

was administered at monthly intervals to one-half of a group of 70 medical students throughout a single respiratory disease season from early October to late May. The incidence of attacks of acute respiratory disease was reduced 40% in the experimental subjects as compared with the controls. The severity of the illnesses was significantly decreased in the experimental subjects as compared with their previous season experience.

The reactions to the injections were mild and consisted primarily of local soreness at the site, lasting one day in the majority of

the students. No jaundice or hepatitis was observed.

The primary object of this small clinical trial of concentrated gamma globulin was not to discover a method of preventing colds, but to determine if possible, whether or not man is capable of forming neutralizing substances for some of the undifferentiated respiratory diseases. A cumulative effect of repeated injections was suggested by the results.

A statistical evaluation of the data shows a 2% or less probability of error, which would indicate that the results were significant.

15631

Effect of Types of Treatment on Development of Antistreptolysin in Patients with Scarlet Fever.*

LOUIS WEINSTEIN AND CLIFFORD C. L. TSAO.[†] (Introduced by Chester S. Keefer.)

From the Haynes and Evans Memorials, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine, Boston, Mass.

During the course of studies on the treatment of scarlet fever with various agents, a somewhat greater incidence of recurrent pharyngitis, with or without a scarlatiniform eruption, was noted in patients treated with penicillin as contrasted with those receiving no therapy or globulin. For this reason, a study of the antistreptolysin titer in the sera of patients with this disease treated by the 3 different methods was carried out. Although it is well recognized that there is no relation between the level of antistreptolysin in the serum and the total antistreptococcal immunity of an individual, studies of this nature are of value, however, in reflecting the response of a host to experience with the beta hemolytic streptococcus. In a similar study, Rantz, Boisvert, and Spink¹ found that the administration of salicylates, sulfa-

diazine, or a "short course" of penicillin had no effect on the mean increase in antistreptolysin. When penicillin was administered over a longer interval, the frequency of antifibrinolysin response was decreased and an antistreptolysin response was also observed less often in the patients in whom bacteriologic relapse did not occur.

Methods. The cases were chosen for each type of treatment alternately and without respect to the severity of their disease. One group received only symptomatic treatment, another human gamma globulin intramuscularly (1 cc per pound of body weight up to 60 cc), and a third was treated with 120,000 units of penicillin daily for 10 days. Cultures of the nose and throat on blood-heart infusion agar and in blood broth were made daily for the first week and every other day thereafter. Serums for determination of antistreptolysin titers were drawn on the day of admission and every 7 days thereafter as long as the patient was in the hospital; a minimum of 3 serums were studied in each case, the last one being obtained at least 21 days after the start of the infection. Antistreptolysin titers were determined by the method of Rantz and Randall.² Only a dif-

* The gamma globulin used in this study was supplied by the American Red Cross.

[†] Visiting Fellow to the Haynes Memorial Hospital, and the Department of Medicine, Boston University School of Medicine, from the Department of Medicine, West China Union University Medical College, Chengtu, China.

¹ Rantz, L. A., Boisvert, P. J., and Spink, W. W., *Science*, 1946, **103**, 352.

TABLE I.
Effect of Various Types of Treatment on Development of Antistreptolysin in Patients with Scarlet Fever.

Type of treatment	Cases with rise in antistreptolysin titer		Avg antistreptolysin titer incr., Units	Cases without rise in antistreptolysin titer	
	No.	%		No.	%
Symptomatic	18	72	300	7	28
Conc. human globulin	9	64	279	5	36
Penicillin	4	13	189	29	87

ference of at least 2 tubes in titration of antistreptolysin was considered as significant.

Results. Twenty-five patients who were given only symptomatic treatment were studied. Of these 18 (72%) developed a rise in antistreptolysin titer, the average increase being 300 units. Seven patients (28%) had no change in antistreptolysin. Of 14 patients treated with globulin, 64% showed an increase in antistreptolysin, with an average of 279 units. The situation was quite different in 33 patients who received 1,200,000 units of penicillin over a period of 10 days; only 4 (13%) showed an antibody response, the average rise being considerably lower than that in the other 2 groups, 189 units. Eighty-seven per cent of the penicillin-treated patients exhibited no increase in antistreptolysin.

Analysis of the patients with respect to development of complications revealed that of the 18 untreated ones who had shown a rise in antistreptolysin titer, 2 developed glomerular nephritis, 2 had recurrent fever without evidence of a localized process, and 1 had proved rheumatic fever. Of the 7 untreated cases who showed no increase in antistreptolysin, 2 had recurrent streptococcal pharyngitis and 1 recurrent scarlet fever. In the globulin-treated group, 2 of the 9 patients who showed an increased antistreptolysin content were classified as rheumatic fever suspects, 1 developed proved rheumatic fever, and 6 showed no complications. None of the globulin-treated individuals who failed to show an antibody response suffered any complications other than cervical lymphadenopathy with fever. Three of the 9 penicillin-treated cases who developed an increased

antistreptolysin titer showed recurrences of Group A *Streptococcus pyogenes* in the pharynx without any other manifestations, and 1 was classified as a rheumatic fever suspect. Of the 29 penicillin-treated cases with no rise in antistreptolysin titer, 3 had a recurrence of *Strept. pyogenes* in the pharynx; in 2 of these, fever was present at the same time.

It is interesting to note that all the cases of rheumatic fever, proved or suspected, and of glomerular nephritis occurred in patients who developed a rise in antistreptolysin titer regardless of the type of treatment received. There appeared to be no relation between the recurrence of streptococci in the pharynx and the antistreptolysin response. In the penicillin-treated group, the incidence of recurrence of streptococci in the pharynx was as great in those who showed an increase in antistreptolysin as in those who did not.

Discussion. These data (Table I) suggest that treatment of patients with penicillin for a fairly long period of time results in a decrease in their ability to form antistreptolysin. Although it is possible that this may reflect a generally decreased formation of antibodies, no conclusions can be drawn concerning the effect of various types of treatment on the total immunologic response to streptococcal infection. As the groups studied were very small, more information obtained from a larger number of patients is necessary.

Conclusions. The administration of concentrated human serum globulin to patients with scarlet fever appears to have no effect on their ability to form antistreptolysin. Treatment with penicillin results in a decrease in the number of persons capable of developing this antibody, and also in the quantity of antibody produced by those who show an increase in antistreptolysin titer.

² Rantz, L. A., and Randall, E., PROC. SOC. EXP. BIOL. AND MED., 1945, **59**, 22.