mucus and has three or four frothy loose movements daily; occasionally has colic. Had appendicitis about five years ago, but recovered without operation. Proctoscopic examination revealed some small ulcerations of rectum with atrophic catarrh, with quantities of stringy mucus. Angulation of sigmoid marked. Except for some tenderness over appendix, abdominal examination was negative.

The patient was put on the test diet before scheduled, and on the third day examination of the results produced the appended report. The specimen has a pasty consistency, a pale yellow and decidedly deficient color, very little odor and shows no gross admixture. Microscopic examination shows no muscle fiber, and an unusual amount of potato remains, containing unchanged starch, and a decided excess of fat, chiefly a soap, but also some free fat and fatty acid crystals. The reaction is slightly alkaline. The sublimate test is negative, but the reaction is slight on account of deficient pigment. The fermentation test for carbohydrate fermentation was positive, albumen putrefaction is negative. Bacterial flora is excessive and chiefly Gram positive.

The patient was put on Takadiastase and ox-gall and was told to continue with his diet. On the third subsequent day another specimen of feces was examined. In the meantime the patient felt a decided improvement, was free from gas, and had only one movement daily.

I could instance many more cases wherein employment of the test diet has been of great help in diagnosis, and toward that purpose have with me complete reports and records which I should be glad to submit to any members of the society. The cases quoted above are typical; full details would demand more time than you can spare me.

It remains to say a few words relative to determination of the clinical significance of faulty sulphate and nitrogen partitions. This subject is still a matter of discussion, but the best authorities and my own experience would seem to warrant the following conclusions:

Relative increase in ethereal sulphates may be due to one of several causes, chief among which may be cited stasis in the bowel, ingestion of decomposing nitrogenous food, improper digestion of food in the stomach and upper intestine, by diminution or absence of hydrochloric acid and bile, the result of excessive or faulty bacterial fermentation in the lower portion of the small intestine and the upper portion of the large intestine. This process may exist without an actual toxemia, and an actual toxemia may exist without this particular putrefactive process, but they are usually associated.

A relative ethereal sulphate excess is commonly associated with an excess of indoxyl sulphate, though not invariably so. Without means of estimating the presence or amount of the actual products of toxemia, the relative excess of ethereal sulphates is used as a guide, although subject to errors as are other guides.

Fault in the nitrogen partition would seem to justify the inference that the hepatic function is disturbed. The decrease in the relative amount of urea nitrogen probably indicates the degree of the fault. With this decrease there is a relative

increase in the amount of one or more of the other forms of nitrogen in the urine. In the severe toxemias of pregnancy, pneumonia, etc., this is chiefly in the so-called ammonia nitrogen and creatinin nitrogen; in digestive disturbances the increase is mainly in the so-called extractive nitrogen, and in lithemic cases and in those of cyclic vomiting, headache or albuminuria, in the purin nitrogen as well, particularly during the acute attack.

In cases of enteritis or colitis, owing to the destruction of cells, the purin nitrogen is often increased.

Faulty nitrogen partition may exist without a toxemia, but a hepatotoxemia without a faulty nitrogen partition is practically unknown. Acidosis frequently accompanies a faulty nitrogen partition, but would seem an evidence of toxemia rather than of the fault in hepatic function, though this is disputed by some.

The fact that the disturbed metabolism is the result rather than the cause of the toxemia, and that it may occur without toxemia, even in mere starvation, makes the subject complex, but we hope yet to learn the complete solution.

In my experiments and practice in this field I have been greatly aided by the painstaking and careful examinations and analysis, the long experience and acute insight of Dr. Frederic Sondern, of New York City, whose reports I quote.

It is my belief that in the recognition of such scientific and chemical research with application of personal knowledge, experience and deductions, we may arrive at diagnoses heretofore deemed impossible.

I realize that this paper is superficial. It is my earnest wish that the subject may be thought worthy of study and that before our next meeting many of you will have found opportunity to give it extended investigation, and have valuable results to report.

