By special roentgenographic technic it was established that the simple pleural effusion extends well above the area of percussion flatness and above the dense radiographic shadow.

On the basis of distinct radiographic zones in simple pleural effusions, several principles have been formulated for locating with greater accuracy the site for thoracentesis.

1 West Eighty-Sixth Street.

THE TREATMENT OF PNEUMOCOCCIC PNEUMONIA WITH CONCENTRATED RABBIT SERUM

ITALO F. VOLINI, M.D.
AND
ROBERT O. LEVITT, M.D.
CHICAGO

There have been few reports submitted concerning the use of rabbit serum in the type specific therapy of pneumonia. This is particularly true of the concentrated and refined serum. The steadily increasing improvements in the character of the serum have indicated the fulfilment of the factors defining a good serum for therapy; namely, first that the intravenous administration be without undue reaction and second that the adequate dose be contained in a small volume. The theoretical and practical advantages that antipneumococcus rabbit serum possesses over horse serum have been pointed out by several observers.[1] These observations, however, have been made with the unconcentrated rabbit serum. Finland and Brown [2] describe the use of the concentrated serum in sixteen cases with two deaths in type I pneumonia. The present report deals with the administration of concentrated and refined rabbit serum in 153 patients, comprising twenty-one different types of pneumococcic infection.

CASE SELECTION FOR SERUM

The principal criterion for the selection of cases suitable for serum therapy was the availability of serum. Owing to the large number of pneumonia patients, the serum supply was generally inadequate. Consequently control comparisons were easy to obtain, practically of an alternate case character. These control data are found in table 2. Serum was not refused even when the outlook was very bad, such as the presence of pulmonary edema or duration of the disease of five or six days, factors which elevate death rate percentages. A positive Francis test or an otherwise good prognosis was frequently utilized to conserve our serum supply for the more necessary or urgent indications. Unquestionably the mortality percentage is thus higher in our series than it would be if a more rigid selection had been employed.

From the Cook County Hospital and the Department of Medicine, Loyola University School of Medicine.
The Pneumonia Committee of the Cook County Hospital and the attending physicians and resident staff cooperated with the authors in this work. The serum used was supplied by the Lederle Laboratories, Inc., the Illinois State Department of Public Health and E. R. Squibb & Sons.

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METHODS OF STUDY

Typing was accomplished by the Neufeld method, applied directly to the sputum. Blood cultures were taken as a routine. Lung puncture, sputum culture and mouse inoculation were employed when difficulties with direct sputum identification were encountered. Repetition of the bacteriologic investigation was performed when the improvement expected did not result, in order to detect possible mistakes in the initial typing.

The intracutaneous test with specific polysaccharide was carried out after serum had been used whenever possible in those cases in which a negative Francis reaction had been present before serum was given.

SENSITIVITY TESTS AND UNTOWARD REACTIONS

The history of possible sensitivity was thoroughly investigated. The ophthalmic test for sensitization was employed as a routine. A positive test was not encountered in the entire series. The intracutaneous testing for rabbit serum sensitivity was discarded early in the investigation because of the frequency of positive readings, especially since we found that the administration of serum in these cases did not result in immediate reactions. No positive intravenous pressor reactions occurred. Difficulty was encountered especially in evaluating pulse rate changes during the course of the pressor test. The significance of this procedure is considered doubtful. We have not encountered an immediate reaction in the entire series.

