The Preparation of Vegetable Soup. Sixty grams each of green or canned French peas, white dry beans, potato, rice, and noodles, and 15 grams of carrot are boiled in water at least four hours. Sufficient water should be added to make one liter—which is sufficient for four feedings. The whole yields 760 calories, of which 6.3 per cent. is protein, fat less than 0.2 per cent., and 43.9 per cent. is carbohydrate. When ready to use, stir up sediment and allow the patient to eat all (including noodles), with the exception of the pea and the bean skins. Onion may be added for flavor if desired.

General Directions for Feeding. The patient should be fed with a spoon by the nurse.

The food should remain in the mouth as long as convenient. Allow water between feedings, not at feedings.

Allowances or corrections are to be made for increase of nitrogen need during the first ten days and during convalescence. At the height of fever, if the patient cannot eat the full quantity, substitute isodynamic quantities of milk sugar. A relative decrease of weight should be reflected in the caloric value of the food on the basis of 4 kilograms of loss per week of disease.

THE THERAPEUTIC USE OF BACTERIAL VACCINES.

WITH THE REPORT OF CASES.

By B. RAYMOND HOOBLER, A.M., M.D.,

ASSISTANT IN CLINICAL PATHOLOGY IN THE CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK.

THIS study does not comprehend a discussion of the various theories of immunity, but is a description of the technique employed in making vaccines, with clinical observations on eight cases in which vaccines were employed.

TECHNIQUE. The technique followed was as simple as routine bacteriological work permitted. The preliminary step was the securing of cultures, either from the blood or pus, and determining the organism that produced the infection. In cases in which a general infection seemed to exist, blood cultures were first tried. If these were negative, then the organism was secured from the seat of local infection.

In cases of localized infection cultures from the pus as well as blood cultures were taken, in order that no unnecessary time might be lost. If blood cultures are positive, it is preferable to make the vaccine from that source, as one is then certain of the infecting organism; whereas cultures from pus are often mixed growths, and much valuable time is lost in plating for pure cultures. Besides

one is not sure which of the germs in the mixed culture is the organism doing the damage.

After the germ had been properly identified and a pure culture grown for eighteen to twenty-four hours on some solid media, such as plain or glyceric agar, the germs were scraped off and mixed with sterile normal salt solution, making an even emulsion. This emulsion was then standardized; that is, the number of germs per cubic centimeter of vaccine was determined by Wright's method. The emulsion was then placed in a bot box, kept at a uniform temperature of 65° C., and allowed to remain there for thirty minutes. After adding a capillary drop of lysol to each 10 c.c. of the emulsion and placing a sterile rubber cap over the neck of the bottle, the vaccine was placed in a refrigerator, and so kept except when using.

This technique is not difficult to master, and need not necessarily be confined to expert laboratory workers. The most difficult part of the process is the determination and isolation of the infecting germ. Care must be taken that spore-bearing germs are not present, as the temperature to which the vaccine is submitted will not kill spores. One may be assured that the vaccine is sterile by planting it on agar and incubating for twenty-four hours. If there is no growth, one is fairly sure that no spore forms or living organisms are present of the aerobic variety; anaerobes, such as tetanus and gas-producing bacilli should be searched for in smears; the clinical symptoms of the patient will suggest the necessity of anaerobic cultures.

The cases to be discussed are divided into two groups:

GROUP I. Those in which the organisms were demonstrated in the blood. Under this three forms of infection are presented: (a) Puerperal septicemia; organism, *Streptococcus*. (b) Septicemia following otitis media; organism, *Streptococcus*. (c) Septicemia accompanying ulcerative endocarditis; organism, *Staphylococcus pyogenes aureus*.

GROUP II. Those in which the organisms were not found in the blood. Under this five different infections are represented, general and local processes: (a) Appendicitis, complicated by pyemia and liver abscess; organism, *Bacillus mucosus capsulatus*. (b) Appendicitis, complicated by pyemia; organism, *Streptococcus*. (c) Puerperal fever, streptococcal endometritis. (d) Pelvic cellulitis, abscess in the cul-de-sac; organism, *Bacillus coli communis*. (e) Infection of the foot followed by cellulitis of the leg, complicated by erysipelas; organism, *Streptococcus*.

