8. Reactions to injections of combined tetanus and diphtheria toxoid are no more frequent or severe than they are with diphtheria toxoid.

9. Prophylactic injections of tetanus antitoxin produce a protective level of antitoxin for only a few weeks. This level is not as high as that after immunization with tetanus toxoid nor does it last nearly as long.

10. It is apparently safe to administer tetanus and diphtheria toxoids to allergic children. Sensitization to the toxoids is rare. This is in contrast to the antitoxins used for passive immunity.

11. In the light of our present knowledge it would seem safer to give an immunized person a stimulating dose of tetanus toxoid after an injury involving probable infection with tetanus spores.

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CHEMOTHERAPY VERSUS COMBINED CHEMOTHERAPY AND SERUM

IN THE TREATMENT OF PNEUMONIA
A STUDY OF 607 ALTERNATED CASES

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The universal acceptance of the value of sulfonamide therapy in pneumonia has left the role of serum as the major current problem in the treatment of this disease. Will the use of serum combined with drug reduce still further the fatality rate? Will it cause a more rapid subsidence of the acute infectious process? These problems have been studied at Bellevue Hospital by using the alternate case method. Since February 1939, all pneumonia patients entering the wards of the First, Second and Fourth medical divisions have been alternated within the pneumococcus types between sulfonamide therapy alone and combined drug and serum therapy. In the present study we are reporting the results up to Jan. 1, 1941 in a series comprising 607 patients thus alternated.

METHOD

As soon as the clinical diagnosis of pneumonia was made, samples of blood and sputum were collected for bacteriologic study. The patient was then immediately placed on sulfonamide therapy without waiting for the results of typing. When the pneumococcus type was obtained, alternate patients in each type were placed in either the drug alone or drug plus serum group. If the patient fell in the drug plus serum group he was given, in addition to the drug, concentrated antipneumococcus rabbit serum. This was administered as soon as the specific type was obtained except when striking clinical improvement already had occurred and serum no longer would be of value. These patients, however, were left in the "drug-plus-serum" group because to remove them would create a statistical error in favor of the drug-alone series. The first therapeutic dosage of serum was usually 100,000 units in uncomplicated cases and 200,000 units or more for known bacteremic or seriously ill patients. This dosage was repeated when necessary. Six patients who would have been due for serum survived less than twenty-four hours and died before typing was completed. These patients, therefore, received no serum but were necessarily counted in the serum group, it being one of the inherent disadvantages of serum therapy that there usually is some delay before serum can be started even under ideal circumstances. With the exception of these six twenty-four hour deaths, all other patients in the serum group who died received serum.

Several different sulfonamide drugs were used during the course of this study: sulfapyridine, dextrose-sulfapyridine, sodium sulfapyridine, sulfathiazole, sulfamethylthiazole and sulfadiazine. When a new drug was introduced, one or more whole wards were shifted from one drug to the other, and all patients entering these wards were treated with the new drug without interfering with the alternation of cases between the drug-alone and the combined therapy groups. There was an occasional failure of response, and occasionally a maintenance dose higher than 1 Gm. every four hours was used. A few patients received sodium sulfapyridine intravenously either to obtain a more rapid absorption or to procure a higher blood concentration of the drug.

Other forms of treatment including oxygen therapy, procedures for maintaining an adequate fluid intake, sedation and various symptomatic measures were used as indicated in both groups of cases.

This study included cases of both lobar pneumonia and bronchopneumonia. No patients were excluded except those with atypical congestive bronchopneumonia terminating some otherwise fatal disease such as carcinoma or heart disease. All other cases of pneumonia were included: systemic disease, no matter how serious, did not disqualify patients. A complete bacteriologic study was carried out in all cases; throat swab cultures were made when sputum was not obtainable; typing was repeated in all of the higher types and whenever the results were not conclusive; typing from the peritoneal exudate and from the brain of the mouse was used to supplement and confirm the findings in every case; admission blood cultures were always procured and repeated when indicated; chest fluid, or any other specimen from a localized process obtainable either ante mortem or post mortem was sent to the laboratory for study. In addition almost every patient had at least one roentgen examination, blood counts, urinalyses and blood chemistry determinations, particularly the sulfonamide drug concentration.

