

oculated group, excluding those patients who contracted the disease elsewhere.

In one hospital in which the nurses had been inoculated, no cases developed after the inoculations, although the nurses continued to care for patients with influenza. Owing to the scarcity of vaccine, some of the nurses, living under identical conditions, were not inoculated, and a high percentage of these contracted severe attacks.

Numerous instances have been observed in which protection appeared to be afforded to inoculated members of families of which all the uninoculated became ill. Similar results were obtained when conditions among the inoculated and uninoculated were comparable, such as in offices, factories and schools, where nearly all were inoculated, or where only a small percentage were inoculated. Illustrating results are as follows:

Of 1,000 persons employed by one company, 481, about one half, received one inoculation; 224 received two inoculations, and ninety-five received three inoculations. From October 28, the date of the first inoculation, to December 8, 138 cases of influenza occurred, only twenty of which were among persons who had had one or more inoculations. Of these, fourteen had had only one inoculation, and the remaining six had but two inoculations. There were thirteen deaths, only two of which followed influenza among the inoculated, and in these two cases only one inoculation had been given.

The mortality from bronchopneumonia in pregnant women has been especially high during the present epidemic. The vaccinations in a fairly large number of such persons appear to have afforded some protection against this complication. The bacteria included in the vaccine belong to the general group of microorganisms associated commonly with chronic infections, such as arthritis, sinusitis and bronchitis; hence some effect should follow its injection. Striking instances of improvement in these conditions have been noted but whether due to specific or nonspecific effects or whether the vaccine acts as an "exfoliative stimulus" according to Larson, liberating preformed specific antibodies, remains to be determined.

From the results obtained thus far, it appears possible to afford a definite degree of protection by prophylactic inoculation to persons against the more serious respiratory infections during the present epidemic of influenza. The duration of immunity is not known, but indications are that it is relatively short.

The vaccine should contain freshly isolated strains of the more important bacteria in approximately the proportions as found in the sputum and lungs in the disease, and since the relative proportions of the bacteria at hand differ so markedly in widely separated communities, judging by the reports, the formula of the vaccine should be made to conform as nearly as practicable to the respective flora of the disease in the communities in which the vaccine is to be used.

A saline vaccine was used as an emergency measure. Owing to the large number of different bacteria that need to be included and the large doses necessary, a lipovaccine, judging by the recent work of Whitmore, ought to possess definite advantages, since reactions should be less severe, the formation of antibodies more marked, and the resulting immunity more enduring.

I am constantly being asked with regard to the use of the vaccine in treatment. Since the severer com-

plications in influenza, such as pneumonia, do not usually begin until the fourth day or later, the vaccine, if given at the onset of the disease might reasonably be expected to afford some protection. The initial prophylactic dose daily for one, two or three days, provided no unfavorable symptoms occur, is recommended. The results obtained are considered preliminary, and final conclusions cannot be drawn at this time. It is indicated that the vaccine used was at least harmless, that a certain degree of protection was afforded, and that prophylactic inoculation against the respiratory infections, so fatal during this epidemic, be studied on a large scale by many according to the principles herein laid down.

#### TREATMENT OF INFLUENZAL PNEUMONIA WITH PLASMA OF CONVALESCENT PATIENTS\*

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The addition of 33 $\frac{1}{3}$  per cent. to the normal population of Washington during the past eighteen months has given us a great military camp with barracks-like overcrowding, yet there is nothing comparable to the military supervision of health conditions.

In the present epidemic, the Medical Department of the Navy is treating not only the officers and their families and the enlisted personnel, but also all civilian employees. Up to December 16, 567 cases of influenza and complicating pneumonias were treated at the Naval Hospital. Of these, 157, or 27.8 per cent., either came in with pneumonia or developed it during the residence.

