Technical Papers

Sudorific Action of Adrenalin on the Human Sweat Glands and Determination of Their Excitability

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Although there is a vast amount of information concerning the responses of the human sweat glands to nervous, thermal, or chemical stimuli, our knowledge regarding the excitability of these glands is very scanty for lack of adequate methods of investigation. Numerous difficult problems of the physiology and pathology of the sweating mechanism, problems still unsolved, can be approached from a new angle by investigating the excitability of the sweat glands.

Recently we have devised a new method (*3*) which has two advantages over Minor's widely used method (*1, 2*): first, the sweat secretion from individual glands can be visualized directly by black spots at the sweat pores of the skin; second, the secretion in minute quantity can be detected with certainty by preventing its evaporation.

Our method will be described briefly. The area of the skin to be examined is painted with 2% or 3% iodine-absolute alcohol solution and dried completely. Then this area is painted again with a mixture of 50 to 100 g fine starch powder and 100 ml castor oil. For observation with great precision, it is desirable to limit the starch grains to about 10 μ in diameter. When sweating occurs, spots or rings of black-stained starch grains appear at the pores of functioning sweat glands and can be seen in a transparent layer of the starch-castor oil mixture, with the magnifying lens or naked eye. The usefulness of this method is illustrated in Fig. 1. The duration and cessation of sweating can be determined by repeatedly wiping the sweat spots with a dry cloth and painting with the starch-castor oil mixture. The secretion of sweat in such a small quantity as 0.00005 mg from one gland suffices to make a sweat spot visible to the naked eye.

Beginning with the work of Elliott, a number of investigators have found a local inhibitory action of adrenalin on spontaneous sweating, but have failed to find its sudorific action on the human sweat glands. Thus, it has become accepted as general knowledge that human sweat glands are not stimulated by adrenalin and this has provided a basis for the concept that the sweat glands in man are innervated by the sympathetic cholinergic nerve fibers. On the other hand, some authors have reported that under certain conditions sweating is elicited by adrenalin, but these findings have been rejected or considered to be not convincing.

Contrary to the accepted view, we have recently demonstrated with certainty by our method a sudorific effect of adrenalin applied intradermally. Adrenalin hydrochloride solution (Sankyo Co., synthetic, $1:10^3$) was diluted with 0.9% sodium chloride solution to various concentrations and 0.1 ml or 0.2 ml was injected into the skin of the forearm, dorsum of the hand, or other regions of the body. With adrenalin of $1:10^3$ to $1:10^4$, sweating began to appear over and around the injection wheal within 1–2 min after injection and spread progressively by forming processes or branches of sweat spots, along with expansion of the anemic area, showing diffusion of adrenalin via the lymphatic channels. As sweating became more evident, the sweat spots increased in size. This sweating response reached its maximum in 1–1½ hr and then

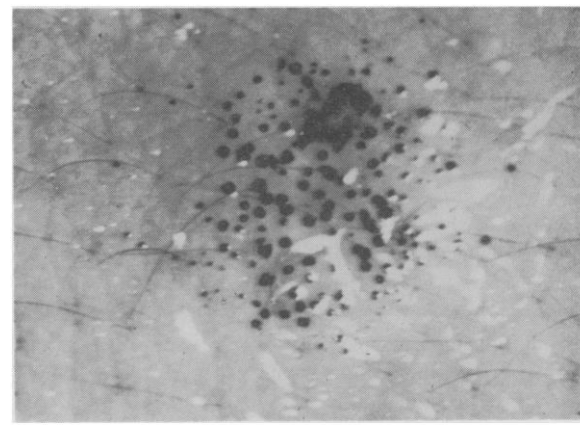

FIG. 1. Sweat spots at individual sweat pores of the extensor surface of the forearm following intradermal injection of adrenalin of $1:10^7$. Photographed 18 min after injection; ×4. Not retouched. The white spots are caused by reflection of light.

declined until it ceased, 4–5 hr after injection. Local anemia generally persisted longer than the sweating. The extent and duration of sweating depended on the concentrations of adrenalin used. The minimal effective concentration for causing sweating on the forearm of the majority of the young healthy subjects tested was $1:10^7$. With such a threshold concentration, the sweat spots disperse evenly over the original wheal of injection (Fig. 1). The sudorific effect of adrenalin was not due to the fluid in which it was dissolved. Injections of 0.9% NaCl solution or HCl solutions of pH corresponding to that of the adrenalin solutions were without effect. When adrenalin was destroyed by ultraviolet rays or by alkali, its stimulating action on the sweat glands was lost. The sweating response to adrenalin was not inhibited by atropine. Cocaine also had no influence on it.