No attempt was made in these cases to limit the patient to vaccine treatment only. In every case the usual routine surgical or medical treatment was carried on, irrespective of the vaccine inoculations. It cannot, therefore, be said that the vaccine treatment was partly or entirely responsible for the cure. It was not the purpose of this paper to prove that vaccines only effected the cure, but rather to present the cases in such a manner as to encourage the use of vaccines

as an adjunct to medical and surgical procedures in certain types of infections which up until now have stubbornly resisted all curative measures.

GROUP I, Case I.—*Puerperal septicemia of forty days' duration; streptococci isolated from the blood; vaccine inoculations given; the temperature came to normal in two days; no further chills.*

Six weeks before admission the patient had been delivered at term of a healthy child. Fever set in immediately and ran a septic course. The patient had daily chills lasting from a half to one hour. During this six weeks the usual routine treatment was followed. She gradually lost her strength; but bedsores developed, the hemoglobin fell to 25 per cent. and the red cells to 1,000,000, and food could not be retained. There was considerable abdominal distention. In this seemingly hopeless condition vaccines were tried.

FIG. 1.—Temperature chart of Case I. Puerperal septicemia; streptococci isolated from the blood; autogenous vaccine used.

Streptococci having been isolated in pure culture from the blood, a vaccine was made, and 50,000,000 bacteria were inoculated on the fortieth day of septic fever. In two days the temperature had fallen to normal (Fig. 1), the chills stopped, and there was an immediate change for the better. The inoculations were repeated every third day, increasing 25,000,000 each dose, until six doses had been given. While the temperature had been lowered and the chills stopped, the patient's vitality was so depressed (the hemoglobin having fallen to 18 per cent.) that she would not respond to supportive measures, and died from inanition. In the light of more recent experience it would seem to me that the doses given were too large and may have contributed to the depression present.

GROUP I, Case II.—*Bacteremia following mastoid disease; streptococci isolated from the blood; treatment by autogenous vaccine and operation; recovery.*

A boy, aged seven years, came into St. Mary's Hospital with the following history: Two weeks previously he began to complain of

general malaise and headache, which lasted a full week. There was no chill; no nosebleed; but there was loss of weight, increasing weakness, and some night sweats. He was feverish at night. There was some earache in the right ear, but no discharge. (Later, the mother said the boy had been complaining of more or less earache for six weeks.) Physical examination showed a poorly nourished, fairly well-developed young boy. The left ear appeared normal. The right ear was reddened, and the drum seemed covered with a small amount of exudate; but was not bulging. The external auditory canal seemed smaller than the left. The chest, lungs, heart, abdomen, and extremities were negative. On admission the temperature was 103.6° ; pulse, 105; the respirations, 40. For the next ten days the temperature was of a septic type (Fig. 2), reaching as high as 105.4° on several afternoons and going to normal or subnormal in the forenoon. The pulse was rarely below 110, and several times as high as 128. On the second day after admission the right ear

FIG. 2.—Temperature chart of Case II, showing the relation of the temperature to vaccine inoculations and operation. A case of mastoiditis; streptococci isolated from the blood.

drum was punctured and bloody serum escaped. Discharge during the next eight days was very scanty. On the fifth day the patient complained of pain in the left elbow and both knee-joints, which were slightly tender and swollen. On the sixth day after admission blood cultures were positive for streptococci. On same day tenderness was made out over the spleen and an endocardial murmur was heard, and two days later swelling was noticed in the subparotid region. The posterior lymph chain showed enlarged, discrete nodes, somewhat tender, but no fluctuation. The swelling in the parotid region rapidly increased, and operation for mastoiditis and sinus thrombosis was performed on the tenth day after admission. The mastoid was found but very little, if at all, involved, and on opening the sinus, a small amount of chocolate-colored material was removed. Cultures were taken, both from the mastoid cells and from the sinus, but were negative. Several glands from the posterior chain were removed.

and found to be acutely inflamed. Two days after operation blood culture was negative.

On the seventh day after admission autogenous vaccine was administered, the initial dose being 17,500,000. Forty-eight hours later a second inoculation of 50,000,000 was given. At this point the operations above referred to were performed. On the three days following operation small daily doses of 5,000,000 streptococci were inoculated. On the fourth day after operation the temperature came to normal and remained practically so, and the patient made a perfect recovery. The fact that the organisms were absent from the blood two days after operation suggests that the infection of the blood stream was transient, as occurs early in pneumonia and typhoid fever, and that the case was a bacteremia rather than a septicemia, and this is further suggested by the immediate recovery after operation.