Without going into the clinical picture of the disease, we may say that the outstanding feature is an overwhelming toxemia. Characterized by headache, muscular fatigue and pain, mental dulness, leukopenia and in many cases nausea and vomiting. Nature's forces, thus paralyzed, failed to respond to ordinary therapeutic measures, especially when pneumonia of whatever etiology complicated the disease. Two factors, we believe, aided in keeping our mortality percentage low in the first days of the epidemic, namely, digitalis and venesection. Isotonic glucose and sodium bicarbonate intravenously and massive doses of camphorated oil were each given in a series of cases without beneficial results. In the later stages venesection was most efficacious in combating dilatation of the heart and flooding of the lungs. Time and again when it seemed that the patient must drown in his own secretions, venesection cleared the bronchi and slowed respiration so that the patient was able to sleep. Blood was drawn with a needle into a sterile 8 ounce nursing bottle so that cultures might be made in each case. Out of forty cultures ten were found positive, showing pneumococcus Type I in 2 cases; Type II in 2 cases; Type IV in 4 cases, and *Streptococcus viridans* in 2 cases. Three patients having positive

\*Owing to lack of space, this article is abbreviated in THE JOURNAL by the omission of several charts. The complete article appears in the authors' reprints.

blood cultures recovered. Pfeiffer's bacillus was grown repeatedly from the sputum, lung puncture and necropsy material, but never from the blood stream.

transient character and were probably due to the rapidity with which the blood was withdrawn. A majority of the men noticed that they gained weight much more rapidly after they had given blood.

The blood thus drawn is sedimented in the ice chest from twelve to twenty-four hours, and an average of 250 c.c. of plasma citrate-salt solution mixture are obtained from every 500 c.c. of blood.

METHOD OF ADMINISTRATION

The plasma is administered intravenously from a graduated container by the gravity method. A small needle and low pressure are used so that fifteen or twenty minutes are consumed in giving the average dose of 125 c.c. The arm selected is elevated and supported with a pillow, care being taken that there is no tight clothing about the shoulders, thus avoiding the possibility of stagnation and agglutination in the vein.

With these precautions taken, it is not essential that the plasma be compatible with the blood of the patient. Indeed, grouping of the plasma and tests for compatibility are eliminated altogether. Doses of less than 100 c.c. are not indicated be-

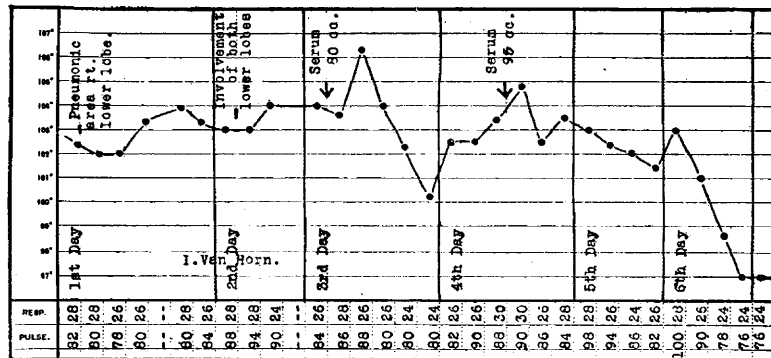


Chart 1.—Temperature, respiration and pulse in a case of influenzal pneumonia in a nurse. The attack began with a severe chill, cough, marked general pains, nausea and vomiting. Physical examination revealed signs of beginning pneumonia in the right lower lobe posteriorly. On the second day the pneumonic area in the right lower lobe showed signs of extending, and a small area was made out in the left lobe. The patient was prostrated, vomited continuously, and was unable to retain anything by mouth. She refused to accept serum treatment. On the third day the patient was much worse. Physical signs of pneumonia were extending in both lower lobes, prostration had increased, vomiting continued, and she was stuporous. Following the injection of plasma there was a chill with a rise in temperature to 106 with no disturbance in pulse or respiratory rate. Sweating was profuse. This was followed by a precipitate drop in temperature to 100 and an improvement of all symptoms. The patient was clear mentally, muscle pains were gone, and vomiting ceased. The following day the temperature again began to rise, the vomiting returned, and all subjective symptoms returned. A second injection of plasma was given and was followed by a slight chill and a rise in temperature. A few hours later the vomiting ceased entirely, the patient brightened up mentally, all pains were relieved, and convalescence was established.

