notably those which have only recently passed from the secondary phase into the phase of latency. On the other hand, individuals with older latent syphilis are likely to exhibit serologic refractoriness, the STS showing either no tendency or little tendency to lose strength. This results in the case having to be classified eventually as serum-fast.

7. DEFINITION OF PENICILLIN FAILURE. Care should be exercised in the determination of failure since patients may develop intercurrent skin eruptions of nonsyphilitic character. Intercurrent infections and smallpox vaccination may produce a temporary elevation of the titre of the quantitative STS. All forms of clinical relapse are generally accompanied by serologic relapse, or by persistently high serologic titres. Treatment failures may be divided into nine categories.

a. Mucous and/or cutaneous relapse is manifested by the appearance of syphilitic lesions of the mouth, genitals, and skin, the latter especially in the anogenital region. There may be lesions of both skin and mucous membranes (mucocutaneous relapse) or of either surface alone. Darkfield examinations should be performed to corroborate the diagnosis. If darkfield examination is negative, repeated quantitative STS should be performed which will reveal a progressively rising titre. In doubtful cases, consultation is desirable.

b. Serologic relapse is manifested by a rising titre of the quantitative STS after the test has become negative or has manifested a previously falling trend. When a serologic relapse is suspected, the patient should be thoroughly and frequently examined, since serologic relapse is usually accompanied or shortly followed by mucocutaneous or some other clinical relapse. Since the titre of the quantitative STS may vary from time to time as a result of laboratory technic—and in different laboratories—it is not sufficient to accept minor fluctuations in the titre as evidence of serologic relapse. *Serologic relapse should be diagnosed only when a series of consecutive tests, performed preferably in the same laboratory, shows persistently increasing titres over a period of 3 to 4 weeks.* In the event that a titred test is not available, a change from a doubtful or negative reaction to a persistently positive reaction will be accepted as adequate evidence of serologic relapse. It should be noted that the titre characteristically rises during and, for a brief period, after penicillin therapy. This elevation is temporary and is not to be considered evidence of serologic relapse.

c. Serum-fastness in primary and secondary syphilis is manifested by a failure of the quantitative STS to show a marked decline within an arbitrary period of 6 months after completion of therapy. Minor fluctuations in the titre may be observed, and also a drop to a lower sustained level, but there is no consistent, gradual, and maintained fall to negative. This condition will be uncommon in primary and secondary syphilis, where it will be considered a treatment failure when present 6 months after completion of therapy. *It will not be uncommon in latent syphilis, in which it will not be considered a treatment failure.*

d. Neurologic relapse (neurorecurrence) may occur as acute syphilitic meningitis, with headache, dizzy spells, fever, and rigidity of the neck. In fulminant cases, coma may supervene rather rapidly. Less commonly relapse in the nervous system may appear as an isolated cranial nerve palsy or paralysis of one or more extremities. Diagnosis should be confirmed by spinal fluid examination. In these cases the neurologist should be consulted for diagnostic assistance.

e. Asymptomatic neurosyphilis is manifested only by an abnormal spinal fluid.

f. Ocular relapse may be manifested by iritis, usually unilateral, or optic neuritis, or neuroretinitis, which may be unilateral or bilateral. The latter conditions may be accompanied by headache, and blurring and progressive failure of vision. In these cases the ophthalmologist should be consulted for diagnostic assistance.

g. Osseous relapse is manifested by severe pain, often nocturnal, in the long bones, most often the tibias, or severe headache when cranial bones are affected. Local tenderness over the affected bone is often very acute. Roentgenograms may assist in the diagnosis.

h. An extremely rare case may occur that is treatment-resistant to penicillin, where lesions fail to heal and living treponemes are present after completion of the treatment course.

i. Other forms of visceral relapse such as hepatitis have so far not been observed but should be watched for.

8. MANAGEMENT OF PENICILLIN FAILURES. *a.* Cases of neurologic relapse and asymptomatic neurosyphilis will be managed in accordance with TB MED 48.

b. All other treatment failures after the 2,400,000 unit course of penicillin will receive a second course of the drug. This will consist of 4,000,000 units of penicillin, given in 80 consecutive intramuscular injections of 50,000 units at 3-hour intervals day and night for 10 days. These patients will be followed during the post-treatment period as described in paragraph 6.

c. Failures to 2 courses of penicillin will be referred to a neurosyphilis center. In theaters of operations suitable arrangements should be provided for expert consultation. Ordinarily these patients will be treated with mapharsen-bismuth in accordance with the following schedule:

Week		
1, 2, 3, 4, 5, 6, 7, 8, 9, 10	Mapharsen intravenously twice weekly, total 20 injections.	Bismuth subsalicylate intramuscularly once weekly, 5 doses.
		Omit bismuth for 5 weeks
11, 12, 13, 14, 15, 16	*Omit* mapharsen 6 weeks	Bismuth subsalicylate intramuscularly once weekly—6 doses
17, 18, 19, 20, 21, 22, 23, 24, 25, 26	Mapharsen as in first course, twice weekly, total 20 injections.	*Omit* bismuth for 5 weeks
		Bismuth subsalicylate intramuscularly once weekly, 5 doses.

Mapharsen dosage: Adjusted approximately to body weight; average dose 60 mg, minimum dose 50 mg, maximum 70 mg.

Bismuth subsalicylate in oil dosage: The standard dose is 0.2 gm of bismuth subsalicylate intramuscularly (not 0.2 gm of elemental bismuth metal).

9. CARDIOVASCULAR, VISCERAL, AND NEUROSYPHILIS. These cases require special hospital management and treatment, and should be referred to the neurosyphilis centers in accordance with the provisions of TB MED 48.

10. CONGENITAL SYPHILIS. Congenital syphilis will be treated according to the stage of disease, as in acquired syphilis.

11. TREATMENT OF CERTAIN ARMY AIR FORCES PERSONNEL. Personnel of the Army Air Forces required to participate in frequent and regular aerial flights may be treated with penicillin, as provided herein, under conditions prescribed by the Commanding General, Army Air Forces.

BY ORDER OF THE SECRETARY OF WAR:

G. C. MARSHALL
Chief of Staff

OFFICIAL:
EDWARD F. WITSELL
Major General
Acting The Adjutant General

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Refer to FM 21-6 for explanation of distribution formula.

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TB MED 183

WAR DEPARTMENT TECHNICAL BULLETIN

VISCERAL LEISHMANIASIS—KALA-AZAR

War Department, Washington 25, D. C. • • • July 1945

This bulletin follows TB MED 182, subject, "Data on Malaria Control." Distribution given TB MED 182 was as follows: AAF (10); AGF (10); ASF (2); T of Opn (Surg) (10); Dept (Surg) (5); Def Comd (Surg) (5); Base Comd (Surg) (5); Island Comd (Surg) (5); S Div ASF (1); Tech Sv (2) except SGO (300); SvC (Surg) (5); GH (5); SH (5); A (Surg) (5); CHQ (Surg) (5); T/O & E 8-500, Med Sv Orgn—(AD) (5), (AF) (5), (FA) (5), (FB) (5), (GB) (5), (HA) (5), (HB) (5), (JA) (5).

This bulletin supersedes paragraph 13, SGO Circular Letter No. 33, 1943

	Paragraph
Introduction	1
Geographic Distribution	2
Etiologic Agent	3
Transmission	4
Clinical Picture	5
Diagnosis	6
Treatment	7
Prognosis	8
Prevention	9

1. INTRODUCTION. *a. General.* Leishmaniasis is infection with protozoan organisms of the genus *Leishmania* which is transmitted by *Phlebotomus* sandflies. Many authorities today group all cases into one of two categories, visceral leishmaniasis, which is infection with *Leishmania donovani*, and cutaneous leishmaniasis, which is due to *Leishmania tropica* or *Leishmania braziliensis*. These organisms cannot be separated by any available procedure, but the distinction is considered necessary on epidemiological and pathological grounds. There is no longer any basis for the separate classification of visceral leishmaniasis in infants, which was formerly attributed to "*Leishmania infantum*." Canine leishmaniasis ("*L. caninum*") probably represents merely an epidemiologic variety of *L. donovani* infection. Whereas cutaneous leishmaniasis usually involves only the skin and subcutaneous tissue and, in some cases, the nasopharyngeal mucosa and submucosa, visceral leishmaniasis always causes widespread lesions. The remainder of this bulletin is devoted to visceral leishmaniasis or, as it is commonly known, kala-azar. These terms will be used interchangeably.

b. Incidence. So far as is known, there is no natural immunity to kala-azar. Although the disease is uncommon in individuals of Caucasian origin in India and China, the low incidence is due apparently to infrequent exposure to the disease. Kala-azar is often sporadic in its occurrence, but it may appear in epidemic form. The disease is particularly common in villages, although it also occurs in cities. In India and China there are particular villages and even individual houses which are known to be foci of kala-azar. Those infected belong predominantly to the lower social groups of the population. Statistics show a higher incidence in males, but it is doubtful that they are reliable, since far more males than females attend hospitals in the Orient. Kala-azar is predominantly a disease of young people, but it is also common in the third decade of life and may occur at any age. In the Mediterranean area the incidence in infants is said to be relatively higher than it is in other areas. Many animals, including especially the hamster, are susceptible to artificial infection, but the

AGO 1115A—July 657607°—45

only animal found to be infected in nature is the dog.

2. GEOGRAPHIC DISTRIBUTION. Visceral leishmaniasis is found in Asia, Africa, Europe, and South America (fig. 1). The incidence varies greatly even in contiguous areas.

a. China. The disease is common in many of the provinces north of the Yangtse River. It is especially prevalent in parts of Kiangsu, Shantung, Honan, Hopei, Anhwei, and Shensi. It is also found in Hupei, Shansi, Szechwan, Kansu, and southern Manchuria (Manchukuo). South of the Yangtse River, a few cases are found in Kiangsu, Chekiang, Kiangsi, and Kwangsi. There is one doubtful report of cases in Canton.

b. India. Kala-azar is found in parts of the eastern portion of the country, including Madras Presidency, Orissa, the United Provinces, and is especially common in Bihar, Bengal, and Assam.

c. Other parts of eastern Asia. The disease has not been reported in Korea, the Japanese Empire, Formosa, the Philippines, Malaya, the Netherlands East Indies, or Burma.

d. Russia. Kala-azar exists in parts of Russian Turkestan and southern European Russia.

e. Mediterranean Area. Kala-azar is found with varying incidence in all the countries bordering on the Mediterranean, especially in parts of Greece, Crete, Yugoslavia, southern Italy, Sicily, Malta, and southern France. It is less frequent, but present, in Palestine, Syria, Turkey, Spain, and North Africa. Cases have been reported in Portugal.

f. Africa. In addition to North Africa (*e* above), kala-azar exists in the Sudan, Ethiopia, Eritrea, Kenya, French Equatorial Africa (Lake Chad region and Gabon), and Nigeria.

g. South America. Visceral leishmaniasis occurs in northern Argentina, Paraguay, and eastern and northern Brazil.

3. ETIOLOGIC AGENT. *a. General.* *Leishmania donovani*, the causal organism of visceral leishmaniasis, is a protozoan parasite which belongs to a group known as hemoflagellates that inhabit the blood or other tissues of vertebrates. Two forms of *Leishmania donovani* are present in its life cycle, the leishmania form—a stage lacking a flagellum—which occurs in man or other mammalian hosts, and a leptomonad or flagellate form which develops in the sandfly intermediate host and in artificial culture media.

b. Leishmania forms. These forms, commonly referred to as Leishman-Donovan bodies, are small ovoid or round unicellular organisms measuring 2 to 4 microns in diameter, which occur in reticulo-endothelial cells and macrophages. The parasites are characterized by a relatively large rounded nucleus usually located on one side of the body and a kinetoplast which appears either as a minute dot or tiny oblique rod (fig. 2). In well-stained specimens, the kinetoplast may be seen to consist of a rodlike parabasal body and a dotlike blepharoplast. Elongated slender "torpedo forms" with blunt or pointed ends may also be observed in man. With Giemsa or Wright's stain, the cytoplasm appears pale blue and the nucleus and kinetoplast red or reddish purple. The leishmania forms grow and multiply at the expense of the host cells which they parasitize. Infected cells become enlarged and finally disintegrate. The liberated parasites are taken up by other endothelial cells or are phagocytosed by polymorphonuclear leukocytes. The organisms are abundant in certain tissues and are present in small numbers in monocytes in the circulating blood.

c. The leptomonad form. These forms result from a transformation which the leishmania forms undergo in the digestive tract of sandfly vectors after they have fed on an infected vertebrate host or in cultures when inoculated on suitable media. The leptomonad forms are spindle-shaped bodies 14 to 20 microns long by 1.5 to 3.5 microns broad, with a more or less centrally placed nucleus (fig. 3). They resemble trypanosomes in shape, but lack an undulating membrane. The flagellum is as long as or longer than the body, and originates from a kinetoplast which lies transversely at the anterior end of the organism. The flagellate forms multiply by longitudinal fission and may be maintained indefinitely in culture. In young cultures, stumpy pear-shaped or oval forms may be common. The leptomonad form moves actively with the flagellum foremost. In cultures,

the leptomonads frequently tend to agglomerate in rosette groups with their entangled flagella directed inwards. Leptomonads may be observed in the midgut of Phlebotomus sandflies by the third day after the leishmania forms have been taken up from an infected mammalian host. As they multiply, the leptomonads move forward to occupy an anterior station in the pharynx and buccal cavity of the sandfly. The leptomonads are presumed to gain access to man when the flies subsequently feed. Inside the body they undergo transformation and multiply as intracellular leishmania forms.

4. TRANSMISSION. *a. The vector.* Sandflies of the genus *Phlebotomus* are chiefly responsible for the transmission of visceral leishmaniasis. These minute blood-sucking vectors are hairy, moth-like insects, capable of penetrating standard mosquito netting and screening. They should not be confused with species of *Culicoides* (gnats or midges) which also are commonly referred to as sandflies. *Phlebotomus* species are weak fliers, having a flight range, at most, measuring a few hundred yards. Consequently, these sandflies are most numerous in the immediate vicinity of their breeding places. The larvae develop in dark, slightly moist places, such as crevices in walls, floors, masonry ruins, under rocks or rubble, in sandy soil, in caves, and along river banks. Larval development requires from several weeks to several months, depending upon the temperature. Daytime shelters for adult sandflies include breeding sites, and also tree hollows and buttresses, animal burrows, and dark sections of human or animal habitations. The average length of life of adult sandflies is estimated to be from 2 to 3 weeks. As with mosquitoes, only the females feed on man or animals. Sandflies are nocturnal feeders, most active on warm, still nights. They attack silently, seeking out the ankles, wrists, knees, and elbows. Often the bites cause a severe local reaction. The recognition of sandflies is aided by their irregular flight with short hops and long pauses and the elevated V-position assumed by the wings when the insects are at rest. Sandflies seldom rise as high as the second floor of a building.

b. Important species. Phlebotomus argentipes is considered the most important vector in India, *P. chinensis* in China, and *P. perniciosus* in the Mediterranean region. Some of the species of sandflies commonly associated with the transmission of kala-azar are listed below:

India: *P. argentipes.*
China: *P. chinensis; P. sergenti* var. *mongolensis.*
Mediterranean: *P. perniciosus; P. major.*
Spain: *P. papatasii.*
Palestine: *P. perfilewi.*
N. Africa: *P. sergenti.*
Sudan, Ethiopia: *P. langeroni* var. *orientalis.*
Brazil, Paraguay: *P. intermedius* (*lutzi*); *P. longipalpis.*

c. The reservoir of infection. In many endemic areas it is probable that man constitutes the important reservoir of infection. In certain areas, such as China, the Mediterranean, and South America, where natural canine infections occur, dogs also may play a part in the epidemiology of kala-azar. Hamsters, and certain other lower animals although susceptible to infection experimentally, are not known to harbor naturally acquired infection.

d. Other possible modes of transmission. Since leishmania forms have been demonstrated in nasal and pharyngeal secretions, urine, and stools of kala-azar patients, the possibility that the parasite may be transmitted through contamination of food or drink, by droplet infection, or by contact, cannot be completely disregarded. However, these modes of infection probably play a minor role, if any, in the spread of the disease.

5. CLINICAL PICTURE. *a. General.* Little is known concerning the dissemination of the parasites immediately following infection. Presumably, the parasites are rapidly spread to many parts of the body. At post-mortem examinations, they are found in endothelial cells in many organs, including the skin, and, especially, the spleen, liver, bone marrow, and lymphoid tissue. The disease is regarded as a reticulo-endotheliosis.

b. Incubation and onset. The incubation period is variable, extending from 2 weeks to 18 months. In the majority of cases, it is believed to be within 2 to 6 months. The onset is also variable. Sometimes it is very slow and insid-

ious, and sometimes it is well defined with a gradual development of high fever over a period of 5 to 7 days, as often happens in typhoid fever. In unusual instances the onset is sudden, with high fever, chills, nausea, and vomiting.

c. Symptoms. There is nothing characteristic about the symptoms of kala-azar. In many instances symptoms are of the vaguest sort for many weeks, suggesting the picture often seen in incipient pulmonary tuberculosis. The degree of prostration is frequently remarkably slight. In one large series of early cases, the symptoms in order of frequency were fever, chills, dizziness, headache, anorexia, cough, sweating, constipation, weakness, loss of weight, diarrhea, malaise, epistaxis, abdominal discomfort, nausea and vomiting, and bleeding gums. In rare instances, attacks of pain occur in the splenic region. In children, irritability, mental clouding, and, rarely, convulsions may appear.

d. Fever. The temperature curve assumes a variable form. It usually shows an irregular remittent or intermittent fever. In some cases, however, fever is well-sustained, and the chart shows an uneven plateau. Occasionally, there are wide swings of temperature, such as occur in septicemia. Double and even triple rises in temperature during a single 24-hour period have been described as characteristic, and should lead one to think of the disease, but they are absent in two-thirds of the cases, and even when present they cannot be considered to be pathognomonic, since they occur in other infections.

e. Physical signs. Patients often do not appear as ill as the temperature would indicate, and in early cases the general examination may reveal little. Enlargement of the spleen is characteristic of established infections with kala-azar. It is an error to suppose that the spleen is necessarily huge, however, since the diagnosis may be made when the spleen is not palpable and is often made when it projects only slightly beyond the costal margin. It should be noted that when the spleen becomes very large it sometimes lies in a horizontal position and sometimes lies vertically. The liver is also enlarged, but the enlargement appears to take place somewhat later than that of the spleen. Tenderness of spleen or liver is unusual. Jaundice and ascites are rare, and when present are perhaps not directly due to kala-azar. An important finding in some cases is enlargement of lymph nodes (the enlargement has no characteristic distribution). Other physical signs are of less importance and are associated chiefly with progressive advance of the disease beyond the early stage. After kala-azar has been active for weeks or months, wasting appears. When blood changes are advanced, pallor and other signs of anemia may be seen. Purpura is an occasional feature. Petechiae are rare and rose spots do not occur. In time, the skin tends to acquire a dusky hue, especially in patients with a dark complexion, but the change is often difficult to make out. The skin may become coarse and dry, and the hair may become scanty. In unusual instances, found for the most part among patients who have been treated inadequately, specific skin lesions may develop. These constitute the so-called post-kala-azar dermal leishmanoid. They occur occasionally on the trunk, but usually on the cheeks and nose (where they may take on a "butterfly" configuration) or lips. Such lesions are originally macular, but become raised and in time nodular. They are associated with depigmentation and do not break down. They contain Leishman-Donovan bodies. Among the incidental findings may be pulsations in the neck vessels, tachycardia, cardiac murmurs, and low blood pressure. The lungs show nothing characteristic.

f. Blood, urine, and stools. The urine and stool show nothing remarkable. The changes in the blood, which are of the greatest importance, are described in paragraph 6*b*.

g. Complications. Patients with kala-azar appear to be peculiarly susceptible to other infections. Stomatitis is common in neglected children. Once established, oral infection may result in noma or cancrum oris, a well-nigh intractable condition. Bronchitis and pneumonia are the commonest secondary infections. In a few instances, nephritis may appear, probably not as a result of kala-azar itself. In advanced cases, edema may be seen, usually because of plasma albumin deficiency.

h. Course. The clinical manifestations usually develop slowly but progressively. In many

cases, the patients have minor symptoms for weeks without reporting sick. Without treatment, the disease usually runs a course, with remissions and relapses, for a period of 2 years or more. During remissions patients may feel, and appear to be, well. In some epidemics, especially in the Sudan areas, the course is relatively fulminating.

6. DIAGNOSIS. *a. Clinical diagnosis.* The diagnosis should always be confirmed by demonstration of the parasite (*c* below). A "therapeutic test" is not considered satisfactory evidence of the disease. The outstanding considerations, apart from demonstration of the parasite, are exposure to the disease, the type of onset and temperature curve (par. 5*d*), palpable spleen and usually palpable liver, and the blood changes (*b* below). Malaria is probably the most frequent source of diagnostic confusion. The two diseases should be separated by parasitologic studies. Other diseases which may need differentiation from kala-azar are schistosomiasis (eggs in stools or urine), relapsing fever (spirochetes in blood), leptospirosis or Weil's disease (agglutination tests, spirochetes obtained by animal inoculation), typhoid fever (blood cultures, agglutination tests), undulant fever (blood cultures, agglutination tests), septicemic conditions such as bacterial endocarditis (blood cultures), pulmonary or abdominal tuberculosis, histoplasmosis, Hodgkin's disease, Banti's syndrome, and blood diseases, especially aleukemic leukemia.

b. Blood studies. (1) The changes in the blood in kala-azar are extremely helpful in diagnosis. The earliest change is a fall in the total leukocyte count, which is due largely to a decrease in granulocytes. While this decrease is not invariably present, it is found in about 80 percent of the cases. Patients with kala-azar may respond to another infection with leukocytosis, but in such cases the leukocytosis is rarely marked. In occasional instances, agranulocytosis develops. There is no eosinophilia. The erythrocyte count falls with varying rapidity. Early cases may be diagnosed before anemia is present, but in established infections anemia is the rule. It may be very severe. Red blood cells tend to be large and hyperchromic. Nucleated forms are unusual. Platelets are also decreased more or less in proportion to the progress of the disease.

(2) The erythrocyte sedimentation rate tends to be increased and may reach high values. The clotting time also tends to increase, but usually is not greatly prolonged. In advanced cases, the bleeding time may be increased.

(3) The plasma proteins undergo a marked change which results in reversal of the albumin-globulin ratio. The globulin fraction begins to increase early in the disease and later may reach extreme values, such as 6 or 8 grams per 100 cc. In advanced cases, the albumin fraction may be much reduced. The relationship of these changes to the qualitative tests which are described below is uncertain. None of these tests is believed to be specific for kala-azar (they are often positive in schistosomiasis and occasionally in other diseases, including malaria). All of these tests may be negative in very early cases which are proved by demonstration of the parasite. Nevertheless, in conjunction with other data, the tests are extremely useful.

