be regarded as chronic cholecystic adhesions (Figs. 6, 7, 8, 9). Most of these cases also show gastric hypermotility six hours after a barium-zoolak meal, turbidity, increased mucin, epithelial cells and bacteria in the duodenal juice. There is usually a history of constipation.

Postoperative Adhesions. Duodenal intubation and visualization offer a practical method of detecting postoperative adhesions after surgery upon the stomach and gall-bladder. In some cases adhesions do not evidently cause pronounced symptoms, while in others the symptoms are suggestive of interference with the patency of the common bile duct or with gastric evacuation (Figs. 12, 13, 14 and 15). In recurrent symptoms after gastro-enterostomy the duodenal-tube is allowed to pass through the anastomosis and outline the jejunum. In perijejunal adhesions the course of the tube in the jejunum is twisted (Figs. 13 and 14).

The conclusions drawn in this paper are based upon an experience of several years on a considerable number of patients, including about 400 established cases. It is not intended that this method should distract from the diagnostic value of the older and well-established methods, but when combined with them at least 90 per cent. of duodenal ulcers and no less than 75 per cent. of gall-bladder disease should be detected even in their incipency. I must emphasize, however, the importance of proper technique.

THE TREATMENT OF EMPYEMA WITH GENTIAN VIOLET.

BY RALPH H. MAJOR, M.D.

DETROIT, MICH.

(From the Henry Ford Hospital.)

OUR conceptions of the etiology, pathology and treatment of empyema have undergone a marked change as the result of observations made during the past two years. It may be a question whether our influenza experience has brought out striking advances in the therapy of that disease, but there can be no doubt that in the treatment of postinfluenzal empyema we have made tremendous strides. Whether these lessons learned in the treatment of postinfluenzal empyema are applicable to other forms of empyema the future must decide.

The treatment of empyema following influenza by the older orthodox surgical methods was followed by such an appalling mortality that many felt we were dealing with a disease quite different from the conventional postpneumonic empyema of the past. Also, postinfluenzal empyema is a complication of bronchopneumonia

and presents many differences when contrasted with an empyema following lobar pneumonia, from which we have gained most of our knowledge of empyema in the past. Moscheowitz,¹¹ however, pointed out that empyema in the past was not a benign condition, the figures at Mt. Sinai Hospital in New York from 1904 to 1914 showing a mortality of 28 per cent. He collected further statistics which show that the death-rate in empyema before the two great influenza epidemics varied from 18.9 per cent (Lilienthal) to 55 per cent (Lavrow). This high mortality was not generally appreciated, however, until empyema was seen *en masse* in the great army hospitals during the past two years as a complication of influenzal bronchopneumonia. The marked fall in the death-rate which followed the policy of delaying operation and of carrying out first a series of preliminary aspirations suggest the interesting query whether these newer methods of treatment would have lowered the empyema mortality in the past.

During the past winter a large number of persons suffering from influenza were treated at the Henry Ford Hospital, where many of these patients developed empyema. It is the purpose of this report to discuss the results obtained in treating these empyema cases, and particularly a group treated by repeated aspirations and intrapleural instillations of gentian violet.

Many differences of opinion prevail regarding the cases to be considered as empyema. Hartwell⁷ in his discussion of empyema uses the term to indicate "a purulent exudate within the general pleural space." "Local collections of pus," he states, "walled off by adhesions are intrapleural abscesses or interlobar abscesses," and as such he excludes them from his discussion. Moscheowitz (*l. c.*), on the other hand, states that "nearly every empyema is an encapsulated one." Aside from these differences in opinion based upon anatomical considerations there are differences in terminology dependent upon the character of the pleural effusion, many observers limiting the term empyema to cases yielding only frank macroscopic pus. Graham,⁴ however, in his summary of reports from the various Base Hospitals notes that the exudate most commonly found is a slightly turbid serofibrinous fluid. In our group of cases all patients showing a turbid pleural fluid containing microorganisms are classed as empyema, the fluid in question varying from a slightly turbid serofibrinous exudate to a thick, creamy pus.

