THE TREATMENT OF LOBAR PNEUMONIA BY FELTON SERUM: THE SEROLOGICAL TYPING OF PNEUMONIA.*

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THERE are certain well-established facts about pneumonia and its treatment by serum. It is known, for example, that 95 per cent of primary lobar pneumonias are caused by the *pneumococcus*. It is known that there are several distinct serological types of the *pneumococcus*, labelled I, II, III, &c., the etceteras being clumped together and called group IV or "x." In the serum-treatment of pneumonia it is important to note that *types I and II pneumococci are responsible for 50 to 80 per cent of all pneumococcal pneumonias, e.g.*, they accounted for 75 per cent of all the pneumonias in the present series of 250 cases.† It is known, largely from animal experiment, that the treatment of type I, and less surely of type II, infections by anti-pneumococcal serum is effective, provided the serum is given early and in adequate dosage. Recent American results on the serum-treatment of pneumonia have supported the experimental evidence. And lastly, it is known that the action of the serum is specific, *i.e.*, a type I serum will benefit a type I infection, but will have no effect on a type II or a type III pneumonia.

In the past the efficient treatment of pneumonia by serum has been hampered by the necessity for injecting large amounts of an unconcentrated serum of low therapeutic value. Modern methods of concentrating the antibodies in serum have resulted in the preparation of anti-pneumococcal sera of considerable potency and refinement. The investigation at the Glasgow Royal Infirmary represents one of the first clinical trials of

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† This series included, besides the serum-treated cases, a large number of lobar pneumonias in Belvidere Hospital. I am indebted to Dr. T. Archibald, Superintendent, and to Dr. J. Montgomery for their co-operation and for the facilities given to examine these cases.

one of these—the Felton serum—in this country. My duty in to-night's symposium is (*a*) to discuss the serological typing of pneumonias, particularly in relation to serum-treatment, and (*b*) to describe the preparation and properties of the Felton serum.

As has been mentioned, the serum-treatment of pneumonia must be specific and must be begun early. It is therefore essential that *an accurate report of the type of infecting pneumococcus must be given as soon as possible*—a bacteriological research. The common method of typing pneumonias is to inject 0·5 to 1·0 c.c. of the saline washings of the patient's sputum into the peritoneal cavity of a mouse. The mouse being especially susceptible to the *pneumococcus*, dies within twenty-four hours of a pnèumococcal peritonitis. The peritoneal exudate is washed out with saline and an agglutination test is done with the resulting pneumococcal emulsion against the type-sera I, II and III, either macroscopically as the Widal reaction is done, or, as we prefer, microscopically on a slide (method of Sabin). While ordinarily the mouse-inoculation method of typing gives satisfactory results, it has certain disadvantages in relation to serum-treatment :—(1) *Typing must be done early.* But it is frequently difficult, sometimes impossible, to get sputum in the earliest stages of a pneumonia. However, even a minimal mucoid spit is often sufficient, although the mouse may not die within twenty-four hours : if no sputum is obtainable, a swab may be taken from the throat. (2) *Typing must be done quickly.* There is a delay of eighteen to twenty-four hours by the mouse-inoculation method. Attempts at serological typing by withdrawing peritoneal fluid from the living mouse four to six hours after injection of the sputum have not, in our hands, been uniformly successful, and we have found it wiser to wait until the animal dies. (3) *Typing must be accurate.* It is generally supposed that typing from the sputum of a pneumonic patient reveals the infecting *pneumococcus.* However, a proportion of healthy people harbour pneumococci in their throats, and so mouse-inoculation of the sputum may result in the isolation of a pneumococcal type which is not the infecting one. Such, in fact, happens, as we have been able to show, by the use of two controls—(1) by repeated examination of the sputum of each case instead of accepting the report on the first specimen, and

(2) by comparing the type isolated from the sputum with that isolated from the blood in those cases which yielded a positive blood-culture. From the former procedure it was learned that 10 per cent of 250 pneumonias would have been incorrectly typed if only one specimen of sputum had been examined—that is, the first specimen yielded a group " x " *pneumococcus* or the organisms were scanty, whereas subsequent specimens gave type I or type II *pneumococcus*. In addition, of course, there was a delay of two to three days in reporting the infecting type. Blood-culture showed that in 4 out of 43 positive cases either type I or II *pneumococcus* was present in the blood (presumably the infecting organism), while a group " x " *pneumococcus* was repeatedly isolated from the sputum. Serological typing from the sputum is therefore not the ideal method of determining the infecting type of *pneumococcus*. Because of the delay in typing and the discrepant results obtained, it has been the practice with the serum-treated cases to commence treatment at once with the polyvalent (types I and II) serum and to continue treatment until the patient was better or the pneumonia was proved not to be either a type I or II infection.