(*a*) *Aldehyde test.* To 1 cc of fresh clear serum, add 1 or 2 drops of commercial formalin. A strongly positive reaction is shown by the development within a few minutes of complete opacity and solidification. If complete opacity develops within 24 hours, the result is still positive. Varying degrees of cloudiness indicate doubtful results. When the serum remains clear, the result is negative, even though it solidifies.

(*b*) *Antimony test.* Dilute a small amount of fresh clear serum ten times with distilled water. Place 2 cc of diluted serum in a test tube 4 or 5 mm in diameter and add from a pipette 2 cc of 4 percent solution of neostibosan in distilled water. Rotate the tube between the palms and then read the result. A heavy flocculent precipitate indicates a strongly positive result, mere cloudiness a doubtful result, and absence of precipitate a negative result. The administration of quinine within 24 hours of the test may cause a false positive result.

(*c*) *Distilled water test.* Obtain, without squeezing, from a skin puncture 20 c mm of blood in a hemoglobin pipette. Empty the blood immediately into a small clean test tube (7 to 8 mm in diameter) containing 0.6 cc dis-

tilled water. Mix the contents by whirling it ten times between the hands. Allow the tube to stand vertically without further shaking. Inspect the tube at the end of 5 minutes for turbidity, and then at intervals of 15, 30, and 60 minutes for settling of the precipitate. Haziness or cloudiness at the end of 5 minutes indicates a positive test. A definite settling of the precipitate within 15 minutes indicates a strongly positive test. If turbidity develops within 5 minutes, but no precipitate settles out in 60 minutes, the test is weakly positive.

c. Parasitologic diagnosis. (1) *General.* Definitive diagnosis of visceral leishmaniasis should be based upon the demonstration of leishmania forms in stained preparations, or the growth of leptomonad forms in cultures inoculated with suspected blood or tissue. In rare instances, parasites may be found in monocytes in the circulating blood, but in general this method is not a practicable means of establishing the diagnosis. If hamsters are available, leishmania infection may be established in these animals by the intraperitoneal injection of blood or, preferably, tissue material. However, since 4 or 5 weeks are required for infection to develop, this procedure does not afford prompt confirmation of a diagnosis.

(2) *Obtaining material for examinations.* Tissue, not blood, is desired for examination. The syringe used for aspiration should be dry in order to avoid distortion or disintegration of the parasites. Possible sources of specimens in which organisms might be found include the spleen, liver, sternal bone marrow, lymph nodes, and skin lesions. The parasite has also been found occasionally in normal appearing skin, in nasal and pharyngeal secretions, and in stools and urine, but these sources are not useful in ordinary diagnostic studies. Liver puncture is not recommended. If enlarged lymph nodes are present and safely accessible, aspirated material or biopsy may show the parasite. Sternal puncture is often successful, provided actual marrow without much blood is obtained. Spleen puncture may furnish diagnostic material when other methods fail to do so. It is, therefore, the most reliable approach. Spleen puncture is not free from danger. It should never be attempted without careful study of the technique which, because of its unfamiliarity, is described in (3) below.

(3) *Spleen puncture.* (*a*) This procedure is simple, but it requires the use of great care. If any difficulty is anticipated, lymph node puncture or biopsy or sternal puncture should be chosen for the first trial in diagnosis. Spleen puncture should be performed only in cases in which kala-azar is suspected because of exposure in endemic areas and when clinical data support the diagnostic impression. It should be done only when the edge of the spleen is well below the costal margin. The blood-clotting time and the bleeding time should be determined beforehand. If the clotting time is significantly prolonged, whole blood should be transfused in amounts sufficient to bring it within normal limits.

(*b*) The procedure should be explained to the patient, with emphasis on the need for him to hold his breath in inspiration at the proper time and on the fact that the puncture takes only a few seconds and is usually painless. It may help to rehearse the procedure with the patient.

(*c*) Only liquids should be allowed for breakfast on the morning the puncture is to be done. Pentobarbital sodium 0.1 gm (1½ grains) may be given by mouth 1 hour before puncture. The patient is placed on an abdominal binder (to be used later) and the abdominal skin is cleansed as usual. The site of puncture is selected midway between the edge of the spleen and the costal margin. It should never be immediately below the costal margin or between the ribs. The skin is anesthetized with 1 percent procaine hydrochloride solution which is injected so as to produce a wheal about 2 cm in diameter in the skin.

(*d*) A dry sterile needle of 17 or 19 gauge and 1¾ to 3 inches in length should be used. It may be introduced with a stylet in place or without stylet and with a sterile air-tight 5 cc syringe attached. The patient is instructed to breathe in and out deeply 10 times and to hold his breath on the tenth inspiration. The operator may count aloud and on the ninth inspiration, say "Now breathe in deeply once more and hold it." The needle is then thrust well into the spleen. It should be held firmly, but not too

rigidly. If a stylet is in place, it is withdrawn and a sterile air-tight 5 cc syringe attached. Suction is produced until a small amount of blood enters the syringe. The plunger is then gently released and the needle is quickly withdrawn. Pressure should be applied gently with the hand over a sterile pad for a few minutes, after which the abdominal binder is closed. The aspirated material should be used for preparing smears and cultures, as described in (4) and (5) below.

(*e*) The patient should not have solid food for 2 or 3 hours, and he should remain in bed until the next day. He should be observed closely and the pulse and blood pressure should be taken frequently for 24 hours. Appropriate steps should be taken at once, if any evidence of bleeding is observed.

(4) *Smears.* Tissue puncture material should be spread as thin as possible, allowed to dry, and, after staining with Giemsa or Wright's stain, should be examined under an oil immersion lens. The examination of stained preparations of such material gives a high percentage of positive results, but long search may be required to find the parasites. In the preparation of smears, large parasitized mononuclear cells are frequently broken and parasites liberated. As a result, free Leishman-Donovan bodies may be found. These must not be mistaken for platelets and hence disregarded; conversely, platelets should not be identified as Leishman-Donovan bodies. When doubtful objects are seen, further search should be made for parasites which show typical morphology and leave no doubt as to the identification.

(5) *Cultures.* When parasites cannot be found by direct microscopic examination of tissue smears, they may be demonstrable in cultures of the tissue material. Since from 1 to 4 weeks may elapse before the flagellates multiply sufficiently to be detected, cultures cannot be relied upon to establish a diagnosis promptly. However, they should be employed routinely whenever possible. They should be used also to confirm the diagnosis of leishmania forms observed in tissue smears. Since the parasites occur in small numbers in monocytes in the peripheral blood, culture of the leukocyte layer of 10 cc of centrifuged citrated blood sometimes may give a positive result. In the case of puncture material, after a smear is made, a few drops of sterile saline solution should be taken up into the syringe. The resulting mixture is then expelled onto the base of a slant of NNN medium. NNN (Novy-MacNeal-Nicolle) medium containing defibrinated rabbit blood is the most satisfactory medium for cultures (TM 8-227). The technique of cultivation of leishmania demands careful attention to aseptic precautions in securing and inoculating the material, as the organisms will not survive in cultures containing bacteria. Cultures for *L. donovani* should be kept as near 22° C. (71.6° F.) as possible. They should never be put in an incubator at 37° C., since the organisms do not multiply at this temperature. The cultures should be examined for parasites every few days and not discarded until at least a month has passed. Rubber caps or stoppers should be used to prevent the cultures from drying, or small amounts of sterile saline may be added from time to time. A platinum loop may be used for obtaining material for examination of the cultures, using precautions to prevent bacterial contamination. The material should be mixed with a small amount of saline on a slide and the actively motile flagellates searched for in the fresh wet preparation, using the high power of the microscope. If negative, a small amount of water of condensation in the culture may be secured with a capillary pipette and examined in the same way. Morphological detail may be observed in smears of culture material stained by Giemsa's or Wright's method.

7. TREATMENT. *a. General.* Patients with fever, severe anemia, or leukopenia should be kept in bed. A well balanced and liberal diet should be given, unless some complication indicates a special regimen. Fluids should be given freely. Special attention should be paid to the care of the mouth in order to secure and maintain cleanliness. Mouth washes should be bland and nonirritating, especially if any lesions are present. If severe anemia, leukopenia, or bleeding tendency exists, transfusions of blood should be given. In cases with secondary infection or cancrum oris, the use of penicillin is advised. In general, the chemotherapy of kala-azar takes precedence over the specific treatment

of other infections which may be concomitant. Splenectomy should never be performed for the treatment of this disease.

b. Chemotherapy. (1) *General.* The early institution of chemotherapy for kala-azar is highly desirable. There are few contra-indications for such treatment, except serious disease of the lungs, heart, liver (aside from disease due to leishmaniasis), and kidneys. The presence of the usual complications of kala-azar is only a further reason for pressing ahead with chemotherapy. At present, neostibosan is considered the drug of choice for general use. Antimony and potassium tartrate has been used in the past for the treatment of kala-azar, but it is more toxic and less effective than neostibosan, and is not recommended. Fuadin should not be used for the treatment of kala-azar. Many infections acquired in the Sudan and a few acquired elsewhere are resistant to the usual treatment. Stilbamidine, a nonstandard drug, has been recommended for use in such cases. It may be obtained as nonstandard Item 1N77830 Stilbamidine, 0.15 gm, 10 ampules in box; unit—box, only by requisition stating full justification for its need. Requisitions for this item must be forwarded by depots or service commands to The Surgeon General's Office for approval. In the United States, patients who may require treatment with stilbamidine should be transferred to one of the hospitals designated for specialized treatment of tropical diseases. In certain oversea areas, it may be possible to procure this drug—which is exclusively of British manufacture—from British sources by local procurement. Permission for the use of other drugs than neostibosan or antimony and potassium tartrate should be obtained from The Surgeon General or in oversea areas from the theater surgeon. Patients who are under treatment should be kept in bed and should be observed closely.

(2) *Neostibosan.* This drug is a standard Medical Department supply item, catalogue No. 1300700, supply unit 10 ampules, each ampule containing neostibosan 0.3 gm. Medical officers in areas where kala-azar is likely to be encountered should check with supply officers to be sure that stocks of this drug are available; if the drug is not in stock, a requisition should be submitted immediately. Neostibosan is described as consisting of para-amino phenylstibonic acid, para-acetyl-amino phenylstibonic acid, antimonic acid, and diethylamine and as containing 41 to 44 percent antimony. The drug is relatively unstable in solution, and should be given only when *freshly* prepared with sterile distilled water. The solution should not be boiled or heated, and it should be used as soon as possible. Neostibosan is administered intravenously in 5 percent solution. For adults, the first dose is 0.2 gm, and subsequent doses are 0.3 gm. The total dose is 3.8 to 5.0 gm (13 to 16 injections). Doses may be given daily, unless untoward effects appear. If untoward effects appear, the drug should be given on alternate days, the dosage reduced, or administration stopped, as the circumstances indicate. The most frequent toxic effects are nausea and vomiting. In rare instances, increased fever, dizziness, urticaria, abdominal and muscular pain, renal irritation, and increased bleeding may appear. It is said that bronchitis and pneumonia may be made worse. A few cases of anaphylactic reaction have been reported.

c. Immediate results of treatment. The response to treatment may be dramatic, but it is usually slow. Reduction of the temperature to normal values may take a week or more, and reduction of the spleen is usually slower. When neostibosan is given in daily doses, the patient may show relatively little improvement until the course of treatment is nearly over. In the great majority of cases, however, improvement is then steady. The return of the white blood cell count to normal values is an important criterion of progress. Cures often result even though the response to treatment appears to be late.

d. Follow-up. The condition of the patient should be carefully appraised at the end of each week following treatment. As a rule, the minimum period of strict hospitalization should be 30 days from the end of treatment. A further convalescent period of at least 30 days is necessary in most cases. In the 4th week after completion of treatment, *Leishmania donovani* should be searched for again in suitable tissue. If parasites are found on this examination, or

symptoms and signs persist which are not otherwise explained, another course of treatment should be given. The length of a second course at this time should be decided by clinical judgment. When relapses occur, they usually appear within 6 months of treatment, but they may appear as much as a year later. The occurrence of a relapse should be established by parasitologic study. The development of cutaneous lesions containing Leishman-Donovan bodies should be considered as a relapse. Later courses are just as effective as first courses of chemotherapy, but in order to avoid failure a second time, consideration should be given to the need for larger doses and a longer course of neostibosan. At present, cure can be demonstrated only by follow-up. Individuals for whom a diagnosis of kala-azar has been established should be reexamined, if possible, every month for 6 months after disposition, and again at the end of a year.

8. PROGNOSIS. Death ensues in 75 percent or more of the untreated cases. When adequate treatment is instituted early in the course, and indicated repetitions of treatment are given, there should be practically no deaths from this disease. Most patients should be free of abnormal findings at the end of a month following treatment and in normal health at the end of another month. Relapses are estimated to occur in not over 5 percent of the cases in China and India; most of these cases are curable by further treatment.

9. PREVENTION. *a. General.* Although much remains to be learned about the transmission of kala-azar and the habits of species of *Phlebotomus* which may serve as vectors, certain effective measures based on present knowledge may be taken to prevent infection of troops with the disease. These include chiefly the segregation of troops at a safe distance from infected native populations, the control of sandfly vectors, and individual protection from the bites of sandflies. Many measures used in malaria control also afford protection against kala-azar.

b. Location of camps. Camp sites should be located on open, elevated, dry, sandy ground when feasible, and as far from native dwellings and domestic animals as possible. The more breeze in a given location, the better.

c. Protection of buildings. Ordinary screening does not exclude sandflies. Occupants of buildings may be effectively protected, however, by the application of DDT residual spray (QM Stock No. 51-I-305) to the entire inner walls, ceilings and fixtures, and to the inside and outside of screens and doors, including a foot or two of the outer wall around their casements. Sandflies entering buildings make frequent short flights along the walls and upon touching treated surfaces usually will be poisoned sufficiently to prevent their biting. Additional protection may be secured by spraying twice daily, at night and in early morning, with an aerosol dispenser or other available insecticide. These measures should be applied in sleeping quarters, shower rooms, latrines, mess halls, theaters, and other buildings where personnel congregate or work indoors at night. Buildings may be made less suitable as sandfly shelters by eliminating cracks and crevices in the walls, by reducing fixtures to a minimum, and by keeping clothing and duffle away from walls where sandflies may seek protection during the daytime.

d. Area control of sandflies. Whenever possible, the area within a radius of 50 to 100 yards of camp sites and quarters should be cleared of rubble, detritus, gardens, vegetation, and needless earthen walls or banks which may serve as breeding places or shelters for sandflies. When removal of vegetation is impractical, it may be sprayed with DDT solution from the ground at the rate of 2 to 4 pounds of DDT per acre, forming a barrier, as recommended against adult mosquitoes (see TB MED 110). To obtain area control, DDT residual spray should be applied to observed and potential *Phlebotomus* shelters and to resting sites on which sandflies alight when approaching a house, thus interposing a barrier between the breeding places of vectors and the dwellings to be protected. These include sites such as stone walls, masonry ruins, piles of stones, tree buttresses, caves, crevices, and animal burrows. When troop concentrations are necessarily in proximity to infected native populations, spraying of their dwellings with DDT residual spray is

advisable. DDT in oil, distributed by aircraft in amounts effective for mosquito control, also greatly reduces the sandfly population.

e. Sleeping nets. Standard mosquito netting does not keep out sandflies. Sleeping nets of mesh fine enough (more than 45 per inch) to keep out sandflies should be used in heavily infested areas, if other effective measures for protection are not feasible. When fine mesh nets are not available or are impracticable, treatment of nets of ordinary mesh with DDT or impregnation with insect repellent may be helpful in excluding sandflies.

f. Repellents. After sundown, quartermaster-issue insect repellent (QM stock No. 51–R–265) should be used on exposed parts of the body. Protection against bites of sandflies lasts for 4 to 6 hours. One application should be made at sundown and a second upon retiring. Regular use of repellent has proved an effective means of preventing sandfly bites.

g. Protective clothing. Long-sleeved shirts and full length trousers should be worn, especially after sundown.

h. Avoidance of exposure. Contact with native populations, which serve as the reservoir of infection, should be restricted to a minimum. Troops should be prohibited from visiting villages, particularly at night, when sandflies usually feed. Since dogs may serve as a source of infection, they should not be permitted around troop installations.

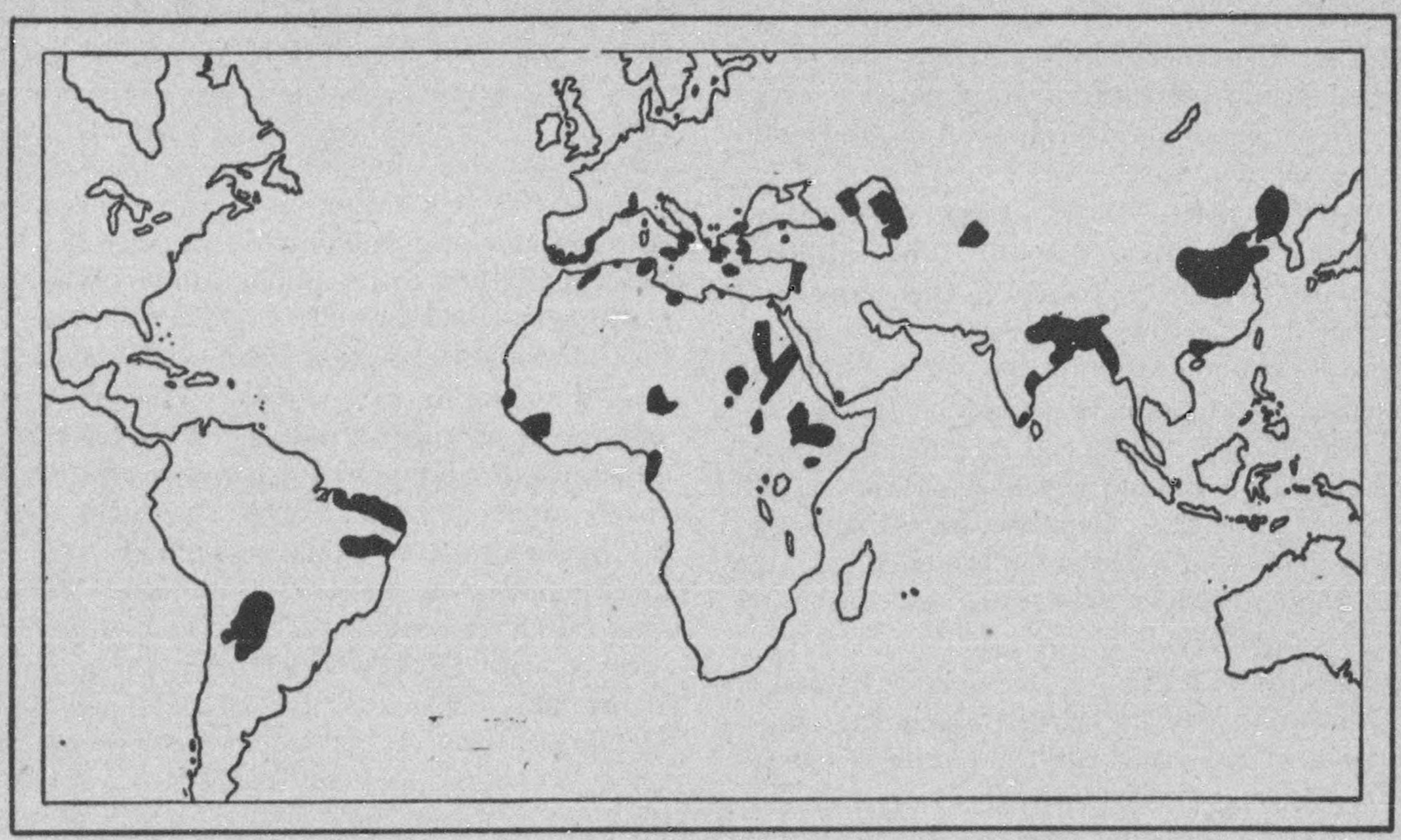

Figure 1. Distribution of visceral leishmaniasis.

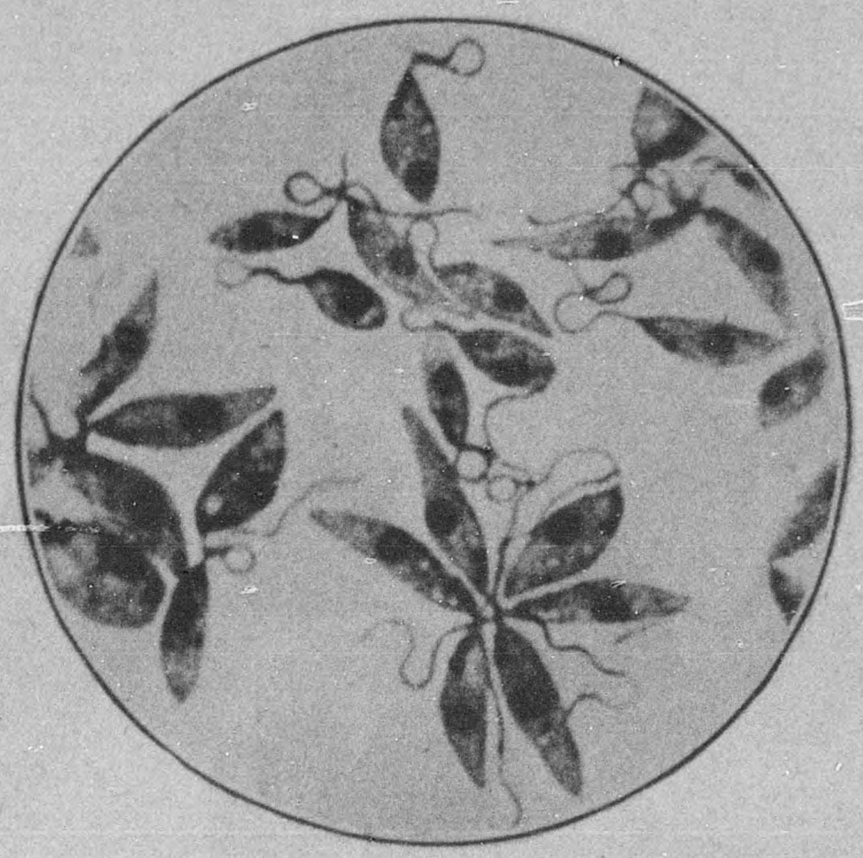

Figure 3.—Flagellate (leptomonad) forms of Leishmania *from culture. (From Army Medical Museum collection.)*

[AG 300.5 (14 Jul 45)]

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Chief of Staff

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Refer to FM 21-6 for explanation of distribution formula.

AGO 1115A

U. S. GOVERNMENT PRINTING OFFICE: 1945

Figure 2. Leishman-Donovan bodies of L. donovani *in stained smear from spleen puncture. (From Army Medical Museum collection.)*

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TB MED 163

WAR DEPARTMENT TECHNICAL BULLETIN

SANITARY CONTROL OF ARMY SWIMMING POOLS AND SWIMMING AREAS

War Department, Washington 25, D. C. • • • May 1945

This Bulletin supersedes SGO Circular Letter No. 118, 2 July 1943

This bulletin follows TB MED 162, subject, "Convalescent Care and Rehabilitation of Patients With Spinal Cord Injuries." Distribution given TB MED 162 was identical to that given TB MED 142.