ANTITYPHOID INOCULATION CONDUCTED AT THE MASSACHUSETTS GENERAL HOSPITAL.*

BY LESLEY H. SPOONER, M.D., BOSTON.

STIMULATED by the results of the Royal Army Medical Corps, which has produced so successfully in British soldiers artificial immunity against typhoid fever, I have carried on at the Massachusetts General Hospital during the past year several series of voluntary typhoid inoculations. In the preparation of my inoculation material or vaccines I have profited by the researches and the results of the British Commission,¹ whose work upon the subject is the most complete at the present time.

The typhoid bacilli grown for twenty-four hours on agar slants are washed into a sterile tube, thoroughly shaken and counted by the Zeiss blood platelet counter. They are then exposed in the water bath to the temperature of 53° C. for

* This work was suggested by Dr. Mark W. Richardson, secretary of the State Board of Health. The financial support was provided by Dr. Richardson, Mr. Frederick W. Lord, of New York, and Mrs. Robert S. Bradley, of Boston.

¹ Leishman and Harrison: Jour. Roy. Army Med. Corps, 1907, viii, pp. 462 and 472; also x, p. 583; also xi, p. 327.

one hour, diluted with the necessary amount of salt solution in a small bottle, and sealed with a rubber nipple. Lysol 0.25% is then added to prevent contamination. The vaccines of any strength may be prepared, but the most convenient is that in which 1 cc. contains 400,000,000 bacilli. They should be kept in the dark, away from dust, at room temperature. Vaccines more than one month old have not been used, although it is probable that they retain their strength much longer. The question of dosage is one over which there has been so much controversy that it seemed best to begin with small doses, repeated at short intervals. In this way it was hoped to avoid severe reaction and general intoxication which sometimes follow doses of 500 and 1,000 M., as used by the Royal Army Medical Corps. In order to determine the effect of small doses, I first inoculated 5 house officers of the Massachusetts Hospital with 50 M. typhoid bacilli, which inoculation was followed by another of 100 M. on the third, fourth or fifth day.

In determining the end results of typhoid inoculation, it is obviously impossible to rely upon the diminished occurrence of typhoid fever among the inoculated because under the ordinary conditions the morbidity is small. One turns naturally at once to a determination of the anti-tropic or immune substances in the blood, and in this work the agglutination test has been selected as the one most satisfactorily employed.

The technic is as follows: Bouillon cultures of the typhoid bacillus are grown at room temperature for twenty-four hours. Drops of this bouillon are placed on slides and mixed with serum, derived from centrifugalized blood, in the following proportions, viz., 1:5, 1:10, 1:25, 1:50, 1:100, 1:500, 1:1,000 and 1:5,000. These preparations are kept at room temperature and are observed under the high-power dry lens after one hour. In the positive cases it is rare to find every bacillus clumped, but it is equally unusual to see many free bacilli in the low dilutions. In all cases the end point is taken to be that in which there are many free bacilli and in which there is some motility, no matter how sluggish. This dilution, which is sharply contrasted with its neighbor, is considered negative and the next stronger taken as positive.

Inoculations were performed with glass "Tuberculin sub-cu." syringes, which were boiled between injections. The commonly selected site for inoculation was at the insertion of the deltoid on the left arm. Alcohol was used as a local antiseptic.

Preliminary agglutination tests were made on all the five house officers above mentioned and were found to be negative, even in the 1:5 dilution, in three, but positive at that ratio in the other two. This fact was explained by further questioning, which showed that one subject when seven years old had suffered from what had been called "slow fever" and the other had received a single typhoid inoculation at another hospital a year before.

All five received 50 M. of the stock vaccine,

which dose was followed on the third day in two cases, the fourth in one and the fifth in the other two by a second dose of 100 M. Widal reactions were tried on various days. They showed that the agglutinating power did not begin to ascend until from the sixth to the ninth day, when a sudden rise took place. This level or even a higher one was maintained for from one to two weeks. Then occurred a slight fall, but the cases continued to show a marked elevation above the normal, which lasted three months after inoculation.