FIG. 3.—Temperature chart of Case III. Ulcerative endocarditis.

GROUP I, Case III.—*Ulcerative endocarditis, pericarditis, and pleurisy with effusion; staphylococci isolated from the blood; vaccine inoculations resulted in these processes clearing up; for one month marked improvement took place, when the patient contracted lobar pneumonia and died.*

Two weeks before admission a boy, aged sixteen years, commenced to have severe pains in the lumbar regions. He lost his appetite and became constipated, and finally had to give up work. He felt considerable palpitation, and was short of breath on exertion. His feet had been swollen for some time. Physical examination was negative, except the heart, which showed the apex beat in the sixth space, three and three-fourth inches from the midline, heaving and forceful; a systolic and a diastolic murmur over the aortic area; a presystolic thrill at the apex; the first sound at the apex, booming preceded by a short rumble; the systolic murmur at base transmitted downward and heard at the apex, but not transmitted to axilla, and a pericardial, to-and-fro friction. Five days after admis-

sion a blood culture was taken, and *Staphylococcus pyogenes aureus* was isolated, and a vaccine was made.

The leukocytes, on admission, were 18,000; the polymorphonuclears, 91 per cent.; large mononuclears, 4.5 per cent.; lymphocytes, 3 per cent.; eosinophiles, 0.8 per cent.; basophiles, 0.7 per cent. Fifteen days later the leukocytes were 50,000; the polymorphonuclears, 80 per cent.; large mononuclears, 14 per cent.; lymphocytes, 6 per cent. On the tenth day after admission the chest was aspirated and fluid obtained. Two days later signs of fluid in the pericardium were made out. The pericardium was aspirated, and over an ounce of clear fluid was obtained. During this period the heart action was very labored, and the pulse reached 132 per minute and was very feeble.

The first inoculation of vaccine was given on the seventh day after admission, and inoculations were given twice a week thereafter, until six had been given. The dosage was as follows:

First inoculation	208,000,000
Second inoculation	312,000,000
Third inoculation	416,000,000
Fourth inoculation	520,000,000
Fifth inoculation	624,000,000
Sixth inoculation	725,000,000

During the first two weeks of vaccine treatment the patient grew gradually worse. During the third week, however, his condition improved and his temperature gradually became normal (Fig. 3). His pulse, which had ranged between 110 and 130, became about 80, and the respirations, which had varied between 35 and 40, decreased to normal. During the third week of treatment his whole appearance changed and his strength steadily increased. After nearly four weeks of normal temperature, during which time marked improvement had taken place in his general condition, he contracted pneumonia and died.

GROUP II, Case IV.—*Pyemia following appendicitis; liver abscess; blood cultures negative; Bacillus mucosus capsulatus isolated from the pus on the fortieth day after operation; the use of vaccines made from this organism was followed by gradual fall of the temperature to normal and perfect recovery.*

J. E., aged forty-six years, came to operation for appendicitis after the usual symptoms. The appendix was found to be gangrenous. Behind the cecum was a small abscess. The appendix was removed, the abscess evacuated, and drainage inserted. The temperature did not rise above 101° on the three days following the operation, but chills, which had preceded the operation, continued and became more prolonged. The two weeks following operation showed a temperature septic in type and the patient's condition grew gradually worse. The wound was kept open and drainage seemed ample during this period. No enlarged liver could be made

out, though the patient became slightly jaundiced during the second week after operation, and occasionally complained of pain in the liver region. No further surgical measures seemed of use, and resort was had to intravenous injections of collargolum, and inunctions of Credé's ointment were given. These measures did not seem to affect favorably the course of the disease. Stock vaccines and antistreptococcal serum were used, with absolutely no results. The patient was in extremis. Blood cultures were entirely negative. A marked grade of secondary anemia was present, the red blood cells being 2,712,000. At this point an autogenous vaccine was made from cultures of *Bacillus mucosus capsulatus*, which was isolated from the pus of the appendix wound.