COMPARATIVE EFFECT ON THE MORTALITY RATE

The effect of the two modes of therapy on the fatality rate is shown in table 1. Of 306 patients treated with chemotherapy alone, 34 (11.1 per cent) died. Of 301 patients treated with chemotherapy plus serum, 44 (14.6 per cent) died. However, if patients dying within twenty-four hours of the start of treatment are excluded, the mortality rates become nearly equal, 9.3 per cent for the drug group and 9.8 per cent for the drug-plus-serum group. It is noteworthy that even in types I, II,

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From the First (Columbia), Second (Cornell) and Fourth Medical Divisions, Bellevue Hospital, and the Departments of Medicine of the Columbia University College of Physicians and Surgeons and Cornell University Medical College, and a Committee for Pneumonia Investigation consisting of Drs. Russell L. Cecil, I. Ogden Woodruff, Asa L. Lincoln and Charles H. Nammack (the latter three, directors of the First, Second and Fourth Medical Divisions respectively) and the authors.

V and VII, in which the value of serum is best established, the fatality rates were not significantly lower in any of the drug-and-serum groups.

COMPARATIVE EFFECT IN BACTEREMIC PATIENTS

In the drug-only group there were 61 bacteremic patients, of whom 20 (32.8 per cent) died, four within twenty-four hours. In the drug-and-serum group, 64 were bacteremic and 29 (45.3 per cent) died, 14 within twenty-four hours. Excluding the twenty-four hour deaths, the mortality rate in the drug group was 28.1 per cent and in the drug-and-serum group 30.0 per cent.

The incidence of bacteremia in this study is 20.6 per cent. This is lower than the incidence in previously reported Bellevue series, because under effective sulfonamide therapy patients rarely develop bacteremia after treatment is commenced. In this series we encountered

TABLE 1.—*Distribution of Cases and Results by Types*

	Drug Only			Drug and Serum		
Type	Cases	Deaths	24 Hr. Deaths	Cases	Deaths	24 Hr. Deaths
I	49	6	1	51	9	3
II	49	4	1	55	10	3
III	31	4	1	32	8	3
IV	9	1	0	7	1	1
V	24	2	1	27	1	1
VI	4	0	0	6	0	0
VII	34	6	1	33	4	2
VIII	25	2	0	26	2	0
IX	3	1	0	2	0	0
X	5	1	0	5	0	0
XI	2	0	0	2	1	0
XII	2	0	0	3	0	0
XIII	5	0	0	1	0	0
XIV	8	1	0	6	2	1
XV	5	0	0	4	0	0
XVI	1	0	0	1	0	0
XVII	9	0	0	7	1	0
XVIII	3	2	0	6	0	0
XIX	8	1	0	5	0	0
XX	7	0	0	4	1	0
XXI	1	0	0	1	0	0
XXII	3	0	0	2	2	2
XXIII	1	0	0	..	..	..
XXIV	3	0	0	4	1	0
XXV	6	1	0	4	0	0
XXIX	4	1	0	3	0	0
XXXI	1	0	0	..	..	..
XXXII	1	0	0	2	0	0
XXXIII	3	1	1	2	1	0
Total	306	34 (11.1%)	6	301	44 (14.6%)	16
Excluding 24 hr. deaths	300	28 (9.3%)		285	28 (9.8%)	

no patient whose blood culture was sterile on admission and became positive during treatment.

There were 4 bacteremic patients in this series whose plates showed innumerable colonies of pneumococci and who recovered. In the Bellevue experience in the prechemotherapeutic era, all such patients died. As it happened, these 4 patients were all in the drug-alone group, and each was treated with a different drug, viz. sulfapyridine, sulfathiazole, sulfamethylthiazole and sulfadiazine. It is remarkable that any patients with such severe infections should recover, and noteworthy that they were all in the drug-alone group.

RESULTS IN EARLY AND IN LATE CASES

In order to evaluate further the effect of the two modes of therapy, all cases were divided according to the duration of illness before treatment was begun. They were grouped into three classes: early (treatment started during the first three days), late (treatment begun on the fourth day or later) and uncertain (duration of illness not ascertainable). The last group for the most part comprised patients entering when moribund, or nearly so, and were consequently usually late cases. The results of treatment are given in table 3.

Of the 158 early cases in which drug-alone treatment was employed there were 7 deaths (4.4 per cent); of the 146 early cases (one twenty-four hour death excluded) in the drug-and-serum group there were 10 deaths (6.8 per cent).