The detailed results are as follows:

	Widal prior to inoculation.	One week after inoculation.	Two weeks.	Three weeks.	One month.	Three months.
W. W. D. (Case 1)	1:5	1:50	1:50	1:50	1:50	1:50
J. G. (Case 2)	1:5	1:100	1:50	1:50	1:50	1:50
R. L. T. (Case 3)	0	1:100	1:100	1:100		1:25
C. H. L. (Case 4)	0	1:100	1:1000	1:500		1:100
C. A. H. (Case 5)	0	1:50	1:100	1:100	1:100	1:50

Cases 1 and 2 were those cited as having been somewhat protected previously, the one by a mild attack of the disease twenty years before, and the other by one vaccine inoculation. Their reaction is of importance and interest in view of the present theory of active immunity. Although it is not evident in the table, both men showed a quicker and sharper response to the inoculation, and in both cases the secondary descent of the Widal curve came earlier. The first observation is thoroughly in accord with the assumption that in the immunized the antibodies are present in the tissues and are merely awaiting a stimulus to bring them forth. It is not possible to explain why the agglutinins, once established, should diminish sooner than in the other cases.

The effect of larger doses remained still to be proved. This point I settled myself by receiving in three successive weeks doses of 100, 200 and 300 M. without appreciable constitutional reaction.

The results were so encouraging that it was decided to place the matter before the authorities of the Massachusetts General Hospital and call for volunteers among the nurses and ward tenders, in an effort to stamp out typhoid fever as contracted within the hospital by these employees.

In the early part of July the nurses were given a talk by Dr. Richardson and myself upon the prevalence of the disease and its incidence in the hospital² and upon measures which might be taken to prevent it. As a result a large percentage of those present volunteered to receive inoculation.

A brief history was taken in every instance to ascertain recent and remote exposure to the

² Spooner: Typhoid Fever: Incidence of the Disease as Contracted within the Massachusetts General Hospital from 1899 to 1908. *Am. Jour. Pub. Hyg.*, vol. xix, no. 4, August, 1909.

disease and whether the nurse had ever suffered from typhoid. All who had even a suspicious record of fever were rejected. The temperature on the day of inoculation was also taken to make certain the perfect health of the individual.

At this time 53 nurses received an initial dose of 50 M., followed at intervals of five days by 100 and 200 M. In all cases local soreness and induration appeared in a few hours. Pain on moving the arm was noted by some, and in three cases, to be mentioned later, small glands were palpable in the axilla. Constitutional symptoms were uncommon, and when present were rarely marked. They were severe enough to make only two nurses decline further inoculation.

The initial Widal reactions were positive in dilutions of 1:5 in 7 cases and absolutely negative in 46. After two weeks the agglutination tests were repeated with the following results:

Dilution of Widal.	Number of Cases.	Percentage of Cases.*
1:5	0	0
1:10	4	8
1:25	6	12
1:50	25	49
1:100	15	29
1:500	1	2

A short talk was then given the ward tenders by the writer, and 9 volunteered for inoculation. For several reasons the treatment was completed in only 6. The agglutination test was absolutely negative in all cases prior to inoculation and two weeks later showed the following results:

1:100	1 case
1:50	4 cases
1:25	1 case
1:10	2 cases†
1:5	1 case‡

The percentages are nearly identical with those stated above, but as a series they are of little value except to emphasize the necessity of repeated inoculation. If one can estimate the comparative importance of the separate inoculations, the second seems to be the most valuable. The first alone is apparently worthless. Although two are far more powerful than one, the third inoculation seems to aid greatly to the immunizing strength.

These and the following cases received doses of 100, 200 and 300 M. at intervals of five days. Two of the ward tenders complained of constitutional reaction, i. e., diarrhea and feverishness, the etiology of which, during the summer, is hard to determine. As a whole, the reaction was no more severe than with the smaller doses.

