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Sensitization of Guinea Pigs to Cotton Linters and House Dust Extracts.

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Since Cooke¹ first directed attention to the importance of house dust as a specific excitant of asthma, there have been many attempts to characterize a hypothetical dust allergen. Its existence, as an entity, was recently questioned by Walzer² on the basis of critical examination of available clinical data pertaining to dust sensitiveness. He found among these data evidence of reactions which he attributed to non-specific irritative principles in extracts of house dust or other dusty substances. Noted also was the fact that no one had succeeded in sensitizing experimental animals to house dust³ nor to suspected parent substances, cotton linters,⁴ kapok fiber dust,⁵ or mold⁶ (*Aspergillus fumigatus*).

Adaptation of the alum precipitation technic devised by Harrison⁷ and employed by Caulfeild, Brown and Waters⁸ in sensitizing guinea pigs to ragweed pollen extracts, has proved effective for establishing anaphylactic sensitiveness to water extracts of linters and house dust, respectively. Comparing anaphylactogenic properties of these extracts led to recognition of a non-specific factor in house dust extracts which induced anaphylactoid symptoms in unsensitized guinea pigs.

Two samples of clean, unused cotton linters were extracted with distilled water saturated with toluene. A 100 g sample was divided into 5 equal portions. To one 20 g portion sufficient solvent (100 ml) was added to saturate the fibers. After agitating for 48 hours, in a jar fixed on a rocking platform, the mixture was transferred to a Buchner funnel. The solution, recovered by suction and mechanical

¹ Cooke, Robert A., *J. Immunol.*, 1922, **7**, 147.

² Walzer, Matthew, *J. Allergy*, 1938, **10**, 72.

³ Ramsdell, Susan G., and Walzer, Matthew, *J. Immunol.*, 1927, **14**, 207.

⁴ Cohen, Milton B., Nelson, Tell, and Reinartz, B. H., *J. Allergy*, 1935, **6**, 517.

⁵ Wagner, H. C., and Rackemann, F. M., *J. Allergy*, 1936, **7**, 224.

⁶ van Leeuwen, W. S., Bien, Z., and Varekamp, H., *Z. f. Immunitätsforsch. u. exp. Therap.*, 1923, **37**, 77.

⁷ Harrison, W. T., *U. S. Public Health Reports*, 1934, **49**, 462.

⁸ Caulfeild, A. H. W., Brown, M. H., and Waters, E. T., *J. Allergy*, 1936, **7**, 451.

pressure, was made up to 100 ml with water and used in the same manner to extract in succession the 4 remaining portions of the sample. Extract recovered from the last portion was made up to 100 ml and sterilized by Seitz filtration.

House dust samples from 2 sources* were heterogeneous mixtures of the sort obtainable from household vacuum cleaners. A 20 g sample of dust was mixed with 100 ml of distilled water saturated with toluene and was agitated on a rocking platform for 24 hours. After standing for 48 hours at 6°C, without agitation, the solid residues were separated and the sterile extract was recovered by Seitz filtration.

To the extracts obtained by the described procedures, a 10% solution of potassium alum was added to final concentration of 1% alum ($\text{Al}_2(\text{SO}_4)_3 \cdot \text{K}_2\text{SO}_4 \cdot 24\text{H}_2\text{O}$). Adjustment of reaction to pH 7 caused appearance of a copious precipitate. The mixture was allowed to stand 24 hours. For sensitizing, this neutral alum-treated extract was shaken and a dose of the suspension was administered subcutaneously. For control and shocking injections, the original sterile water extracts were used, with NaCl added to concentration of 0.9%, just before intravenous administration.

Anaphylactic sensitivity to the original water extracts of linters and dust, respectively, has been demonstrated in guinea pigs sensitized by subcutaneous injection of the alum-treated extracts. Guinea pigs were not sensitized after intraperitoneal injection of untreated water extract of linters, in 0.9% NaCl, administered in single or multiple doses totaling 5 or 6 ml.