TABLE 2.—*Bacteremic Cases and Results by Types*

	Drug Only			Drug and Serum		
Type	Cases	Deaths	24 Hr. Deaths	Cases	Deaths	24 Hr. Deaths
I	16	5	1	14	6	3
II	13	4	1	12	7	2
III	5	2	1	8	4	2
IV	0	0	0	2	1	1
V	4	1	1	6	1	1
VI	0	0	0	0	0	0
VII	5	3	0	8	4	2
VIII	6	1	0	7	1	0
IX	2	1	0	0	0	0
X	0	0	0	0	0	0
XI	0	0	0	0	0	0
XII	1	0	0	0	0	0
XIII	0	0	0	0	0	0
XIV	1	0	0	2	2	1
XV	0	0	0	0	0	0
XVI	0	0	0	0	0	0
XVII	0	0	0	0	0	0
XVIII	1	1	0	2	0	0
XIX	1	1	0	0	0	0
XX	0	0	0	1	1	0
XXI	0	0	0	0	0	0
XXII	0	0	0	2	2	2
XXIII	0	0	0	..	..	..
XXIV	0	0	0	0	0	0
XXV	4	1	0	0	0	0
XXIX	1	0	0	0	0	0
XXXI	1	0	0	..	..	..
XXXII	0	0	0	0	0	0
XXXIII	0	0	0	0	0	0
Total	61	20 (32.8%)	4	64	29 (45.3%)	14
Excluding 24 hr. deaths	57	16 (28.1%)		50	15 (30.0%)	

In the "late" group (omitting twenty-four hour deaths) there were 117 cases in the drug group with 14 deaths (12.0 per cent) and a total of 110 cases in the drug-and-serum group with 11 deaths (10.0 per cent). In the "uncertain" group (omitting twenty-four hour deaths) there were 26 in the drug group with 7 deaths (26.9 per cent) and 28 cases in the drug-and-serum group with 7 deaths (25.0 per cent). Combining the "late" and "uncertain" groups we have a total of 143 cases with 21 deaths (14.7 per cent) in the drug group and 138 cases with 18 deaths (13.0 per cent) in the drug-and-serum group. Thus it can be seen that the fatality rate in the patients treated early, whether by

TABLE 3.—*Results in Early Cases (First Three Days) Compared with Those in Late Cases and in Cases of Uncertain Duration*

	Cases	Total Deaths	24 Hour Deaths	Fatality Rate with 24 Hour Cases Excluded
Early				
Drug only	158	7 (4.4%)	0	4.4%
Drug and serum	147	11 (7.5%)	1	6.8%
Late				
Drug only	122	19 (15.6%)	5	12.0%
Drug and serum	118	19 (16.1%)	8	10.0%
Uncertain				
Drug only	27	8 (29.6%)	1	26.9%
Drug and serum	35	14 (40.0%)	7	25.0%

drug alone or by drug and serum, was about one-half the fatality of the late and uncertain cases combined; this emphasizes anew the well known fact that early treatment is essential if the best results are to be obtained. The additional routine use of serum did not materially affect the outcome in the early, in the late or in the uncertain group.

COMPARATIVE EFFECTS ON RAPIDITY OF RECOVERY

It is not easy to judge the effect of the two modes of therapy on the rapidity of recovery. We have elected to estimate this by making composite temperature curves (charts 1 and 2) of the type I and of the type II cases in the two therapeutic groups in which survival

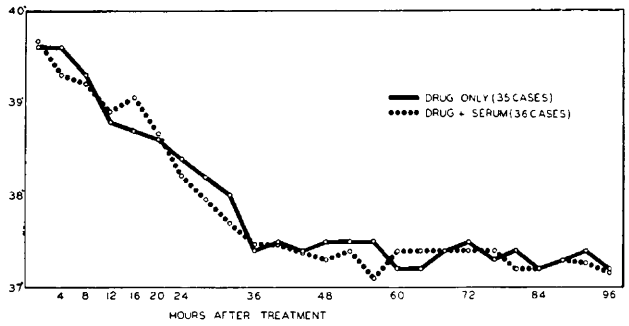

Chart 1.—Comparative temperature response in type I cases.

occurred. In these two types the effect of serum therapy has been most completely studied, and if differences in rapidity of response are to be found they should be apparent here. As can be seen, there is no significant difference in the two temperature curves for each type, nor could any consistent difference in the two therapeutic groups be noted clinically. The serum was given at varying intervals after the start of drug treatment, depending on the speed of typing but usually within the first twenty-four hours.