	Paragraph
Introduction	1
Responsibilities	2
Scope of Sanitary Control	3
Disease Hazards	4
Swimming Pool Inspections	5
Laboratory Examinations of Swimming Pool Waters and Interpretation of Such Examinations	6
Recommended Practices and Standards for Swimming Pools	7
Beaches and Other Natural Swimming Places	8
Facilities at Swimming Pools and Swimming Beaches	9
Sewerage and Water Facilities	10
References	11

1. INTRODUCTION. The purpose of this bulletin is to provide Medical Department officers with information dealing with the provision of swimming facilities and with essential requirements for the protection of personnel using such facilities. The requirements presented are considered the minimum necessary to control effectively the spread of disease by waters used for swimming.

2. RESPONSIBILITIES. Under the general provisions of paragraph 2, AR 40-205, the Medical Department exercises sanitary supervision over Army swimming pools and Army swimming areas. The construction of pools and the maintenance and operation of equipment and appurtenances is a function of the Corps of Engineers. The control of swimmers and pool attendants is usually the responsibility of a recreation officer or other officer designated by the local commending officer.

3. SCOPE OF SANITARY CONTROL. The sanitary supervision of pools and areas includes the following:

a. Inspections and recommendations pertaining to, and technical supervision of, all features of operation which would affect the health or safety of the swimmers.

b. Laboratory examinations of the water and the interpretation of such examinations.

c. Recommendations relative to the location and construction of pools and areas, so far as the location and construction may affect the health or safety of the swimmers.

d. Sanitary surveys to determine possible sources of pollution and their significance.

4. DISEASE HAZARDS. Bathing in waters polluted by sewage, by human or animal excrement, or from the secretions and discharges of bathers, is a possible means of acquiring disease.

a. Diseases which may be contracted by swimming in polluted water are: eye, ear, nose, and throat infections; skin infections; certain gastrointestinal infections; and very rarely such diseases as spirochetal jaundice (Weil's disease). The more common infections attributed to swimming are sinusitis, otitis media, and conjunctivitis. The intestinal disorders

740A—May 637201°—45

are rarely contracted from swimming pools, but may be when polluted streams or beaches are used. It is still questionable whether poliomyelitis is transmitted through swimming areas.

b. In endemic areas, schistosomiasis may be acquired by bathing in natural bodies of water containing schistosome cercariae or artificial pools fed from an infested source. Waters harboring the intermediary snail and contaminated by excrement containing the ova of the parasite serve as the source of infection. Swimming and unnecessary entrance in fresh water, ponds, streams, and canals should be prohibited in endemic areas.

c. In any particular instance where the surgeon finds evidence that disease is being transmitted through a swimming pool, or area, or where these bathing facilities constitute a menace to health of the troops, the pool or area should be closed at once. Adequate corrective measures should be established before further use is permitted.

5. SWIMMING POOL INSPECTION. Routine inspections of swimming pools should be made by the medical inspector or his assistants to insure that swimming pools are operated in a safe and sanitary manner, giving particular attention to the following items:

a. Supervision of bathers. A qualified attendant should be on duty at all times when the pool is open to use by bathers. The attendant should be in full charge of bathing and have authority to enforce the rules of safety and sanitation recommended in *e* below.

b. Maintenance of swimming-pool rooms, dressing rooms, shower rooms, and toilets. The swimming pool, dressing rooms, and appurtenances should be kept clear at all times. The use of DDT residual spray on lockers and on the walls of dressing rooms and toilets is recommended where flies, mosquitoes, or other insects may be a problem.

c. Quality control of swimming pool waters.

(1) *Residual disinfection.* (*a*) Chlorine at a residual concentration between 0.4 and 0.6 part per million is the preferred disinfecting agent for swimming-pool waters. Operating tests should be made frequently to insure this concentration of free chlorine at peak loads in the pool.

(*b*) Chloramine disinfection is slower and should not be employed. As far as possible, chloramines should be eliminated by the use of higher rates of chlorination. With the use of ammonium alum as a coagulant, or with the ammonia naturally present in the pool water, it may not be possible to eliminate chloramines. If chloramines are present, the residual "chlorine" concentration in the pool water should be maintained between 0.7 and 1.0 part per million.

(2) *pH.* The pH of the swimming pool water should be maintained between 7.2 and 7.6.

(3) *Clearness.* If the water is of suitable clarity, an observer standing outside the pool should be able to see clearly, from a horizontal distance of 10 yards, a black disk, 6 inches in diameter on a white field, lying on the bottom of the pool at its deepest point.

(4) *Temperatures.* The water in any swimming pool should not be artificially heated to a temperature above 78° F. It is desirable that air temperatures should be about 5° F. warmer than pool temperature.

d. Operating records. Full daily records should be kept, showing: the total number of swimmers; the maximum number of swimmers using the pool at one time; the length of time pumps and filters are in operation; the amount of chemicals added; when each filter is washed and cleaned; when the pool is cleaned; the results of all tests made of the quality of the water, including at least one test for residual chlorine made at the end of each swimming period.

e. Regulations. Regulations pertaining to the operation of a swimming pool should be published by competent authority and posted where they will be seen by all swimmers. The following are suggested:

(1) The orders, instructions, or requests of the pool attendants will be complied with by all swimmers.

(2) Not more than ---- swimmers will be allowed within the pool enclosure at one time.

(3) All persons will take a shower bath with warm water and soap before entering the pool

enclosure. Swimming suits will not be worn in the shower bath. The soap will be rinsed off with warm water and the swimming suit put on without drying the body.

(4) Expectoration, blowing the nose, or urinating into the pool is forbidden.

(5) No articles of food will be carried into the bathhouse or pool enclosure.

(6) No person who has a cold, sore, ulcers, or other skin diseases, discharges from the ears, who is wearing a bandage of any kind, or is otherwise sick will be permitted to enter the pool enclosure.

(7) No person reported by the surgeon as having, or as being a carrier of, an infectious disease will be permitted to enter the pool enclosure.

(8) No person other than swimmers who have complied with these regulations will be allowed within the pool enclosure, except the pool attendants.

6. LABORATORY EXAMINATIONS OF SWIMMING POOL WATERS AND INTERPRETATION OF SUCH EXAMINATIONS.

a. Collection of samples. It is desirable, wherever facilities permit, to collect one or more samples weekly from swimming pools. Samples should be collected only when the pool is in use and preferably during periods of heaviest bathing loads. The samples should be collected in sterile containers containing sodium thiosulfate to neutralize the chlorine residual.

b. Coliform test. None of the five 10 ml. portions of the water examined should be positive by the confirmed test for coliform organisms.

c. Bacteria count on standard nutrient agar. Not more than 15 percent of the samples should contain more than 200 colonies per ml. when incubated 24 hours at 37° C. on standard agar.

7. RECOMMENDED PRACTICES AND STANDARDS FOR SWIMMING POOLS.

a. Construction plans for new swimming pools, and major improvements to existing pools, should be forwarded to service command or theater headquarters for approval prior to starting construction, regardless of the source of funds. Standard swimming pool plans may be requested through channels from the office of the Chief of Engineers for the following pools and bathhouses:

Pools and bathhouses	Size	Drawing numbers
Standard swimming pool (inclosed).	42′ x 100′	701–140 to 701–157, inclusive.
Standard swimming pool, type A, standard bathhouse.	60′ x 100′	701–160 to 701–166, inclusive, 701–180 and 701–181.
Standard training pool, type B, standard bathhouse.	82′ x 165′	701–170 to 701–176, inclusive, 701–180 and 701–181.
Standard swimming pool, type C, standard bathhouse (inclosed).	50′ x 100′	701–190 to 701–196, inclusive, 701–200 and 701–201.

Additional reference material may be found in *Recommended Practice for Design, Equipment, and Operation of Swimming Pools and Other Public Bathing Places*, an official report (1942) of the American Public Health Association, 1790 Broadway, New York, N. Y.

b. Location of swimming pools. Swimming pools should be located at sites where dirt and debris will not be carried or blown into the pool, and as far as possible from dirt roads, dusty parade grounds, and railroad yards, because dirt and cinders reaching the pool interfere with proper disinfection and general cleanliness. Trees and shrubbery enhance the appearance of a pool, but pools should not be placed so that falling leaves and blossoms will reach the water. Pools should not be placed in low areas subject to flooding, and the top of the pool should be well above the surrounding ground level.

c. Design, construction, and operation features of swimming pools. (1) *Chlorinators.* Chlorine apparatus should be located where it can be readily observed and serviced, and where gaseous chlorine leaks will not endanger the swimmers in the pool or in the bathhouse. Cylinders containing chlorine gas, and chlorinators supplied from such cylinders, should not be located in pits, basements, or where chlorine gas cannot flow into the atmosphere by gravity at the floor level.

(2) *Material.* Pools should be constructed of an impervious material. The bottom surface

and the walls of the pool should be as smooth as possible to facilitate cleaning and the movement of deposits to the main drain. The walls and bottom should be light in color, which can be accomplished by using white portland cement in the original concrete mixture or by painting the surface with a satisfactory waterproof paint. Sand or dirt bottoms are insanitary and should not be used.

(3) *Circulation.* In the design of a new pool, provision should always be made for complete circulation of water through all parts of the pool. Fill and draw pools are not recommended.

(4) *Depth.* The bottom of the ordinary rectangular pool should slope so that the water varies in depth from 3 feet 6 inches at the shallow end to from 8 to 11 feet at the deep end.

(5) *Diving equipment.* Facilities are desirable for practice or instruction in diving and for teaching troops how to get off sinking ships. The maximum safe elevation of diving boards and diving platforms above the surface to the water, in relation of various depths of water, is given in the following table:

Minimum depth of water	Maximum safe elevation above water	
	Diving board	Diving platform
8 ft	3 ft	5 ft
9 ft	5 ft	7 ft
10 ft	7 ft	9 ft
11 ft	10 ft	12 ft

(6) *Inlets.* Inlets are defined as the fixtures installed integrally with the pool structure through which water is introduced into the pool. They should not be considered to include the supply lines directly connected with drinking water systems, for which see (9) below. Inlets should be located at such points as to produce uniform circulation of water throughout the entire pool. The flow to the inlets should be controlled by valves on headers which feed a number of inlets, or by placing a valve on each inlet line so that approximately 75 percent of the fresh water may be directed to the shallow area. A rectangular pool having a length of 75 feet or more should have inlets at the shallow and at the deep end. If the width is greater than 40 feet, or if the length exceeds 100 feet, inlets should be provided on approximately 20-foot centers at both sides and at both ends. Inlets should be located approximately 18 inches below the overflow rim.

(7) *Outlets.* Outlets should be located at the deepest point to facilitate recirculation and draining. The outlet pipe should be large enough to meet the requirements for recirculation and for filter backwashing. The outlet pipe should connect to a trench which is covered with a grating having an area at least 10 times the area of the pipe. The grating should be of such design as to prevent swimmers' fingers or feet from being caught and also of sufficient weight to prevent removal by the swimmers. In the modern hopper type pool bottom, the main drain or outlet grating should include nearly all of the flat area in the bottom of the hopper.

(8) *Sewers.* No direct connections to sanitary sewers should be permitted. All pool drains to sewers should be broken at a point where any sewage which may back up from the sewer will overflow to waste instead of being permitted to reach the pool. Pumping of pool drainage to an elevation above any possible backing up of sewage may be needed in some cases.

(9) *Interconnections.* No interconnections should be permitted between swimming pools and water supplies used for drinking. An open surge tank connected to the recirculation pump suction is recommended. The potable supply line should be float-valve controlled and an airgap of at least the diameter of the pipe plus 1 inch should be provided between the end of the pipe and the rim of the tank. It is not desirable to discharge make-up water direct to the pool; however, if an open surge tank cannot be provided such practice is acceptable. If this is done, an airgap should be provided between the water line and the highest pool level.

(10) *Overflow gutters.* Overflow gutters of ample size to carry off normal amounts of overflow water should extend completely around the pool, and should be easily accessible for cleaning. Drains in the gutter should be spaced on 10-foot centers, and the bottom of the gutter should be pitched 3 inches in 10 feet to the drains. The gratings should be kept free of foreign materials in order to prevent stoppage.

(11) *Steps and ladders.* Steps and ladders should be recessed and of an impervious material of such design that they can be easily cleaned. They should be so designed and constructed that no water is left on them when the pool is empty. Most of the factors in relation to steps and ladders affect safety rather than the sanitary conditions of the pool. Transition from one level to another in a pool or bathhouse should be made with ramps and not with steps or stairs. When step holes are used, provision should be made to provide drainage to prevent dirt accumulation.

(12) *Walks.* Walk areas should have a nonslip finish, should have a pitch of 3 inches in 10 feet and be not less than 4 feet in width. It is desirable to provide walk widths of 6 to 10 feet. The pitch of the walk should be in one direction only, either to drains at the fence line, which is the common practice and believed most desirable, or to drains at the edge of the pool. A 6-inch curb should be placed at the outside edge of the walk on which are set the fence posts. Between the edge of the pool and the walk there should be a curb 3 to 6 inches high and 12 inches wide, the top surface of which should have a nonslip finish. Hose connections should be provided so that all of the walk areas can be reached with 50 feet of hose.

(13) *Filters.* (*a*) The filtration equipment should be of sufficient capacity to result in an 8-hour turnover of the pool water at a filtration rate of 3 gallons per square foot per minute. If batteries of four filters are provided, the recirculating pump will provide a backwash of about 12 gallons per square foot per minute, a bare minimum for filter washing. If less than four units are provided, a separate wash water pump will be necessary which should provide a backwash rate of 15 gallons, or more, per square foot per minute.

(*b*) Filters at swimming pools should be backwashed when the loss of head gauge shows that the friction head through the filter has reached approximately 7 feet or after the filter has been operated 4 days. Backwashing the units daily is not recommended. Each filter should be washed separately, in order to obtain a satisfactory wash rate, and over a sufficient period to remove all dirt from the bed. This can be determined by observing the turbidity of the wash water as it discharges to waste.

(*c*) All filters and piping at pools should be fitted with drain plugs and sloped to a low point to facilitate draining and to prevent damage from freezing when the pool is closed.

(*d*) As a standard for swimming pool filtration plants, reference should be made to American Society of Civil Engineers' Manual of Engineering Practice No. 19, entitled "Water Treatment Plant Design," adopted 23 July 1939.

(*e*) Pressure filters should be equipped with air release lines to allow for releasing air which may become entrapped within the tank. Such a line should be tapped in at the highest point of the tank and carried to the front of the filter and fitted with a valve within reach of the operator. Gauges should be provided on the filter influent and effluent lines to allow for determining the loss of head through the filter bed.

(14) *Hair and lint catcher.* A hair and lint catcher, preferably the type with a clamp cover and basket strainer, should be provided in the pump suction line to retain hair and lint that would otherwise injure the pump or clog the filter bed. An extra strainer basket should be provided, and a vacuum gauge installed between the catcher and the pump which will indicate the degree to which the strainer is clogged. The strainer should be cleaned daily, and more often if indicated. It may be desirable to install valves on either side of the catcher to allow for removal of the strainer without the loss of considerable water into the equipment room.

(15) *Water heater.* For indoor pools, means should be provided for heating the recirculated water. Steam or hot water should not be added to the pool direct. Steam carries considerable rust and scale into the pool, and the direct connection to hot water lines constitutes a cross connection.

(16) *Suction cleaner.* Suction cleaners should be provided and used to remove sediment and other accumulations from the pool bottom. They are desirable because they per-

mit cleaning without draining the water from the pool. There are two main types of equipment.

(*a*) Built-in suction cleaners utilize the recirculation pump with a separate suction line running to the side of the pool to which is attached the cleaner hose. This type is recommended for small pools only. The line from the side of the pool to the pump suction should be not less than 3 inches in diameter. The connection on the side of the pool should be 12 inches below the overflow rim and located so that all parts of the pool can be reached with 50 feet of hose. If necessary, two connections should be provided. Ordinarily, little cleaning is necessary in the shallow end of the pool, since the swimmers and the incoming fresh water keep any sediment moving to the deep end.

(*b*) Portable suction cleaners consist of a low capacity pump with power, mounted on a small truck which can be wheeled around on the pool walk. The pump discharge can be spilled to the walk drains. This type of cleaner is used at large pools.

(*c*) Pools should be cleaned at frequent intervals to prevent the accumulation of large amounts of sediment.

(17) *Alum and soda ash.* (*a*) Alum is used in connection with the filtration of swimming pool water to increase the efficiency of the filtration process. It is not considered a process of coagulation, as is the case in treating water for drinking purposes, since a pool seldom has facilities for mixing and settling, nor are such considered essential. Usually there is provided an alum pot for feeding the chemical to the system; however, an open type feeder is preferred, in order that dosage can be determined more accurately and less cleaning and maintenance are required. The open type feeder consists of a small box, into which the water flows, and which is controlled by a float valve. The outlet is connected to the recirculation pump suction. Alum is placed in the box and the rate of feed can be regulated by adjusting the flow of water from the box by means of the float valve. Alum, whether fed by a pot or open type feeder, should be added to the recirculation pump suction.

(*b*) The amount of alum to be added to the system is that necessary to form a floc on the upper layers of the filter sand (approximately 0.1 to 0.5 grain per gallon based on the capacity of the pool). Alum should be added to the system *only after* the filters have been backwashed, and should be added slowly so that the feeding will extend over a period of 8 to 12 hours. The purpose of this slow rate of feeding is to prevent the precipitate from forming in the pool. In order to obtain the proper reaction, there should be present in the water 20 parts per million of alkalinity. If less than this is present, 0.5 grain of soda ash should be added per grain of alum.

(*c*) In most pools, the tendency is to add too much alum. Many pools, especially indoor ones, use no alum with satisfactory clarity resulting. In addition to using soda ash, caustic soda, or lime to provide the required alkalinity, sufficient amounts of one of these chemicals should be added to maintain a pH between 7.2 and 7.6.

(18) *Size of pool.* The size of the pool required for a permanent station is based on the maximum current swimming load, or the number of swimmers expected to use the pool at any one time. The strength of the unit is the principal factor in estimating the swimming load, but other factors must also be considered, such as climatic conditions, other recreational facilities, and the location of the pool. In general, 27 square feet should be provided for each swimmer, computed on the maximum expected load. Under average conditions, the sizes given below are approximately the minimum:

Strength of command	Maximum current swimming load	Surface area of pool
500	55	1,500 sq ft
1,000	92	2,500 sq ft
2,000	133	3,600 sq ft

d. Disinfection of swimming pool water. (1) The recirculating system and the chlorinator should be placed in operation sufficiently in advance of the swimming period to insure a safe concentration of residual chlorine in the pool water during periods of use as shown in paragraph 5*c*(1).

(2) If ammonia is present, the concentration should not be permitted to exceed about one-quarter of the concentration of residual chlorine. Tests for free ammonia should be made occasionally to determine whether an excessive concentration prevails.

(3) The orthotolidine arsenite test for free chlorine and chloramines should be made occasionally to determine whether or not interfering substances such as manganese or nitrites are present which may produce false readings with the orthotolidine reagent used in the test for residual chlorine.

(4) In general, equipment for feeding chlorine as a gas should be provided when the amount of water recirculated exceeds about 200,000 gallons per day. Hypochlorinators are usually preferred when the quantity of water is less than about 100,000 gallons per day. Between these approximate figures, the selection will depend upon several factors, such as the type of water being treated, the amount of chlorine to be added, the number of months that the pool is to be used each year, the cost of available types of feeding apparatus, and the availability and relative cost of chlorine as compared to that of chlorine compounds.

(5) The use of fill and draw pools or intermittent disinfection with hypochlorites is not recommended. Fill and draw pools are difficult to maintain in good sanitary condition at all times. Intermittent disinfection with hypochlorites does not give satisfactory chlorination, especially during fluctuating bathing loads, and hence water of safe bacterial quality cannot be assured.

e. Swimming loads.

Type of pool	Maximum bathing load limit
Artificial pool with recirculation, filtration, and continuous chlorination, and 0.4 ppm residual chlorine at all times.	Not less than 50 gallons of recirculated water per bather. Assumes all bathers take preliminary showers.
Fill-and-draw pool with continuous chlorination, continuous recirculation through multiple inlets, and maintenance of 0.4 ppm chlorine residual at all times, but no filtration.	Not less than 50 gallons of new water per bather (e. g., a 100,000-gallon pool with a total daily bathing load averaging 250 per day must be emptied and refilled every 8 days).
Flowing-through pool with continuous chlorination of incoming water, dispersal of water through multiple inlets, and maintenance of 0.4 ppm chlorine residual.	Not less than 50 gallons per bather (e. g., maximum of 1,440 bathers per day for 50 gpm flow). Chlorine residual requirement tends to limit pool size for any given flow.
Flowing-through pool fed by well, clear springs, or small stream, without disinfection.	One person per 500 gallons of new water added to the pool.
Fill-and-draw pool with intermittent disinfection.	1 person/400 gallons between disinfections. 1 person/100 gallons between changes.

8. BEACHES AND OTHER NATURAL SWIMMING PLACES. *a. Site selection.* The principal factor involved in the selection of a site for a swimming beach is freedom from sewage pollution. In considering the dangers from sewage pollution, it is well to emphasize that dilution and the time to flow are factors of great importance. The hazards from a relatively small amount of sewage in close proximity to a swimming area is far greater than a large amount at a considerable distance.

b. Destruction of small hosts of schistosome parasites. Copper carbonate (3 pounds per 1,000 square feet of water surface to be treated) may be used to kill the snail intermediate hosts. A concentration of 10 parts per million of copper carbonate after 48 hours of contact destroys free-swimming cercariae as well as snails. Copper sulfate may be substituted when copper car-

bonate is not available. Doses of this magnitude will destroy fish and other aquatic life. Because of the amphibious habits of the snail hosts of some schistosomes, chemical treatment of the water should be supplemented by the application of slaked lime to the ground and along the shoreline of the water. Measures for killing snails have their greatest usefulness where the infested bodies of water are small. Prevention of pollution of water by feces, infected individuals, or reservoir hosts will reduce the number of infected snails.

c. Bacterial quality of water at beaches. (1) Under the heading of beaches are considered swimming places along small streams, rivers, lakes, and tidal waters.

(2) It is not considered practicable or desirable to recommend any absolute standard of safety for waters of outdoor bathing places. Nor is the arbitrary wholesale condemnation of such places warranted without definite epidemiological evidence. Safety of such waters for swimming should be based upon information obtained by thorough sanitary surveys, and results of routine bacteriological examinations.

(3) As a means of determining the suitability of natural waters for swimming, the following classification is given, based upon the presence of *E. coli.* These limits may have to be altered in some cases, in view of existing local conditions and of the findings of a sanitary survey:

Classification	Average E. coli per 100 m.
Class A (good)	0 to 50.
Class B (fair)	51 to 500.
Class C (poor)	501 to 1,000.
Class D (very poor)	Over 1,000.