At the height of the epidemic, a suggestion came from Boston Chelsea Hospital that the serum from convalescent patients might be of curative value. We at once determined to give the method<sup>1</sup> a thorough trial, but we chose to use citrated plasma rather than the serum obtained by clotting and centrifuging.

The apparatus and procedure as used by us has already been described.<sup>2</sup> Blood plasma is obtained by this method with the minimum of labor and danger of contamination. A larger amount of plasma is obtainable and the excess fluids added are a distinct advantage in view of the profuse perspiration following its administration. We believe that the failure of this method of treatment has been due in many cases to its having been tried half-heartedly, owing to the difficulties and labor involved in the collection of the plasma or serum.

On being discharged to the convalescent wards, the pneumonia patients are sent to the laboratory for Wassermann tests, and their venereal history is carefully inquired into. If convalescents are accepted, they are bled twice after being about the ward from four to six days, in amounts of from 300 to 500 c.c., with several days intervening between the bleedings. In only two instances have the donors mentioned sensations of faintness; these were of

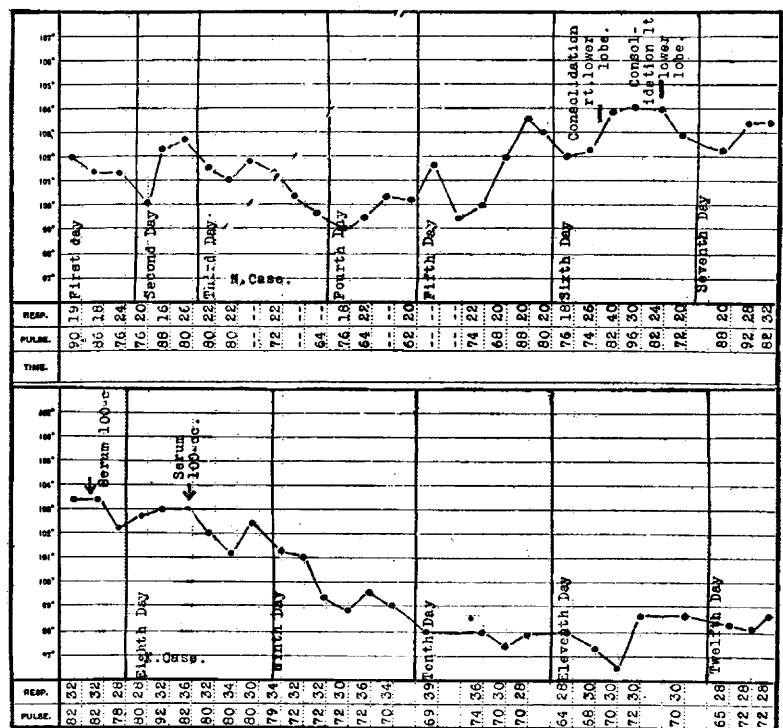


Chart 2.—Temperature, respiration and pulse in a case of influenzal pneumonia in a pharmacist who on the fifth day complained of being weak and worn out. No definite physical signs were made out. On the following day he was stuporous, showed marked prostration, and developed a severe cough. Physical examination revealed small pneumonic areas in both lower lobes. Twenty-four hours later he was given 100 c.c. of serum. There was no chill or reaction following it, but there was an immediate and marked improvement in his mental condition and entire relief from muscular pain. The injection was repeated on the following day and no reaction followed it. Next day the temperature reached normal.

cause they may produce uncomfortable reactions in the patients without giving any permanent relief of their symptoms.

1. The details of the method were later published by McGuire, L. W., and Redden, W. R.: Treatment of Influenza Pneumonia by the Use of Convalescent Human Serum, J. A. M. A. 71: 1311 (Oct. 19) 1918.  
2. Hartman, F. W.: New Methods for Blood Transfusion and Serum Therapy, J. A. M. A. 71: 1658 (Nov. 16) 1918.