TABLE 1.—*Types of Serum Treated Cases*

Type of Pneumonia	No. of Cases	Deaths		Bacteremia		
		No.	Per Cent	No.	Dead	Per Cent
I	30	2	6	6	1	16.7
II	34	3	8.8	6	3	50
III	14	3	21	0	0	0
IV	11	1	9	2	0	0
V	2	0	0	1	0	0
VI	1	0	0	0	0	0
VII	26	2	7.6	3	1	33
VIII	16	3	18	0	0	0
XII	2	0	0	0	0	0
XIV	2	1	50	1	1	100
XV	1	0	0	0	0	0
XVII	1	0	0	0	0	0
XVIII	3	0	0	1	0	0
XIX	1	0	0	0	0	0
XX	1	0	0	0	0	0
XXIII	1	0	0	1	0	0
XXIV	1	0	0	1	0	0
XXV	2	0	0	0	0	0
XXVIII	1	0	0	0	0	0
XXIX	2	0	0	1	0	0
XXXI	1	0	0	0	0	0
Totals	153	15	9.8	23	6	26

Corrected mortality (4 deaths under 18 hours) 11 deaths, 7.2 per cent

Thermal reactions were studied carefully because of their great frequency in the early phases of this study. This corroborates the observations of other investigators using rabbit serum. While the inherent thermogenic properties of the serum are very important, the controllable factors in this type of reaction are numerous. The rapid administration or dilution of the serum was found to be the important feature in producing chill and elevation of temperature. There was very little constancy or relationship to the particular injection in the divided dose method. This led us to try the single total undiluted dose method. The advantages of this procedure are obvious. The concentrated refined rabbit serum lends itself admirably to this technic, especially in the highly

concentrated unitage. It soon became apparent that the serum could be given at a more rapid rate without danger. The procedure now is to administer the first cubic centimeter in a period of two minutes, then the entire remainder at a rate of 1 cc. a minute. If the

TABLE 2.—*Control Types of Cases Not Treated with Serum*

Type of Pneumonia	No. of Cases	Deaths		Bacteremia		
		No.	Per Cent	No.	Dead	Per Cent
I	49	13	26	10	4	40
II	34	16	47	6	4	67
III	18	11	61	1	1	100
IV	3	2	67	0	0	0
V	6	5	83	4	3	75
VI	2	0	0	0	0	0
VII	17	6	35	4	4	100
VIII	8	1	12	2	1	50
IX	3	1	33	0	0	0
X	1	0	0	0	0	0
XII	5	2	40	1	0	0
XIII	2	0	0	1	0	0
XIV	2	0	0	0	0	0
XVI	1	0	0	0	0	0
XVII	2	0	0	0	0	0
XVIII	2	2	100	0	0	0
XIX	5	2	40	1	1	100
XXI	1	0	0	0	0	0
XXIII	1	1	100	0	0	0
XXVIII	1	1	100	0	0	0
XXIX	1	0	0	0	0	0
Totals	164	63	38.4	30	18	60

patient is receiving intravenous fluid at the moment serum administration is decided on, the needle of the syringe containing the total dose is pushed through the latex tubing near the intravenous needle and the serum is given at the rate already indicated. Otherwise the serum is given intravenously, directly from the syringe

TABLE 3.—*Age Distribution of Serum Treated Patients*

Age Group, Years	Number of Patients	Deaths
1-10	2	0
11-20	12	1
21-30	20	1
31-40	47	3
41-50	39	7
51-60	26	2
61-70	3	0
71-80	3	0
81-90	1	1
Over 50	33	3

TABLE 4.—*Race and Sex Distribution of Serum Treated Patients*

Race and Sex	Number	Deaths
A. White		
Male	75	7
Female	17	0
B. Negro		
Male	41	5
Female	14	1
C. Mexican		
Male	5	2
Female	0	0
D. American Indian		
Male	1	0
Female	0	0
Total		
Male	122	14
Female	31	1

at the indicated rate. One is cautioned to aspirate a minimal amount of blood into the syringe to indicate the intravenous position of the needle. The last sixty-nine consecutive patients in this series were treated by the single total undiluted dose technic with an incidence of only 8 per cent of thermic reactions compared to 28 per cent in our preceding eighty-four cases. With the highly concentrated unitage, this method requires only from ten to twenty minutes. A maximum of 35 cc. as the initial and total dose was given in this way without thermic reaction. A unitage concentration of 5,000 per cubic centimeter or over is particularly adaptable. We have tested the practicability of this method by having twelve interns inject sixty-nine patients. We believe that the therapeutic efficiency of the serum is enhanced by this method of administration.