AGE OF PATIENTS

The patients comprising this study were older, on the whole, than those in most other reported studies, the average age for the entire group being 49.3 years. The distribution by age is shown in table 4. The average age for the drug group was 49.2 years, for the drug-plus-serum group 49.3 years. There were no deaths in either group in patients under 30 years of age. Between 30 and 50 the fatality rate was 3.4 per cent in the drug group and 4.9 per cent in the drug-and-serum group. For patients 50 or more years of age, the fatality rate was 16.1 per cent in the drug group and 16.8 per cent in the drug-and-serum group.

DRUG LEVELS AND AMOUNT OF SERUM USED

Blood level estimations were done frequently on most of the patients during the active stage of the disease.

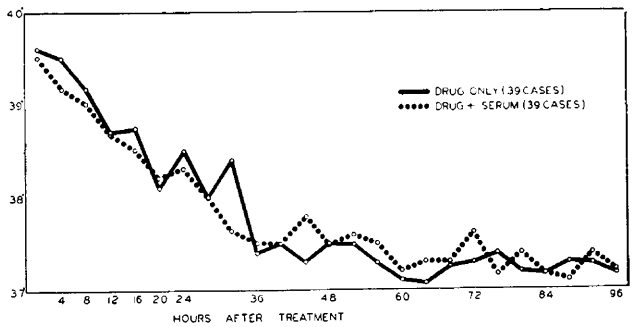

Chart 2.—Comparative temperature response in type II cases.

Our data are not complete enough, however, to allow us to draw any definite conclusions. In experimental infections in animals treated with sulfonamides, Marshall [1] has shown that the percentage of animals surviving depends on drug dosage and drug level, high doses and levels increasing the survival rate. It is probable that this applies to human cases of pneumonia also, but we are unable to state what constitutes the optimum blood level of drug. In practice the estimation of blood levels has been of value chiefly for those patients who have not responded satisfactorily or who have had impaired renal function. If failure of a patient to respond appears to be due to a low blood level, parenteral or increased oral administration of the drug can be used. An initial dose of 2 Gm. was used in all our cases. That a larger initial dose would have saved a substantially greater number of patients seems to us unlikely.

The amount of serum used varied from 80,000 to over 600,000 units; for patients who died but survived long enough to receive serum, the average dose was 260,000 units.

RESULTS ACCORDING TO DRUG USED

There seemed to be no significant difference in the fatality rates for the different sulfonamide compounds used, although several of the compounds were not tried extensively enough to offer conclusive evidence on this point (table 5). All the compounds were potent remedies for pneumonia, although the dextrose-sulfapyridine solution used (10 per cent in 50 per cent dextrose given orally) was a little less efficient than the other drugs in the cases of bacteremia. This may have been due to the slower absorption of this drug. The sodium sulfapyridine cases comprise those in which tablets of this drug were administered orally. A few patients were given supplementary intravenous injections of sodium sulfapyridine but were not treated exclusively in this way.

TABLE 4.—*Distribution of Cases and Results by Age*

	Drug Only				Drug and Serum			
Age	Cases	Deaths	24 Hour Deaths	Fatality Rate with 24 Hour Deaths Excluded	Cases	Deaths	24 Hour Deaths	Fatality Rate with 24 Hour Deaths Excluded
Under 30	33	0	0	0	32	0	0	0
30 to 50	118	4	0	3.4%	124	8	2	4.9%
50 and over	155	30	6	16.1%	145	36	14	16.8%
Total	306	34	6	9.3%	301	44	16	9.8%

COMPLICATIONS OF PNEUMONIA

The complications are listed in table 6. All of the 10 patients with pneumococcic endocarditis diagnosed clinically died regardless of the type of therapy used, and none of the patients with pneumococcic meningitis following pneumonia recovered. There were 11 patients with empyema in the drug-alone group; of these 2 died (1 within twenty-four hours and 1 with pneumococcic endocarditis) and 4 came to thoracotomy. Of the 13 empyema patients in the drug-and-serum group 4 died (1 within twenty-four hours, 1 with meningitis and 1 with probable pneumococcic endocarditis), and 7 required thoracotomy. The remaining empyema patients in each group had thin fluid and recovered on repeated thoracenteses and continued oral administration of the drug. Fluid was demonstrated or suspected on admission in 7 of the 11 cases in the drug-alone group and in 5 of the 13 cases in the drug-and-serum group. There were 5 cases of sterile serous effusion in the drug-alone group and 16 in the drug-and-serum group; of these cases, in 2 in the drug-alone group and in 7 in