An alternative method which would quickly and accurately determine the type of the infecting *pneumococcus* is therefore desirable. *Blood-culture* fails because the organism may be isolated from the blood only in 20 to 30 per cent of pneumonias; in the present series 43 out of 184, or 24 per cent, were positive. *Lung-puncture* has been advocated and the risk is probably minimal, but the method is not always successful. In a small series done in conjunction with Dr. Montgomery, of Belvidere Hospital, only 50 per cent were positive. In both of these methods there is also the disadvantage of delay—twenty-four hours or longer. A method with which we are at present experimenting, and which has been used in America as an index for the continuance of serum-treatment, may solve the problem, since by its use an accurate report of the type of infecting *pneumococcus* may be given a few hours after the patient's admission. It depends on the injection of an initial dose of polyvalent (I and II) anti-serum. At a suitable time (half to one hour) after the injection, blood is withdrawn by capillary tube from the patient's ear or finger, the serum is separated and is tested for the presence of

agglutinins to types I and II *pneumococci*. If, for example, agglutinins to type I are present and none to type II, it is concluded that the pneumonia is a type II infection, since the corresponding agglutinins contained in the infected serum have been neutralized, while those for type I are still circulating in the blood.

The serological typing of pneumonias has other uses apart from its relation to serum-treatment — in diagnosis, for example. But particularly in epidemiological studies, it indicates the incidence of the different types which may vary in the same country from year to year or in different countries at the same time. This is important in regard to mortality statistics. It is known that type I and group " x " are the least virulent varieties of the pneumococcus—type III is the most virulent but is rare in this country; type II is more virulent than type I. Hence a proportionately high incidence of type II infections would in itself tend to raise the pneumonia mortality rate in a particular district. Typing helps to prove the infectivity of pneumonia, *e.g.*, in a family or in the wards of a hospital. It is also the means of discovering " carriers " of the more virulent and infective types. These may be either healthy contact carriers or convalescent carriers: the latter may harbour the infecting organism in the throat for a considerable time after the infection, *e.g.*, in the present series the examination of cases three to six months after recovery showed that a fair proportion of them still " carried " the infecting *pneumococcus*.

The following table shows the distribution of 250 pneumonias in the serological types:—

LOBAR PNEUMONIA: TYPE-INCIDENCE.

	Total Cases (G.R.I. + Belvidere) 250.			
Type	I	II	III	IV
	83	104	5	58
	33·2%	41·6%	2%	23·2%
	G.R.I.—57 Cases (+ 3 untyped).			
	16	25	1	15
	28·2%	43·8%	1·7%	26·3%

BLOOD CULTURE: Total Cases 184: 43 positive, 24%.
G.R.I. 60 Cases: 11 positive, 18%.
Mortality: 18 Cases, 44%.

The Felton Serum.

The initial preparation of the Felton anti-pneumococcal serum is on orthodox lines. Horses are immunized with killed virulent cultures of the organism, then bled and the serum separated. Twenty per cent anhydrous sodium sulphate is added to the unconcentrated serum and allowed to stand in an incubator at 37° C. until a precipitate forms. After filtration the precipitate is dialized in running water for 5 to 7 days. The content of the dializing sac is then adjusted to a pH of 4·6, at which point a second precipitate forms. This precipitate is removed, and the supernatant fluid containing the antibodies plus globulin and some albumin is readjusted to a pH of 6·8 and diluted in 4 to 5 times its bulk of cold distilled water. The white precipitate which forms contains practically all the protective substances in the original serum and is dissolved in concentrated form in normal saline. There is thus a concentration of antibody and also elimination of the albumin fraction, which is largely responsible for the thermal and anaphylactic reactions. As regards the properties of the serum, it is antibacterial—not antitoxic. It is rich in agglutinins, opsonins, &c., which act directly on the *pneumococcus* and make it susceptible to phagocytosis. Hence it prevents further proliferation of the infecting organism. In addition it neutralizes the poisonous product of the *pneumococcus* which circulates in the blood—a specific soluble carbohydrate substance which is associated with the capsule of the organism. The serum does not affect the progress of already consolidated lung, but by counteracting the pneumococcal poisons it may indirectly combat anoxæmia and cardiac failure.