Objection may be raised to the inclusion in our discussion of certain cases as postinfluenzal empyema, on the ground that they were simply cases of streptococcus pneumonia complicated by streptococcus empyema. As certain of these cases were not observed until after the onset of the empyema, and as the symptoms of influenza show much variation, this objection has some weight. On the other hand these cases of empyema occurred during the height of the influenza epidemic, presented a similar clinical picture, ran the

same clinical course and had bacteriological findings identical with those cases of influenza observed from their onset. Because of this similarity and the lack of definite evidence to the contrary all the cases of empyema occurring during this epidemic have been considered as a single group. Also it must be emphasized that at the present time we have no definite criteria, either clinical or pathological, by which postinfluenzal streptococic empyema can be differentiated from empyema following a primary streptococcus bronchopneumonia occurring during an influenza epidemic, or in fact from an empyema complicating a measles bronchopneumonia.

The study of our series of cases, although small, brings out some points of interest. In all there were admitted to the hospital 312 cases with the clinical diagnosis of influenza; 40 of these cases, or 12.5 per cent, developed empyema, and of these 17 died, a mortality of 42.5 per cent. This mortality is higher than that reported in a summary of 25 army camps collected by Graham, which was 30.2 per cent, but not so high as that reported from some of the Base Hospitals—for instance, Camp Funston with 84 per cent and Camp Wheeler with 65 per cent. These statistics, however, like many of those published, lose much of their value because of a failure to distinguish between the mortality of empyema and that due to bronchopneumonia. Graham (*l. c.*) has also pointed out that in the army statistics much of the discrepancy is due to differences in definition of the term empyema. In those camps in which the term empyema was limited to cases showing frank pus the mortality was the lowest, while in the camps including also cases of serofibrinous effusions the mortality was much higher. The latter classification was used in our series and doubtless accounts in great measure for the high mortality. The differentiation made by Graham agrees with the observations of many writers, and our cases also show that the serofibrinous exudation corresponds in time to the presence of an acute pneumonic process, and consequently the period in which most deaths occur.

The conclusion of Moscheowitz (*l. c.*) that when a patient dies with an empyema in the acute stage the cause of death is the pneumonia and not the empyema is shared by most observers. Fifteen of our 17 deaths occurred in the presence of an acute demonstrable pneumonia, 10 of them within one week after admission to the hospital. Eleven of the fatal cases showed a serofibrinous exudate, 6 showed frank pus. One of the latter, however, died from streptococcus peritonitis following ulceration of the bowel and one other patient was a case of neglected empyema admitted *in extremis*.

The disastrous experience following too hasty operative intervention in empyema was so uniformly noted in the influenza epidemic as to constitute the most important single observation made on this subject during the past two years. Rodman¹⁴ noted in his work at Camp Bowie that the mortality was 45 per cent in the cases

in which the method of early operation was employed. Later, when he aspirated until frank pus appeared, the mortality dropped one-half. Stone¹⁵ reported a mortality of 61.2 per cent in 85 patients operated upon immediately following the establishment of the diagnosis. Among 190 patients operated upon after a series of preliminary aspirations the mortality fell first to 12.6 per cent and a later series showed a still lower rate of 9.5 per cent. Following a series of such experiences reported from various parts of the country the method of preliminary aspiration rapidly became the method of choice, and its value was emphasized particularly in the report of the Empyema Commission⁴ and in a more recent article by Moscheowitz (l. c.). A number of methods of closed drainage also made their appearance; the method of Mozingo,¹⁰ irrigation with Dakin's solution through a trocar; the method of Phillips,¹² irrigation through a catheter, and the method of Harloe,⁶ who inserted a catheter into the chest through which the pus was aspirated at various times, and which was clamped off during the intervals. Each of these three methods gave excellent results in the hands of their originators. A similar treatment was employed by Manson,⁹ who treated a series of cases by repeated irrigation with chlorinated soda through a catheter. He treated 43 patients by this method; all were cured and no secondary operation was necessary. In discussing the excellent results obtained by many observers who employed first aspirations followed later by operation it must be emphasized that their low mortality was due partly at least to the fact that they were treating the more resistant patients of their series, the others having already succumbed to an acute bronchopneumonia.