1. Marshall, E. K., Jr.: Experimental Basis of Chemotherapy in the Treatment of Bacterial Infections, Bull. New York Acad. Med. **16**: 723-731 (Dec.) 1940.

the drug-and-serum group there was demonstrable or suspected fluid on admission. There were 5 cases of nonputrid lung abscess, and it is our impression that perhaps more abscesses as sequelae of pneumonia will be seen in the future than in the past, because some of the most acutely ill patients with heavy bacteremia, who in the past did not survive the acute stage of the disease, now live long enough to allow tissue breakdown to occur. This subject of pleural and parenchymal complications of pneumonia under modern therapy will be reported in detail in a subsequent communication.

TABLE 5.—*Distribution of Cases and Results According to the Drug Used*

	Drug Only						Drug and Serum					
	Cases	Deaths	24 Hour Deaths	Bacteremia	Deaths	24 Hour Deaths	Cases	Deaths	24 Hour Deaths	Bacteremia	Deaths	24 Hour Deaths
Sulfapyridine	152	16	2	31	8	2	144	23	6	26	11	5
Sodium sulfapyridine	33	4	0	8	3	0	48	5	3	12	5	3
Dextrose sulfapyridine	68	8	2	12	6	1	52	7	3	10	5	2
Sulfathiazole	15	1	1	2	1	1	28	3	0	8	3	0
Sulfamethylthiazole	9	1	0	2	1	0	7	1	1	3	1	1
Sulfadiazine	29	4	1	6	1	0	22	5	3	5	4	3
Total	306	34	6	61	20	4	301	44	16	64	29	14

The latter patient went into labor after being in the hospital twenty-four hours and also had a thin empyema which was cured without surgery. All these patients were in the seventh or eighth month of pregnancy and only 1 did not deliver during the acute stage of the disease.

Four of the women in this series were pregnant; 2 were in the drug-alone and 2 in the drug-and-serum group. All recovered. Two were bacteremic; 1 had 12 colonies per cubic centimeter of blood and recovered on drug and serum; the other had innumerable colonies in the blood and recovered on sulfadiazine alone.

DRUG AND SERUM REACTIONS

The toxic reactions ascribed to the sulfonamide drugs are listed in table 7. There were not enough cases in which treatment by every one of the individual drugs was given to make a comparative table of incidence which would be of statistical significance. However, it can be said that there was frequent and severe nausea and vomiting with sulfapyridine, dextrose sulfapyridine and sodium sulfapyridine, considerably less nausea and vomiting with sulfathiazole and sulfamethylthiazole, and practically none with sulfadiazine. The serious toxic reactions were infrequent with any of the drugs and were rather well distributed.

TABLE 6.—*Complications (607 Cases)*

	Drug Only	Drug and Serum	Total
Endocarditis	7	3	10*
Meningitis	4	3	7
Empyema	11	13	24
Serous effusion	5	16	21
Pericarditis	0	1	1
Lung abscess	3	2	5
Otitis media	2	1	3

* In three of these cases the diagnosis was confirmed at autopsy.

Only one fatality due to chemotherapy occurred, a case of toxic hepatitis and aplastic anemia due to sulfapyridine. In 1 of the sulfamethylthiazole cases already reported,[2] peripheral neuritis developed following the administration of 72 Gm. of the drug.

2. Solomon, Saul, and Kalkstein, Mennasch: Sulfamethylthiazole in Treatment of Severe Type II Bacteremic Pneumonia, New York State J. Med. **41**: 270-272 (Feb. 1) 1941.

Serum reactions consisted in a small number of chill reactions and an occasional mild serum sickness. Once a questionable anaphylactic reaction possibly contributed to a patient's demise an hour after the serum had been administered.