A sudden influx of typhoid cases at the Chelsea Naval Hospital induced the officers in charge of that institution to have inoculation performed upon the nurses. Accordingly 4 officers and 10 men were vaccinated. None were accepted who had had typhoid or who were running a temperature. Three of the number showed a positive

agglutination in a dilution of 1:5. Eleven were absolutely negative. The results after three weeks were:

1:100	4 cases
1:50	7 cases
1:25	3 cases

In the early part of September, 23 more Massachusetts Hospital nurses, chiefly in the entering class, were inoculated with the larger dose, i. e., 100, 200 and 300 M. The reaction was no greater locally than before, but two had headache and nausea during the night following inoculation, which disappeared the next day. Two nurses showed a positive Widal reaction of 1:5, and 21 were completely negative. At the expiration of two weeks the results were as follows:

1:100	4 cases
1:50	14 cases
1:25	4 cases
1:10	1 case

The results of similar inoculations upon 4 more house officers complete the work. From absolutely negative Widal's they showed, two weeks after inoculation, positive reactions in dilutions of 1:100 in one case and 1:50 in the others. The former, that of the writer, has persisted in that strength for two months.

As a matter of comparison 4 convalescent typhoid patients, two weeks after normal temperature had been reached, were studied. Their agglutination reactions performed in the same way were positive in dilutions of 1:500 in one case, 1:100 in another and 1:50 in the other two.

Before making a plea for regular hospital inoculation it was decided to question the nurses as to the exact extent of inconvenience from this method of immunization. Fifty nurses were consulted and reported their feelings in detail. In 46 the local reaction was only "slight." In these there was very slight difficulty in moving the arm. The local reaction was more severe in the remaining 4, being characterized by all as "considerable." Motion of the arm was more painful and in some almost difficult. All these symptoms lasted less than twenty-four hours. In three cases tender axillary glands were palpable on the day of inoculation, which disappeared by the following morning. Twenty-nine nurses suffered from no general reaction. In 18 it was trifling, consisting of slight headache and mild malaise, which was felt the afternoon and night following inoculation, disappearing on the next day. Three nurses experienced severe headache and nausea during the reaction period. One of the latter, the only case in the training school, was absent from duty for a half day.

Finally, all the nurses affirmed without exception that they would have undergone the inoculation, even if they had known the severity of the reaction and the general inconvenience, provided that it carried with it the hope of immunity, as suggested in the present instance. This is a matter of utmost importance, since by means of such statistics the medical profession should be

* Two nurses received fewer than the regular number of inoculations and have been omitted from this table.

† Both received only two inoculations.

‡ One inoculation only.

urged to acquaint the public of the ease with which immunity can probably be acquired.

The severity of the reaction does not bear a direct relation, however, to the degree of immunity conveyed. The greater number of those showing the higher agglutinating power suffered only slight local and no constitutional reaction. On the other hand, several with smaller amounts of agglutinins complained of more violent general disturbance. The following table indicates this relation:

LOCAL REACTION.						
	1:10.	1:25.	1:50.	1:100.	1:500.	Total.
Slight	4	7	20	14	1	46
Considerable	1	..	3	..	..	4
						50
Palpable glands	..	..	2	1	..	3
GENERAL REACTION.						
Absent	1	6	11	10	1	29
Slight	3	1	9	5	..	18
Considerable	1	..	2	..	..	3
						50

To summarize,³ 103 people have been inoculated. Of these, 74 were Massachusetts Hospital nurses, 9 house officers and 6 ward tenders. Fourteen were vaccinated at the Naval Hospital. Of this number, 6, or 5.8%, reacted in dilutions of 1:10; 14, or 13.6%, 1:25; 56, or 54.4%, 1:50; 26, or 25.2%, 1:100; and 1, or 1%, 1:500. In other words, 94.2% of those inoculated showed agglutination tests in dilutions of 1:25 or more; and 80.6%, in 1:50 or more.