REACTIONS FOLLOWING ADMINISTRATION

In approximately 75 per cent. of the patients there is a response of some kind within two hours. This may be manifest by chilly sensations or a frank chill

One fourth of the cases show no reaction or only perspiration, yet get the same though perhaps less prompt results from treatment. Chart 2 is that of a pharmacist who would not give in to the infection until pneumonia developed, areas of consolidation were made out in both lower lobes, and the respiration rate was 32 per minute. Two doses were administered within a twelve-hour period. Almost immediately there was a complete change in the mental attitude and physical condition. At the end of twenty-four hours the temperature was normal. As expressed by the patient himself, a heavy weight seemed to be lifted off him in such a way as could only be appreciated by one who had experienced it. Again and again we have seen patients pass from the preliminary stage, after treatment, into sound sleep, like that of a child, to awake hours later feeling perfectly well, ready to eat anything.

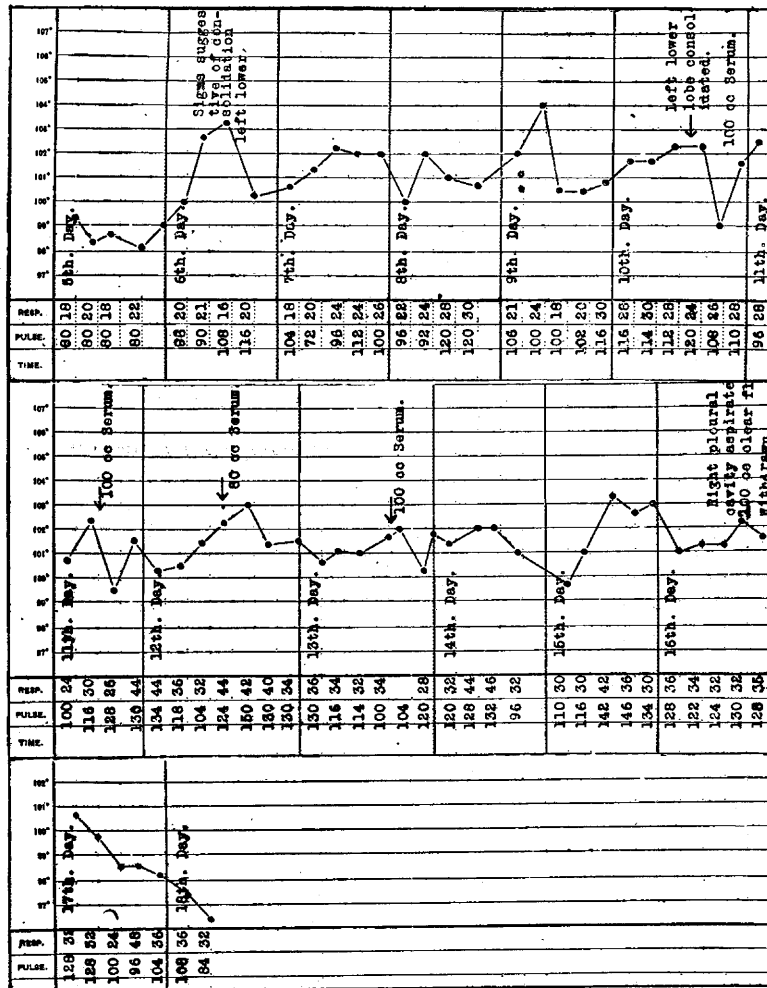


Chart 3.—Temperature, respiration and pulse in a case of influenzal pneumonia complicated by pleurisy with effusion.

lasting several minutes, a rise in temperature of from 1 to 2 degrees, and drenching perspiration. The use of hot water bottles and extra blankets at this time affords comfort to the patient and encourages perspiration. In our experience these reactions do not weaken or prostrate the patient, but leave him with a slower pulse, freer and easier respirations, and a reduced if not a normal temperature. At the same time the subjective symptoms of headache, muscle pain and mental depression are relieved in a marked degree.