(4) In determining the safety of water at natural swimming areas or outdoor bathing beaches, emphasis is laid upon the results of sanitary surveys rather than bacteriological examinations. When bacteriological examinations are made, inoculations in lactose broth will be made of three 10 ml., three 1.0 ml., three 0.1 ml., and three 0.01 ml. portions. The number of positive and negative tubes of each dilution will be reported under Remarks or on the reverse side of the Form 8–126. If, for example, three 10 ml., three 1 ml., and one 0.1 ml. portions are positive, the results will be reported as follows:

10 ml. 3+0−
1 ml. 3+0−
0.1 ml. 1+2−
.01 ml. 0+3−

In the foregoing example, the "average" number of coliform organisms, is computed at 400 per 100 ml. Thus the quality of the sample is within the range specified for Class B waters.

9. FACILITIES AT SWIMMING POOLS AND SWIMMING BEACHES. *a. Dressing rooms.* (1) There should be provided one large dressing room of sufficient size to accommodate 25 percent of the maximum current swimming load at one time. A sufficient number of hooks should be provided to accommodate the clothing of all swimmers. Floors, walls, partitions, and furniture in dressing rooms should be of easily washable material. They should be kept clean at all times and scrubbed daily with strong soap and water. All floors should have a nonslip finish and pitch 3 inches in 10 feet to drains. A hose connection should be provided in each dressing room. Pools to be used jointly by both sexes should have separate dressing, toilet, and shower facilities.

(2) For outdoor pools and swimming areas, the open court type dressing area is recommended. This type of area does not have a roof and thus the sunlight is allowed to enter; adequate natural ventilation is also afforded. A section of roof, 4 to 5 feet in width, should extend along one side or end of the dressing room to provide protection for dressing in the event of rain.

b. Showers. The minimum number of showers provided should be in the proportion of 1 for each 30 persons at the time of the maximum load during continuous swimming. When swimming by classes there should be at least 1 shower per 10 swimmers for the largest class. All showers should be provided with an adequate supply of hot water and soap. Two methods may be employed to furnish hot water to the showers; the first consists of a hand-controlled mixing valve at each shower which allows the bather to adjust the temperature of the water. The second consists of a temperature regulator located at the heater

which mixes all water going to the showers. This regulator is set to deliver water having a temperature range from 90° F. to 110° F. Only one line is run to the showers which delivers water of this temperature. The advantage of this latter method is the saving of pipe and valves, and the protection against scalding. If it is believed necessary, a single cold water shower can be installed in the shower room for those who desire a cold shower after taking the soap shower in the warmer water.

c. Toilets. (1) Toilets should be divided into two classes, "wet" and "dry." The wet toilets are intended for use by wet swimmers and are located adjacent to the shower room; the dry toilets serve the dressing rooms and are located off the dressing area. For the men the wet toilets should consist of one seat and one urinal, and for the women one or two seats depending upon the size of the pool. The wet units should be so placed that persons using them must pass through the shower room before entering the pool.

(2) For the dry toilets, 1 seat and 1 urinal should be provided for every 25 men, or fraction thereof, of the maximum current swimming load, and 2 seats for every 25 women of the maximum current swimming load.

(3) The prison type toilet with a seat not affected by frequent washing and disinfection is recommended, and preferably the units should be wall hung to allow the floor to be cleaned more easily.

d. Control fungous infections. Current Army practice will be followed in the control of fungous infections.

e. Suits and towels. All suits and towels should be washed with soap and boiling water, rinsed, and thoroughly dried each time they are used.

f. Life guards. One or more life guards should be on duty at all times during swimming hours.

g. Copper sulfate treatment. (1) Copper sulfate is not recommended for the control of algae growths in waters having a high alkalinity, because a milky precipitate of the carbonate or hydroxide is formed which not only increases turbidity but also renders the free copper ion noneffective. If the water is of such character that copper sulfate can be used, the amount needed may vary from 0.5 to 5.0 parts per million. Early preventive treatment is desirable. Copper sulfate is toxic to fish and therefore should be used with caution where fish are present in swimming areas. At pools, algae may be killed by draining and washing down the walls and bottom with a solution containing about 5 parts per million copper sulfate, or by sunning the empty pool for 1 day or more.

(2) Superchlorination is recommended for killing algae when copper sulfate cannot be used successfully, or it may be used to replace completely the use of copper sulfate because of its added advantage of complete sterilization. Superchlorination should be applied only after the swimmers have left the pool. It consists of building up a chlorine residual of 10 to 15 parts per million. After this residual has been obtained, the chlorinator is shut off but recirculation is continued. Under ordinary conditions, by the following day the residual will have dropped to a point that is safe for swimming; however, if necessary the chlorine content can be reduced by adding fresh water, or with a small amount of sodium thiosulfate solution. The advantages of this treatment are that all algae will be killed, any iron will be precipitated, the system will be sterilized, and the water will be clear and free from turbidity.

10. SEWERAGE AND WATER FACILITIES. Adequate sewerage facilities for the disposal of wastes from toilets and showers and for the overflow or waste of the pool should be provided. Proximity to adequate water mains is also necessary. For these reasons, consideration should be given to the location of the pool near to existing facilities of this nature.

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WAR DEPARTMENT TECHNICAL BULLETIN

CHANCROID, LYMPHOGRANULOMA VENEREUM, AND GRANULOMA INGUINALE*

War Department, Washington 25, D. C. • • • April 1945

This Technical Bulletin rescinds paragraphs 5, 6, and 7, S. G. O. Circular Letter 74, 1942, subject, "Diagnosis and Treatment of the Venereal Diseases"

	Paragraph
Section I. Chancroid.	
Definition	1
Distribution	2
Epidemiology	3
Course	4
Diagnosis	5
Treatment	6
Prophylaxis	7
II. Lymphogranuloma Venereum.	
Definition	8
Distribution	9
Epidemiology	10
Course	11
Diagnosis	12
Treatment	13
III. Granuloma Inguinale.	
Definition	14
Distribution	15
Epidemiology	16
Course	17
Diagnosis	18
Treatment	19

Section I

CHANCROID

1. DEFINITION. Chancroid (soft chancre) is a localized venereal disease caused by the *Hemophilus ducreyi*, transmitted only by direct contact, and characterized by painful single or multiple genital ulcers, often complicated by suppurating inguinal bubo. The incubation period is usually 3 to 5 days, but may be shorter or longer.

2. DISTRIBUTION. The incidence of chancroid in the continental United States is comparatively low; but it is so much higher in most oversea theaters of operations, especially those in tropical and semitropical countries, as to be a problem of military importance.

3. EPIDEMIOLOGY. The disease occurs primarily among peoples that live on a low hygienic level. There are probably symptomless carriers, usually female.

4. COURSE. The disease begins as a vesicopustule which breaks down rapidly. The pustule soon ruptures, leaving a sharply circumscribed, shallow ulceration. The edges may become ragged and undermined. The base is moist and covered with necrotic, grayish exudate. When this is removed, an uneven base of purulent granulation tissue is revealed. The lesion is surrounded by erythema and is usually very painful. Multiple lesions may develop rapidly by auto-inoculation. Induration is usually absent in untreated lesions, but boggy induration may be present if local treatment has been applied.

The lesions occur in the following sites in order of frequency: in the male—prepuce, frenum, shaft, and anus; in the female—labia, clitoris, fourchette, vestibule, anus, and cervix. Spread by auto-inoculation may take place anywhere in the perigenital zone.

Regional adenitis frequently develops within a few days to 2 weeks. The bubo is usually large,

*This bulletin is based upon recommendations made by the Subcommittee on Venereal Diseases of the National Research Council.

AGO 462A—Apr. 637401°—45

unilateral, soft, fluctuant, acutely inflamed, and tender. Untreated, it has a tendency to rupture at a single point. However, it may subside without suppuration.

Phimosis and paraphimosis may occur. There is a tendency to spontaneous healing, both of genital lesions and of bubo, with scar formation. Systemic reactions are mild or absent.

5. DIAGNOSIS. All patients with penile ulcers of any description should be admitted to a hospital for diagnosis and treatment.

Since primary syphilis may clinically resemble chancroid, and since mixed infections of these two diseases may occur (the chancre appearing in the chancroid), the diagnosis of syphilis must be confirmed or ruled out by laboratory tests.

Local antiseptic applications must not be made until at least three negative darkfield examinations of the lesion or of lymph node puncture material are obtained on successive days. A blood serologic test for syphilis should be made on admission, repeated once a week for the first month, and at monthly intervals for 3 months unless a diagnosis of syphilis is established earlier.

The diagnosis of chancroid may be aided by the laboratory examination of stained smears from the lesion, or by culture of pus from the lesion or the bubo.

6. TREATMENT *a. Chemotherapy.* (1) *Systemic.* Sulfadiazine should be administered in all cases. One gram (15 grains) four times a day for 5 to 7 days is recommended.

(2) *Local.* Nothing but cleanliness (soap and water) is necessary.

(3) If the patient is sulfonamide-sensitive, local application of mild antiseptics (Zephiran, 10 percent aqueous solution or 3½ percent tincture; gentian violet, 2 percent aqueous solution; potassium permanganate, 1:10,000 aqueous solution, or one 5-grain tablet to 3 liters of water) may be used.

b. Surgical treatment. (1) The bubo should never be incised. If fluctuation is present, aseptic aspiration with a 16-gauge needle is recommended; this may be repeated if necessary. Sulfadiazine ointment should be applied to the puncture wound.

(2) Marked phimosis or paraphimosis may be treated by immersion and soaking in hot magnesium sulfate or saline solutions during systemic sulfonamide therapy. Circumcision or dorsal slit is undesirable and is rarely necessary.

7. PROPHYLAXIS. Personal cleanliness is important. The standard U. S. Army chemical prophylactic kit, PRO-KIT (Item No. 9118000), has proved valuable in the prevention of chancroid.

Section II

LYMPHOGRANULOMA VENEREUM

8. DEFINITION. Lymphogranuloma venereum (also known as lymphogranuloma inguinale, lymphopathia venereum, and by numerous other names) is a systemic virus disease, acquired venereally, and characterized by a small evanescent herpetiform initial lesion frequently followed by regional lymphangitis and adenitis.

9. DISTRIBUTION. It is world-wide in distribution but is seen with greater frequency in tropical and semitropical climates.

10. EPIDEMIOLOGY. This disease is generally acquired through sex contact. The existence of asymptomatic carriers is suggested by the numerous individuals with positive Frei tests without clinical signs or symptoms of the disease.

11. COURSE. The disease usually begins as a trivial and transitory, painless, small erosion, papule, or herpetiform vesicle or ulcer, of the penis, vulva, vagina, peri-anal area, or anal or rectal canal which frequently escapes the patient's notice.

The invasion of the lymph nodes usually occurs from 10 to 30 days after infection. Inguinal adenitis is often bilateral and occasionally subsides without suppuration. During this stage, constitutional symptoms (prostration, malaise, fever, meningitis, meningo-encephalitis, or other bizarre manifestations) may be observed. The lymph nodes may fuse to the skin. Multiple areas of softening occur in the matted nodes followed by break-down and the development of numerous sinuses. Extensive scarring accompanies healing. The anorectal syndrome is more frequently found in the female and is characterized by rectal pain, discharge of blood and pus from the anus, a tendency to-

ward extreme chronicity, and the production of rectal strictures.

12. DIAGNOSIS. *a. Laboratory tests.* (1) *Cutaneous (Frei) reaction.* Only the chick embryo (yolk sac) antigen supplied through normal channels (item No. 1703300) will ordinarily be used. Directions for its use and for interpretation of the test will be found with each package.

A positive Frei reaction cannot be relied upon absolutely to establish the lymphogranulomatous nature of any clinical condition, since it is known that, in untreated infections with lymphogranuloma venereum, skin sensitivity persists for many years, probably for a lifetime. A positive test may, therefore, mean only that the patient has had lymphogranuloma venereum at some time in the past, rather than that his present symptoms are caused by this disease. False positive Frei reactions may occur in other related virus infections.

A diagnosis of lymphogranuloma venereum should not be made on the basis of a positive Frei reaction in the absence of clinical signs.

A negative Frei reaction in the presence of a clinically suspicious lesion of at least 3 weeks' duration is of value in excluding the diagnosis of lymphogranuloma venereum.

(2) *Complement fixation test for lymphogranuloma venereum.* This test is still in the experimental stage and is not advised for general use.

b. Differential diagnosis. Lymphogranuloma venereum must be differentiated from malignant tumors, Hodgkin's disease, tularemia, amebic proctitis, tuberculosis, meningo-encephalitis, pyogenic infections, plague, chancroidal bubo, granuloma inguinale, and syphilis. Syphilis should be ruled out by darkfield examinations of material from genital lesions or regional lymph nodes and by serologic examinations which should be repeated monthly for at least 3 months. Low titre false positive serologic tests for syphilis may occur in this disease.

13. TREATMENT. *a. Local.* The fluctuant nodes may be aspirated; but incision and drainage should not be used. Radical excision is inadvisable because of the risk of lymphatic obstruction and chronic swelling of the penis, scrotum, or vulva.

b. Chemotherapy. Sulfadiazine should be administered in a dose of 1 gram (15 grains) three times daily for 21 days.

c. Surgical. Patients with late complications, who do not respond to sulfonamide therapy, should be handled in the following manner:

(1) *Rectal stricture.* Prolonged gentle dilatation, preferably manual. Colostomy should not be performed unless dilatation is impossible because of location of the stricture, or has failed.

(2) *Peri-rectal abscess.* Surgical incision and drainage.

(3) *Fistula-in-ano.* Should be excised where possible.

Section III

GRANULOMA INGUINALE

14. DEFINITION. Granuloma inguinale is a chronic disease due to infection with a Donovan body, which is possibly of bacterial nature. It is a mildly contagious, progressive disease, characterized by a sharply defined, granulomatous, usually painless, initial lesion, involving the skin of the genital or inguinal region, and spreading gradually by continuity or contiguity. Rarely, it is a systemic disease involving bones, joints, and viscera. Granuloma inguinale is a distinct disease entity and should not be confused with lymphogranuloma venereum.

15. DISTRIBUTION. The disease has a world-wide distribution but is seen more often in tropical and semitropical countries.

16. EPIDEMIOLOGY. Some doubt exists concerning the manner of spread of granuloma inguinale. The consensus is that it is venereally acquired and that its communicability is low. There appear to be marked differences in racial and individual susceptibility.

17. COURSE. The disease starts as a vesicle, papule, or nodule. The surface epithelium becomes excoriated or eroded, leaving an ulcer with a beefy red granular base. An early lesion may be a clean, raised, velvety, smooth tuft of granulation tissue, situated at the mucocutaneous border of the vaginal orifice, at the preputial orifice, or on the glans or inner surface of the prepuce. The margin of the lesion is sharply defined. The granulation tissue, if traumatized, bleeds easily. The lesions are not painful unless grossly secondarily infected.

There is very little tendency to spontaneous healing. The lesions spread by continuity or contiguity. Extension is often slow. There is a predilection for moist contact surfaces, particularly in the cruroscrotal folds, the groins, and the cleft and folds of the buttocks. The advancing border of the lesion has characteristic rolled edges, the granulation tissue piling over onto the bordering epithelial surface.

The ulcerative process may remain more or less stationary for many years. Secondary elephantoid enlargement of penis, scrotum, or labia may occur. The lesions may heal with scar formation at one margin and progress at another. There are three types of lesions: exuberant, ulcerative, and cicatricial.

Ultimately, marked impairment of general health may occur, ending in extreme cachexia and death.

18. DIAGNOSIS. The clinical appearance of a chronic ulcerative process involving the skin of the groin and genital areas, without involvement of the lymph nodes, is characteristic of the disease. The demonstration of Donovan bodies confirms the diagnosis.

For this demonstration, spreads should be made from scrapings or punch biopsy of *clean* granulation tissue, and stained by Wright or Giemsa stain. Histologic study of tissue sections taken by biopsy from a peripheral area of diseased tissue may demonstrate the pathognomonic large cells with cystic spaces containing Donovan bodies.

Lymphogranuloma venereum, chancroid, carcinoma, and syphilis should be considered in the differential diagnosis, and appropriate diagnostic tests should be performed. A blood serologic test for syphilis should be made weekly the first month and at monthly intervals for 3 months unless a diagnosis of syphilis is established earlier.

19. TREATMENT. *a. Fuadin (a complex antimony compound).* This drug is also known as neoantimosan and stibophen. It is supplied in ampules containing 6.4 percent solution (0.064 gm fuadin, 1 grain, in 1cc). Fuadin solution is given intramuscularly. The first three doses of 1.5 cc, 3.5 cc, and 5 cc are given on successive days, followed by 5 cc two or three times weekly until complete healing has taken place; and, in order to prevent relapse, continued at weekly intervals for 6 months after complete healing. The most commonly reported oxic symptom is vomiting. Rarely, joint and muscle pains may appear. If any toxic symptom occurs the dose should be reduced.

b. Antimony and potassium tartrate (tartar emetic). If there is no response to fuadin therapy after 6 weeks of treatment, antimony and potassium tartrate should be administered. This preparation contains about 36 percent antimony. One percent solution should be freshly prepared, using if available Medical Department supplies of sterile distilled water or physiological saline, rather than local supplies. The solution should be perfectly clear and free of sediment. It is sterilized by *gentle* boiling for 5 minutes. Solutions should not be autoclaved. The drug is best tolerated 2 to 3 hours after a light meal. It is administered intravenously and should be given slowly. Since the solution is very irritating, the needle should be wiped off with a sterile sponge and there should be no extravasation. The patient should remain recumbent for at least an hour after treatment. The first dose is 3 cc (0.03 gm tartrate). Provided no untoward reaction occurs, subsequent doses are given on alternate days and are increased on each occasion by 3 cc (0.03 gm tartrate), until the maximum individual dose of 12 cc (0.12 tartrate) is reached. If no toxic reaction appears the maximum tolerated dose may be given 3 times weekly for 15 doses. The toxic effects of antimony and potassium tartrate include coughing immediately upon injection, which is not important; nausea, vomiting, dizziness, and collapse. Transient electrocardiographic changes without corresponding clinical manifestations have been reported. If a toxic reaction other than coughing occurs during administration the injection should be stopped at once. Following any toxic effect, the subsequent dose or doses should be reduced or omitted according to the circumstances.

c. Healing under antimony is enhanced by adequate concomitant treatment of gross secondary infection. This may be accomplished by local application of daily wet dressings with weak solutions of potassium permanganate or

sodium perborate. Penicillin given intramuscularly every 3 hours, in injections of 10,000 units each, in a total dosage of 400,000 units, is also recommended for the treatment of secondary infection.

[AG 300.5 (11 Apr 45)]

By order of the Secretary of War:

d. X-ray therapy combined with chemotherapy has yielded promising results.

e. Surgical excision of the entire diseased area may be necessary as a last resort. If used, it must be followed by chemotherapy.

G. C. MARSHALL
Chief of Staff

Official:
J. A. ULIO
Major General
The Adjutant General

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U. S. GOVERNMENT PRINTING OFFICE: 1948

TB MED 138

WAR DEPARTMENT TECHNICAL BULLETIN

CHOLERA

War Department, Washington 25, D. C. • • • February 1945

This bulletin supersedes par. 2 of SGO Circular Letter No. 33, 2 February 1943.

This bulletin follows TB MED 137, subject, "Physical Reconditioning for Bed and Ward Ambulant Patients." Distribution given TB MED 137 was as follows: AGF (5); ASF (2); T of Opns (25); S Div ASF (1); Dept (5); Base Comd (5); Is Comd (5); Arm & Sv Bd (2); Def Comd (5); Tech Sv (2); SvC (10); Named & Numbered GH (60); Numbered GH (NP) CZ (45); Named SH (Including RH & Numbered SH) (40) except AAF (0); M Conc C (55); Gen Disp (ZI) (10); Fld Hosp (15); Hosp Tn (2); Hosp Ship Plat (5); Hosp Ship Complements (15); Conv. Ctr (15); Conv. Camp (10); Vet Gen Hosp (10); Vet Sta Hosp (10); Vet Evac Hosp (5); Vet Conv Hosp (5); Portable Surg Hosp (5); Evac Hosp (750 bed) (40); Evac Hosp (SH-400 bed) (30); Conv Hosp (20) except AAF (0); Gen & Sp Sv Sch (5); Enlisted Techn Sch 8 (1); USMA (2); ASTPU (3); ROTC (2); Army Med Tng C (60); Ind Sta (10); Sv C Lab (5); A (5); CHQ (5); D (55); AF (55); One copy to each of the following: T/O & E 3-25; 4-45; 4-145; 4-232; 5-35; 5-72; 5-95; 5-275; 6-35; 6-55; 6-65; 6-75; 6-95; 6-175; 6-325; 6-355; 6-365; 6-395; 7-85; 9-12; 11-25; 17-55; 17-125; 18-25; 19-35; 20-42. Two copies to each of the following: T/O & E 2-22; 4-152; 4-260-1; 5-386; 5-535S; 6-12; 6-45; 8-22; 8-26; 8-520; 9-35; 9-76; 10-22; 10-165; 10-217; 11-15; 17-15; 18-10-1; 18-35; 19-55; 20-46; 44-15; 44-25; 44-75; 44-115; 44-125; 44-225S; 44-315; 55-120-1. Three copies to each of the following: T/O & E 5-192; 7-95; 8-27; 10-45; 10-175; 17-115; 44-135; 44-320; 55-110-1; T/O & E 5-21 (5); 5-251 (6); 5-510S (35); 8-28 (10); 8-519 (15); 8-534 (5); 8-537T (15); 8-550 (60); 8-550S (45); 8-560 (40); 8-572S (5); 8-580 (40); 8-581 (30); 8-590 (20); 8-591T (15); 8-595T (10); 8-650 (10); 8-750 (10); 8-760 (10); 8-780 (5); 8-790 (5); 10-95 (7); 10-125 (6).

	Paragraph
General	1
Geographic Distribution	2
Course	3
Diagnosis	4
Treatment	5
Prevention	6

1. GENERAL. Cholera is an acute enteric infection in which the *Vibrio comma* is the specific etiologic agent. Although the organism may persist in nature under favorable circumstances for at least a few days, infection is usually traceable to patients in the immediate neighborhood. Patients in the incubation stage and those with mild symptoms or subclinical infections are important potential sources. Convalescent patients may remain carriers of virulent organisms for a short period of time. Recent studies have cast doubt upon the existence of true carriers. Susceptible individuals acquire the disease through the ingestion of food, drink, or other material contaminated by feces which contain the specific organism. Attacks of cholera in an exposed group of individuals often appear to be distributed capriciously, probably because of the occurrence of subclinical attacks in the community. It is widely believed that any preexisting intestinal disturbance predisposes to the disease. Contamination of water is one of the most important means of spreading cholera. Flies may play an important role. Epidemics are seasonal, since their development is favored by climatic conditions, such as high temperature, high relative humidity, and intermittent heavy rainfall. In some areas, epidemics are associated with floods. Once a cholera epidemic gets under way, unless effective control is exercised, it rapidly sweeps

through an unprotected population and spreads along lines of communication with a speed proportional to that of the available means of transportation.