Many scattered instances are reported in which the empyema cleared up under the preliminary aspirations and resort to operation became unnecessary. At the onset of our empyema experience repeated aspiration was performed on the patients with the object of preparing them for a subsequent operation. It was thought at the time that this preparation would be assisted by the use of some bland antiseptic solution capable of destroying bacteria without causing any marked irritation of the pleural surfaces. The solution used for this purpose was an aqueous solution of gentian violet, which has been shown by the investigations of Churchman^{12,3} to possess a high bacterial value *in vitro* for most Gram-positive organisms, and also to have a value in the treatment of suppurative processes.

The procedure was as follows: The chest was aspirated by means of a Potain aspirating outfit, the fluid withdrawn and 100 c.c. of an aqueous solution of gentian violet introduced into the chest through the aspirating needle by means of a Luer syringe. This solution was allowed to remain until the next aspiration. At first a dilution of 1 to 10,000 was used, followed later by dilutions of 1 to 5000 and

1 to 1000. Later in the series the first instillations were used in the strength of 1 to 5000, followed rapidly by an increase in strength to 1 to 1000. As this method was followed in a number of the earlier cases by a sterilization of the pleural exudate and clearing up of the empyema the procedure was extended to all the cases coming under observation. The greater number of the cases cleared up under this treatment, there were some failures, and in a few instances it is now apparent that surgical intervention should have been resorted to earlier.

Twenty-seven cases in all were treated in this way. Of this number 14, or 51.8 per cent, were cured; 8, or 29.6 per cent, were not cured by this procedure but later came to operation; 5, or 18.5 per cent, died. Of the fatal cases 3 died of pneumonia present on admission and persisting during treatment, while 1 patient died of peritonitis having its origin in a diphtheritic enteritis with ulcer formation and perforation of the intestine. This mortality of 18.5 per cent, although admittedly high, is mostly a pneumonia rather than an empyema mortality, and compares favorably with the mortality statistics previously quoted and also with those of Ingraham,⁸ who reports an operative mortality of 31.8 per cent, and of Gray,⁶ whose mortality was 21 per cent.

The character of the fluid obtained in the successful group of cases varied. In 3 instances it was serofibrinous, 2 of these patients clearing up after two treatments and the third after six treatments. A fourth patient showing a similar fluid cleared up after two aspirations without the use of any gentian violet. This recovery was not included in the statistics for this reason. All of these showed a pure culture of *Streptococcus hemolyticus* in the pleural fluid. Another patient with bronchopneumonia developed a sterile serofibrinous effusion that disappeared with one aspiration, the case resembling one reported recently by McCrae,¹² who describes a turbid pleural effusion in a case of lobar pneumonia that cleared up following one aspiration.

In 6 of the 14 successful cases frank pus was obtained at the first aspiration and the fluid continued to be quite thick and purulent, later becoming thinner and finally disappearing altogether. This group is of considerable interest in showing that cases with frank pus do clear up following repeated aspiration and gentian violet instillations, and that rib resection with open drainage is not the only method whereby such cases can be cured.

In 5 of the cases the fluid was at first serofibrinous but later became markedly purulent and remained so until it cleared up. In all, 11 out of the 14 showed frank pus during the course of treatment, and belong to the group of undisputed empyema cases.

Bacteriological studies of the pleural fluid in the 27 cases treated by aspiration and gentian violet injections showed the hemolytic streptococcus present in pure culture in 17 cases; associated with the

B. influenzae in 4; associated with the pneumococcus in 2; associated with both the pneumococcus and *B. alkaligenes* in 1; while in 1 instance the *Streptococcus hemolyticus*, pneumococcus and *B. influenzae* were all found at various times in the fluid; in 2 of the cases the pneumococcus was grown in pure culture. In those cases showing more than one organism in the pleural fluid the bacteriological findings varied with different aspirations, one microorganism growing at one time, another at other times and often both together.