Chart 1 is that of a nurse who refused the treatment until there was involvement of both lower lobes, and she was too ill to care what happened. In addition to other symptoms, she vomited constantly. Within two hours after she had received 80 c.c. of plasma, the temperature began to fall and the vomiting ceased. This relief lasted only eight hours, but a second injection (against which she was alert enough to protest strongly) was followed by cessation of vomiting and uneventful recovery.

Those pneumonias developing in the hospital and treated within forty-eight hours have shown the most clear-cut and striking results, due, we believe, to the neutralization of the toxin or toxins freeing natural forces to combat secondary invaders. In these cases the physical signs do not extend, but may persist for several days. In the terminal stages circulation is so poor and the lung involvement so extensive as to make this treatment uncertain and unsatisfactory because serious symptoms may be aggravated rather than relieved.

POTENCY OF PLASMA

In the first cases we injected only the compatible plasma; hence we were unable to pool that drawn from the various convalescents. With this procedure it was found that 25 per cent. of the plasma was very potent, 65 per cent. was moderately potent, and 10 per cent. was inactive. The

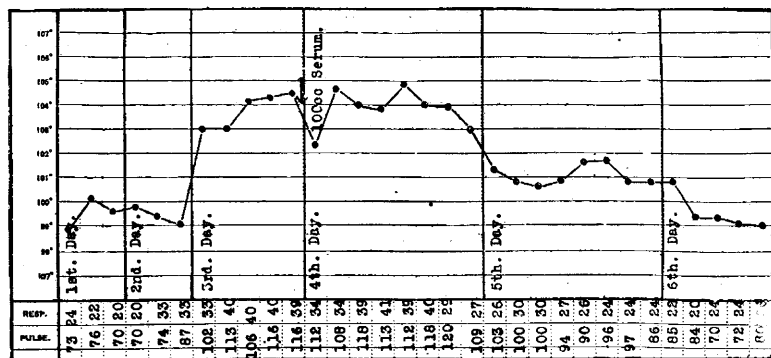


Chart 4.—Temperature, respiration and pulse in a case of influenzal pneumonia in a woman who was a superintendent of nurses and refused to give up her duties until prostrated. On the third day the temperature rose to 103, pulse 113, and respirations 40. Signs of pneumonic areas in the lower lobes of both lungs were made out. One hundred c.c. of serum were administered intramuscularly. During the next twenty-four hours the temperature fluctuated between 104 and 105, and then began falling by lysis, accompanied by improvement in both pulse and respiration. The patient was discharged on the twelfth day.

plasma collected as late as thirty days after the temperature had become normal seems to be potent, as is also that of convalescents who were treated during their pneumonia.

Agglutination and complement fixation tests with five strains of the influenza bacillus and twelve different serums were uniformly negative. Agglutination tests on Types I, II and III pneumococci were likewise negative. Unfortunately no such tests were made with the diplostreptococcus, which was present in many of the early cases.

RESULTS OF TREATMENT

Complications of any kind interfere markedly with recovery. Pleurisy, and particularly pleurisy with effusion, seems to neutralize the beneficial properties of the plasma. Chart 3 is that of a patient first treated five days after suggestive signs of pneumonia were made out. Each of four injections was followed by temporary improvement, but he grew weaker until

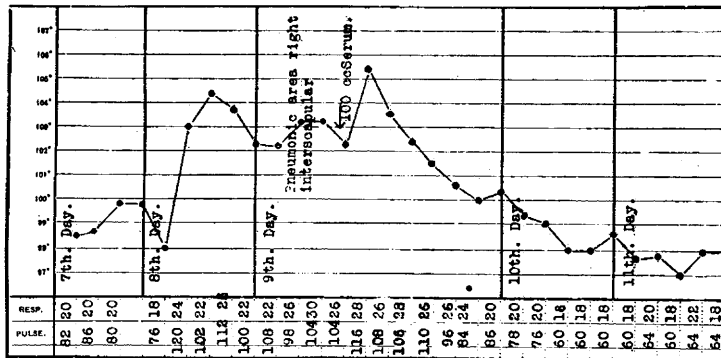


Chart 5.—Temperature, respiration and pulse in a case of influenzal pneumonia developing five days after temperature became normal.

the sixteenth day, when, following the aspiration of 200 c.c. of fluid from his right pleural cavity, the temperature dropped to normal and an uneventful recovery was made.

