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Active Hypersensitivity from Inhalation of Finely Atomized Fluid Antigens.*

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Recent reports indicate that influenza may be successfully treated by inhalation of finely atomized particles (aerosol) of specific antiserum.[1-3] If further investigation confirms these reports, it is likely that this form of treatment will be attempted on a large scale. Because the supply of human convalescent serum is limited, antiserums of other than human origin will in all probabiity be used. The possibility must be considered that a foreign serum used in this manner may produce active as well as passive sensitization and thus bring about a dangerous state of hypersensitivity. It is also of great importance to know whether or not this method of treatment will produce serious allergic reactions such as anaphylactic shock, asthma, or pneumonitis in patients who are already hypersensitive to the particular antiserum used.† In order to answer these questions as well as to explore further some of the basic mechanisms which concern "natural" acquired sensitivity, blood serum from animals commonly used for the production of therapeutic antiserums (rabbits, goats, swine, and horses) and egg albumin were tested in a manner which would simulate their use under the conditions mentioned above.

The procedures employed in this study were essentially the same for each of the 5 antigens tested as illustrated by the following example: A group of 24 guinea pigs weighing 300-350 g each was subdivided into 3 groups of 8 each. Group 1 was placed in a closed chamber and exposed for 20 minutes to an atmosphere into which undiluted sterile swine serum was continuously atomized. This administration of serum by inhalation was repeated daily for 5 successive days. The finely atomized particles of serum were diffusely and densely distributed throughout the 27x14x14-inch exposure chamber. Group 2 received a single intraperitoneal injection of 0.5 cc of swine serum. Group 3 received no treatment and served as controls.

Fourteen days after the first treatment with swine serum, precipitin titers were determined on the pooled serums from each group using the antibody dilution method of Cannon and Marshall; see Table I.

Four weeks after guinea pigs had been injected with or had first inhaled swine serum, animals of all 3 groups were exposed to finely atomized swine serum. In every instance, the animals which had been previously treated, either through inhalation or by injection of

TABLE I.
Antibody Response Following Administration of Antigen.

Antigen used	Manner of administration	Antibody titer
Swine Serum	Inhalation (Aerosol)	<1:10
	Injection	*
Rabbit Serum	Inhalation (Aerosol)	<1:10
	Inj.	1:512
Goat Serum	Inhalation (Aerosol)	1:40
	Inj.	1:640
Horse Serum	Inhalation (Aerosol)	1:80
	Inj.	1:80
Egg Albumin	Inhalation (Aerosol)	<1:10
	Inj.	1:10

* Serum was unusable because of bacterial contamination.

* This investigation was aided in part through the Influenza Commission, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Division, Office of the Surgeon General, U. S. Army.

1 Smorodintseff, A. A., Gulmow, A. G., and Tshalkina, O. M., *Z. f. Klin. Med.*, 1940, 756.

2 Henle, W., Stokes, J., Jr., and Shaw, D. R., *J. Immunol.*, 1941, **40**, 201.

3 Smorodintseff, A. A., and Shishkina, O. I., *Arkiv. Biologischeskikh Nauk*, 1938, **52**, 132.

† References to literature concerning immunologic response to inhaled antigens may be found in Ratner, B., *Allergy, Anaphylaxis and Immunotherapy*, Williams and Wilkins, Baltimore, 1943.

swine serum, exhibited varying degrees of anaphylactic shock. This was characterized by dyspnea, coughing, sneezing, roughening of the coat, and prostration. A moderate to marked hyperemia and edema of the conjunctivæ also developed. Swine, rabbit, goat, and horse serum each caused approximately the same degree and type of allergic reaction in specifically sensitized animals regardless of whether the initial, sensitizing dose had been inhaled or given parenterally. Of 56 sensitized animals which were treated in this manner, 3 died in the chamber during exposure to an atomized specific antigen. Two of these had been sensitized by a single intraperitoneal injection of 0.3% crystalline egg albumin, the third by inhalation of the same substance. Other than this, however, anaphylactic reactions were sub-lethal and symptoms usually subsided within a few hours after each exposure to aerosol. Control animals gave slight or no reactions. Four weeks after sensitization by inhalation of various antigens, 14 guinea pigs were injected intravenously with 0.3 to 0.5 cc of the specific antigen. Twelve of the 14 animals in this group died of typical anaphylactic shock.

It has been suggested that repeated inhalations of small doses of anti-influenzal serum might be used prophylactically. A second series of experiments, using goat serum alone, was conducted to determine whether or not widely spaced inhalations of smaller quantities of serum would also produce a state of active hypersensitivity. Guinea pigs and rabbits were exposed to aerosols of undiluted or diluted (1:10) goat serum for 20 minutes at weekly intervals. Upon the third of the weekly exposures, mild reactions were observed. By the fifth week of such treatment, allergic reactions were quite marked and were in every way similar to those previously described.

Histologic studies of tissues from animals which were autopsied two days following the last of several (5 or 6) 20-minute exposures to atomized antigen revealed acute inflammatory changes in lungs, trachea, and nasal mucosæ. These were present to some extent in all of the animals, including controls, but were more pronounced in those which had been previously sensitized by injection or inhalation of the specific antigen.

From these observations it is apparent that active sensitization can be readily accomplished by inhalation of finely atomized fluid antigen and that serious allergic reactions, even fatal anaphylactic shock, may occur when hypersensitive animals inhale aerosol of specific antigen.

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Experimental Basis for the Chemotherapy of *Trichomonas vaginalis* Infestations. I.

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Clinical reports clearly indicate that an entirely satisfactory therapeutic agent is not established for the treatment of *Trichomonas vaginalis* infestations. *In vitro* studies of the trichomonacidal effect of various compounds can supply only collateral data for future therapeutic trial. Such factors as prolonged exposure of the parasite to the medication mixture, the intervention of tissue exudates, and preparatory cleansing and drying of the site of infection lead to divergence of *in vitro* and clinical findings.

The data reported in this paper were obtained from tests of a number of proprietary compounds which were solicited from the manufacturers, as well as others selected for reasons of theory or convenience. The list will be enlarged in future studies by investigation of many compounds suggested by clinical literature and will be supplemented by