Since inoculations have been started there have been no cases of typhoid fever contracted at the Massachusetts Hospital among the nurses, house officers or ward tenders, or in those inoculated at the Chelsea Naval Hospital.

The results of this work are striking, inasmuch as high agglutinating power has been produced with small doses of vaccine and with slight constitutional reaction. Furthermore, although it may be doubted whether agglutinating power is necessarily synonymous with immunity, yet it is hard to believe that agglutinins can exist in the blood to such an extent without a considerable degree of immunity.

It is, therefore, impossible at the present time to say definitely how strong the immunity acquired through inoculation is, or how long it will last. There would seem to be no doubt, however, in the first place, that nurses, ward tenders, physicians and others who are brought into intimate relation with typhoid patients should submit to inoculation; secondly, that those who plan to make a journey into districts known to be subject to typhoid fever should be inoculated; and thirdly, inoculation is likely to become advisable and more or less general in districts where typhoid is epidemic. This would seem to be especially appropriate for other members of a family in which typhoid is present. Finally, a necessity for inoculation against typhoid will probably be

³ In this summary eight cases have been omitted because they have received fewer than the required number of inoculations.

always with us. About 4% of all typhoid patients become what are known as chronic carriers of the disease, that is to say, they may harbor in the urine or stools the typhoid bacillus for a long term of years. No matter, therefore, how careful we may be as to the supervision of our milk and water supplies, there will always be the danger of typhoid epidemics arising from infection of the milk or the water through the typhoid carrier. It is possible, of course, that methods may be devised for the cure of this persistence of the typhoid organism in certain individuals, but the outlook for the elimination of the typhoid carrier cannot be said at present to be hopeful.

NOTE. — I am indebted for hearty co-operation in this work to Dr. Frederic A. Washburn, of the Massachusetts General Hospital; to Miss Pauline L. Dolliver and Miss Georgianna J. Sanders, of the Massachusetts Hospital Training School for Nurses, and to the officer in charge of the United States Naval Hospital at Chelsea. I wish to take this means of thanking also those house officers, nurses and ward tenders of the Massachusetts Hospital and of the Naval Hospital for their aid in furthering an investigation which should be of some advantage to mankind.

THE REPRODUCTION OF PAIN AS A MEANS OF MAKING DIFFERENTIAL DIAGNOSES.*

BY HENRY T. HUTCHINS, M.D., BOSTON.

As pain is the most frequent symptom with which the physician and, more especially, the surgeon has to deal, it would seem that the study of this symptom could not be pursued in too great detail. Our lack of knowledge of the origin and meaning of pain is considerable when we think how often we meet with it as a symptom. This paper is, in part, a plea for the more careful study and investigation of pain as opportunities present themselves in the daily work of the physician. Our lack of knowledge of pain, as a symptom of a definite lesion, too often leaves us in doubt as to the proper course to pursue toward its relief. An accurate knowledge of the origin, character, duration and location of pain is essential to the making of a correct diagnosis in many cases.

It would be a great help if we could know the normal sensibilities of every organ and tissue in the body. Some work to this end has been done under local anesthesia. The normal sensibilities of the tissues encountered in making incisions into the abdomen under local anesthesia have been accurately described by many operators. The sensibilities of many of the abdominal organs have been studied in like manner, — the stomach, intestines, gall bladder, urinary bladder, ureters and pelvic organs.

Frequently, when palpating different parts of the body, especially the abdomen and pelvis, pain is caused in structures perhaps in no way diseased, e. g., pressure over the abdominal aorta, over deep nerve trunks, the ovary, etc. Most infrequently is an attempt made by questioning the patient, to find out whether the pain produced has ever been experienced spontaneously under apparently normal conditions. If, while making an examination which causes pain by pressure over a tender area, the insufficient question, "Does that hurt you?" could be replaced

* Read before the Boston Obstetrical Society, Oct. 20, 1909.