FIG. 4.—Temperature chart of Case IV, showing the temperature curve before and after inoculation. A case of pyemia with liver abscess following an appendix operation.

The first inoculation of the autogenous vaccine was made on the forty-fifth day after operation; thereafter two inoculations each week were made, with doses as follows:

First inoculation	40,000,000
Second inoculation	50,000,000
Third inoculation	50,000,000
Fourth inoculation	50,000,000
Fifth inoculation	55,000,000
Sixth inoculation	55,000,000
Seventh inoculation	70,000,000
Eighth inoculation	70,000,000
Ninth inoculation	110,000,000
Tenth inoculation	110,000,000
Eleventh inoculation	110,000,000

Inoculations were then given weekly for a month at the same dosage, viz., 110,000,000.

After the first inoculation there was a slight fall in temperature (Fig. 4). After the second there was a decided fall. Chills, which had occurred regularly every day for forty-five days, ceased. The patient's general condition improved. The temperature remained between 99° and 102° for a month after inoculations began, during

which time signs of a liver abscess became evident. The abscess was opened and drained. *Bacillus mucosus capsulatus* was found in the pus from this abscess also. The temperature came gradually to normal after the abscess was opened, and the patient made a perfect recovery. Nearly one year later he reports himself in perfect health.

GROUP II, Case V.—*Postappendicular pyemia; abscess in the shoulder-joint; vaccine made from the pus; improvement after the second inoculation; perfect recovery.*

M. M., a woman, aged thirty years, was taken ill, eight days before admission, with the symptoms of appendicitis. At an operation performed immediately the appendix, perforated and gangrenous, was found enclosed in an abscess cavity, well walled off. Drainage was inserted and wound left open. The temperature for the first day after operation did not rise above

FIG. 5.—Temperature chart of Case V; postappendicular pyemia. The temperature curve before and after inoculations.

99.5°, but on the days following rose each afternoon and became septic in type. Five days after operation the wound was explored, but no pus pockets were made out; the abdomen was not rigid, and there were no signs of general peritonitis. On the ninth day after operation the left shoulder-joint was very painful, considerably swollen, and markedly tender. This continued until the seventeenth day after operation, when joint was aspirated and a seropurulent fluid obtained. Cultures from this fluid yielded a pure growth of streptococci. Several blood cultures were taken, none of which were positive. On the twentieth day after operation the right sterno-clavicular joint became swollen, tender, and slightly reddened, and the overlying tissue reddened. The leukocyte count on admission was 33,000; 89 per cent. polymorphonuclears; five days after admission, 33,300; 93 per cent. polynuclears.

On the twenty-second day after operation the first inoculation of autogenous streptococcic vaccine was given, the dose being 2,500,000. This was repeated daily until twelve inoculations had been given.

The temperature gradually came to normal (Fig. 5); her general condition improved from the first inoculation; the joint symptoms gradually disappeared, and the patient made a complete recovery. After the vaccine treatment was begun, all surgical and other medical measures were omitted. At the time inoculations were begun the patient was in a very critical condition.

GROUP II, Case VI.—*Puerperal fever, developing on the sixth day of the puerperium; blood culture negative; intra-uterine culture showed streptococci; stock streptococcic vaccine from a streptococcic septicemia was given, and the temperature came to normal, but rose on the second day; autogenous vaccine was then given, and the pulse, temperature, and respirations came to normal.*

A woman, aged thirty years, was delivered of a child at full term. For five days after delivery the temperature was normal; the uterus was contracted and the patient seemed to be doing well. On the sixth day the temperature suddenly rose to 105° in the morning

FIG. 6.—Temperature chart of Case VI; puerperal fever.

and dropped to normal in the afternoon. The next day it rose in the morning to 105.4° and fell in the afternoon (Fig. 6). The patient exhibited the usual symptoms of septic infection—rather drawn facies, rapid respiration, rapid pulse, extreme restlessness. On the sixth day of this septic infection blood cultures were taken, and no growth resulted. Cultures were taken at the same time from the uterine cavity. The cervix was patulous and considerable discharge was present. The intra-uterine cultures yielded a pure streptococcic growth, and a vaccine was made from this.

