreign matter is apt to have been introduced.

(e) In all severe wounds, proper surgical treatment, including cleansing, removal of foreign bodies, and debridement, is of equal importance to antitoxin in preventing tetanus.

D. IMMUNOLOGIC THERAPY

1. CASES: Specific immuno-therapy is but one of the triad usually employed. The other two (which are more important) are: *correct surgical care* (including removal of foreign bodies, debridement, drainage and avoiding cauterization) and *careful symptomatic treatment.*

(a) Although definitely indicated in the treatment of tetanus, antitoxin is of limited value. It cannot neutralize toxin already bound to nerve cells, and therefore cannot be expected to relieve symptoms. Its use is indicated mainly in a prophylactic sense, in that it can be expected to neutralize uncombined toxin still in body fluids and still being produced in the wounds.

(b) Total mass dosage up to several hundred thousands of units has been recommended by some. However, conservative opinions are to the effect that the total dosage given over a period not exceeding three or four days should rarely exceed 100,000 units. Some authorities feel that 40,000 units will accomplish as much as larger dosage. The proper dosage probably lies somewhere between 10,000 and 100,000 units. In using antitoxin, serum sensitivity must be ruled out or desensitization employed.

(c) Intravenous or a combination of intravenous and intramuscular injection is the generally accepted method of administering tetanus antitoxin therapeutically. Ordinarily beneficial results of serum therapy will accrue from that given within the first 4 days, and continuation beyond this point is probably unnecessary.

2. FOR EXPOSURES: As outlined under artificial passive immunity.

RABIES

A. TEST FOR SUSCEPTIBILITY: None

B. ACTIVE IMMUNITY

1. INHERENT: Not known
2. NATURALLY ACQUIRED: Not known
3. ARTIFICIALLY ACQUIRED: By subcutaneous administration of antirabic vaccine of which there are several types differing

chiefly in method of preparation. All are based on an attenuated or "fixed" strain of rabies virus, the virulence of which has been fixed so that it is highly virulent for lower animals when inoculated intracranially, but of extremely low virulence when given subcutaneously. Most of the methods, notably those devised by Semple, Harris and Cumming, require the killing of the fixed virus by chemicals or heat. The method of Hoegyes employed in Georgia consists of a highly diluted living fixed virus. The original Pasteur method employs a combination of living and dead fixed virus.

(a) The production of immunity by antirabic vaccine or "treatment" is slow, probably requiring several weeks to reach a maximum. Fortunately, the incubation period of rabies, varying from 15 to 90 days (averaging 4 weeks), is long enough to permit the production of an adequate degree of protection before active infection can begin.

(b) Immunity production is accelerated by repeated daily injections. The Semple and Harris methods employ 14 daily doses, while that of Hoegyes, as employed by the Georgia Department of Public Health, has a range of dosage varying from as low as 12 for very superficial exposures, to 45 for severe exposures about the face. The size of the dose varies from 1 to 2 c.c.

(c) The incidence of rabies in persons who are actually bitten by rabid animals and who receive prophylactic treatment is less than 0.1 percent as compared with an incidence of 10 to 15 per cent without treatment. The efficiency of antirabic treatment in protecting man against the development of rabies from the bites of or equivalent exposure to rabid animals seems to depend on such factors as:

  (i) Location and severity of the wounds. Prophylactic treatment fails most often after severe, multiple lacerations about the face (especially the lips). Next in order of seriousness are punctures on the bare hands, especially the fingers. Least dangerous are bites on the legs and feet.

  (ii) Prompt administration: While supportive evidence is meager, it is the prevailing opinion that delay in commencing antirabic treatment lessens its efficiency.

(d) Duration of immunity is not known, except that it is relied upon to protect against all re-exposures occurring within six months following immunization. Very recent experimental evidence indicates a much longer duration.

(e) Complications: The only serious complication is treatment paralysis, which is very rare, occurring only once in every 4,000 or 5,000 persons treated. In spite of its rarity, the possibility of treatment paralysis is an important argument against the promiscuous administration of antirabic treat-

ment to persons not directly exposed to the infection. (See g.)

(f) Types of exposure warranting antirabic treatment:
  (i) The bite or scratch of a known rabid animal.
  (ii) The bite or scratch of a suspected rabid animal, that is, one in which rabies cannot be excluded by observation or clinical and laboratory methods.
  (iii) The direct contact of saliva of the known or suspected rabid animal with fresh, open abrasions not more than 24 hours old.
  (iv) Young children who have been in contact with known or suspected rabid animals whose degree of exposure is unknown.
  (v) Neurotic individuals not considered exposed, but whose sanity is threatened unless treatment is given.

(g) Circumstances not warranting antirabic treatment:
  (i) Getting saliva on the bare skin in the absence of fresh, open abrasions.
  (ii) Contact of saliva with cuts or scratches which are more than 24 hours old, and are "scabbed over."
  (iii) Bites through heavy clothing where the cloth is not torn.
  (iv) Drinking the milk of rabid cows.
  (v) Bites which occurred more than seven days prior to onset of symptoms in the animal.
  (vi) Bites of animals which live and show no definite symptoms one week after biting.

C. PASSIVE IMMUNITY

1. INHERENT: Unknown
2. ARTIFICIALLY ACQUIRED: None

D. IMMUNOLOGIC THERAPY

1. CASES: None
2. EXPOSURES: (See P-3.)