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## Cutaneous reaction to pneumococcic filtrates.

By W. P. LARSON.

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Pneumococcus filtrates supplied by Olsen have been injected into mice intraperitoneally. A limited number of mice which received one injection of the filtrate in this way, when killed 24 to 48 hours later, showed marked congestion of the lungs. Microscopic sections showed congestion with hemorrhage throughout the lungs.

The filtrate was injected intracutaneously in 17 normal individuals, as well as three convalescent pneumonia cases who had received pneumonia antitoxin. Nine of the 17 healthy individuals gave a positive skin test and 8 a negative reaction. The convalescent pneumonia patients were all negative. The positive skin tests were present in about 8 hours following the injection, reached the height of their reactions in about 24 hours, after which they began to fade. At the end of 48 hours the reactions had all disappeared.

These observations, considered with those presented by Olson, indicate that his filtrates contain a soluble toxin.

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## Studies on pneumococcus filtrates.

J. G. OLSON. (Introduced by W. P. Larson).

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Following the work of W. P. Larson<sup>1</sup> on the production of an antipneumococcus serum by means of whole pneumococcus cultures treated with Sodium Ricinoleate, studies were made to determine the mode of action of the serum. Used clinically, Larson's serum promptly and strikingly relieves the symptoms of intoxication in a large percentage of cases of pneumonia; and inasmuch as the serum does not appear to possess a high titre of

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<sup>1</sup> PROC. SOC. EXP. BIOL. AND MED., 1925, xxii, 172.

animal protective bodies, as ordinarily measured, other avenues of approach were tried.

It developed that we could produce the clinical and pathological symptomatology of pneumonia in suitable animals with certain sterile pneumococcus filtrates intraperitoneally, and they may thereby be caused to develop dyspnea, prostration, and even death. At autopsy the lungs show congestion, infiltration, hemorrhage and even hepaticization.

Such filtrates, when injected into the skin of certain animals, *e. g.*, rabbits, produce a reaction, in 16 to 24 hours, for an area of redness one to several centimeters in diameter may develop, such a reaction slowly fading over a period of several days. By suitable dilution, it has been found possible to so control the dosage, that 0.1 cc. will cause an area of redness 1.0 cm. to 1.5 cm. in diameter to appear, and reaches a maximum in 16 to 24 hours.

The phenomena described may be successfully produced in other animals than those mentioned.

It is obvious, of course, that a restricted line of procedure must be followed in the preparation of the filtrates.

We have found that sera prepared by Larson's method possess, in high degree, power to prevent both the lung changes mentioned, and also the cutaneous reactions. Moreover, sera from certain animals that have been given one or more injections of such filtrates are found to possess power to prevent the reactions. There seems to be a definite quantitative relationship between the ability of a serum to inhibit the lung phenomena and to prevent cutaneous reactions. What is especially interesting is the fact that it is also apparently possible to measure the relative therapeutic power of such sera on the basis of their ability to inhibit the cutaneous or pulmonary changes, both in experimental animals and in clinical cases of pneumonia.

From the above experiments it would appear that a toxin specific to the pneumococcus has been demonstrated and that the action of the Larson serum and of the serum produced by the injection of the toxin is antitoxic. Indications are that the toxin may be of value in the production of active immunity to pneumococcus infections and may be utilized as a measure of resistance.

Exhaustive experiments designed to throw light on the nature and mode of action of the toxin and antitoxin are being carried out.