Serum sickness (delayed reactions), such as arthralgia, urticaria and fever, occurred in 28 per cent of the cases. There was no relationship between the thermic reactions and the frequency of serum sickness.

CLINICAL RESULTS

This statistical study from the Cook County Hospital of a series of 153 patients with pneumococcic pneumonia treated by type specific antibody rabbit serum demonstrates a death rate less than one third, almost one fourth, that of the non-serum treated mortality. The

TABLE 5.—*Lobe Distribution of Serum Treated Patients*

Lobe	Number	Deaths
Right upper	17	3
Right middle	10	1
Right lower	53	4
Left upper	8	1
Left lower	42	3
Multilobar	23	3

TABLE 6.—*Relationship of Duration of Disease to Mortality of Serum Treated Patients*

Day of Disease Serum Was Given	Number	Deaths	
		Number	Per Cent
1st	6	0	0
2d	29	3	10.3
3d	44	1	2.2
4th	39	6	15.3
5th	23	3	13.0
6th	6	0	0
7th	3	1	33.0
8th	3	1	33.0

figures in tables 1 and 2 illustrate this rather vividly. Of the fifteen deaths that resulted, four occurred within eighteen hours after the administration of serum. If these deaths are removed from the statistics the death rate would be lowered to 7 per cent. The control series approximates very closely the serum treated figures in the several important variables, namely age, type of pneumococcic infection, bacteremia and seasonal incidence. There were thirty positive blood cultures in the control cases and twenty-three in the serum treated cases.

Table 3 shows thirty-three serum treated patients over 50 years of age with three deaths. These include eight type III cases with two deaths and nine type II pneumonias with one death.

A study of the temperature curves following serum administration in the patients who recovered shows a descent to normal within eighteen hours, a crisis termination, in seventy-seven patients. Normal temperature readings appeared in a forty-eight hour period in sixty-one cases.

An analysis of the deaths reveals the following important data: Fifteen deaths occurred. Four of these were

of bacteremic patients. Four occurred within eighteen hours after admission. No autopsies were permitted on these four. Autopsy showed in two patients suppurative pericarditis and in the remaining patient an acute pneumococcic endocarditis type VII. Deaths were restricted to types I, II, III, IV, VII, VIII, XIV (table 1).

COMPLICATIONS

This series shows relatively few complications. This tends to confirm the observations that there is probably an advantage in the penetrating and diffusing properties due to the smaller size of the rabbit serum pneumococcus antibody. Empyema occurred in five patients, all of whom recovered. Two patients with pericarditis and one with acute endocarditis died. One patient with acute suppurative otitis media complicated by meningitis with type IV pneumococcus obtained from the spinal fluid recovered. There were two other cases of otitis media, one showing extension to the mastoid. The usual supportive and symptomatic measures were utilized in the general treatment. Digitalis was not employed.

Intravenous fluids and oxygen were liberally administered. The need for these measures was distinctly less-

TABLE 7.—*Dosage Analysis (Includes Total and Repeated Doses)*

	Dosage					
	Cc. per Patient			Units per Patient		
Type of Pneumonia	Average	Maximum	Minimum	Average	Maximum	Minimum
I	33.5	120	10	123,800	250,000	100,000
II	27	55	14	117,600	240,000	46,500
III	51.8	120	12	135,000	180,000	100,000
IV	26	40	15	155,600	231,000	92,500
V	20	20	20	120,000	120,000	120,000
VI	20	..	..	160,000		
VII	21.6	50	5	210,000	450,000	70,000
VIII	27.6	40	18	139,300	180,000	70,000
XII	38.5	40	37	116,000	120,000	111,000
XIV	38	40	36	180,000	180,000	180,000
XV	100	..	..	400,000		
XVII	20	..	..	60,000		
XVIII	33	40	20	133,000	160,000	80,000
XIX	41	..	..	165,000		
XX	40	..	..	200,000		
XXIII	40	..	..	120,000		
XXIV	80	..	..	240,000		
XXV	32.5	45	20	140,000	180,000	100,000
XXVIII	40	..	..	120,000		
XXIX	41	..	..	165,000		
XXXI	40	..	..	120,000		