The number of treatments employed before recovery varied greatly. While in one instance only one treatment was necessary thirty-eight had to be employed in another case. The average has fourteen to sixteen. There was no appreciable difference between the number of treatments necessary in cases in which frank pus or where serofibrinous fluid was obtained at the first aspiration. These results are of interest in emphasizing that in all cases the fluid after a few aspirations became purulent and that the presence of a serofibrinous fluid indicated only that the patient had been aspirated at an earlier stage.

In the successful cases two noteworthy effects of treatment were observed: a gradual lowering of temperature and a diminution in the amount of fluid obtained at thoracentesis. While a decrease in the amount of fluid was usually a good sign, yet this alone without a lowering of temperature did not prognosticate a favorable outcome, as it occurred in a few patients who failed to clear up. This failure of the amount of fluid obtained at tapping to serve as a prognostic index is probably to be explained anatomically—a failure to drain the cavity thoroughly because of inaccessible pus pockets.

A study of the temperature curves in all of the successful cases showed that the treatments very soon reduced the fever. In some instances this fall was rapid and a normal temperature was reached in from two to seven days. Such a reduction was, however not the rule, and the average length of time before a normal temperature was reached was fifteen days, during which time the patients were treated from once a day to once in three or four days. In our experience those patients who were treated frequently, as often as every day in the beginning of the temperature, made, as a rule, the most rapid and satisfactory recoveries. In several instances the patients after a week or longer of normal temperature showed sudden rises of temperature which persisted for a few days but disappeared when treatment was resumed. Several patients also showed complications in the form of erysipelas and acute arthritis which complicated the picture of the temperature curve and undoubtedly extended the febrile stage.

In contrast to this fall of temperature in the successful cases the unsuccessful ones showed neither rapid nor gradual response to aspiration and gentian violet instillation. In most of these cases this treatment did not produce freedom from fever for a single day.

In one case there were occasionally remissions of one to two days followed by periods of fever lasting from one to two weeks. One other case showed marked reaction to tapping and fever-free periods of a week at times. This patient was later operated upon at his own request.

The absence of microorganisms in the pleural fluid was, of course, a favorable sign, but one which, as a rule, appeared late in the course of treatment. In many patients also the fluid was not wholly sterile at the time of the last aspiration, although the number of microorganisms was very greatly reduced. The leukocyte count, while it steadily fell as the patients responded to treatment, showed such great variations that it could not be used as a very reliable prognostic index.

The result of these observations indicates that definite response to the treatment should appear within two or three weeks of frequent treatments if this method is to result in recovery. If this response is absent, successful results with this treatment are doubtful and thoracotomy is indicated.

Moschowitz (*l. c.*) in discussing the pathology of empyema lays stress upon the presence of ruptured subpleural pulmonary abscesses and states that irrigation of empyema cavities with irritating solutions such as Dakin's solution results in coughing and choking. In our experience the presence of such communications between the bronchus and the pleural cavity was strikingly shown by the appearance of a violet-stained sputum in 19 of the 27 cases treated. In the first cases noted the question was raised whether the appearance of the dye-stuff in the sputum was not due to penetration of the lung by the aspirating needle. While this possibility cannot be absolutely ruled out, further observation led to the conclusion that it was unlikely. In all aspirations extreme care was used not to penetrate the lung itself; the appearance of the dye-stuff in several cases was instantaneous upon introduction of the gentian violet into the pleural cavity; also in other patients the dye-stuff was coughed up suddenly several days after the intrathoracic injection. In another group of patients the frequent expectoration of thick pus led to the conclusion that a bronchopleural fistula was present.