THE FATAL CASES

Of the 78 patients who failed to survive, 22 were admitted moribund or nearly so and died within twenty-four hours of admission. Of the remaining 56, 26 had some other serious systemic disease in addition to pneumonia. A list of the chief additional diseases occurring in the fatal cases is presented in table 8. The average age of the patients who died was 59.4 years for those receiving drug alone and 61.8 years in the drug-and-serum group. Although alcoholism occurs frequently in our Bellevue patients, for lack of reliable data we have not listed it as an associated systemic disease unless there was accompaning hepatomegaly and jaundice. It will be noted that many of the associated diseases were or of themselves would have become fatal, but because pneumonia precipitated the patient's death the case was nevertheless included in the series.

TABLE 7.—*Serious Toxic Reactions: Based on 607 Cases of Pneumonia Treated with Sulfonamide Drugs*

Rash	5
Gross hematuria	6
Hemolytic anemia	2
Aplastic anemia and toxic hepatitis	1*
Granulocytopenia	6
Peripheral neuritis	1†

* Fatal case. † Followed sulfamethylthiazole.

TABLE 8.—*Associated Systemic Disease (Fatal Cases)* *

	Total Cases		24 Hour Deaths	
Disease	Drug Only	Drug and Serum	Drug Only	Drug and Serum
Heart disease				
Compensated heart disease	2	8†	0	4‡
Decompensated heart disease	1	4	0	1
Chronic nephritis with uremia	1	2	0	0
Prostatic hypertrophy with uremia	2	0	0	0
Diabetes				
With ketosis	1	2	0	0
Without ketosis	2	1	0	1
Syphilis (latent)	1	2	0	1
Leukemia				
Acute myelogenous	1	0	0	0
Acute lymphatic	0	1	0	1
Chronic lymphatic	0	1	0	1
Alcoholism with enlarged liver and jaundice	1	1	0	1
Chronic pulmonary tuberculosis	1	0	0	0
Total cases	13	22	0	10

* When more than one associated disease was present only the more serious disease is listed.
† Includes two old hemiplegias and one recent myocardial infection.
‡ Includes one old hemiplegia.

COMMENT

Fleming,[3] Bullowa, Osgood, Bukantz and Brownlee[4] and Finland, Lowell and Spring,[5] by in vitro experiments, have demonstrated that pneumococci are killed more easily by sulfapyridine plus antipneumococcus

3. Fleming, A.: The Antibacterial Action in Vitro of 2 (*p*-Aminobenzenesulfonamido) Pyridine on Pneumococci and Streptococci, Lancet **2**: 74-78 (July 9) 1938; Serum and Vaccine Therapy in Combination with Sulfanilamide or M. & B. 693, Proc. Roy. Soc. Med. **32**: 911-920 (June) 1939.

4. Bullowa, J. G. M.; Osgood, E. E.; Bukantz, S. C., and Brownlee, Inez E.: The Effect of Sulfapyridine Alone and with Serum on Pneumococcic Pneumonia and on Pneumococcus-Infected Marrow Cultures: Results in Four Hundred and Thirty-Seven Pneumococcic Pneumonia Patients Rotated for Treatment, Am. J. M. Sc. **199**: 364-380 (March) 1940.

5. Finland, Maxwell; Lowell, F. C., and Spring, W. C., Jr.: Clinical and Laboratory Studies on the Use of Serum and Sulfapyridine in the Treatment of the Pneumococcal Pneumonias, New England J. Med. **222**: 739-747 (May 2) 1940.

serum than by either agent alone. MacLeod,[6] in experimental type III infections of mice, Kepl and Gunn,[7] in early type I infections in rats, and Powell and Jamieson,[8] using a variety of types in rats, have obtained better results with sulfapyridine and serum together than with either agent alone. However, Wright and Gunn[9] failed to get better results in type III infections in rats with combined therapy than with sulfapyridine alone, or in the longer established type I infections.[7]

Haviland,[10] in studying type I pneumonia in human beings, found that administration of serum as well as drug maintained antibodies in the blood during the whole course of the disease. He suggests that, instead of waiting for the appearance of antibodies (which with drug treatment alone may not occur for several days after the temperature has fallen to normal), 100,000 units of serum be given routinely four hours after the start of chemotherapy. This is a theoretical consideration which is yet to be shown to have practical application, particularly since it has been demonstrated[11] that some patients may recover without demonstrable antibodies in the blood and that others may die despite the presence of a high titer of antibodies.