Anaphylactoid symptoms, interpreted as evidence of a non-specific toxic factor, were observed in unsensitized animals following an initial intravenous injection of water extract of house dust. These symptoms were watering eyes, dyspnea and scratching of nose and eyes. Contractural spasms or coughing did not occur. Autopsy revealed emphysematous lungs, spotted with numerous punctate hemorrhages. Clotted blood was found in both thoracic and peritoneal cavities in animals dying from or sacrificed while recovering from anaphylactoid symptoms. Damage indicated by hemorrhagic areas was much more extensive than observed in animals exhibiting anaphylactic shock of like severity.

Recognition of an inherent toxic principle in house dust extract rests upon differences in doses required to induce ante- and post-mortem evidence of anaphylaxis in sensitized guinea pigs, and ana-

* Sample HD-E obtained from B. G. Efron, M.D., New Orleans, La. Sample HD-P obtained from H. S. Bernton, M.D., Washington, D. C.

TABLE I.

Animal No.	Body wt, g	Sensitizing dose	Sample	Incubation period, days	Body wt, g	Test injection, ml	Symptoms
78	330	1 ml Linters extr.	C-5	27	459	1.0	Moderate anaphylaxis
84	363	1 " " "	C-5	54	604	2.0	Severe " "
142	355	2 " " "	C-5	133	739	2.0	Moderate " "
444	318	2 " " "	C-16	29	520	3.0	" " "
489	305	2 " " "	C-16	47	413	4.0	Fatal " " 4 min.
435		None—Control	C-16		496	5.0	None " "
487		" " "	C-5		418	4.5	" " "
490		" " "	C-5		573	4.6	" " "
498		" " "	C-16		665	5.0	" " "
479	237	2 ml Dust extr	HD-E	32	460	0.4	Fatal anaphylaxis 4 min
481	259	2 " " "	HD-E	39	390	0.4	" " " "
483	262	2 " " "	HD-E	57	598	0.4	Moderate " "
486	247	2 " " "	HD-E	57	528	0.4	Fatal " " 30 min.
566	276	2 " " "	HD-P	33	469	0.8	Fatal " " 4 "
504		None—Control	HD-E		473	1.0	None Moderate anaphylactoid
509		" " "	HD-E		340	2.0	" " " "
510		" " "	HD-E		327	2.0	" " " "
503		" " "	HD-E		416	2.0	Fatal " "
564		" " "	HD-P		465	0.8	None " "
567		" " "	HD-P		470	0.8	" " " "
573		" " "	HD-P		331	3.0	Moderate anaphylactoid

phylactoid symptoms in the unsensitized animals. Whether the inherent toxic principle detected in two samples of house dust is responsible for non-specific positive cutaneous reactions in human subjects has not been determined. However, in associated clinical trials, house dust extract "E" has been found to possess skin whealing agents of unusual potency.

Specimen results appear in Table I.

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Aortic Pressure and the Diastolic Volume Law of Energy Output in Cardiac Contraction.

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The conclusion of Starling and Visscher¹ that the oxygen consumption of the isolated heart under constant chemical and temperature conditions is determined solely by the initial length of its muscular fibers has been the subject of some disagreement. Stella² asserted that at constant initial fiber length, the energy output of the tortoise ventricle in contraction varied with the arterial resistance. It was shown, however, by Moldavsky and Visscher³ that a systematic error in measurement of diastolic ventricular volume occurred in Stella's experimental procedure and that when this error was obviated by suitable means the energy output in contraction was found to depend only upon initial fiber length and was entirely unrelated to pressure or work conditions.

Kiese and Garan⁴ have attacked this problem again with the mammalian heart-lung preparation. In a series of exact studies they have shown that the oxygen consumption of the heart is significantly greater when a diastolic ventricular volume increase is brought about by raising the inflow, and therefore the minute volume, at constant arterial pressure, than when the same diastolic volume is obtained by increasing the aortic pressure, keeping the inflow constant at a low level. Stated in numerical terms, they found in a typical experiment that in order to have identical oxygen consumptions the

¹ Starling, E. H., and Visscher, M. B., *J. Physiol.*, 1927, **62**, 243.

² Stella, G., *Ibid.*, 1931, **72**, 247.

³ Moldavsky, L. F., and Visscher, M. B., *J. Physiol.*, 1937, **91**, 23.

⁴ Kiese, M., and Garan, R. S., *Arch. f. Exp. Path. u. Pharmac.*, 1938, **188**, 226.