

THE TREATMENT OF PNEUMONIA

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Spontaneous recovery from pneumococcic pneumonia depends upon the production by the body of sufficient specific antibodies to unite with all of the pneumococcus antigen (the capsular carbohydrate). This union of antibodies and antigen sensitizes the pneumococci so that they can be destroyed by phagocytosis or lysis. There are two methods of treatment of pneumonia by which the immunological processes of the body can be assisted in attaining a concentration of specific antibodies sufficient to bring about recovery of the patient. One of these consists of the intravenous administration of type-specific antipneumococcus serum, and the other is the method of chemotherapy. Antipneumococcus serum augments the supply of naturally formed antibodies and thus hastens arrival at the stage where antibodies are present in excess of the antigen or capsular carbohydrate. The newer chemotherapeutic agents, on the other hand, act by retarding the multiplication of the pneumococci. The production of antibodies proceeds at its normal rate and, in successfully treated cases, the autogenous supply of antibodies rapidly attains a concentration sufficient to unite with all of the retarded supply of antigen.

Both serum therapy and chemotherapy have proved effective in greatly reducing the mortality rate of pneumococcic pneumonia. With serum therapy the average mortality rate is now approximately 15 per cent; with chemotherapy it is 6 to 8 per cent. Although chemotherapy has a distinct statistical advantage, serum therapy has not been superseded. Further developments in chemotherapy may entirely supplant the use of antipneumococcic serum but, in the meantime, much work must be done concerning the effectiveness of combined treatment with serum and chemotherapeutic agents.

Sulfapyridine and sulfathiazole appear to be equally effective in the treatment of pneumococcic pneumonia, but sulfapyridine causes a more abrupt fall in temperature than does sulfathiazole. Flippin, Schwartz and Rose¹ observed a critical drop in temperature within twenty-four hours in 66 per cent of patients treated with sulfapyridine and in 50 per cent of patients treated with sulfathiazole. In 32 per cent of the patients treated with sulfathiazole, however, crisis did not occur until after seventy-two hours, while it was delayed to this extent in only 13 per cent of the patients who received sulfapyridine. The average duration of hospital care was the same in the two groups of patients.

Nausea and vomiting are more common in patients treated with sulfapyridine than in those who receive sulfathiazole. Drug rashes result more frequently from sulfathiazole than from sulfapyridine. Pepper and Horack² demonstrated that sulfathiazole recrystallizes in the kidney

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tubules, whereas sulfapyridine usually crystallizes in the renal pelves and ureters. They believe that the renal complications following the use of sulfathiazole will be more serious than those from sulfapyridine. Hepatitis, granulocytopenia, agranulocytosis and hemolytic anemia are rare complications of sulfapyridine therapy and apparently occur even less frequently after the use of sulfathiazole. Before a final decision can be reached concerning the relative merit of the two drugs, both preparations must be studied more thoroughly.

Sulfapyridine and sulfathiazole are administered by mouth, and the sodium salt of both drugs can be given by intravenous injection in 5 per cent solution. The initial oral dose of either preparation usually is 2 grams, and additional doses of 1 gram each are given at intervals of four hours, day and night. The optimum concentration of either drug in the blood is approximately 5 mg. per 100 cc. but favorable responses have been observed with lower concentrations. Treatment is continued until the temperature has returned to normal and has remained there for forty-eight hours. When it is necessary to administer the sodium salt of either drug by intravenous injection, because of severe nausea and vomiting or for some other reason, the usual dose is 2 to 4 grams. Subsequent injections can be given daily or more often, according to the concentration of the drug in the blood.

The development of certain of the manifestations of drug toxicity should be taken as an indication for stopping either sulfapyridine or sulfathiazole. Leukopenia with granulocytopenia, agranulocytosis, acute hemolytic anemia, hematuria, anuria, dermatitis, conjunctivitis, and drug fever are principal contraindications for further use of the preparations. The appearance of any of these conditions calls for the vigorous forcing of fluids in order that the drug may be eliminated from the body as quickly as possible. Transfusions are advisable whenever severe anemia develops. It may be difficult to distinguish between drug fever and fever due to the pneumonia. Long and his coworkers³ pointed out, however, that drug fever occurs most commonly from the fifth to the ninth day of therapy while patients who have received adequate treatment for pneumonia usually have a normal temperature long before this. The reappearance of fever in a patient whose clinical course is otherwise satisfactory suggests that the fever is due to the drug.

