strophanthin. The period of supernormality has in many cases been followed by a period of prolonged subnormality.

In the nonrhythmic preparation, the development of supernormality may result in the production of 2 or more responses following a single electrical stimulation. Such Lucianni groups have been directly attributed to supernormality by Ashman and Hafkesbring.[1] In the spontaneously rhythmic preparation, supernormality may result in the production of occasional extrasystoles, of regular coupling of beats, and of shorter or longer bursts of tachycardia. In this stage there may be multiple beat foci and with severe poisoning fibrillation may ensue. The similarity of this series of events to the effects seen with toxic dosages of the digitalis-like drugs on the mammalian ventricle is striking and there seems no reason to doubt that the mechanism is the same for the two cases.

The methods by which we have produced supernormality in the ventricular preparation are those which will cause its production in the nerve trunk (Graham[2, 3]). Moreover, the subnormal period (Graham[4]) may be found in the two preparations following supernormal period (see also Ashman and Wooley[5]). The results of these experiments, thus offer further indication of the similarity in the two preparations, of the fundamental processes concerned with the recovery of electrical excitation following a response despite the very great differences in their manifest time functions.

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Relation of Muscle Receptive Substance to the Contractile Mechanism. Responses to Heat and Drugs.

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This paper reports further work in an investigation of muscle-receptive substance and contractile mechanism in smooth muscle

1 Ashman, R., and Hafkesbring, R., PROC. SOC. EXP. BIOL. AND MED., 1925, **23**, 162.

2 Graham, H. T., *Am. J. Physiol.*, 1933, **104**, 216.

3 Graham, H. T., *Am. J. Physiol.*, 1934, **110**, 225.

4 Graham, H. T., *Am. J. Physiol.*, 1935, **111**, 452.

5 Ashman, R., and Wooley, E., PROC. SOC. EXP. BIOL. AND MED., 1925, **23**, 159.

fibers, already reported briefly.[1, 2, 3] The results here reported seem to confirm the hypothesis that "This receptive substance is very labile to heat."[2] They seem to prove that the receptive substance can be destroyed without "killing" the contractile mechanism. The results, therefore, suggest that the receptive substance is not, as Langley[4] postulated, a side chain of the contractile mechanism, but rather an independent structure or substance as postulated by Dixon.[5]

Method. The muscles here studied were the iris muscles of fetal pigs about 5 days before birth (length, 260 mm, plus or minus 10 mm). The fetuses were obtained from the recently killed mother, quickly excised, measured, and the marked heads placed in a mixture of hog saline and saline ice. For testing, the eyes of 7 fetuses of a litter were excised, placed in small individual pyrex glass cups in pairs, and covered with a glass plate. One eye of each pair was used as a control, the other for the test. The action of a drug or of a temperature change was measured by measuring the short diameter of the pupil before and after application. This measurement was made with fine bow dividers under illumination by both transmitted and reflected light, and the value read off on a diagonal scale. This value was corrected for any simultaneous change in the control.

To determine the lability of the receptive substance to heat of 40°C, 6 of the 7 pairs of eyes were placed in a thermoregulated physiological saline bath at 40°C and a pair removed at regular intervals and cooled in a mixutre of saline and saline ice. The unheated pair of eyes was used as a control in the subsequent tests. The destruction of the cholinergic receptive substance was measured by the amount of decrease in pupil constriction to 3 drops of 0.3% carbaminoyl choline hydrochloride dropped onto the cornea. The tonus in the dilator muscle fibers was measured by the amount of dilation after atropinizing the carbaminoyl choline treated muscles with 2 drops of 0.01% atropine sulfate. To test the irritability and contractility of the contractile mechanism after destruction of the receptive substance, the eyes were rapidly cooled or heated, and the amount of pupillary constriction or dilation measured.

Results. The facts here reported were derived from a study of

[1] Shaklee, A. O., and Christensen, K., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1619.

[2] Shaklee, A. O., Christensen, K., and Oppenheimer, H. E., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 225.

[3] Shaklee, A. O., Christensen, K., and Kaplan, A., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 399.

[4] Langley, J. N., *J. Physiol.*, 1905, **33**, 374; 1907, **36**, 347.

[5] Dixon, W. E., and Ransom, F., *Ergebn. d. Physiol.*, 1912, **12**, 765.

TABLE I.
Data.

Heating, Temp.	0	35°-40°C	Additional Heating at 40°C						42°
" , Durat. (min.)	0	15±	15	30	60	90	120	150	30
Cbmcl. (Const., %)	100	104	72	42	7	4	0.5	0	0
Atrop. (Dil., %)	100	102	64	35	8	7	1.7	0	0
Cooling (23°-0°) Const. %							5±	5±	0
Warming (0°-37°) Dil. %							10±	10±	0

Abbreviations: "Durat.," duration; "Cbmcl. (Const., %)" gives the average amount of pupillary constriction to 3 drops of 0.3% carbaminoyl choline hydrochloride, expressed in % of the control; "Atrop. (Dil. %)," the subsequent average dilation to 2 drops of 0.01% atropine sulfate.

more than 6 successive litters, 42 fetuses, 84 eyes, 2136 careful measurements with a background consisting of a study of 99 other litters on the same general problem.

Findings and Tentative Conclusions. 1. Both the radial and constrictor muscle fibers, in the unheated eyes, and in those heated less than about 120 min at 40°C, possessed tonus; for after the pupil was constricted by carbaminoyl choline, paralysis of the cholinergic receptive substance by atropine, produced dilation. 2. The cholinergic receptive substance was completely destroyed by heating at 40°C, without destroying the contractile mechanism; for the amount of pupillary constriction that could be produced by carbaminoyl choline became progressively less as heating went on, until, at the end of about 120 min, it was entirely gone. Yet, after this complete destruction of receptive substance, cooling the eye produced constriction and warming produced dilation; while eyes in which the contractile mechanism had been "killed", by heating at 42°C for 30 min, gave no response to like changes in temperature.

Corollary: 1. The cholinergic receptive substance in the muscle fiber is independent of the contractile mechanism. 2. Carbaminoyl choline and atropine act on a cholinergic receptive substance in the sphincter of the iris. 3. These findings suggest further, that, in the process of "stimulating" a receptive substance in the living animal, the acetylcholine liberated from a nerve ending, may act as a catalyst on the receptive substance, causing it to discharge a second "stimulating" substance into the contractile mechanism of the muscle fiber. 4. The findings are in harmony with our former findings, and with the chemical theory of neuro-muscular transmission.