The duration of the patient's stay in the hospital after the development of empyema is a question that must be taken into consideration in the choice of a method of treatment. This question has not been studied in detail in many of the empyema reports doubtless because of the difficulty in tracing these cases which in the army camps were frequently transferred. Ingraham (*l. c.*) states that the average stay of his cases in the hospital was 78 days—22 days before operation and 56 days following operation. Gray (*l. c.*) found the average number of days in the hospital to be 92 at Fort Des Moines. Tinker and Wattenberg¹⁶ have reported in

their studies on the treatment of empyema some interesting figures. Their series comprise 80 cases—all but 6, however, were operated upon elsewhere and transferred to them for after-treatment. The average stay of the patients in their hands was only 34 days, but as the average length of suppuration before admission was four months their general average was over five months. One of their patients had been suppurating eleven months before coming into their hands and another was under treatment for five months before recovering.

The average stay in the hospital necessary for our cases, which were cured by aspiration and gentian violet instillation, was 76 days, the longest 120 days, the shortest 25 days. The average length of stay in the group unsuccessfully treated and later subjected to thoracotomy was 101 days, the longest 112 days and the shortest 92 days. The patients who were operated upon were discharged from the hospital on the average of 39 days after operation. This indicates that the previous treatment of the patient by aspiration and intrathoracic injection had not, as a rule, rendered the surgical problem more difficult nor delayed the time of recovery. In one conspicuous example a bilateral empyema by means of this treatment cleared up on one side, and the remaining empyema being limited to one side, proved a simple surgical problem. The average length of stay of all patients was 84 days, which compares favorably with the figures above mentioned. This period of time could doubtless have been somewhat shortened by an earlier operation in a few of the cases which failed to improve rapidly after treatment and who in the light of our experience now should have been operated upon sooner. Our cases also were kept in the hospital on the average of a month with a normal temperature before discharge, a period which doubtless could be considerably shortened.

The cases in this series have been followed closely in order to ascertain the after-results of the treatment. One of the patients died subsequently after discharge from the hospital from what was apparently acute cholecystitis. This patient had responded very readily to treatment, and at the time of her discharge showed nothing abnormal in the chest but the presence of some pleural thickening. Nine of the patients returned to the hospital in response to recall letters and showed only the signs of a thickened pleura on the affected side. All of these persons are at work and consider themselves cured. The physical signs at present do not indicate an excessive pleural thickening and none of them show any recognizable deformity. Four other patients have been followed by letter and have made perfect recoveries. Letters from their physicians of 2 of these state that they have recovered entirely and show only slight signs of a thickened pleura. There have been no relapses. This point has been very carefully studied, and this report has been delayed largely because it was desired to allow a sufficient

time to elapse to be sure the patients were cured. It has now been over four months since the last patient was discharged from the hospital.

Summary. In a series of 27 cases of postinfluenzal empyema, 14, or 51.8 per cent, were cured without operation by repeated aspiration and intrapleural instillations of gentian violet. No relapses occurred and no deformities of the chest developed. The presence of frank pus was no contra-indication to treatment by this method. It is possible that some of these cases would have recovered without the use of gentian violet installations, yet because of the prompt symptomatic response to such injections and the rapid diminution or disappearance of bacteria in the pleural fluid it was evident that the dye-stuff possessed a very definite bactericidal value.

The most valuable indication that a patient is responding to treatment is a lowering of temperature immediately following aspiration, which persists and gradually reaches normal. A diminution of microorganisms or a frequent absence of them in the aspirated fluid is a favorable sign, but only when there is a temperature response to aspiration. Patients who failed to show such reactions to treatment in 15 to 20 days in our experience did not recover by this method. If the aspirations and instillations are not effectual within this time surgical intervention is indicated. This method of treatment should delay the operation only slightly longer than usual while making an attempt to clear up the empyema during this period. Failures were due usually to inability to empty the pus because of extensive pocket formation—a fact demonstrated at operation.

In the great majority of the cases repeated aspiration after thorough cocaineization of the skin was performed without any great discomfort. The absence of any drainage tube through the chest wall permitted the patients great freedom of movement, both while in bed and later when they were walking about.

It is difficult to discuss the amount of time necessary for treatment by this method because of the limited number of cases treated. All of the patients were kept under observation in the hospital for a much longer period than necessary. This has lengthened considerably the average duration of stay in the hospital for this series of cases. Many of these patients were up and about the hospital for four or five weeks before discharge, receiving during this time one to two treatments a week. Such patients could be discharged earlier and have the occasional aspirations carried out in the out-patient department.