During the time that sulfapyridine or sulfathiazole is being administered, daily measurements should be made of the concentration of the drug in the blood. Failure of the drug to produce a satisfactory response may be due to inadequate absorption from the gastro-intestinal tract, and in a situation of this kind, the intravenous administration of the sodium salt is called for. Severe disturbances of the blood picture seldom occur early in the course of treatment but complete blood counts

should be made daily after the third or fourth day. The urine should be examined for blood each day.

Although the first measure to be employed in the treatment of pneumonia is the administration of sulfapyridine or sulfathiazole, the typing of cases of pneumococcic pneumonia by the Newfeld reaction should not be neglected. There are cases in which, in addition to chemotherapy, serum therapy should be instituted promptly, and this, of course, is impossible unless the type of the invading pneumococcus is known. Combined therapy is advisable in patients who are seriously ill when first seen or who are found to have a positive blood culture, as well as in elderly individuals and in pregnant women. It is also indicated in patients who are unimproved after forty-eight hours of treatment with sulfapyridine or sulfathiazole, in spite of a satisfactory concentration of the drug in the blood. Unfortunately, in the latter group, the delay in serum administration obviously places serum therapy at a distinct disadvantage.

Antipneumococcus serum prepared from horses or rabbits may be obtained for all of the numerically most important types of pneumococci. The serums are now highly refined so that most of the reaction-producing factors have been eliminated. Rabbit serum has the advantage of being more quickly and economically produced and of greater concentration. Moreover, fewer people are sensitive to rabbit serum than to the serum of horses. Before serum of any kind is given, however, a history should be taken concerning such manifestations of allergy as asthma, hay fever, and hives as well as with reference to the previous use of either rabbit or horse serum. In addition, the conjunctival test for serum sensitivity, and if this is negative, the intravenous test should be carried out. If these tests reveal evidence of serum sensitivity, serum therapy should be employed only in urgent situations. The serum should be well diluted with sterile physiologic salt solution and should be given very slowly.

There is still some difference of opinion as to whether or not the total dose of antipneumococcus serum should be given in a single injection or in several injections at intervals of one or two hours. Practically all workers agree, however, that the total estimated dose should be administered within the first twelve hours of treatment. The usual dosage employed is 100,000 units for all types of pneumonia except types II and III, and 200,000 units for types II and III. In the case of elderly individuals and in those with involvement of more than one lobe, these amounts may be doubled. After the amount decided upon has been administered, it usually is best to wait for twelve hours before considering the use of additional serum.

Although the modern treatment of pneumonia has greatly simplified

THE TREATMENT OF PNEUMONIA

the problem of general care of the patient, there are certain principles that must be kept in mind. The patient should be isolated and every measure should be taken to insure physical and mental rest. Adequate nursing care is essential; the position in bed should be as comfortable as possible and should be changed as necessary. Fluids should be given at frequent intervals and in amounts sufficient to keep the twenty-four hour volume of urine up to 1500 cc. In seriously ill or delirious individuals and in those who are greatly troubled with nausea and vomiting, it will be necessary to administer 5 per cent glucose in physiologic salt solution in order to maintain this level of urine output. The diet may be liquid or soft, depending upon the general condition of the patient. Prompt treatment of the pneumonia and the use of a cleansing enema as necessary are the two most effective measures in the prevention of distention. Codeine may be necessary for cough, and severe pain will at times necessitate the use of morphine. A many-tailed bandage often is very helpful in relieving less severe pleural pain. Sedatives should be given at night to secure restful sleep. Digitalis is administered only in the event that auricular fibrillation or evidence of congestive heart failure develops.

Because of the greatly shortened course of pneumonia treated successfully with sulfapyridine or sulfathiazole, the administration of oxygen is necessary much less frequently than formerly. Oxygen therapy has not diminished in value, however, and should be employed, preferably by means of an oxygen tent, whenever there is cyanosis, undue tachycardia, shallow respiration with a rate above 40 per minute, or great restlessness and delirium.

REFERENCES

1. Flippin, H. F., Schwartz, L., and Rose, S. B.: Comparative effectiveness and toxicity of sulfathiazole and sulfapyridine in pneumococcal pneumonia, *Ann. Int. Med.*, 13:2038-2049, (May) 1940.
2. Pepper, D. S. and Horack, H. M.: Crystalline concretions in the renal tubules following sulfathiazole therapy; widely patent foramen ovale in a patient aged 77, *Am. J. M. Sc.*, 199:674-679, (May) 1940.
3. Long, P. H., Haviland, J. W., Edwards, L. B. and Bliss, E. A.: The toxic manifestations of sulfanilamide and its derivatives with reference to their importance in course of therapy, *J.A.M.A.*, 115:364-367, (August 3) 1940.