By determining the minimal effective concentration of adrenalin applied intradermally, we have attempted to measure the excitability of the sweat glands (*4*). This was expressed as usual by the reciprocal (or its logarithm) of the threshold concentrations of adrenalin. The excitability of the glands on the forearm thus measured was, as described above, 10^7 in more than 80% of the healthy males and females tested, aged 14 to 24

yr, and it was 10^6 in the remaining subjects. An excitability of 10^8 was rarely found. The sweat glands of the arm, leg, and trunk exhibited about the same excitability. No seasonal variation in the excitability was found, as measured by the adrenalin method, in the healthy adult subjects, at environmental temperatures of 4° to 27° C. In younger subjects, aged 1 to 12 yr, and in older subjects aged 62 to 77 yr, the excitability was found to be much lower. In the majority of the children of 1 to 5 yr, sweating was not produced even with adrenalin of $1:10^4$. These findings indicate that the excitability of the human sweat glands reaches its highest level at the age of about 14 yr in both sexes, but decreases in senility. However, it must be noted that the sweat glands of newborn infants tested within one week after birth exhibited almost the same excitability as that of their puerperal mothers (Nagashima). Whether some hormone or humoral agent exists for increasing the excitability of the sweat glands and maintaining it at high levels, remains to be decided by further investigations.

References

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Two Crossover-Selector Systems: New Tools in Genetics

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The current interest in mutation rate as a fundamental biological process might well be paralleled by the study of a related process, namely, crossing over. Not only does a single agent, irradiation or heat, affect both processes, but crossing over itself produces some mutants (*1*, *2*). Therefore the finding that a new agent, chemical or physical, is an inducer of crossing over greatly increases the probability that the same agent will turn out to be mutagenic, and vice versa. Mutation studies are intrinsically laborious, although special methods have been devised by H. J. Muller and others both to speed and to improve the search for mutagenic agents and conditions in *Drosophila melanogaster*. Whereas mutagenic agents may act with a frequency of about 1×10^{-4}, crossover inducers may act to the extent of 1×10^{-2} or 1×10^{-1}. Hence a short way to find a new mutagen among several substances might be through first demonstrating its effect upon crossing over.

The availability of a new and rapid way of finding crossovers among large numbers of zygotes, to be described here, confirms the strategy of investigating the many genetically interesting chemicals, such as carcinogens, by screening for the induction of crossing over in advance of more extensive experiments on their possible mutagenic properties. However, the usual studies on changes in apparent crossing over in *Drosophila* females are subject to previously unappreciated sources of error (*3*, *5*). This suggests that more exact data may be obtained from studies on the induction of crossovers in heterozygous males, where none are normally expected, but such experiments have usually been almost as laborious as mutation studies. The present paper describes two plans to simplify the detection of crossovers. The first plan has been implemented by five special stocks, some of which have required two years to synthesize and are at present propagated only at the University of North Carolina.[1]

The first plan eliminates all noncrossover offspring, which may represent 99% of a whole experiment and even 100% of many families within the test. The 1% remaining, an average frequency for crossovers in a successful induction experiment, develop freely. The plan requires four dominant genes, each of which is lethal to egg or larva when homozygous. Two of the lethals must be closely linked in coupling phase on one side of the spindle attachment (see genotype of ♂ in Table 1), and the other two should be located in the opposite arm of the homologous chromosome and as close together as possible. The mutants Minute(3)y, Glued, Stubble, and bithorax-Dominant, at loci 40.2, 41.4, 58.2, and 58.8, respectively, meet these requirements. Such a stock is fertile, and provides the males for experimental purposes. Females used in place of a recessive test-cross stock have the alternated arrangement of the same lethals, as shown in Table 1, or else *My* bx^D/*Gl Sb*, either of which is easily carried in balanced stock. When experimental matings are made the noncrossover zygotes all die: one quarter of them are killed by homozygous *My/My*, another quarter by *Gl/Gl*, a third quarter by *Sb/Sb* and the remaining noncrossovers by bx^D/bx^D. Most spontaneous crossovers are also killed by one or more of these combinations, but the wild type crossovers formed in males will survive. Table 1 includes only noncrossovers and single crossovers, and it omits gametes expected less often than 0.3% of the time. The full checkerboard would be 16×16 and would contain 256 kinds of zygotes. These have been figured out, and no confusion as to the origin of any adult will result unless triple crossover wild type eggs, probability 1.6×10^{-6}, are formed.

Thus the vast majority of the F_1's die, in egg or larval stages in this illustration, and the crossovers, although rare, become very conspicuous as the only adults. The need for classification of the adults under the microscope is directly proportional to the success of the inducing agent. Classification determines whether a crossover contains two dominant mutant markers, expected in most instances of male-formed crossovers (top half of Table 1), or an odd number of dominants, expected from the rare female-produced crossovers, which affect only 0.3% or 0.6% of the eggs. Test-crosses to wild may verify any doubtful classes of crossovers.

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