Two of three fatal cases showed extensive fibrinous pleurisy with an effusion of about 200 c.c. of sero-sanguineous fluid, containing many pneumococci in each pleural cavity. The third case showed an encapsulated empyema on the left side from which Group I pneumococci were cultivated. One of the two patients mentioned above had a pneumococcus Type IV septi-cemia, the organism producing green coloration in different culture mediums. Treatment in all three cases was begun late, either because we did not see the cases until late or because definite signs of pneumonia were not made out until late.

Up to the present time, forty-six cases of influenzal pneumonia have been treated with three deaths resulting, making the mortality percentage 6.5. Of 111 patients untreated, twenty-eight died, giving a mortality percentage of 25.2, or about four times the percentage mortality among forty-six treated cases.

CONCLUSIONS

1. The toxemia of influenza seems to be neutralized by the plasma from convalescent patients.
2. Certain care being exercised, tests for compatibility are eliminated.
3. A large percentage of all plasma is active, and most satisfactory results are obtained by pooling the different lots.
4. Sharp reactions are followed by the most prompt improvement, but are not essential to success.
5. Pneumonia must be diagnosed early and treated immediately if a large percentage of recoveries are to be obtained.

OPERATIVE TREATMENT OF GUNSHOT WOUNDS OF THE SPINE WITH GRAVE PARALYSES \*

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It appears to be generally held that operation is contraindicated in recent gunshot wounds of the spine when there is complete or almost complete paralysis and sensory loss below the level of the cord injury. From a number of reported observations, however, it seems clear that paralysis ranging from slight to most extreme may be associated with wounds in the neighborhood of the spine without involvement either of bone or of dura. The hopeless destruction of the cord by the missile or by bone fragments can be determined without operative intervention in not a few cases, and in these operation is of no avail. There are many cases, on the other hand, in which such cord destruction cannot be shown unequivocally by roentgenographic and clinical examination and the study of the course of the missile, instances in which operation may reveal a partially severed, contused or compressed cord. Basing my opinion on several experiences with cases of this type, I believe that these patients should be given the benefit of doubt as to the completeness of the cord lesion, and that operation should be performed in the hope of encountering remediable conditions.

My special purpose in the present contribution is to discuss a group of cases of gunshot wound of the spine in which the dura is intact in the presence of complete or almost complete paralysis, the lesion in the cord being attributable to commotion or concussion or to both combined. In the fatal cases examination discloses either a diffuse or a focal necrosis in the affected part of the cord with a varying degree of surrounding edema. Sometimes all the cord elements are destroyed at this level, but more frequently greater or lesser portions remain intact. The presumption is that in the favorable cases, those in which functional recovery occurs to a varying degree, edema was a prominent element in the lesion. There is, then, a group of cases of gunshot wounds in the spinal region, with intact dura and with grave paralysis, in which the possibility of return of function exists. In injuries by shell fragments, the chances of recovery from the wound are greatly reduced or even entirely eliminated if a deep-seated wound infection is added to the cord lesion with its complications. In addition to the indirect effect on the cord of the type of injury in question, there may be fragments of bone or epidural clots directly compromising the dura, the removal of which would aid in recovery and reduce the likelihood of epidural infection. It is chiefly, however, for the elimination of infection, and not with the expectation of relieving pressure on the cord, that I believe prompt operation is indicated in these cases. This point of view received support in a series of spinal wounds under my care at British Casualty Clearing Station No. 17 last year. Of twenty-two patients with spinal wounds accompanied by manifestations of severe damage to the cord, four fell into the category of

\* From Mobile Hospital No. 2, A. E. F.