At the time the culture was taken, 50,000,000 stock streptococci were inoculated. (This strain of streptococcus was obtained from a blood culture taken from a previous case of puerperal septicemia.) The temperature came to normal the next day. Later it rose again, and on the third day the autogenous vaccine was inoculated, the dose being 100,000,000. The temperature again came to normal, being the twelfth day of the puerperium, and was followed by the

pulse and respiration. The patient had no further fever during the puerperium, and made a complete recovery.

GROUP II, Case VII.—*Pelvic abscess; Bacillus coli communis was isolated from the pus; after many autogenous inoculations the temperature came to normal.*

Two weeks before admission, after working hard, the patient began to flow, many clots coming away. This gradually increased and she became very weak. She had high fever at times, chills and sweats for three days preceding admission, and severe pain in the pelvis. Physical examination showed the abdomen to be slightly tender and rigid. The pelvis was tender on both sides, and over the

FIG. 7.—Temperature chart of Case VII, pelvic abscess. *Bacillus coli* infection.

uterus very rigid. The cervix was patulous. A large mass was made out filling the entire cul-de-sac, and very tender on palpation. An operation was made in the cul-de-sac and a large amount of pus evacuated. The fever continued, although drainage seemed ample.

The first inoculation was given on the twenty-second day of the disease. Thereafter inoculations were given twice a week, with dosage as follows:

First inoculation	25,000,000
Second inoculation	50,000,000
Third inoculation	50,000,000
Fourth inoculation	50,000,000
Fifth inoculation	75,000,000
Sixth inoculation	75,000,000
Seventh inoculation	100,000,000
Eighth, ninth, tenth, eleventh inoculations	100,000,000
Twelfth inoculation	150,000,000
Thirteenth inoculation	200,000,000

The temperature came gradually to normal and no further abscesses were formed in the pelvis (Fig. 7).

TYPE II, Case VIII.—*Infected foot, followed by cellulitis of the leg and later erysipelas; streptococci were found in the pus from the foot; a stock vaccine was used, and after two inoculations the temperature came to normal.*

A young colored woman, a nurse, acquired an infection of the foot. The wound was opened and drained. Cultures from the pus showed streptococci. The temperature before the operation was 104.8°. The usual wet dressings were applied, but the temperature continued high. Two days after operation the patient complained of the leg being painful and stiff. The next day the edges of the wound appeared discolored, and within a few hours signs of erysipelas appeared, and extended up the leg. These were painted with carbolic acid, followed by alcohol. The leg was greatly swollen and tender, and signs of phlebitis were present. The temperature was continuously high, between 103° and 105°. On the day erysipelas was noted a stock vaccine of streptococci was used, 50,000,000 being the initial dose. This was followed by no apparent result. The temperature and pulse remained persistently high for the next three days, when the second inoculation of 100,000,000 stock

FIG. 8.—Temperature chart of Case VIII; infected foot; erysipelas. Stock vaccine used.

streptococci was given. This was followed by an immediate fall in temperature, the first in ten days, falling to 100.5°. The next day it did not go above 101.4°, and on the following day it came to normal and remained so (Fig. 8). The pulse likewise fell to normal coincident with the temperature, and the patient went on to complete recovery. It should be noted that surgical measures went hand in hand with vaccine treatment, particularly the treatment of the erysipelas with carbolic acid and alcohol painting, and also that the fall in temperature took place about the usual time in the course of erysipelas.

GENERAL SUMMARY. 1. Closely following Wright's method,¹ vaccines were made in eight cases from germs isolated from the blood, when this was possible; otherwise from pus taken from the point of local infection. Two types of vaccines were used—autogenous, and stock vaccine, made from germs secured from sources other than the patient. Of the cases reported, six received autogenous

¹ Transactions of Harvey Society of New York, 1907.

vaccine only; one received, first, stock, then autogenous vaccine; and one received stock vaccine only.

2. The cases reported comprise two of septicemia, one of malignant endocarditis, two of pyemia following appendicular operations, one of puerperal fever, and two of local infection.

3. Classified as to infecting organisms, there were five cases of streptococcic infection, one case of *Bacillus coli communis* infection, one case of *Bacillus mucosus capsulatus* infection, and one case of *Staphylococcus pyogenes aureus* infection.

4. In cases reported, improvement showed itself by a fall in temperature, reduction of pulse rate, and improvement in the general condition. The time taken to bring about these results varied from twenty-four hours to two weeks.

