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A Method for Determining the Chill-Producing Properties of Anti-Pneumococcic Serum.*

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Following the intravenous injection of concentrated, anti-pneumococcus horse serum, there frequently occurs a systemic reaction of varying intensity. The reaction comes on usually in from 30 to 60 minutes after the injection, and begins almost always with a chill, which is accompanied and followed by an elevation of temperature.

It seems that this reaction is not an essential factor in the beneficial effects of the serum, indeed it is considered by many to be a distinct disadvantage and to be responsible for some limitation of a more general employment of the serum therapy. Unfortunately there has been no method devised to determine, in advance of its use, whether the serum to be employed contains chill-producing properties, and so this knowledge is obtained only after the occurrence of the reaction in a treated patient. The present communication is a report of a successful imitation of the reaction in dogs, thus affording a method of determining before its clinical employment, the presence or absence of the chill-producing factor in any given sample of serum.

In the first experiments, it was found that a serum which had produced a typical reaction in a patient, produced a corresponding reaction when injected into the jugular vein of a dog. On the other hand, a serum which had failed to give a reaction in a patient, also failed to give one in a dog. Following these initial experiments, a considerable number of serums, which had been or subsequently were used in the pneumonia wards at Harlem Hospital, were tested. The experimental results were in striking agreement with the clinical ones.

The procedure in the animal test is as follows: The dogs selected are of the short-haired variety, of a weight between 5 and 10 kilos; the temperature is taken by rectum before and at 20 minute intervals after the serum injection; the thermometer is inserted the same distance for each reading; the serum is injected into the jugular vein, no local anesthesia or operative exposure being necessary.

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The criterion of a positive reaction is a rise of temperature of 1.5°F or more, occurring within 60 to 75 minutes, and maintained for at least an hour. A chill may or may not be present, apparently unrelated to the degree of temperature elevation. In a typical, strong reaction, there is first a definite chill, coming on within half an hour after the injection; the rise in temperature is observed about 10 minutes later, and reaches a maximum of 2°F or more in about 15 minutes. The temperature remains elevated for 2 hours or longer The dose of the serum required to produce effects varies from 1 to 10 cc., practically the same as that required in patients.

Just as in patients, there is some variability in the responsiveness of different dogs to the test, and it is desirable in the selection of animals to make a preliminary control test, not only to determine the reaction to a known chill-producing serum, but the lack of reaction to a non chill-producing serum as well. The same dog may be used 6 or more times without the development of tolerance. On the other hand if the injections are too widely spaced, anaphylactic phenomena occur.

The accompanying table is illustrative of the experimental results.

TABLE I.

Serum	Test on Dogs		Test on Patients	
	Dose	Effect	Dose	Effect
	cc.		cc.	
No. 1	1	+2.2°F	2	Chill
" 1	5	Marked chill, +3.5°F	—	—
" 2	10	None	10	No chill
" 3	4	Marked chill, +3.3°F	4	Marked chill
" 7	10	None	20	No chill
" 11	10	+1.0°F	10	Mild chill
" 14	5	+1.9°F	5	Chill
" 14	10	Chill, +2.2°F	—	—
" 18	10	+2.0°F	10	Chill
" 23	3	+1.2°F	—	—
" 23	5	Chill, +2.0°F	5	Chill
" 24	10	None	10	No chill

From work already done it appears possible to differentiate chill-producing from non chill-producing serums before these have been subjected to the various procedures for refinement. This, and attempts to determine the nature of the chill-producing factor will be reported later.