The unitage presented as described on the manufacturer's label.

ened in the serum treated patients, owing to the frequent abrupt recovery shortly after the use of the serum. The serum treated patients did not receive sulfanilamide or sulfapyridine. The latter drugs were employed for some patients of the control series.

SUMMARY AND CONCLUSIONS

Concentrated and refined antipneumococcus rabbit serum is an efficient therapeutic agent in the type specific treatment of lobar pneumonia. This controlled study demonstrates the mortality rate of the non-serum treated patients four times that of the rabbit serum series. Sensitivity to the therapeutic rabbit serum is rarely encountered. It is remarkably free from immediate reactions and produces a relatively small percentage of thermal and delayed serum reactions. It lends itself to the concentrated single total dose administration, which procedure saves much time and probably enhances its therapeutic efficiency.

Cook County Hospital.

RENAL COMPLICATION IN SULFAPYRIDINE THERAPY

REPORT OF FIVE CASES WITH ONE DEATH

Y. F. TSAO, M.D.
MARY E. McCRACKEN, M.D.
JI CHEN, M.D.
P. T. KUO, M.D.
AND
C. L. DALE, M.D.
SHANGHAI, CHINA

In view of the rapidly increasing popularity in the use of sulfapyridine by the medical profession, it seems wise to report in detail five cases of hematuria, some of which were complicated with abdominal pain resembling that of renal or ureteral origin and one of which was complicated with uremia and was fatal. A special report by the Council on Pharmacy and Chemistry of the American Medical Association,[1] based on reports received from about 100 investigators, mentioned toxic renal manifestations of sulfapyridine as very rare cases in which there is temporary hematuria, which in some cases has been quite severe. In the same issue of THE JOURNAL three cases of hematuria, one presenting visible blood, occurring in association with the administration of sulfapyridine were reported by Southworth and Cooke[2] of New York. In two of their cases there were severe abdominal pain of renal and ureteral origin and nitrogen retention in the blood. Antopol and Robinson[3] reported formation of uroliths in the urinary tract of rats, rabbits and monkeys fed with sulfapyridine. Gross, Cooper and Lewis[4] produced urinary calculi containing 6.4 per cent sulfapyridine and 64.1 per cent acetylsulfapyridine in twenty-seven of thirty-nine rats by the administration of 1 Gm. of sulfapyridine per kilogram of body weight by mouth in two weeks or less. They also found that these urinary calculi caused death in some and varying degrees of renal damage in other animals by complete or partial urinary obstruction, with associated hematuria, pyelonephritis and nonprotein nitrogen, as well as retention of sulfapyridine. We are in accord with Southworth and Cooke that, as far as we can determine, there is no report of cases of renal complication in human beings other than the three they have reported and the four cases of gross hematuria, usually accompanied by ureteral pain, mentioned in a report of fifty cases of pneumococcic pneumonia by Graham,[5] nor have we seen any report of a death due to such renal complication.

REPORT OF CASES

CASE 1.—M. N. W., a girl aged 6 years, weighing 29 pounds (13 Kg.), was admitted April 3, 1939, with the chief complaint on admission of fever and cough of three days' duration. There was no history of former urinary disease. Routine

From the departments of urology and pediatrics of the American Hospital for Refugees, and the departments of pathology and biochemistry, Pennsylvania Medical School of St. John's University.

All the sulfapyridine used in our hospital was prepared by Société Parisienne d'Expansion Chimique under the trade name "Dagenan." The chemical formula given is 2-(para-aminobenzene-sulfonamidepyridine).

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