5. The number of inoculations given before the temperature came to normal permanently varied with the individual case, from three to seventy-five days, and from two to fifteen inoculations.

6. The number of organisms inoculated as a "dose" varied with the organism given. The following table shows the initial and maximum doses employed:

	Initial.	Maximum.
Streptococcus (3 cases)	50,000,000	100,000,000
Streptococcus (1 case)	50,000,000	200,000,000
Streptococcus (1 case)	2,500,000 (daily)	
<i>Bacillus coli communis</i>	25,000,000	200,000,000
<i>Bacilli mucosus capsulatus</i> . . .	40,000,000	110,000,000
<i>Staphylococcus pyogenes aureus</i> .	200,000,000	725,000,000

In streptococcic infections two methods of dosage were employed, large doses (50,000,000 to 100,000,000) twice a week; or small doses (2,500,000 streptococci) given daily. The latter method gave excellent results in two cases. As a rule, the doses are increased gradually, that is; by one-tenth of the initial dose.

CONCLUSIONS. 1. Bacterial vaccines, if properly used, can do the patient no harm.

2. Autogenous vaccines should be used when possible. Stock vaccines are uncertain, but they may be used when there is delay in securing autogenous vaccines.

3. The technique of preparing vaccines is simple and should be made a part of the routine laboratory work in every well-equipped hospital.

4. Chronic infections yield more readily to the use of vaccines than acute fulminating infections; and local processes are more easily controlled than general infection.

5. If a vaccine is to be of service, it will usually show results within one week or ten days.

Acknowledgment is made of valuable suggestions from articles by W. Gilman Thompson, M.D.,² and Drs. Barr, Bell, and Douglas,³

² AMER. JOUR. MED. SCI., August, 1900.

³ Lancet, 1907, i. 499.

on the vaccine treatment of septic endocarditis, and Drs. Sutcliffe and Bayly⁴ on streptococcic septicemia. I wish to acknowledge also the many useful suggestions of Dr. Thomas W. Hastings.

THE PRESENT STATUS OF TUBERCULIN THERAPY.

BY WILLIAM C. VOORSANGER, M.D.,

VISITING PHYSICIAN TO THE MOUNT ZION HOSPITAL, SAN FRANCISCO; CLINICIAN TO
SAN FRANCISCO TUBERCULOSIS CLINIC.

WHEN Koch, in 1890, introduced tuberculin as the long-sought cure for a dreaded disease, he was hailed as a deliverer. But Koch either did not understand his own remedy, or the scientific world misinterpreted his teachings. It is needless to dwell upon the disastrous results following the use of the original "Tuberculin," founded upon the principles of active immunity. It was not understood—large doses were given—and results were in many cases negative—in others fatal. But a few great and far-seeing minds realized that Koch had introduced a remedy which was destined to live. The majority of physicians dropped the new remedy with as much avidity as they had taken it up. Thanks, however, to a few German physicians, led by Koch, and to Trudeau, in this country, work upon tuberculin continued, developed, and improved until a new tuberculin is given us, and a new and better method of administration, with better results and no fatalities. Again the scientific world is inflamed and the pendulum is swinging the other way. Apathy has given way to enthusiasm, and it is well to pause a bit, lest this very enthusiasm lead us to discredit a method which, when used rationally and understandingly, is unquestionably a most valuable aid in the treatment of tuberculosis.

Before a physician is qualified to use tuberculin he should be able to answer satisfactorily four questions: (1) What is tuberculin? (2) What is the theory of its action? (3) What are the various kinds of tuberculin? (4) What is the dosage?

Let me briefly consider the first two questions together, from the theoretical point of view. Arloing and Courmont were the first to discover agglutinins for the tubercle bacillus. Their experiments showing that tubercle bacilli have agglutinating action and that antibodies were present in the blood of a tuberculous patient, were fought by the German observers, denied by Koch and his pupils, in particular Rahhinowitz. Jürgens⁵ is of the view that the agglutinins are only an evidence of the presence of soluble tubercle bacillus substances in the circulation. A few years after Arloing

⁴ Lancet, 1907, ii, 367.

⁵ M. Wolff and H. Mühsam, Deut. med. Woch., 1908, No. 35.