Bullowa, Bukantz and de Gara[12] have presented suggestive evidence that the presence of free capsular polysaccharide in the blood stream implies a more serious prognosis than does bacteremia alone and that sulfapyridine, alone or even with specific serum, may not cure such patients. They state that "it remains for further observations to determine whether or not a greater reduction in mortality of pneumococcal pneumonias, or other pneumococcal infections, may be accomplished by the inclusion of this laboratory criterion as a guide to therapy."

With respect to the application of experimental results to the treatment of patients, the literature is replete with opinions as to the role that serum should play in the treatment of pneumonia, but, as Finland[13] points out, there is little basis for estimating the relative efficiency of combined therapy compared with chemotherapy alone, in spite of the large number of cases included in a host of clinical reports.

To the best of our knowledge, only two studies have appeared on the use of serum in other ways than merely in seriously ill patients, Bullowa and his associates[4] have reported a series of 324 cases rotated in treatment three ways; the mortality rate in the group receiving serum alone was 17.3 per cent, in the group receiving sulfapyridine alone, 8.1 per cent, and in the group treated with both agents, 11.2 per cent. Dowling, Abernethy and Hartman[14] have recently reported a series of 162 cases alternated between drug therapy and combined therapy; the mortality rate was 12.5 per cent in the drug alone group and 9.8 per cent in the drug plus serum group. The authors felt that the patients who received serum as well as sulfapyridine responded more promptly, and that serum seemed to be a valuable adjunct to sulfapyridine in patients over 40 years of age.

Our clinical results confirm the previously reported failures in smaller series to affect the mortality rate to any significant extent by using serum routinely in addition to chemotherapy, regardless of the stage of the disease in which treatment is started. We have not noted more prompt responses in the patients receiving combined therapy.

What, then, is the present role of serum in the treatment of pneumonia? There will probably be no disagreement with the statement that serum should be used for patients who cannot tolerate the sulfonamide drugs or for those who fail to respond satisfactorily within twenty-four to forty-eight hours to drug therapy. However, our study certainly provides no argument for the routine use of serum in the treatment of all cases of pneumonia. Whether the patient was treated early or late in the disease, whether bacteremia was present or not, whether the patient was young or old, and regardless of the presence or absence of systemic disease, our results were the same in the drug-alone as in the drug-plus-serum group. The group of patients who cannot tolerate sulfonamide therapy probably should include those who have had a previous serious reaction to such therapy, e. g. granulocytopenia, hepatitis or hemolytic anemia. When sulfonamide therapy has to be discontinued before its full benefit has been obtained, administration of serum may be helpful in furthering the response or in preventing relapse.

In our private practice we have used serum several times with gratifying results for patients who failed to respond to chemotherapy. Whether these patients would not eventually have recovered without the additional use of serum we cannot say. Our Bellevue study would lead us to believe that they would have done so. In the Bellevue group there were a number of delayed responses to chemotherapy. We were constantly on the lookout for patients in the drug-only group to whom we might feel that an injustice had been done in not giving serum, but when the completed data were analyzed we found no such cases.

SUMMARY AND CONCLUSIONS

1. A series of 607 cases of pneumococcic pneumonia was alternated in treatment, by type, between chemotherapy and combined chemotherapy and serum therapy.

2. The fatality rate in the drug-alone group was 9.3 per cent, in the drug-and-serum group 9.8 per cent. The fatality rates were 11.1 per cent and 14.6 per cent respectively if twenty-four hour deaths were included.

3. In the bacteremic cases the fatality rate was 28.1 per cent with drug alone and 30.0 per cent with drug and serum. If twenty-four hour deaths were included, the fatality rates became 32.8 per cent and 45.3 per cent respectively.

4. In contrasting the results of treatment in the cases treated early with those in cases treated late in the disease, the additional use of serum did not lower the fatality rate in either group.

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5. The average response as judged by rapidity of fall in temperature in type I and type II cases was not enhanced by the use of serum.

6. No essential differences were noted in the therapeutic response obtained with the various drugs used —sulfapyridine, sulfathiazole, dextrose sulfapyridine, sodium sulfapyridine, sulfamethylthiazole and sulfadiazine.

7. Of the 78 patients who died, 48 either entered the hospital in a near terminal condition and died within twenty-four hours or had some other severe systemic disease in addition to pneumonia.

8. The present role of serum in pneumonia appears to be its use in the treatment of patients who cannot tolerate the sulfonamide drugs or who do not respond satisfactorily within twenty-four to forty-eight hours to sulfonamide therapy.