2. GEOGRAPHIC DISTRIBUTION. The best known endemic center of cholera is in the region of the lower Ganges River in Bengal, eastern India. The disease is said to be always present in this area. Other endemic areas may exist in Burma, southern China, and elsewhere, but their continuous existence is uncertain. Cholera often spreads throughout India and Burma. In recent years relatively few cases have appeared in Ceylon or to the west of India. During the summer in many years, cholera spreads extensively to the eastward. For some years before the war, British Malaya and the Netherlands East Indies (except for a small, somewhat questionable, epidemic in Celebes in 1937–39) were practically free of the disease. The same was true of the Philippines, except for the years 1930–34. Cholera often appears in Thailand, French Indo-China, Hong Kong, and Canton. It spreads northward through the ports of the China coast (such as Swatow, Amoy, Foochow, Wenchow, Shanghai, Tsingtao, and Tientsin). From these ports, the disease invades neighboring inland areas, especially the valley of the Yangtse River through which it reaches far into the interior. Formosa, the Ryukyu Islands, and Japan proper for many years before the war were kept relatively free of cholera, although the tendency for it to reach these islands from China is great. Very few, if any, cases of cholera have ever been reported from the Japanese Mandated Islands or Guam. In the years 1930–34 an extensive epidemic occurred in many parts of the Far East, reaching as far north as Peiping, China. Cholera was also widespread in 1938–39. The great epidemics of the nineteenth century reached all but the coldest parts of the world. The potential distribution of cholera, therefore, is nearly universal. In all parts of the Far East especially, the danger of epidemics is ever present.

3. COURSE. *a. Symptoms and signs.* The incubation period is usually from 1 to 3 days. Premonitory symptoms of depression, lack of energy, and simple diarrhea sometimes occur. In epidemics, mild cases may be seen which show only malaise and diarrhea throughout. In ordinary cases, the onset is sudden, with profuse, watery stools which quickly lose all fecal characteristics. The stools are voluminous and frequent; they are of a light grayish color and contain small mucous flocculi. Tenesmus is uncommon. Vomiting, which is copious, is often precipitate and free of nausea and retching. Prostration rapidly becomes severe. Dehydration may reach an extreme degree in a very short time, so that it is obvious in the thickening of the blood (the specific gravity may rise nearly to 1.070) and in the shrinking of all the tissues. There is great thirst. Patients are apathetic but clear in mind. In addition to huge quantities of fluids, large amounts of mineral metabolites are lost, especially chlorine, sodium, and calcium. There is a strong tendency toward acidosis, and a marked shift may occur in the acid-base balance of the blood (pH as low as 7.07 and bicarbonate reserve as low as 18 vols. per 100 cc, with total base reduced by 10 percent, have been reported). Muscular cramps may be widespread and severe. The circulation is profoundly affected, with peripheral collapse and low blood pressure rapidly developing to marked degree. The secretion of urine often fails and uremia often appears in severe cases. The skin temperature may be subnormal, though the rectal temperature remains elevated. In severe cases, the rectal temperature also falls. In some instances, a stage of "reaction" develops, with high temperature and the appearance of complications, such as pneumonia.

b. Duration and outcome. The course is usually run in a few days (average, 3 to 5). In fatal cases, death may occur in a few hours or after several days. Even in recent years, epidemics among neglected patients show a fatality rate of 50 to 70 percent. When proper treatment is promptly applied, the case fatality rate should not be over 8 to 10 percent.

4. DIAGNOSIS. *a. General.* The possibility of cholera should be brought to mind by epidemiologic considerations. In and near endemic areas, it is essential to be informed of cases suspected of being cholera among native populations. The recognition of the first few cases of cholera in an area is a matter of vital importance. At the start of an epidemic, rela-

tively mild ambulatory cases which are exceedingly dangerous as potential source of spread may be mistakenly diagnosed as food poisoning or dysentery. In the presence of an epidemic, every person having diarrhea or gastrointestinal disturbance should be regarded as a cholera suspect until proved otherwise. Cholera must be separated from: acute bacillary dysentery, in which the stool content is different and tenesmus is present (except in mild cases), and in which collapse is rare in adults; food poisoning, in which distressing vomiting with nausea and retching, and headache are common; clinical froms of malaria (chiefly falciparum malaria), in which intestinal symptoms and collapse occur; heat exhaustion and other conditions in which a state of shock develops.

b. Specific. (1) Cholera is diagnosed specifically by the identification of *Vibrio comma* in stool cultures. Fecal smears stained with carbolfuchsin diluted 1 to 10, showing the comma forms with the "fish in stream" appearance, are suggestive. The final diagnosis, however, requires culture of the organism from stool specimens and identification by agglutination.

(2) Specimens of feces from cases or suspected carriers should be planted (two or more loopfuls of liquid feces or mucus) without delay in several tubes of alkaline (pH 8.0 to 8.4) peptone water (peptone 1 percent, NaCl 0.5 percent) and incubated at 37° C. for 6 to 8 hours. Other intestinal organisms are inhibited somewhat at this alkalinity, and the vibrio if present will become concentrated at the surface. Examine the surface growth microscopically for typical gram-negative, slightly curved, motile rods. Streak onto nutrient or infusion agar. Typical 24-hour colonies resemble those of the other enteric gram-negative bacilli. Suspected colonies may be tested with specific *V. comma* agglutinating serum using a slide technique and a 1:20 antiserum dilution.

(3) Colonies giving a positive slide agglutination should be isolated and their identity confirmed by macroscopic tube agglutination and biochemical studies. *V. comma* produces acid without gas in glucose, maltose, mannite, and sucrose. Lactose may become acid in 14 days. Nitrites are produced from nitrates; indol is positive and gelatin is liquefied. Macroscopic tube agglutinations should be done at 37° C. for 2 hours rather than at 56° C., since rapid lysis of the vibrio occurs at the higher temperature. It should be noted that *V. comma* is sometimes strongly or completely inhibited on the selective media such as EMB agar or SS agar used for the isolation of other enteric pathogens.

(4) To isolate the cholera vibrio from suspected water, 100 cc samples are inoculated into 10 cc of 10 percent peptone water and incubated for 6 to 12 hours at 37° C. The surface growth is examined as outlined in (2) above.

5. TREATMENT. *a. General.* A patient with cholera represents a therapeutic emergency. The prompt institution and intelligent management of therapy are essential. Since it usually happens that a group of patients (often a very large number) must be treated at the same time, some general plan of action should be prepared and adhered to unless cogent reasons for deviations appear. An outline of the essential part of the treatment is given in *f* below. As in all severe infections, good general medical and nursing care are important. Patients with subnormal temperatures should be kept warm. During the early stages of the disease, little or no attempt should be made to give the patient food, except such as he may be able to take in liquid form.

b. Isolation. See paragraph 6*a*.

c. Replacement of fluids and electrolytes. At present this is without doubt the most important form of treatment, far outranking any available drug or serum therapy. Those who are familiar with the urgency of this form of treatment in young children with dysentery will recognize the similarity of the situations. However, even in moderately severe cases of cholera the problem is much more difficult and persistent. During the acute stage, patients usually can retain only very little of the fluid taken by mouth (advantage should be taken, however, of any possibility that they can retain fluid taken by this route). Reliance must be placed, therefore, upon intravenous injections. Subcutaneous injections are not recommended.

d. Types of solutions. If sufficient supplies of standard solutions and standard sterile distilled water for intravenous administration are not available, solutions should be freshly prepared with distilled water and freshly sterilized. Many "reactions" described in cholera

are due to pyrogenic impurities in water. However, in grave emergencies when large groups of patients must be treated, the administration of fluid should not be withheld because of inability to use ideal technique. Plasma and whole blood generally are not necessary in cholera and *may be very harmful.* The state of shock which accompanies cholera is not in itself an indication for plasma. Plasma and blood should be given only when specific reasons for giving them are known to exist. The three solutions described below, with or without dextrose and thiamin, are given intravenously to meet various needs which develop in the course of cholera (see *e* below).

(1) Isotonic saline: sodium chloride 9 gm per liter.

(2) Hypertonic saline: sodium chloride 14 gm per liter. This solution should be prepared by adding sodium chloride (ACS) 14 gm to about 1,100 cc of freshly distilled water and boiling to the point where the volume is 1,000 cc.

(3) Alkaline saline: sodium bicarbonate 18 gm and sodium chloride 6 gm per liter. This solution should not be sterilized by heat because of the attendant loss of carbon dioxide. The following technique may be employed: Dissolve sodium chloride (ACS) 6 gm in about 1,100 cc of freshly distilled water and sterilize by boiling to the point where the volume is 1,000 cc. Add immediately sodium bicarbonate (USP) 18 gm which has been taken directly from the original container and weighed in a sterile vessel. Cool the solution to body temperature and use it at once.

(4) Dextrose to make 5 percent solution should be added to physiologic or hypertonic saline, but not more than 50 gm of glucose should be given in 1 hour or 400 gm in 24 hours. It is desirable, but not essential, to add thiamin chloride 1 mgm for every 25 gm of glucose.

e. Determination of amount, frequency, and type of fluid. (1) The inexperienced physician needs first to learn that patients with cholera usually require relatively huge amounts of fluid and that such treatment may have to be continued over a surprisingly long period. Secondly, he must learn that too much fluid is dangerous, particularly if given after the blood has approached its normal specific gravity. The criterion which has been most used in an effort to be exact is the specific gravity of the blood which is normally from 1.056 to 1.058. As the normal value is closely approached, the rate of fluid administration should be slowed, but the patient must be watched to see that further large losses of fluid are not occurring and do not begin again. The specific gravity of the blood may be determined by the copper sulfate method (see the *Bulletin of the United States Army Medical Department*, number 71, December 1943, page 66), if circumstances permit. Such determinations are by no means necessary for thoroughly satisfactory treatment of patients. In general, judgment must be based especially on the blood pressure; but color and consistency of the blood, rate of the pulse, and amount of urine are also helpful. The development of palpitation, restlessness, pain in the chest, coughing, or edema indicates that too much fluid has already been given. Most patients should have 2 liters of fluid in the first 2 hours. For some time, more fluid is necessary every 3 to 4 hours. The usual rate of continuous infusions (50 to 60 drops per minute) is quite inadequate. It may be necessary to give as much as 6 to 8 liters in the first 24 hours, although 4 or 5 liters are often sufficient. Intravenous fluid may have to be given well into or through the second 24 hours.

(2) In general, physiological saline is the fluid to be used. In regard to the use of glucose, see *d* (4) above. Some observers believe that hypertonic saline in limited amounts gives better results, especially in early cases (before dehydration is severe). As has been pointed out above, the tendency to acidosis is strong. Most patients have an alkali deficit when they come under treatment, and all may develop this condition later if a favorable response is not secured. Hence, it is advised that treatment begin with a limited amount (500 cc) of alkaline saline solution. The further administration of this solution must depend upon observation of the patient. The rate and depth of respiration are not good guides to the presence of acidosis in the acute stage of cholera, though they may be in the later stages. Ketone bodies are not necessarily present in the urine in acidosis due to cholera. Determination of the pH, the carbon dioxide combining power, or the urea content of the blood would be helpful, but such

studies are often impossible. If measurement of urine volume is possible, it is helpful. Continued lack of urine formation is associated with the development of acidosis. The reaction of the urine may be used, within limits, as a guide to the further need for alkali. In the past, many patients have been overdosed with the result that clinical alkalosis appeared.

f. General routine. The following plan is recommended as an initial procedure: Isolate the patient and make certain that all members of the staff understand the system of isolation and disinfection and the need for continuous close observation of the patient and his treatment. Begin at once to administer fluid by vein and give 2,000 cc in the first 2 hours. Of this amount, 1,500 cc should be physiological saline solution with 75 gm glucose and 3 mgm thiamin hydrochloride. The remainder of this amount of 2,000 cc should consist of 500 cc of alkaline saline solution; if available, it is convenient to give the alkaline solution at the start. This amount of saline solution is almost never sufficient to cover the needs of a patient, although it is often not necessary to supply more alkaline solution. Further physiological saline solution, often in the amount of 1,000 cc, will be needed every 3 or 4 hours in many cases. The amount and type of such fluid must be determined in accordance with the principles outlined in *e* above.

g. Chemotherapy. Under no circumstances should the prompt institution of parenteral treatment with liberal amounts of fluid be neglected because of the use of chemotherapy. The value of the sulfonamides and penicillin in the treatment of cholera is uncertain. Because of the frequent failure of renal secretion, it is believed that sulfadiazine and other well absorbed sulfonamides should not be given by any route. Reports of the results of giving sulfaguanidine are difficult to evaluate. The use of sulfaguanidine is suggested; if it is given, full doses should be administered: 5 gm four times a day or 3.5 gm six times a day for 4 or 5 days. The clinical value of penincillin has not been determined. Although the vibrio is gram-negative, the drug has been shown to exert an effect *in vitro*. Penicillin in large dosage therefore should be tried in a suitable series of patients, with adequate controls. Full accounts of the results of chemotherapy in cholera are desired.

h. Various drugs. Numerous drugs of a great variety have been used in the past, most of which rest on no rational basis and have not been shown to be efficacious. Their use is considered to interfere with the proper treatment of the patient, especially during the acute stage. Included in this group are digitalis, epinephrin, hypnotics, sedatives, and laxatives. In some cases with collapse, the injection of caffeine sodium benzoate may be helpful.

i. Special forms of treatment. No bactericidal or antitoxic serum which is known to be efficacious is available. Claims have been advanced for cholera bacteriophage, but clear evidence of its value is lacking. Its use is not recommended.

j. Convalescence. Once convalescence is established, it usually proceeds rapidly. Patients should be allowed to resume normal activity only gradually. Suitable restrictions must be imposed for the first 2 weeks. The diet should soon be liberal. Most patients can be expected to return to duty in about 30 days.

6. PREVENTION. *a. Isolation.* Patients and proved carriers should be strictly isolated. Special care must be taken in the disposal of excreta and vomitus and all articles which are contaminated by them. Patients' clothing, bedding, and eating utensils should be disinfected by boiling. All attendants should soak their hands in an antiseptic solution and wash them with soap and water *immediately* after handling patients or any article contaminated by them. A cholera ward should be screened and remote from any general source of water and from any mess or kitchen.

b. Foreign quarantine. Cholera is a quarantinable disease as defined in intenational sanitary codes. Military personnel found or suspected to be infected with cholera are subject to the provisions of such international sanitary regulations except, of course, as their application may be modified by martial law or by the necessity of the military situation. Traditional practice provides for detention of cases and suspects traveling internationally by boat or aircraft until the individual is determined to be uninfected. Decisions are ordinarily based upon physical inspection, evaluation of contact

history, epidemiology of the disease in areas departed, and stool examinations when indicated. Freedom of the stool from cholera vibrios is usually required for release from detention. U. S. Army policy considers that effective immunizations, conditions of sanitation in military carriers and stations, and the constant medical surveillance maintained over personnel traveling in military traffic are adequate guarantees, and that evidence of valid immunization and freedom from symptoms of cholera at the time of travel may be taken to fulfill quarantine requirements without further ado, in order to avoid delay en route.

c. Immunizations. (1) Although cholera vaccination is of proved value, reliance must not be placed upon vaccination as the sole means of preventing cholera. Vaccination is definitely secondary in value to sanitary measures for protection of water and food. These measures must be applied vigorously, even though all personnel are immunized against cholera.

(2) Cholera vaccination is required for personnel stationed in or traveling to or through Asia, including the area around the Persian Gulf, the Philippines, the islands of the East Indies and far western Pacific. It may be required in other areas at the direction of The Surgeon General, or at the discretion of the local surgeon when danger from cholera exists. Initial vaccinations consists of two subcutaneous injections of cholera vaccine at a 7- to 10-day interval. The first dose is 0.5 cc and the second dose 1.0 cc; stimulating doses of 1.0 cc should be administered every 4 to 6 months during danger of infection. Additional doses of 1.0 cc each will be given whenever in the opinion of the surgeon stimulation of immunity is indicated (see par. 4*g*, TB MED 114).

d. Water supply. When the danger of cholera exists, particular care should be exercised to safeguard water supplies. In the case of fixed installations, a special sanitary survey of the water system should be made by a qualified sanitary engineer, as provided in paragraph 11*a*(3), AR 40–205, unless such a survey has been made within 6 months previously. A chlorine residual of not less than four-tenths part per million (0.4 ppm) will be maintained in the active part of the distribution system at all times, and daily or more frequent tests of the residual will be made. In the case of field supplies, water will be checked to insure maintenance of required chlorine residuals until consumed. Drinking water that, due to its organic or mineral content, can not be effectively chlorinated should be boiled and then chlorinated to protect from subsequent contamination. Whenever possible, water should be coagulated, settled, and filtered prior to use, either in fixed filter plants or by portable or mobile purification units. All personnel should be specifically directed not to consume water except from sources approved by the surgeon.

e. Food and food handlers. Food should be eaten only in authorized places, and other establishments should be declared "out of bounds." Native help should be excluded as food handlers at military installations. Personal hygiene, especially the proper cleansing of hands, should be rigidly enforced for all personnel handling food. Fresh fruits and vegetables must be cooked before being eaten, or else soaked for 30 minutes in a concentrated solution of Compound Germicidal Rinse (1 unit dissolved in 8 gallons of water). Compound Germicidal Rinse is QM Stock No. 51–C–1606. Stool cultures on all food handlers should be made at regular intervals. The importance of reporting any symptoms or signs of an intestinal upset, even one loose stool, should be impressed on all food handlers. Individuals known to have been infected should not be permitted to handle food for a period of 3 months after return to duty and then only after three negative stool cultures have been obtained. Careful attention should be paid to the washing and disinfection of eating and cooking utensils, in accordance with AR 40–205 and changes thereto. If boiling water is not available for disinfection, then after washing and rinsing, the dishes and cooking utensils should be immersed in a solution of Compound Germicidal Rinse (1 unit in 25 gallons of water) for a period of at least 1 minute. After cleansing, dishes and cooking utensils should be air dried. During the drying and storage periods they should be protected from insects and dust.

f. Fly control. The control of flies is especially important in areas where cholera is present. Adequate screening of kitchens, messes, isolation wards, and latrines should be

provided and maintained in good repair. Proper disposal of organic waste materials should be enforced to prevent breeding of flies. In the field it is essential that flies be denied access to human feces by flyproof construction of latrines. When native labor is employed, proper latrine facilities should be provided and their use enforced. Destruction of adult flies by the use of insecticides, traps, and swatting should receive close attention, especially in sick wards, kitchens, mess halls, and latrines. DDT may be used to kill adult flies by applying as a residual spray and to kill fly larvae in organic wastes by applying as a spray or powder. Residual spray (5 percent DDT in kerosene, QM Stock No. 51-I-305) applied to surfaces on which flies commonly rest will remain lethal to flies alighting on such surfaces for 2 or more months. The recommended rate of application is 200 mg per square foot (1 quart per 250 square feet). Screens, walls, ceilings, light fixtures, garbage racks, and latrines should be treated. To kill fly larvae in pit latrines, it is recommended that DDT residual spray be applied evenly over the fecal contents at the rate of 2 ounces per latrine box hole (½ ounce per square foot). Or, 1 ounce of 10-percent DDT powder (Larvicide, DDT powder, dusting, QM Stock No. 51-L-122) may be used (¼ ounce per square foot). This treatment should be repeated twice a week unless local experience indicates that less frequent application will suffice.

[AG 300.5 (31 Jan 45)]

By order of the Secretary of War:

G. C. MARSHALL
Chief of Staff

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Major General
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For explanation of symbols, see FM 21-6.

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TB MED 167

WAR DEPARTMENT TECHNICAL BULLETIN

SCHISTOSOMIASIS JAPONICA

War Department, Washington 25, D. C. • • • June 1945

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This bulletin follows TB MED 166, subject, "Films for Reconditioning for Bed and Ward Patients in ASF Hospitals." Distribution given TB MED 166 was identical to that given TB MED 145.

	Paragraph
General	1
Geographic Distribution	2
Etiologic Agent	3
Transmission	4
Course	5
Diagnosis	6
Treatment	7
Follow-up	8
Prognosis	9
Prevention	10

1. GENERAL. Three species of blood flukes are important agents in the production of human disease *Schistosoma hoematobium*, *S. mansoni*, and *S. japonicum*. These parasites belong to the class of trematodes in the Phylum Platyhelminthes or flatworms. The three species have similar life cycles, but their respective molluscan intermediate hosts are different. Man becomes infected by each species in much the same way. After reaching maturity, *S. haematobium* characteristically settles in the venous plexuses of the urinary bladder. In maturity, both *S. mansoni* and *S. japonicum* inhabit branches of the superior and inferior mesenteric veins. The diseases produced by these flukes have essentially the same pathogenesis, and differ chiefly because of variations in the anatomical regions involved and consequent variations in symptomatology. The same symptoms may appear in all three infections during the early stages. The disturbances produced by *S. haematobium* arise mainly in the genito-urinary system, but the lower colon and rectum also occasionally may be involved. Both *S. mansoni* and *S. japonicum* cause disturbances principally in the small intestine, colon, and rectum; rectal lesions are less commonly due to *S. japonicum*. All three parasites may give rise to hepatic lesions, but severe hepatic cirrhosis, splenomegaly, and ascites are common late results of infection with *S. mansoni* and more especially with *S. japonicum*. In general, infection with *S. japonicum* is more severe and appears to be more resistant to available chemotherapy than is the case with disease due to the other blood flukes. The available methods of treatment can be applied without variation to any of the three forms of schistosomiasis. In a broad sense, the same methods of prevention are applicable. Apart from these generalities, the remainder of this bulletin is devoted to infections with *S. japonicum*, or schistosomiasis japonica. This infection is sometimes referred to as oriental schistosomiasis or as Katayama disease (from the name of one of the Japanese areas in which it occurs).

2. GEOGRAPHIC DISTRIBUTION. *a. General.* The extent of schistosomiasis japonica is determined principally by the distribution of

the species of snails which serve as intermediate hosts. The established occurrence of the disease is limited to Japan, Formosa, China, the Philippines, and Celebes; foci may exist in upper Burma along the Chinese border. (See fig. 1.)