It is a very great pleasure to acknowledge the assistance of Dr. Frank J. Sladen and Dr. F. Janney Smith in the preparation of this report, and the aid received from Drs. L. G. Byington, L. S. Fuller and R. L. Schaefer, whose careful observation and treatment of the patients contributed largely to the success of the treatment.

BIBLIOGRAPHY.

1. Churchman, John W.: Selective Bactericidal Action of Gentian Violet, *Jour. Exper. Med.*, 1912, xvi, 221.
2. Churchman, John W.: Treatment of Joint Infections by Lavage and Direct Medication, *Ann. Surg.*, 1915, lxi, 409.
3. Churchman, John W.: Treatment of Acute Infections of the Joint by Lavage and Direct Medication, *Jour. Am. Med. Assn.*, 1918, lxx, 1647.
4. Grnham, E. A.: Empyema in Base Hospitals, Report to the Surgeon-General, War Surgery and Medicine, Washington, August, 1918, No. 6, vol. i.
5. Gray, Horace: Pneumonia and Empyema, *Boston Med. and Surg. Jour.*, 1919, clxxx, 475.
6. Harloe, Ralph F.: Treatment of Empyema, *Jour. Am. Med. Assn.*, 1919, lxxiii, 1874.
7. Hartwell, John A.: Treatment of Empyema, *Ann. Surg.*, 1919, lxx, 55.
8. Ingraham, C. B., Roddy, John, and Aronson, Joseph D.: A Study of Empyema Cases at Camp Doniphan, *Surg. Gynec. and Obst.*, 1918, xxvii, 554.
9. Munson, Frank M.: Treatment of Empyema by a Closed Method, *Jour. Am. Med. Assn.*, 1919, lxxiii, 1404.
10. Mazingo, Arvine E.: Surgical Treatment of Empyema by a Closed Method, *Jour. Am. Med. Assn.*, 1918, lxxi, 2662.
11. Moschowitz, Alexis V.: Newer Conceptions of the Pathogenesis and Treatment of Empyema, *Am. Jour. Men. Sc.*, 1920, clx, 660.
12. McCrae, Thomas: Treatment of Empyema in Lobar Pneumonia by Early Aspiration, *Canada Med. Assn. Jour.*, 1920, x, 162.
13. Phillips, H. B.: Empyema at Camp Mills, L. I., *Jour. Am. Med. Assn.*, 1919, lxxii, 1274.
14. Rodman, John S.: Empyema, *Ann. Surg.*, 1919, lxx, 49.
15. Stone, W. J.: Management of Postpneumonic Empyema, *Proc. Am. Soc. for Clin. Investigation*, September 6, 1919, x, p. 786.
16. Tinker, Martin B., and Wattenberg, John E.: Treatment of Chronic Empyema, *Ann. Surg.*, 1919, lxx, 545.

THE ADVANTAGE OF SERUM THERAPY AS SHOWN BY A COMPARISON OF VARIOUS METHODS OF TREATMENT OF ANTHRAX.

By JOSEPH C. REGAN, M.D.,

LECTURER ON CONTAGIOUS DISEASES, LONG ISLAND MEDICAL COLLEGE, AND ASSISTANT
RESIDENT PHYSICIAN, KINGSTON AVENUE HOSPITAL.

(From the Kingston Avenue Hospital, of the Bureau of Hospitals, Department of
Health, New York City, Dr. R. J. Wilson, Director.)

VARIOUS methods of local therapy of anthrax have been in use for many years past, and are still widely employed either alone or in conjunction with other measures. If one has the time to consult the literature dealing with the subject, whether it be in periodicals or in text-books, it is at once evident what wide differences of opinion exist as to the most effective method of treatment. This is unfortunate and is liable to lead one to the conclusion that most all the usual methods give about the same results and it is not therefore a vital matter which one is employed in the individual case. This view-