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BURNS OF THE HAND

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As most persons are dependent on the use of their hands for a living, a minor burn of the hands may be a distinct handicap and a major burn a catastrophe. Improperly treated minor burns may easily become major ones, and improperly treated major ones may result in the loss either of the hand or of the life of the patient himself.

The treatment of burns of the hand differs sufficiently from the treatment of burns elsewhere on the body to justify calling particular attention to the difference. In a previous paper [1] the early and late treatment of burns in general was discussed. Certain suggestions made in that paper for treatment of burns of the extremities need to be amplified.

Burns of the hand are caused primarily by explosion, by fire or by contact with hot liquids. The hands of the nonindustrial worker are usually exposed and therefore are more frequently burned than other parts of the body. In the agony of pain and fright the hands are often used to put out flames elsewhere on the patient's own body or on that of some one else. The ungloved hand is obviously more severely burned in instances in which sticky hot liquids or oils are spilled, in which there is a single flash of flame, as in some explosions, or in which momentary exposure to steam occurs. Burns are not often severe if the patient happens to be wearing gloves that can be removed quickly before too deep penetration of the causal agent. Grease-soaked gloves that fit tightly at the wrist and are hard to remove when ignited produce a much deeper burn than would occur if the gloves had not been worn. If hot liquids are spilled over woolen or cotton mittens with knit elastic wristlets, the heat of the liquid is often held in the fabric, resulting in injury to the deeper structures. Since the household mangle has become a popular addition to many home laundries frequent and extremely extensive burns of the hand have been seen. In the latter cases the trauma caused by the crushing action of the roller complements the trauma from the heat of the ironer.

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EARLY TREATMENT OF FRESH BURNS OF THE HAND

The heavy skin on the palmar surface is a natural protective barrier to all injuries, including burns. The dorsum of the hand is likewise toughened to some degree as compared with unexposed portions of the body. However, it is also a corollary that the tougher the hands, the dirtier they are likely to be. Débridement and complete cleansing of burns in the latter group of patients are much more difficult and less certain of success.

Burns of the hands alone are generally less shocking than burns received elsewhere on the body. The patient is more or less accustomed to receiving injuries to his hands, so the element of fright is not as great. Because the hands are exposed, pain from friction of the coverings or clothes on the burned surface is thereby avoided. When the hands are toughened and calloused they are less likely to be as sensitive to pain as some normally unexposed area. If shock does exist, it is to be combated in the usual fashion, with heat to the body, intravenous administration of fluids or transfusion of serum, morphine and the body in the Trendelenburg position. In all cases, pain is enough of a factor to warrant the routine administration of some type of sedative or analgesic.

A good first aid measure is to place the injured hand immediately in a bowl of clean water so that all the burned surfaces are below the water level. The patient will experience pain when the hand is first immersed, but this will quickly be relieved as the air is excluded from it.

After the initial pain and shock have been treated, one proceeds with the treatment of the local area. This should take the form of a careful débridement. All children and hypersensitive adults should be given a general anesthetic for this procedure. In stoical adults with a high threshold for pain adequate analgesia is often obtained with a sufficiently large dose of morphine.

The débridement consists of a thorough cleansing with a solution of 50 per cent green soap and 50 per cent hydrogen peroxide. The finger nails are clipped if they are not to be used for traction (explained later in the paper). All blisters are opened and the raised dead skin is removed. The inside of a raised blister in the hair-bearing areas must be considered as having been contaminated by the dirty surface hairs which were drawn into it as the skin was raised by the fluid formed beneath it. Some surgeons prefer to leave the blisters unbroken in areas not bearing hair, such as the palmar surface. In my experience the ones left unbroken frequently break or go on to infection through small cracks in the macerated surrounding skin. On excessively hairy hands, if the hair has not been burned off it should be removed by extremely careful shaving—even over the burned surfaces. If this is not done the hairs are later enmeshed in either the eschar or the crust that is formed. When the burn heals, the removal of either the crust or the eschar is both hindered and painful if the hairs have been allowed to become caught in it. After being cleansed and debrided, the hand is flushed with physiologic solution of sodium chloride and then soaked in some mild antiseptic solution, such as hexylresorcinol solution or solution of merthiolate. Occasionally a 70 per cent solution of alcohol is used for a final wash, but there are two objections to its use: First, it is extremely painful if the patient is not