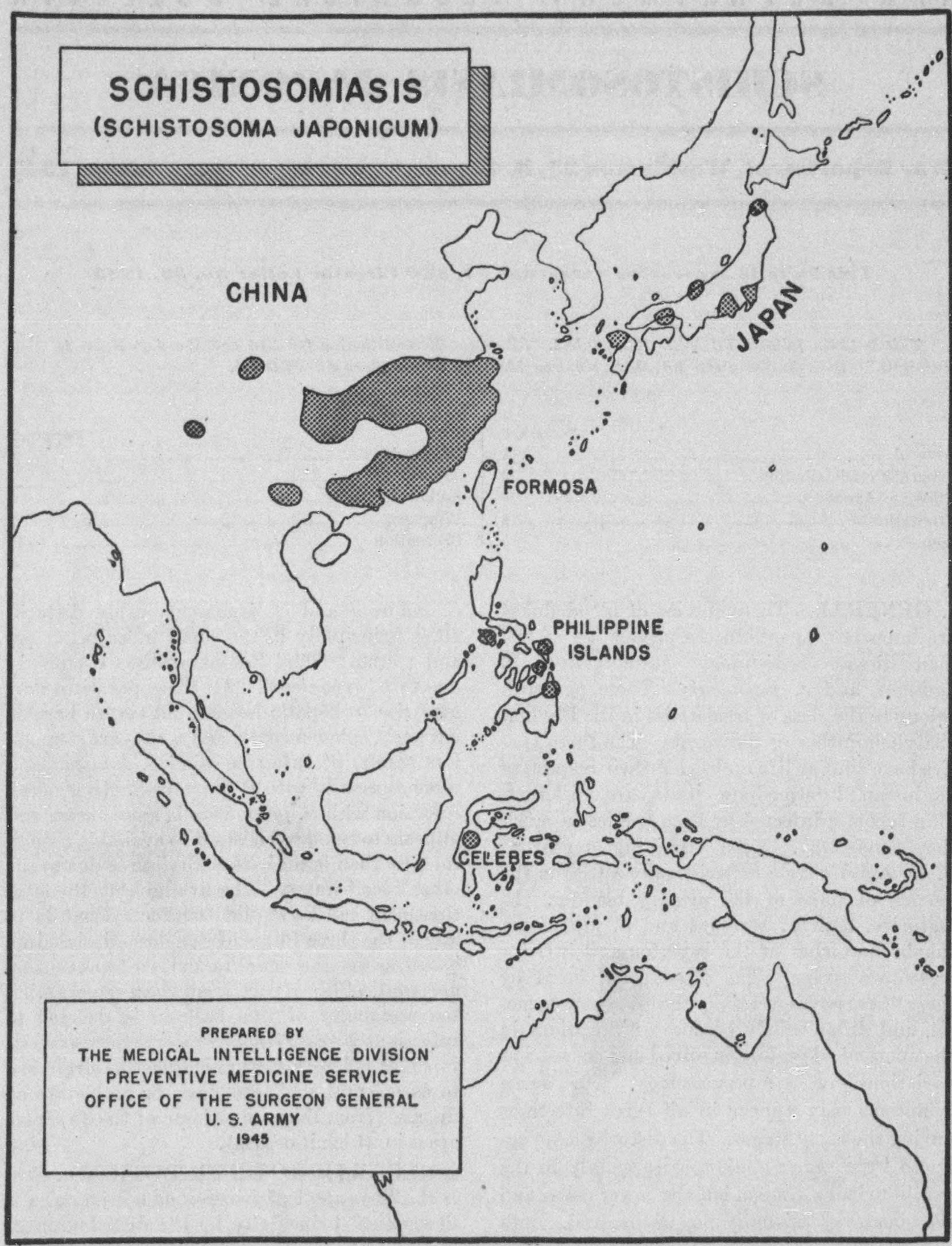

Figure 1.

b. Japan. Five foci are well known. These involve small areas, but at least in the past the rate of infection has been high. Four of these foci are on the main island of Honshu: In the prefecture of Ibaraki, on the lower reaches of the Tone River, not far to the northeast of Tokyo; in the prefecture of Shizuoka, about Lake Ukishima, near Numadzu; in the prefecture of Yamanashi, near Kofu, north of Mt. Fuji; in the prefectures of Okayama and Hiroshima, along the Ashida River in the Katayama district. The fifth focus is on Kyushu, the southern island, in the prefectures of Saga and Fukuoka, along the Chikugo River, near Kurume. In addition, reports of surveys show individuals passing schistosome eggs in the prefectures of Fukui, Tochigi, and Aomori, on the Island of Honshu. According to a recent unconfirmed report, schistosomiasis exists on the Island of Shinkoku.

c. Formosa. According to one report, a focus exists near Shinchiku, in the northwest part of the island. It is possible that schistosomiasis occurs elsewhere on the island.

d. China. Schistosomiasis is widely distributed in central and southern China, where very large numbers of people are infected. It has not been found north of the tributaries of the Yangtse River. In all probability, the distribution of schistosomiasis in China is wider than is yet realized.

(1) *Southern areas.* Schistosomiasis is found in Kwangsi Province in the valley of the Si River (region of Pinyang). Kwangtung has endemic areas on the Si River (about Takhing or Tehking), on the Pei River (area of Kukiang or Shiuchow), and on the Han River (Meihsien). Fukien has areas about Futsing and Minhow (Foochow). Chekiang includes areas about Yungkia (Wenchow) and Taichow and extensive districts about Hangchow Bay (including Ningpo, Shaohsing, and Kiahsing) and in the Chientang River basin from Hangchow to Chuhsien and Kaihwa. Chekiang and Kiangsu together present a heavily infected area about the Tai Lake.

(2) *Yangtse River areas.* Schistosomiasis occurs in areas which are thickly scattered throughout the drainage basin of the Yangtse, especially on its southern side, from the outskirts of Shanghai (Kiangsu Province), near its mouth, to Ichang in Hupeh Province. The infection is especially prevalent in the Hankow-Wuchang area (Hupeh). It is also prevalent about several large lakes and their tributaries and effluents, including Chao Lake (Anhwei Province), Poyang Lake (Kiangsi), and Tungting Lake (Hunan). West of Ichang, the disease has been reported only along the Min River south of Chengtu.

(3) *Yunnan.* An endemic area exists in the region of Tali on the Lake Erh-hai. Cases have also been reported on the Burmese border.

e. The Philippines. Schistosomiasis has been reported to occur especially on the Island of Leyte, and also on Samar, Mindoro, and in the region of Surigao in the northern part of Mindanao.

f. Celebes. A focus has been reported in the Lake Lindoe region in the central portion of the island.

3. ETIOLOGIC AGENT. *a.* Unlike other trematodes, the adult worms of *Schistosoma* have separate sexes. The female worms of *S. japonicum* are long and slender, measuring about 2.5 cm by 0.03 cm. The males are shorter and thicker; the sides of the posterior part of the body curl ventrally to form a groove in which the female worm is enclosed during most of her life. The female deposits eggs in the small venules of the intestinal wall. Some of these eggs gradually are extruded into the lumen and are discharged in the feces.

b. Since the eggs are usually fully developed when passed, they hatch within a few hours upon dilution of the feces with fresh water, liberating a ciliated free-swimming larva known as a miracidium. Upon reaching a suitable snail which can serve as intermediate host, the miracidium invades the soft tissues of the mollusc where it undergoes development and asexual multiplication requiring several weeks. The ultimate result is the production of numerous free-swimming, fork-tailed cercariae, the infective stage for man.

c. Cercariae emerge from infected snails over a period of several months. The cercariae are microscopic in size, their bodies measuring only about 0.15 mm in length. They tend to collect near the surface of the water. They are short-lived and must reach their final host within 1 or 2 days in order to continue their development. If cercariae are successful in contacting the skin or mucous membrane of man, or appropriate

animals, they drop their tails, rapidly penetrate the tissue, and enter the venous circulation. After traversing the lungs and heart, the young worms that reach the intra-hepatic portions of the portal vein mature and pair. They then proceed against the blood stream to small branches of the mesenteric veins where they settle down. Those that settle in small vessels elsewhere for the most part are unable to complete their development, die, and are absorbed. Mature worms are sexually paired in the mesenteric venules where egg deposition occurs. Eggs first appear in the feces from 4 to 6 weeks following invasion of the body by cercariae. In the absence of effective treatment, adult worms may live and continue to deposit eggs for many years (perhaps 10 or 20 years).

4. TRANSMISSION. *a.* Schistosomiasis is most prevalent in irrigated regions where the abundance of canals, ditches, and pools of stagnant water provide a favorable environment for the snail intermediate hosts. Only certain species of snails belonging to the genera *Katayama*, *Oncomelania*, and *Schistosomophora* are suitable for the larval development of *Schistosoma japonicum*. Sources of infection are limited to regions where these species are present. The snails are amphibious in their habits and because of their small size (3 to 10 mm in length) may easily be overlooked unless careful search is made of vegetation above the water line. They apparently prefer water which is slightly acid, and are most abundant in still water and sluggish streams with grassy banks. Rapidly flowing water, however, cannot be regarded as necessarily safe, since cercariae may be washed into the stream from more favorable snail habitats located higher up. Inundated rice fields and ponds are particularly dangerous sources of infection. Infested water may be quite clear and show no gross evidence of contamination.

b. Infection is generally acquired by wading, swimming, bathing, or otherwise coming in contact with water infested with cercariae. Contaminated drinking water is another but apparently less important source of infection. Cercariae consumed in drinking water presumably enter the tissues by penetrating the buccal mucosa. A few minutes of contact with heavily infested water are sufficient to produce a clinical infection. Ordinary clothing does not significantly impede penetration of the cercariae into the skin.

c. Spread of schistosomiasis is favored by poor sanitation which allows contamination of water with feces containing eggs. Use of human excrement to fertilize rice fields is an important factor in the prevalence of schistosomiasis. However, animals other than man may also be involved in the spread of the disease. Dogs, cats, field mice, horses, cattle, and water buffalo may harbor *Schistosoma japonicum* and serve to disseminate the infection among snails.

5. COURSE. *a. General.* The lesions and symptoms of schistosomiasis japonica are due to the presence of the worms and their eggs, and probably also to substances given off by both worms and eggs. It is customary to divide the course of the disease into three stages, but these stages are continuous, and, therefore, clinical phenomena attributed to the different stages may overlap. The first stage corresponds to the period from the penetration of the body by cercariae to the settling down of paired mature worms in the mesenteric venules. The second stage corresponds to the period in which eggs are deposited by female worms in the small vessels of the intestinal wall. Many of these are extruded into the lumen of the gut and appear in the feces. Others are carried in numbers, which increase as time goes on, into the liver, mesenteric lymph nodes, and to a lesser degree other abdominal organs. In unusual cases, eggs may be found in the lungs, heart, brain, or other parts of the body, including the skin. Vastly more eggs, however, are always found in the intestinal wall and liver than elsewhere. The presence of eggs in the tissues gives rise to small abscess-like formations, which, in the case of the intestine, often rupture and release their contents into the gut. In practice, the symptoms associated with the first stage may be inseparable from those of the second stage. The symptomatology of these stages, therefore, is described under one heading (*b* below). The third stage, which is associated with proliferation and repair of damaged tissues, is described in *c* below.

b. Early symptoms. The early symptoms are variable in time of appearance and in intensity.

It should be remembered that the symptoms are not necessarily a measure of the severity of the infection. Early symptoms are often transient and may be overlooked. In some cases, a papular rash or itching, or both, may appear immediately after exposure. However, the first symptoms usually are noted between 3 and 10 weeks after infection (most commonly after about 5 to 6 weeks). The earliest symptoms include fever, chills, sweats, itching, unproductive cough, headache, stiffness of neck muscles, chest pain, epigastric pain, general abdominal discomfort or crampy pain, and pain in the back or legs. (Stiffness of the neck is described as apparently of muscular origin.) Anorexia and weight loss are often striking. Diarrhea may develop somewhat later or may be present at the same time; it is not usually severe in the beginning. The picture of subacute appendicitis occasionally develops. In some instances, signs of involvement of the central nervous system appear, including confusion or stupor, muscular weakness, changes in reflexes (especially hyperactivity), and rarely epileptiform seizures. Urticaria, with large or small lesions, edema, signs suggestive of bronchopneumonia, and abdominal tenderness (especially in the epigastrium), may be present. Lymph node enlargement, either regional or generalized, may be demonstrable. The liver and, at a somewhat later stage, the spleen are often palpable. X-ray pictures of the lungs may show scattered areas of infiltration. In rare cases, peripheral thrombosis has been attributed to the local deposit of eggs. In the early stages, the blood characteristically shows a rapidly increasing white cell count, with marked eosinophilia. These changes in the blood may reach striking proportions. As time goes on, they tend to disappear. At first there is no anemia. After deposition of eggs has begun, the stools may contain blood and mucus, as well as eggs. These symptoms may last from 2 to 10 weeks. There may be relapses and remissions, but spontaneous cessation of early symptoms ultimately occurs in most cases, if reinfection does not occur.

c. Late sequelae. As time goes on, affected tissues react to the increasing numbers of eggs deposited in them by extensive proliferation and repair. The results which may develop after a number of years include: thickening of the intestinal wall and formation of papillomata; thrombosis of mesenteric, portal, or splenic veins; cirrhosis of the liver, splenomegaly, and ascites. Emaciation may be extreme. When these lesions develop, associated symptoms usually appear only 3 or more years after infection. The clinical picture approximates that of Banti's syndrome. Dysentery may appear from time to time, but is often absent. At this stage, frequently, if not usually, the stools do not contain schistosome eggs. Anemia may be severe. The leukocytes are often reduced in number, but may be within normal limits or slightly increased. Eosinophilia is rarely present. The disease may last for many years.

6. DIAGNOSIS. *a. Clinical.* (1) In the early stage, a history of exposure is a most important clue to the diagnosis. Particularly significant is membership in a group of individuals with the same exposure and a similar clinical course. The clinical findings of outstanding significance are urticaria, itching, fever, cough, diarrhea, palpable liver, and (somewhat later) palpable spleen. The diagnosis should be confirmed by the demonstration of ova in the stools. If necessary, proctoscopy may be used as an aid in diagnosis, provided personnel trained in the use of the instrument are available. It may be possible to see beneath the normal appearing mucosa clusters of small yellowish nodules. Specimens containing ova may sometimes be obtained when ova cannot be demonstrated in the stools. Early schistosomiasis must be separated from allergic reactions to agents other than schistosomes and from many febrile diseases, such as dengue, malaria, kala azar, typhoid fever, and tuberculosis. An enlarged and tender liver may cause confusion with amebic or other forms of hepatitis, including infectious hepatitis. When the dysenteric picture is present, amebic and bacillary dysentery, and intestinal tuberculosis must be excluded. Involvement of the appendix may suggest the presence of subacute appendicitis.

(2) In the late stage, schistosomiasis japonica may be inseparable on clinical grounds from Banti's syndrome or hepatic cirrhosis from other causes. Splenomegaly is more marked in this disease than in ordinary portal cirrhosis. Late schistosomiasis japonica may resemble

kala azar or chronic malaria. These diseases, however, are often associated with febrile episodes which are rare in late schistosomiasis; they are rarely, if ever, associated directly with ascites.

b. Laboratory. (1) *General.* Specific diagnosis is established by the demonstration of the typical eggs in the stool specimen, or by allowing the eggs to hatch and identifying the miracidia. Difficulty may be encountered in finding eggs at some stages of the disease.

(*a*) Eggs discharged in the feces are usually mature and contain fully developed ciliated miracidia. However, many of the eggs first passed after infection may be immature. The eggs measure 70 to 100 microns in length by 55 to 65 microns in width and have well-rounded ends. They may have a light yellowish-brown color or may be hyaline. When the egg is properly oriented, a minute spinose process resembling a recurved hook extending from a depression on one side of the egg near the end is sometimes visible. In a viable mature egg, the miracidium may be seen squirming within the shell and moving its cilia in rhythmic fashion. Detail is obscured and the appearance altered in some specimens by adherent tissue remnants and fecal debris. Occasionally stools may contain eggs in which miracidia have disintegrated.

(*b*) The miracidium of *S. japonicum* is a very active, free-swimming organism which propels itself by means of cilia covering its surface. When observed in the water after hatching, the miracidia show a fishlike movement. A small, primitive gut is present at the cone-shaped anterior end, and on each side of this structure is a gland which apparently secretes a lytic substance. Slightly posterior to these is a second pair of glands which open laterally. Two flame cells, conspicuous because of the rhythmic movement of their cilia, are present in each side of the body. Proliferating germ balls are located in the posterior end of the larva. Use of the high power, or oil immersion lens, is required to distinguish the detailed structure of the miracidium.

(2) *Stool examination.* Several techniques may be used to detect the eggs in stool specimens. Since the eggs (or miracidia) are difficult to demonstrate in early and also very late cases, the diagnosis of schistosomiasis should not be excluded by a single negative stool examination.

(*a*) *Examination of a direct smear.* A simple smear of feces mixed with a drop of physiological saline solution on a slide reveals the eggs in many specimens from heavy and well-established infections. Smears should be made from any blood or mucus present in the stool specimen and preferably from the surface of the stool. When negative results are obtained, this technique should be supplemented by other procedures listed below. Concentration of eggs by zinc sulfate flotation is not satisfactory.

(*b*) *Sedimentation.* A portion of the stool specimen is comminuted in 5 to 10 parts of tap water poured into a conical urinalysis glass and allowed to sediment for 30 to 45 minutes. The supernatant fluid is decanted and the sediment resuspended by the addition of water. The process is repeated three or four times until the lighter debris has been removed and the supernatant fluid is relatively clear. After the final washing, the sediment is transferred to a slide by means of a pipette and examined for the eggs, using the low power of the microscope. Several smears should be examined before a negative report is made. Sedimentation and examination should be completed within 6 hours after dilution of the feces, otherwise hatching may occur. If eggs are not demonstrable by the sedimentation technique, an egg-hatching technique should be employed.

(*c*) *Egg-hatching technique.* The sedimentation technique is carried out on a generous portion of the stool specimen as described above. The final sediment is transferred to a graduate cylinder or, preferably, a large Erlenmeyer flask, and the container filled with water free from chlorine. It is allowed to stand preferably at a temperature of 30° C., for 6 to 12 hours, or overnight, to permit the eggs to hatch. The free-swimming miracidia collect near the surface of the water. The small area at the top of the flask concentrates the organisms so that they are more easily detected. The miracidia may be readily observed in proper light by use of a hand lens. They appear as minute, white, boat-shaped bodies swimming rapidly in a straight course. The miracidia must not be confused

with free-living ciliates which sometimes contaminate water. To confirm the identification, a few of the organisms should be transferred to a glass slide and examined under higher magnification. A dilute aqueous iodine stain may be added to facilitate identification.

(*d*) *Acid-ether technique.* Approximately 1 gram of fecal material (about the size of a pea) is thoroughly emulsified in 5 cc of 40 percent hydrochloric acid (40 cc concentrated hydrochloric acid diluted to 100 cc) in a small vial. The material is filtered through two layers of moist gauze stretched over the top of a 50 mm funnel into a 15 cc centrifuge tube. An equal quantity of ether is added, and the tube is stoppered with a gloved finger, and shaken thoroughly. It is then centrifuged for 1 minute at 1,500 rpm. Upon removal from the centrifuge, the debris floating at the acid-ether junction is loosened by ringing with a clean applicator, and the acid and ether layers are rapidly poured off and discarded. The same applicator is used to stir the sediment in the few drops of fluid remaining; the sediment is then transferred to a slide and examined under a coverslip.

(3) *Eggs in tissues.* Diagnosis sometimes may be established by the demonstration of eggs in tissue prepared by the usual techniques. The eggs are recognized by the characteristic shell. Often, however, they are collapsed, and in old infections they may be calcified.

(4) *Serological and skin tests.* Positive skin reactions appearing within 15 minutes may be obtained following intradermal injection of group-specific antigens prepared from extracts of adult schistosomes, cercariae, or infected snail tissues. Controlled skin tests, precipitin, and complement fixation reactions with schistosome antigens may be helpful as adjunct diagnostic procedures in cases in which eggs cannot be demonstrated. However, general use of these techniques in Army hospitals is precluded by the fact that the antigens are not available for distribution.

(5) *Other laboratory studies.* In the early stages, leukocytosis is often present, with total counts ranging from 12,000 to 20,000 and sometimes to 60,000 or more. Eosinophilia is common and when present is an important finding, especially when a marked increase occurs rapidly. The presence or absence of other intestinal parasites should be determined. The percentage of eosinophils may reach 80. Except in the late stages, anemia is not necessarily present. There is usually an increase in the globulin fraction of the plasma proteins. The erythrocyte sedimentation rate is elevated in some cases. The urine is not remarkable. The stools do not show any characteristic abnormalities other than the presence of eggs, although blood and, especially, mucus are often present in the early stages. The spinal fluid has been reported as normal, even in patients with central nervous system involvement.

7. TREATMENT. *a. General.* The treatment of late schistosomiasis with established hepatic disease is not discussed here. In early schistosomiasis, if significant constitutional symptoms or diarrhea are present, the patient should be confined to bed. The diet should afford a liberal supply of all the essential nutrients. Supplementation with four multivitamin tablets a day is recommended. If diarrhea is present, the diet should be bland or soft.

b. Chemotherapy. (1) Drug treatment should be instituted at the earliest possible time. Compounds of trivalent antimony are the most effective known agents. Pentavalent antimony preparations, such as neostibosan, are relatively ineffectual. Most of the reported cases of schistosomiasis japonica have been treated with one of two trivalent antimony compounds, antimony and potassium tartrate or fuadin. So far as is known, no adequate comparison has been made of the efficiacy of these drugs in the treatment schistosomiasis japonica. Recommended doses of fuadin, however, are less toxic than those of antimony and potassium tartrate. Other drugs have been used in the treatment of infections due to *S. haematobium* and *S. mansoni.* Available reports do not establish the superiority of any of these other drugs. Their relative value in infections due to *S. japonicum* is problematic. At present, it is recommended that patients with schistosomiasis be treated with fuadin or with antimony and potassium tartrate. The courses recommended below are planned to provide approximately equal amounts of antimony, in order to permit comparison of the two drugs on this basis. Authority for the trial use of

other chemotherapeutic agents in the United States should be obtained from The Surgeon General, or, in oversea theaters, from the theater surgeon.

(2) All available preparations of antimony possess toxic properties which are potentially dangerous. Nevertheless, the early institution of chemotherapy for schistosomiasis is imperative, unless the presence of another serious disease contraindicates it. Antimony compounds should always be given with care, especially with close observation of the patient's reactions to their administration. It should be remembered that small dosages are often followed by therapeutic failure. Among the toxic effects which have been reported are depression of the circulation and respiration, and irritation of the central nervous system, liver, and kidneys. Sudden death during injection has been reported. In general, antimony compounds are contraindicated in the presence of disease of the heart, liver, or kidneys. As a rule, they should not be administered concurrently with other metals or potential cardiac depressants, such as emetine.

c. Fuadin. This drug is also known as neoantimosan and stibophan. The solid contains 13.6 percent antimony. It is supplied in ampules containing 6.4 percent solution (approximately 0.064 gm fuadin in 1 cc). Fuadin solution is given intramuscularly and should be injected slowly. The first three doses of 1.5 cc, 3.5 cc, and 5.0 cc are given on successive days. On the fifth and subsequent alternate days, 5 cc are given, provided no toxic effect other than nausea appears, until a total of 16 doses has been administered (75 cc of solution, containing 0.653 gm of antimony). The only commonly reported toxic symptoms are nausea and vomiting. Rarely, joint and muscle pains may appear. If toxic symptoms occur, the subsequent dose should be reduced or the administration temporarily or permanently discontinued, according to the circumstances. The results of treatment should be checked as described in paragraph 8. The course of treatment may be repeated after 2 weeks' rest. However, if a course of fuadin is ineffectual, it is recommended that the patient receive antimony and potassium tartrate.

d. Antimony and potassium tartrate (tartar emetic). (1) This preparation contains about 36 percent antimony. It is recommended that it be administered in a concentration of 0.5 percent. Solutions should be freshly prepared, using if available Medical Department supplies of sterile 5 percent glucose in physiological saline solution, sodium chloride isotonic solution, or distilled water (preference in that order), rather than locally prepared diluent. If the diluent is prepared locally, it should be freshly distilled and sterilized. Every effort should be made to avoid the use of solutions containing pyrogens or the introduction of pyrogens during the preparation of solutions. Solutions of antimony and potassium tartrate should be perfectly clear and free of sediment. If a freshly opened clean supply of drug is available, with aseptic precautions it may be removed from the container, weighed, and transferred to sterile diluent, using sterile spatula and weighing vessels. With a fresh, clean supply of drug, sterile diluent, and careful technique, such a solution may be administered intravenously without sterilization. If doubt exists regarding the suitability of available supplies or technique, antimony and potassium tartrate solutions should be sterilized by gentle boiling for 5 minutes. They should not be autoclaved.

(2) Antimony and potassium tartrate is best tolerated 2 or 3 hours after a light meal. It should be administered intravenously and should be given slowly. Since the solution is very irritating to the tissues and may cause sloughing, the needle should be wiped off with a sterile sponge and there should be no extravasation. The patient should remain recumbent for at least an hour after treatment. The first dose of the 0.5 percent solution is 8 cc (0.04 gm tartrate). Provided no untoward reaction occurs, subsequent doses are given on alternate days and are increased on each occasion by 4 cc (0.02 gm tartrate), until 28 cc (0.14 gm tartrate) are being given. If no toxic reaction appears, a total of 15 doses is given (360 cc of solution, containing 0.648 gm antimony). The toxic effects of antimony and potassium tartrate include coughing immediately upon injection, which is not important; nausea; vomiting; stiffness of joints and muscles; sense of constriction of the chest; pain in the upper abdomen; bradycardia; dizziness; and collapse. Transient electrocardiographic changes with-

out corresponding clinical manifestations have been reported. If a toxic reaction other than coughing occurs during administration, the injection should be stopped at once. Following any toxic effect, the subsequent dose should be reduced or the administration of the drug temporarily or permanently discontinued, according to the circumstances. The course of treatment should not be repeated until after 2 weeks have elapsed without treatment.

8. FOLLOW-UP. In many cases, it is necessary to give more than one course of treatment. Hence, it is essential that the results of treatment for schistosomiasis be carefully checked. As chemotherapy becomes effective, eggs which are passed cease to contain viable miracidia. They appear dark, shriveled, and do not hatch when placed in water. When treatment is successful, eggs ultimately cease to appear. If viable eggs are present 4 weeks or more after a course of treatment is finished, it may be concluded that treatment has failed to kill all the worms present. Stool examinations should be done at least every week during treatment, at the end of a course of treatment, and at intervals thereafter for at least 3 months, but individuals should not be retained in the status of patients for this purpose alone. Individuals who have had schistosomiasis should be reexamined from time to time for a year following treatment. If eggs with living embryos are found, treatment should be reinstituted after a suitable interval has elapsed following the previous treatment.

9. PROGNOSIS. The proportion of patients with schistosomiasis japonica who acquire the late lesions of the disease is unknown. The amount and frequency of repetition of infection are important elements in determining the severity of the infection. The prompt administration of treatment has been found to relieve the early symptoms, including at least in some instances even severe manifestations of central nervous system involvement. It is believed that chemotherapy when instituted early is effective in preventing the development of severe sequelae. If cirrhosis of the liver is well established, chemotherapy does not influence the course.

10. PREVENTION. *a. General.* Prevention of schistosomiasis in military forces depends primarily upon avoidance of contact with fresh water infested with cercariae. Control measures to interrupt the life cycle of the parasite by killing the snail intermediate hosts, or by preventing the pollution of water with feces containing eggs are of lesser immediate importance.

b. Avoidance of exposure. (1) Swimming, bathing, and laundering of clothes, and the washing of vehicles in fresh water ponds, streams, and canals should be prohibited in endemic areas. Surveys by trained personnel should be accomplished as early as possible to locate infested bodies of water, and appropriate warning signs should be posted. The apparent absence of snails does not guarantee freedom from cercariae. Educational lectures and propaganda posters should be freely utilized to indoctrinate troops in the necessity for avoiding contact with infested water. Orders regarding avoidance of exposure should be strictly enforced by the imposition of fines, or other appropriate punishment.

(2) When practicable, rubber hip boots, waders, rubber gloves, or other waterproofed clothing should be worn by personnel whose duties require that they work in unsafe water. Care should be taken not to splash water on unprotected parts of the body.

(3) Shower bath water for small units required to remain away from their base should be provided from Lyster bags in which the water is treated as described in *c* (2) below. The Lyster bag can be hung at a suitable height from a branch, or from a support stretched between two trees. Improvised showerheads should be prepared beforehand and connnected to the faucets of the Lyster bag by a rubber hose. Use of such an expedient will minimize infractions of bathing discipline.

(4) In case of accidental or necessary entrance into water suspected of containing cercariae, immediate bathing with soap and brisk rubbing of the skin with a towel or article of clothing may reduce the chance of infection.

c. Treatment of water. Only water treated so that cercariae are killed should be used for bathing, laundry, vehicle washing, and drinking purposes. Maximum use should be made of subsurface water as a source of supply. Usual methods of filtration and chlorination cannot be relied upon to remove or destroy

cercariae. Recommendations for the treatment of water in areas where schistosomiasis is a hazard are summarized below.

(1) The standard portable (or mobile) sand filter purification units will not remove all cercariae; hence, sufficient chlorination to kill cercariae must also be employed. The newly standardized diatomaceous earth filter, however, is effective in filtering out cercariae.

(2) Application of chlorine sufficient to provide 1 part per million residual at the end of 30 minutes contact is sufficient to kill cercariae. It is important to note that this contact time exceeds that normally required for Lyster bag treatment. When employing Lyster bags, a satisfactory procedure which affords a margin of safety for the destruction of cercariae is to add sufficient calcium hypochlorite (grade A) to provide 1 part per million of residual chlorine after 10 minutes contact. An additional ampule of calcium hypochlorite should then be added and the water allowed to stand 30 minutes before use. When using canteens, treatment with two halazone tablets for clear water and four tablets for turbid or colored water is adequate to kill cercariae after 30 minutes contact.

(3) Water can be rendered free of infective cercariae by heating to 125° F. or by storage for 72 hours. In either case, the water should be chlorinated before use.

d. Destruction of snail hosts. Copper sulfate or copper carbonate (3 pounds per 1,000 square feet of water surface to be treated) may be used to kill the snail intermediate hosts. A concentration of 10 parts per million of copper sulfate after 48 hours of contact destroys free-swimming cercariae as well as snails. Because of the amphibious habits of the snail hosts of *Schistosoma japonicum*, chemical treatment of the water should be supplemented by the application of slaked lime to the ground and vegetation on the banks and along the shoreline of the water. Measures for killing snails have their greatest usefulness where the infested bodies of water are small. Their value is limited in places where extensive areas must be treated.

e. Disposal of feces. Prevention of pollution of water by proper disposal of human feces from infected individuals is a control measure which reduces the number of infected snails. However, domestic animals such as dogs, cats, cattle, and water buffalo often harbor *Schistosoma japonicum* and may serve to spread the infection.

[AG 300.5 (28 May 45)]

BY ORDER OF THE SECRETARY OF WAR:

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Chief of Staff

OFFICIAL:
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Major General
The Adjutant General

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Refer to FM 21-6 for explanation of distribution formula.

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TB MED 114

WAR DEPARTMENT TECHNICAL BULLETIN

IMMUNIZATION

War Department, Washington 25, D. C. • • • 9 November 1944

This Technical Bulletin rescinds S. G. O. Circular Letter No. 162, 28 November 1942, and all other S. G. O. directives on immunization

This bulletin follows TB MED 113, subject, "Medical and Sanitary Data on Borneo." The distribution given TB MED 113 was as follows: Armies (3); Corps (3); Sv C, Attn: Sv C Surg (3); Sv C, Attn: Tng Div (1); Depts (2); Def C (3); D (3); T of Opns (5) except SWPA (17); Base C (2); Numbered Air Forces (20) except 8th and 12th (30); ASF UTC (3) Med Sv Sch for 0 (1); Med Techn Sch (1); Med Dept RTC (1); AAF Sta (Cont) (1); Named Gen Hosp (Cont) (1); Sta Hosp (Cont) (1); Reg Sta Hosp (Cont) (1); Med Lab (Army) (1); Med Lab (Gen) (1); Med Lab (Dept) (1); Med Lab (Sv C) (1); PE (CG) (1); PE (The Surg) (1); PE (Int O) (1).

	Paragraph
Introduction	1
Standards, Procurement, Shipment, and Storage of Prophylactic Biologicals	2
Precautions To Be Taken When Administering Biologic Products	3
Technical Instructions	4
Immunization Records	5
Appendix.	

1. INTRODUCTION. *a.* The purpose of this bulletin is to furnish technical instructions concerning the agents and methods for accomplishment of the various immunization procedures in accordance with section III, AR 40–110, 15 September 1942 (under revision).

b. The indications for the various immunizations, the personnel to be immunized, and the required administrative procedures are described in section III, AR 40–210, 15 September 1942 (under revision). The technical instructions and information regarding the procurement, supply, shipping, and storage of biologic products contained herein should be carefully read by all medical officers.

2. STANDARDS, PROCUREMENT, SHIPMENT, AND STORAGE OF PROPHYLACTIC BIOLOGICALS. *a. Standards.* All biologicals obtained in this country for use in the Army must conform to the National Institute of Health requirements for the production and sale of such materials. If procured abroad, these agents must conform to standards equivalent to those of the U. S. National Institute of Health or the British Therapeutic Substances Act.

b. Procurement. See current War Department Supply Bulletins (8 series) for information regarding procurement of the various immunizing agents. Requisitions for Army Air Forces stations should be submitted to the Commanding General, Headquarters Air Service Command, Patterson Field, Fairfield, Ohio, Attention: Medical Supply Unit, ASCSE8NC.

Typhus and cholera immunizations may be

RESTRICTED

obtained at named general hospitals, regional station hospitals, 750-bed or larger station hospitals, ports of embarkation, general dispensaries, staging areas, and all stations of the Army Air Forces. In special circumstances where casuals or units are ordered overseas from a post not serviced by one of the above installations, typhus and cholera vaccines may be requisitioned for immunization of these specific groups.

In order to use most efficiently the limited supply of yellow fever vaccine, stocks are maintained in the United States only at ports of embarkation, general dispensaries, staging areas, and stations of the Army Air Forces. Casuals and units proceeding overseas may obtain yellow fever inoculation at any of the above installations.

c. Shipment and storage. Smallpox vaccine (Item No. 1609000) and yellow fever vaccine (Items Nos. 1613000 and 1613200) should be shipped and stored at freezing temperatures as indicated in paragraphs 4*a* (1) and (2) below.

All other agents referred to in this publication should be stored at temperatures between 2° and 10° C. (35.6°–50° F.). Lower temperatures should be guarded against, since freezing may result in breakage of the containers or harm to the product. However, these materials are relatively stable and will not necessarily lose their potency if kept at ordinary outdoor or room temperatures over reasonable periods of time. When necessity requires the shipment or storage of these materials at temperatures higher than those recommended, the agents should be carefully inspected before use for evidence of physical change.

3. PRECAUTIONS TO BE TAKEN WHEN ADMINISTERING BIOLOGIC PRODUCTS. *a.* The present medical program of the Army requires the administration of various prophylactic and therapeutic biological preparations to large numbers of individuals. As some individuals may be expected to show reactions of varying degree, because of sensitivity, to the substances injected, all medical officers should be impressed with the occasional seriousness of such reactions and the precautions to be taken against them. Prior to the injection of any biologic product, inquiry should be made as to whether or not the individual who is to receive the injection has previously shown any unusual degree of sensitivity to a foreign protein. If the individual gives a history of such sensitivity, the surgeon will take the indicated precautionary measures, such as tests for sensitivity, the administration of the required material in a series of small and more frequently repeated doses, or desensitization, in order to avoid a possible serious reaction. Persons with significant allergy to eggs should not be given vaccines prepared by cultivation in eggs. These include typhus, yellow fever, influenza, and Rocky Mountain spotted fever vaccines. History of sensitivity may be elicited by questioning concerning food intolerance for eggs. The existence of allergy may be substantiated by intradermal skin test beginning with 1:1000 dilution of the vaccine and increasing to 1:100, and 1:10 if no reaction occurs with the higher dilution. The amount injected intradermally should be as small as possible (0.02 to 0.04 cc). See paragraph 9*f*, AR 40–210, 15 September 1942, regarding exemption from immunization.

b. While reactions of sensitivity occur in only a very small proportion of individuals, on rare occasions they may be of sufficient gravity to require prompt action. A solution of epinephrine hydrochloride (1 to 1000) injected subcutaneously in doses of 0.3 to 0.8 cc. is sufficient to control mild allergic manifestations. If indicated, this dose may be repeated after a few minutes. For severe reactions larger doses may be used. Whenever a biologic product is to be used, epinephrine will be available and ready for immediate injection, if required. Practically all dangerous reactions begin within approximately one-half hour after receiving an injection. If an individual has a dangerous allergic reaction to any biologic agent or drug, the date, type, and severity of the reaction will be recorded in the space provided on the Immunization Register (WD, AGO Form 8–117, formerly WD, MD Form 81).

c. Upon the occurrence of local or constitutional reactions, remarkable in severity or frequency, to any biologic product, a report will be made to The Surgeon General, including the following data: product and dosage given; maker's name, lot number, and expiration date of the material; if an immunizing agent, which

injection in the series produced the reaction (e. g., first, second, stimulating dose); description of type of reactions encountered and their frequency (number of injections given and number of reactions noted). Samples of the biologic product under suspicion should be kept, including both opened and unopened packages, but should not be forwarded unless so directed by The Surgeon General.

d. To avoid the possibility of infection resulting from parenteral injections, it is of the utmost importance that meticulous aseptic technique be exercised at all times, including the use of a freshly sterilized needle for each injection.

4. TECHNICAL INSTRUCTIONS. *a. Smallpox.* The only effective method for the prevention or control of smallpox is vaccination with a potent vaccine. If smallpox occurs within a command or if it is known that there has been exposure to cases of the disease, it is more practical in most instances to vaccinate all of those exposed than to attempt the selective vaccination of the nonimmune contracts. The procedure requires little time and those individuals who are already immune will respond with minimal reactions.

(1) *Storage of vaccine.* Smallpox vaccine, if exposed to temperature above 5° C. (41° F.), will lose its potency very rapidly. It is therefore extremely important that smallpox vaccine be kept below this temperature at all times. A temperature of about −10° C. is desirable and even colder levels will do no harm and are definitely preferable to temperatures above freezing. Because of the glycerin in smallpox vaccine, there is no danger of breakage of the capillary tubes. The best methods for storage of the smallpox vaccine are:

(*a*) Place in the freezing room of a refrigeration plant or in the freezing compartment of a mechanical refrigerator.

(*b*) Lacking mechanical refrigeration facilities, the vaccine, in suitable metal containers, should be placed directly on ice. In no instance should smallpox vaccine be allowed to stand at room temperature, if such temperature is above 5° C. (41° F.).

(2) *Shipment.* Unless proper care is afforded smallpox vaccine in transit, it may deteriorate and be useless upon arrival. Shipments should be made by the most rapid and direct route and must be so timed that the vaccine will not be allowed to remain in a post office or express office over a holiday or week end. Upon arrival at the destination, the vaccine must be placed immediately in storage as indicated above.

When using smallpox vaccine in a dispensary or clinic, only sufficient vaccine for 1 hour's vaccinations should be removed from the icebox at one time.

For ordinary shipments by parcel post, express, etc., the package containing the smallpox vaccine preferably should be placed between blocks of dry ice. The entire package should then be wrapped carefully with cellucotton or other insulating material and placed in a heavy cardboard carton, heavy wrapping paper, or other suitable mailing container.

For shipments in transit for extended periods such as those made by boat, smallpox vaccine should be placed in the freezing compartment of a refrigerator unit and held at freezing temperatures, that is below 0° C. (32° F.).

Because of the perishable nature of this material and the brevity of the period of expected potency, the amounts requisitioned should not be in excess of the anticipated needs for approximately 2 months. In addition, it is recommended that, for use overseas, smallpox vaccine of acceptable quality be purchased locally, whenever possible.

(3) *Method of vaccination.* The multiple pressure method is the one of choice. The arm should be prepared for the vaccination by washing with soap and water and thoroughly dried before application of vaccine. If desired, ether or acetone may be applied to the area and allowed to dry completely before the vaccine is deposited on the skin.

Note.—Alcohol, especially if medicated, should not be used, as remaining traces of this antiseptic may inactivate the vaccine.

After the arm is prepared, the vaccine is deposited on the cleansed area and the vaccination is accomplished by the multiple pressure method. This entails the holding of the needle parallel to the skin and pressing the side of the needle point through the drop of vaccine about 30 times. The motion should be perpendicular to the skin and just enough pressure should be

applied so that the elasticity of the skin will pull a small bit of the epidermis over the point of the needle at each pressure. The total area of the vaccination should not be greater than ⅛″ in diameter and should not be deep enough to result in bleeding. No dressing should be applied to the vaccinated area.

(4) *Interpretation of results of vaccination.* If potent vaccine is used and if the proper technique is employed, one or another of the three types of reactions described below should follow vaccination.

(*a*) *Vaccinia* (primary reaction). This type of reaction occurs in persons not immune to vaccinia or smallpox. Characteristically, a papule appears about the third day at the site of vaccination. This becomes a vesicle on the fifth or sixth day and is surrounded by a band of erythema. The maximal extent of the vesicle and erythema is attained about the tenth day. Following this, the erythema subsides. The vesicle becomes a pustule and a crust forms which usually comes away about the twenty-first day.

(*b*) *Vaccinoid* (accelerated reaction). This reaction occurs in individuals partially immune to vaccinia or smallpox. A papule appears in about 36 hours at the site of vaccination. The vescile develops more rapidly than in the primary reaction and is surrounded by an erythematous area of considerably less extent. The height of the reaction is reached in about 4 to 8 days after which there is a rapid subsidence.

(*c*) *Immune* (immediate reaction). This reaction occurs in persons immune to vaccinia or smallpox. A papule and small area of redness occur usually within the first 24 hours after vaccination and the peak of the reaction is past within 3 days. This reaction must never be recorded unless there is full assurance that a potent vaccine has been used and the reaction has actually been observed 2 to 3 days after vaccination.

If none of these reactions occurs, the vaccine was inert or improper technique was employed and the vaccination should be repeated as many times as necessary. In order to distinguish with certainty among the four possible readings, it is necessary to make inspections at 2 to 3 days and at 8 to 10 days after the vaccination. Since the transfer of personnel during the period immediately following vaccination may render the proper interpretation and recording of reactions much more difficult and increase the chances of error, vaccination should not be performed at any induction or reception center unless there is assurance that the recruits will be available for inspection at the station for at least a week.

b. Typhoid fever and paratyphoid fevers. Vaccination against typhoid fever and the paratyphoid fevers produces a considerable degree of immunity. However, this immunity may not suffice to protect against unusually large doses of the infecting organisms. Accordingly, typhoid vaccination in no instance should be considered as a substitute for the proper sanitary control of food and water as prescribed in AR 40–205 and AR 40–210.

(1) *Type of vaccine.* The triple typhoid vaccine used in the Army is manufactured and distributed by the Army Medical School. This vaccine contains 1000 million *E. typhi*, and 250 million each of *S. paratyphi* and *S. schottmuelleri* per cubic centimeter.

(2) *Method of vaccination.* (*a*) The initial vaccination consists of the subcutaneous injection of three doses of the triple vaccine administered at intervals of 7 to 28 days, the longer interval enabling administration of the three doses concurrently with tetanus toxoid. The first dose is 0.5 cc of the vaccine and the second and third doses are 1.0 cc each. Care should be taken that the injections are made into the superficial subcutaneous tissue. Injections given deeply, particularly into the muscle or into a vein, are more apt to produce untoward reactions.

(*b*) Revaccination is accomplished by the subcutaneous administration of 0.5 cc of the triple vaccine annually to those individuals who have been given the initial vaccination series described above.

(3) *Reactions.* A large proportion of individuals will exhibit reactions to typhoid vaccination. These reactions are extremely variable, both in nature and degree, and usually occur within 24 hours. Local redness, heat, and tenderness at the site of injection are usually seen. Occasional systemic reactions are encountered which are characterized by general malaise, headache, slight elevation of temper-

ature, and rarely by actual chills with secondary rise in temperature. It is preferable to avoid the simultaneous injection of another agent which may in itself give rise to reactions of this type. The administration of typhoid vaccine within a period of a week following yellow fever vaccination should be avoided, if possible, although in case of necessity, lesser intervals or even simultaneous immunizations may be accomplished.

c. Active immunization against tetanus. (1) *Type of toxoid.* The material used is tetanus toxoid, plain (fluid).

(2) *Method of immunization.* (*a*) *Initial immunization.* This consists of a series of three subcutaneous injections of tetanus toxoid (plain), 1 cc each administered with intervals of 3 to 4 weeks between doses. This "initial immunization" produces an active immunity to tetanus. Subsequent reinforcement of this immunity is accomplished by the administration of a stimulating or recall dose of toxoid. The prophylactic use of tetanus antitoxin is therefore unnecessary after the completion of the initial immunization series. Instead, an emergency stimulating dose of tetanus toxoid should be administered as indicated below.

(*b*) *Subsequent injection of tetanus toxoid.*

1. A single stimulating dose of 1 cc of tetanus toxoid is injected subcutaneously approximately 1 year after the initial series and need not be repeated except as indicated in *2* below.

2. In addition to the above initial and stimulating immunization, an emergency stimulating dose should be administered to those indicated below as soon as practicable after the injury (preferably within 24 hours) when deemed advisable by the responsible medical officer:

(a) Individuals who incur wounds or severe burns on the battlefield.

(b) Patients undergoing secondary operations or manipulations of old wounds.

(c) Others who incur punctured or lacerated wounds, severe burns, or other conditions which might be complicated by the introduction of *Cl. tetani* into the tissues.

d. Use of tetanus antitoxin. The administration of tetanus antitoxin is limited to the following:

(1) To patients presenting clinical evidence of tetanus.

(2) To individuals who incur wounds or other conditions which necessitate protection against tetanus, but who either have not previously completed the initial immunization with tetanus toxoid or whose identification tags or immunization records fail to show such immunization.

These individuals should be passively immunized with at least 1,500 units of tetanus antitoxin and also actively immunized with tetanus toxoid by completion of the initial series.

Due consideration should always be given to the possibility of allergic reactions when injecting tetanus antitoxin because it contains horse serum (see par. 3).

e. Yellow fever. The administration of yellow fever vaccine is required for personnel traveling to or through or stationed in areas in which yellow fever is endemic or epidemic. See footnote ([8]) at end of appendix.

(1) *Nature of vaccine.* The yellow fever vaccine used in the military service consists of a special strain (17D) of living yellow fever virus which has been attenuated through cultivation in chick embryos. The vaccine is prepared from chick embryo material, placed in ampules and then rapidly frozen, desiccated, sealed, and stored at a temperature not higher than 0° C.

(2) *Shipment and storage.* The responsibility for proper storing, packing, and shipping of all yellow fever vaccine lies with the medical supply officer of the depot. He will determine the best method of shipment in each instance. He will take the necessary steps to insure that the vaccine is held at a temperature below 0° C. while in transit and he will notify the officer who made the requisition of the exact time and place of delivery. A commissioned officer will personally receive the vaccine from the carrier immediately upon delivery, and will place it in storage at a temperature not above 0° C. Ordinarily, the freezing compartment of a refrigerator makes the safest available storage place for the vaccine. During "defrosting" periods, the vaccine must be transferred to the freezing compartment of another refrigerator to protect it from temperature change. Yellow fever vaccine must be used immediately after removal from the refrigerator, as the virus

becomes completely inactive and worthless after 3 or 4 hours at room temperature. Vaccine exposed to room temperature for longer than 1 hour should not be used.

(3) *Package information.* The ampules of yellow fever vaccine now supplied are of two sizes, one containing the desiccated equivalent of 5 cc, and the other of 1 cc of the concentrated vaccine. With each 5-cc ampule is provided a rubber-stoppered bottle containing about 55 cc of sterile normal salt solution. The 1-cc ampule is accompanied by a small bottle which contains 10 cc of sterile normal salt solution. The 5-cc ampule, when diluted with sterile saline in the manner described below, will provide 55 cc of diluted vaccine, sufficient for more than 100 injections. The 1-cc ampule, when diluted with 10 cc saline, furnishes sufficient material for 20 injections. It is technically impracticable to produce and distribute this vaccine in ampules smaller than 1 cc (20 doses). The diluted vaccine which remains unused after 1 hour will be discarded.

(4) *Technique of dilution and injection.* (*a*) *Using the 5-cc ampule.* With a sterile needle and syringe remove through the cap 5 cc of sterile saline and add this to the desiccated vaccine in the ampule. Suspend the vaccine in the saline by shaking the ampule, or by forcing the fluid in and out of the syringe. When the vaccine has been completely suspended, draw the entire contents of the ampule into the syringe and inject this 5 cc of concentrated vaccine through the rubber cap into remaining salt solution in the saline bottle. This will provide about 55 cc of an approximately 1:10 dilution of yellow fever vaccine, which is then ready for use. The dose of this diluted vaccine is 0.5 cc injected subcutaneously.

(*b*) *Using the 1-cc ampule.* Remove 1 cc of salt solution from the 10-cc saline bottle, and suspend the desiccated vaccine in this 1 cc of saline. Inject this amount of concentrated vaccine into the 10-cc bottle of saline and mix thoroughly. This will provide about 10 cc of 1:10 dilution of yellow fever vaccine which is then ready for use in the manner described above.

(5) *Precautions.* (*a*) The vaccinating dose is one injection of 0.5 cc of the 1:10 dilution of the concentrated vaccine. Every precaution must be taken to avoid giving improperly diluted vaccine.

(*b*) After an ampule of vaccine has been opened, any vaccine which remains unused after 1 hour will be discarded.

(6) *Reactions from yellow fever vaccine.* About 5 percent of those receiving this vaccine may exhibit a slight febrile reaction on the fifth to the seventh day. Yellow fever vaccine preferably should not be given concurrently with smallpox vaccine. When both of these vaccinations are to be done, it is suggested that the yellow fever vaccine be given first and that at least 5 days elapse before the smallpox vaccination is done. With the exception of smallpox vaccine, there is no strong objection to the simultaneous administration of yellow fever vaccine and other vaccines or tetanus toxoid. However, an exaggerated reaction to triple typhoid vaccine may result if it is administered to individuals who are actually experiencing a febrile reaction to a previously administered dose of yellow fever vaccine, and, therefore, the administration of typhoid vaccine within the 7-day period following yellow fever vaccination should be avoided, when practicable.

f. Louse-borne typhus fever. Typhus vaccination is required for all military personnel stationed in or traveling through defined endemic areas. See footnote ([6]), at end of appendix. This vaccination should be performed before arrival in an endemic area. Vaccination should be considered merely an adjunct to, and never a substitute for, effective louse control. Vaccination does not always prevent infection but greatly modifies the severity of the disease.

(1) *Type of vaccine.* Typhus vaccine consists of a suspension of killed epidemic typhus rickettsiae prepared by an egg yolk-sac culture method.

(2) *Method of vaccination.* (*a*) The initial vaccination consists of two injections of the vaccine, 1 cc each, administered subcutaneously at intervals of from 7 to 10 days.

(*b*) A stimulating dose of 1 cc of typhus vaccine should be administered at the beginning and in the middle of the typhus season which means about 1 November and 1 February. Other 1 cc doses of typhus vaccine may be given whenever in the opinion of the surgeon this additional stimulation of immunity is indicated.

g. Cholera. Cholera vaccination is required for all military personnel stationed in or traveling through defined endemic areas (see footnote (7) at end of appendix) or elsewhere, at the discretion of the surgeon, when danger from cholera exists.

Vaccination against cholera is definitely secondary in value to sanitary measures. These measures and other pertinent procedures for the sanitary control of food and water must be applied vigorously, even though all personnel are immunized against cholera.

(1) *Type of vaccine.* Cholera vaccine consists of a suspension of 8,000 million killed cholera vibrios (*V. comma*) per cubic centimeter.

(2) *Method of vaccination.* (*a*) The initial vaccination consists of two subcutaneous injections of cholera vaccine at an interval of from 7 to 10 days. The first dose is 0.5 cc and the second dose 1 cc.

(*b*) A stimulating dose of 1 cc of cholera vaccine should be administered every 4 to 6 months as long as serious danger of infection is present. Additional 1-cc doses of cholera vaccine may be given whenever in the opinion of the surgeon this additional stimulation of immunity is indicated.

h. Plague. Under present conditions plague vaccine is to be administered only when personnel are under serious threat of exposure to plague. The indiscriminate administration of plague vaccine in the absence of definite indications for its use is not warranted. The most effective measures for the prevention of bubonic plague is the avoidance of contact with infected rodents and fleas.

(1) *Type of vaccine.* The vaccine consists of a suspension of 2,000 million killed plague bacilli per cubic centimeter.

(2) *Method of vaccination.* (*a*) The initial vaccination consists of two subcutaneous injections of plague vaccine with an interval of from seven to ten days. The first dose consists of 0.5 cc and the second dose of 1.0 cc.

(*b*) Additional 1-cc doses of plague vaccine may be administered whenever in the opinion of the surgeon stimulation of immunity is indicated. Repetition oftener than every 4 to 6 months is not considered warranted.

i. Influenza. (1) *Type of vaccine.* Influenza vaccine is a killed suspension of type A and B influenza viruses which were grown in eggs. (See TB MED 85, 15 August 1944.)

(2) *Method of vaccination.* One dose of 1 cc is given subcutaneously at the direction of the theater surgeon or The Surgeon General in the face of an outbreak or threatened outbreak of influenza. Repetition of this dose after 90 days, should another outbreak become apparent, is considered advisable.

j. Diphtheria. Immunization of military personnel against diphtheria is not a routine procedure and should be undertaken only when a definite hazard from this disease exists. When time and facilities permit, preliminary Schick testing may be done and only the positive reactors should be immunized. However, because of the time required, the meticulous care necessary to obtain reliable results, and other inherent difficulties, mass Schick testing will seldom be feasible and the entire group requiring immunization should be given toxoid in the manner described below.

(1) *Type of immunizing agent.* The material to be used is diphtheria toxoid, plain.

(2) *Method of immunization.* Reactions to diphtheria toxoid are more common in adults than in children and, therefore, it is desirable to begin with a dosage of 0.1 cc, subcutaneously, and to limit further immunization to those who do not react severely to this test dose. The occurrence, after any dose in the series, of local edema or induration more than 6 cm in diameter, or a marked constitutional reaction with fever over 101° F., is a contraindication to further doses. The group given the test dose should be inspected after 48 hours. Those who have not experienced severe reactions may be given the first regular immunizing dose of 0.5 cc at this time. From this point subsequent doses are given at 3-week intervals, the second and third immunizing doses being 1.0 cc. Even though the entire series cannot be completed for some individuals because of reactions, this procedure should raise the general level of immunity sufficiently to prevent an epidemic of diphtheria.

k. Scarlet fever. Immunization of military personnel against scarlet fever is seldom indicated. Under certain circumstances, however, this procedure may be applicable for the pro-

tection of nurses, ward attendants, and others in close association with cases of scarlet fever. The material supplied for this purpose is scarlet fever streptococcus toxin. As the injection of this material may be attended by severe reactions, special care must be exercised in its use. The protection against streptococcal disease afforded by this material is not complete.

l. Rocky Mountain spotted fever. Vaccination alone is not a dependable method for the prevention of Rocky Mountain spotted fever. The immunity produced, however, is apparently sufficient to modify the severity of the case and prevent death when the disease is acquired within a year subsequent to vaccination. Chief reliance for prevention should be placed on avoidance of ticks and frequent inspection of the body (once or twice a day) with prompt removal of ticks. Attachment of the infected tick for 4 to 6 hours is probably necessary for transmission of the infection.

(1) *Immunization.* Mass vaccination is not recommended in the Army, but it may be used when authorized for certain individuals or groups such as patrols and guards who come into frequent contact with the brush, and who are located in regions where danger from Rocky Mountain spotted fever is particularly great. Vaccination is probably of no value when given after the bite of an infected tick. It is valueless in treatment.

(2) *Supply.* Request for Rocky Mountain spotted fever vaccine should be made to the respective service command surgeon. In order to provide a basis for authorization the request should indicate the number and type of personnel in whom its use is proposed, and the reasons for considering the degree of danger particularly great among the personnel proposed for immunization. Requests from the Third, Fourth, Seventh, Eighth, and Ninth Service Commands will be approved at the discretion of the respective service command surgeon. Requests from other service commands will be forwarded with the recommendations of the service command surgeon to The Surgeon General for review.

(3) *Type of vaccine.* The vaccine consists of a suspension of killed Rocky Mountain spotted fever rickettsiae prepared by the egg yolk-sac culture method.

(4) *Method of immunization.* The subcutaneous administration of three doses of 1 cc each, at intervals of 7 to 10 days shortly before the tick season begins, is the recommended procedure.

m. Measles. Immune serum globulin (human) may be administered following a known exposure either to produce temporary complete immunity or to produce partial immunity for the purpose of modifying the severity of the disease. In the Army this procedure ordinarily should be reserved for debilitated, susceptible patients and exposed susceptibles who must be protected for military reasons.

(1) *Nature of the material.* Immune serum globulin is a clear, colorless solution of the gamma globulin fraction of human serum containing most of the antibodies against measles. It is relatively stable, may be shipped like other biologicals, and should be stored at 2° to 10° C. (35.6° and 50° F.).

(2) *Method of use.* The degree of protection afforded varies principally with the size of the dose and the interval between exposure and the time of administration. In adults, 10 cc of immune serum globulin (human) injected intramuscularly within the first week following exposure ordinarily will produce complete immunity of 2 to 3 weeks duration; 5 cc usually produces modification. Modified measles is characterized by a prolonged incubation period (up to 21 days) followed by slight fever and a transient rash. Administration of the large dose subsequent to the first week of the incubation period may produce only modification. After the appearance of the rash, it is ineffective.

(3) *Reactions.* Intramuscular injection is followed by little or no reaction other than the slight local discomfort incident to the volume of material injected. The material should not be administered intravenously as injections by this route have caused sharp febrile and shock-like reactions.

n. Rabies. (1) *Type of vaccine.* Rabies vaccine (Semple type) is a phenol killed suspension of the virus obtained from rabbits. It is a nonstandard item to be purchased as needed. While the Semple type of vaccine is most commonly used, the chloroform inactivated material may be used. In some localities, other types such as Pasteur, Hogyes, Harris, and Cum-

mings may be the only ones available in which event they may be utilized.

(2) *Method of vaccination.* This vaccination is given at the direction of the surgeon. Usually the contents of one vial are injected subcutaneously every day for 14 days when an individual has been bitten by a rabid animal. However, in the case of face bites, the treatment is continued for 21 days. If the vaccine used is prepared according to the method of Pasteur, 24 doses in 21 days are routinely required. In the case of bites by an animal suspected of being rabid, the animal should be confined and kept under observation for evidence of rabies, vaccine being given on the appearance of definite clinical evidence of rabies in the animal or if histologic evidence of rabies is found at post-mortem. If the animal cannot be confined and watched or has been destroyed so that laboratory examination is impossible, the decision as to whether or not to give vaccine will have to be made on the basis of individual circumstances, but it should not be withheld if there is any suspicion that the animal was rabid. In the case of face bites, since the incubation period is shorter than for bites of the extremities, the vaccine series should be started at once without awaiting confirmation of the diagnosis in the animal.

5. IMMUNIZATION RECORDS. The required immunization records are prescribed in section III, AR 40–210. The detailed administrative procedures in the preparation and disposition of immunization records will be published in a War Department circular. Entries in the Service Record, WD AGO Form 24, are prescribed in TM 12–230.

APPENDIX I

SUMMARY OF IMMUNIZATION REQUIREMENTS[1]

ROUTINE

Immunization	Agent and catalog No.	Required		Initial series			Stimulating doses	
		For duty in U. S.[2]	For duty overseas[3]	No. of doses	Individual dose	Recommended interval between doses[4]	When indicated	Amount
Smallpox	Smallpox vaccine (No. 1609000).	Yes	Within 1 yr. (all theaters).	1	Contents 1 capillary tube.		Every 3 yrs. and in presence of the disease.	Contents 1 capillary tube.
Typhoid—paratyphoid.	Triple typhoid vaccine (No. 1730000).	Yes	Within 1 yr. (all theaters).	3	1st dose—0.5 cc; 2d dose—1.0 cc; 3d dose—1.0 cc.	7 to 28 days.	Annually, and in presence of the disease.[5]	0.5 cc.
Tetanus	Tetanus toxoid (Nos. 1612500 and 1612700).	Yes	Same as for duty in U. S.	3	1.0 cc	Minimum of 21 days.	One year after initial series and upon occurrence of wounds or burns, as directed by the medical officer.	1.0 cc.

See footnotes on p. 14.

APPENDIX I

SUMMARY OF IMMUNIZATION REQUIREMENTS—Continued

SPECIAL

Immunization	Agent and Catalog No.	Required		Initial Series			Stimulating Doses	
		For duty in U. S.[2]	For duty overseas[3]	No. of doses	Individual dose	Recommended interval between doses[4]	When indicated	Amount
Typhus(louseborne)	Typhus vaccine (No. 1612800).	No	Yes, for movement to or through defined endemic areas[6].	2	1.0 cc	7 days	Seasonally about 1 Nov. and 1 Feb. in endemic areas and in the presence of the danger of typhus.	1.0 cc.
Cholera	Cholera vaccine (No. 1601500).	No	Yes, for movement to or through defined endemic areas.[7]	2	1st dose—0.5 cc; 2d dose—1.0 cc.	7 days	At 4–6 month intervals in the presence of danger of cholera.	1.0 cc.
Yellow fever	Yellow fever vaccine (Nos. 1613000 and 1613200).	No	Yes (10 days or more before reaching endemic area).[8]	1	0.5 cc of the proper dilution.		Every 4 years	0.5 cc of the proper dilution.
Plague	Plague vaccine (No. 1607000).	No	Only on special order or in presence of definite plague hazard.	2	1st dose—0.5 cc; 2d dose—1.0 cc.	7 days	At 6-month intervals in the presence of danger of plague.	1.0 cc.
Influenza	Influenza vaccine (No. 1605900).	No	No	1	1.0 cc			

See footnotes on p. 14

APPENDIX I

SUMMARY OF IMMUNIZATION REQUIREMENTS—Continued

OCCASIONAL (for details see par. 4)

Immunization	Agent	Indication	No. of doses	Individual dose	Interval between doses	Stimulating doses
Diphtheria	Diphtheria toxoid plain (No. 1604100).	Outbreak of diphtheria	4	0.1, 0.5, 1.0, 1.0 cc	48 hrs. between 1st and 2d; 3 to 4 weeks for remainder.	Usually none.
Scarlet fever	Scarlet fever streptococcus toxin (No. 1608300).	Seldom indicated	5	See directions on package.	1 week	None.
Rocky Mountain spotted fever.	Rocky Mountain spotted fever vaccine (nonstandard).	Only for personnel exposed frequently to infected ticks.	3	1.0 cc	7 to 10 days	Repeat series annually if indicated.
Measles (passive)	Immune serum globulin (human) (No. 1605500).	Prevention or modification in susceptible contacts under special conditions.	1	5 to 10 cc within 10 days after exposure.		Usually none.
Tetanus (passive)	Tetanus antitoxin (No. 1611000).	Wounded personnel who have not received initial toxoid series.	1	Not less than 1,500 units.		Usually none.
Rabies	Rabies vaccine (nonstandard).	When bitten by rabid animal	14 or 21[9]	See directions on package.	1 day	None.

See footnotes on p. 14.

FOOTNOTES FOR PAGES 11-12-13

[1] The administration and recording of immunizations will be kept up-to-date as prescribed. Inoculation of inductees should be initiated as soon as feasible after induction (exception—smallpox, unless there is assurance that the individual will be available for inspection at the station for at least 1 week). When troops are alerted for duty overseas, necessary stimulating and special inoculations will be started as soon as possible, although it may be necessary to complete some of the immunizations at staging areas, ports of embarkation, or on transports. Navy and Marine Corps personnel who have fulfilled Navy immunization requirements should be accepted as satisfying the respective Army requirements for equivalent service. Navy requirements which differ materially from those of the Army are:

a. Smallpox: Vaccination at 4-year intervals.

b. Triple-typhoid: Annual stimulating dose of 0.1 cc administered intracutaneously.

c. Tetanus: Alum-precipitated toxoid used. Initial immunization by two 0.5-cc injections with interval of not less than 4 nor more than 8 weeks. Stimulating doses of 0.5 cc after 1 year, then every 4 years, 1 month before entering a combat zone, and upon occurrence of wounds or burns.

[2] In addition, all male Army Air Forces personnel eligible and physically qualified for oversea duty are required to obtain typhus, cholera, and yellow fever initial immunizations. No stimulating doses of these special vaccines should be given such personnel prior to receipt of orders moving personnel to Army Air Forces staging areas or their equivalent. All installations processing Army Air Forces personnel will provide for the administration of these special immunizations.

[3] The requirements of this column are primarily for personnel on first departure from the United States for oversea duty. Personnel going to an oversea theater after brief absence from that or another theater will be assumed to have completed the initial immunization requirements for duty in the theater from which they departed. In no case will such personnel be required to repeat the initial series of immunizations. They should be given only the additional or stimulating doses necessary for service in the areas to or through which they are returning. Personnel making intra- or inter-theater movements or returning to the United States should be immunized before departure in accordance with existing requirements for travel to or through the areas concerned.

[4] The prescribed time interval between doses of the various agents should be adhered to, but, when this cannot be done, the missed dose should be administered as soon as possible and the series completed. A new series should not be started. The lapse of a period up to several years since the administration of the initial series of any of the routine or special immunizing agents shown above does not necessitate repetition of the initial immunization, even though no stimulating doses have been given in the interim. If an initial series has been given at any time in the military service, a single stimulating dose ordinarily will raise the immunity to a satisfactory level.

[5] The interval between the three doses of the initial series of triple-typhoid vaccine may be 7 to 28 days. The 0.5 cc stimulating dose should be given only to those who have completed an initial vaccination series with Army triple-typhoid vaccine.

[6] Typhus vaccination is required for personnel stationed in or traveling through Asia, Africa, Europe (including the British Isles), the mountainous regions of Central and South America (including Mexico, but excepting Panama), Alaska, the Southwest Pacific Area, and certain islands in the South Pacific (see POM). In highly endemic areas, stimulating doses should be given about 1 November and 1 February and additional doses whenever unusual risk of exposure exists.

[7] Cholera immunization is required for personnel stationed in or traveling to or through Asia, including the area around the Persian Gulf, and the islands of the East Indies.

[8] Yellow fever immunization is required for those stationed in or traveling to or through the endemic areas which are defined as follows: In the Eastern Hemisphere, that portion of Africa lying between latitude 18° south and the northern borders of French West Africa, French Equatorial Africa, and the Anglo-Egyptian Sudan, including the islands immediately adjacent thereto. In the Western Hemisphere, the mainland of South America lying between latitudes 13° north and 30° south, including the islands immediately adjacent, and Panama, including the Canal Zone. However, transit through the Panama Canal with brief sojourns within the terminal port cities or military posts within the Canal Zone will not be considered as travel through an endemic area. In order to comply with the quarantine regulations of certain countries, individuals traveling to these countries through the endemic areas as defined above must have been vaccinated not less than 10 days nor more than 4 years before entering an endemic area. The individual must carry an immunization register or certificate of immunity.

[9] Rabies vaccine is administered for 14 days when the material used was not prepared according the the technique of Pasteur, and when the wound is elsewhere than on the face. Rabies vaccine is continued for 21 days when the vaccine was prepared according the the technique of Pasteur, and when the wound is on the face. The directions for giving this vaccine are contained on printed material which accompanies each set of ampules. Rabies vaccine is administered at the discretion of the medical officer. It should not be given until definite clinical evidence of rabies is observed in the animal or a diagnosis has been established by histologic technique except in the case of face wounds when it should be begun immediately, or in case the suspected animal is not available for examination.

[AG 300.5 (28 Oct 44).]

BY ORDER OF THE SECRETARY OF WAR:

G. C. MARSHALL,
Chief of Staff.

OFFICIAL:

J. A. ULIO,
Major General,
The Adjutant General.

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IBn 11 (2): T/O 11-15
IBn 11 (1): T/O 11-25
IBn 17 (3): T/O 17-115
IBn 17 (2): T/O 17-15
IBn 17 (1): T/O 17-55; 17-125
IBn 18 (2): T/O 18-35
IBn 18 (1): T/O 18-25
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IC 8 (2): T/O 8-22; 8-26
IC 9 (2): T/O 9-76
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For explanation of symbols, see FM 21-6.

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