disciplined Shetland sheep dogs showed significantly less activity than any other animals ($p = 0.001$, Friedman analysis of variance). In another test the experimenter sat silently in a room for 10 minutes and recorded the amount of time the pups spent in contact with him. In this test the *indulged* Shetland sheep dogs differed significantly from all other dogs in that they rarely approached the experimenter ($p = 0.001$, Friedman analysis of variance). From these results it is clear that a specific test for a specific breed may facilitate expression of the effects of early rearing.

The conditions of rearing were continued over a second period, when the pups were 11 to 15 weeks of age, and all tests were readministered, with essentially the same results.

In the follow-up observations and tests, the indulged beagles, in contrast to all other animals, underwent dramatic changes, in time, although all animals were maintained under standard conditions. On a weekly test in which the time taken to catch each animal was recorded, these animals became exceedingly shy and wary of being caught when approached by various human beings, including the experimenter ($p = 0.05$, t test). Thus, it appears that changes in the behavior of certain animals may occur that are seemingly independent of the current environment and belatedly dependent, instead, upon the mediation of past experiences.

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26 December 1957

New Test for Tranquilizers

The clinical success of the tranquilizing drugs has yet to be matched by a comprehensive experimental account of their behavioral effects. However, there has been impressive progress in certain areas. For example, a number of studies have dealt with the effects of tranquilizers on the behavior of experimental animals in the presence of stimuli associated with punishment ("anxiety" or "fear" situations) (*1, 2*). Tranquilizers have also impaired animal performance in discrimination tasks (*3*). The present report describes a somewhat different approach to "tranquilization." The findings suggest an aspect that is not associated with punishment or "fear reduction" and that is expressed in improved rather than impaired performance. Pigeons have served as subjects in this work.

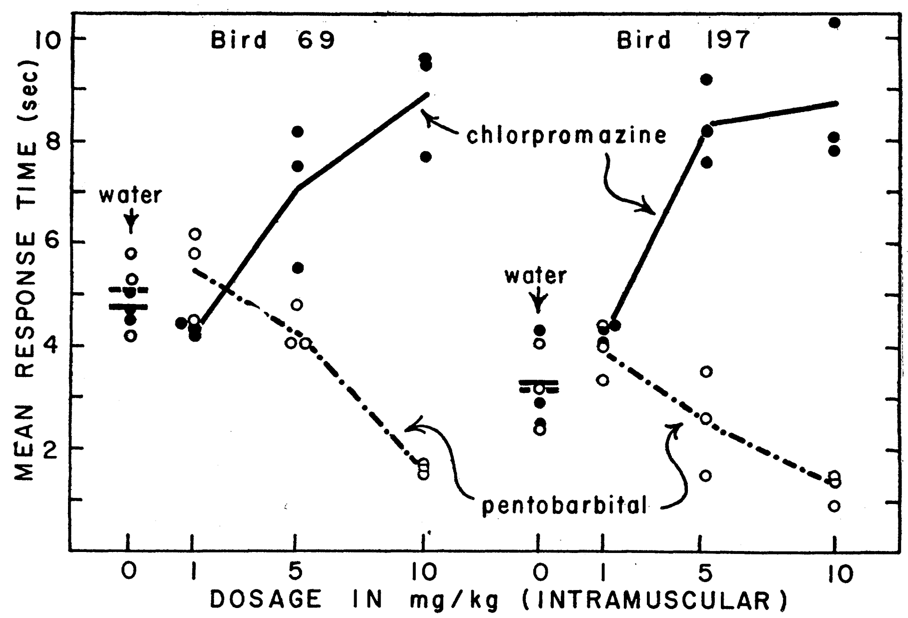

Fig. 1. Dose-response curves from two birds. Individual sessions appear as circles and dots; lines join the means of three sessions. The higher the curve, the longer, on the average, the bird stood still to gain food reinforcement.

The basic idea of the method may be stated simply. A pigeon is trained to stand still in a particular location. The longer it stands continuously in the designated spot, the more likely it is to receive food reinforcement. The bird's performance of this "standing response" is recorded as a function of drug dosage.

The method has been applied in a brief study as follows. The bird was placed in a closed, cubical chamber. A food magazine set in the front wall of the chamber operated automatically to present grain to the bird. Small photocells were located on one side wall and on the rear wall of the chamber. The cells were placed at about the height of the pigeon's head when it stood erect. Opposite the cells, in the front wall and in the other side wall, were small electric lamps. When the bird stood in a circumscribed area near the center of the chamber, its head cast a shadow over both photocells simultaneously. When the bird was in any other position, one or both cells received light from the lamp opposite. If the bird stood in the correct position and cut off light continuously from both cells for a sufficiently long period, it gained access to the food magazine for 5 seconds. A translucent disk on the front wall of the chamber glowed whenever the bird was in the right position. The length of time that the bird stood continuously in the correct position is defined as the "response time."

The hungry pigeon (weighing about 80 percent of the weight it attained when it was allowed to feed freely) was trained as follows. First it was allowed to become familiar with the food magazine, and then it was given food whenever it happened by chance to stand in the correct position for half a second or so. As in other instances of operant conditioning (*4*), the bird spent more and more time in the correct position, and the response time required to bring food was gradually increased.

Each experimental session lasted 2 hours. During this time, the bird received approximately 30 food reinforcements, averaging one every 4 minutes. This schedule was maintained by varying the response time required for reinforcement. With each reinforcement, the response time required to bring food the next time was increased by 2 seconds. Every 4 minutes the required response time was automatically reduced by 2 seconds, regardless of the bird's behavior. Thus, if the bird averaged more than one reinforcement in 4 minutes, it gradually increased the response time required, while if it averaged fewer reinforcements, the response time gradually decreased. No matter how "well" the pigeon performed (that is, how long, on the average, it stood continuously in the critical position), an equilibrium was reached such that the bird was reinforced about every 4 minutes. (Of course, if the bird had not performed the correct response at all it would not have been reinforced, but this situation did not arise in the experiment described in this report.) Counters totaled the number of response times that fell in each of ten intervals covering the range from 0 to 30 seconds. The average response time for each 2-hour session was computed from these totals.

Although the correct position was such that the bird was not required to stand perfectly still but could move its head somewhat while remaining within bounds, the task proved a difficult one. Well-trained birds stood for an average of only 5 to 6 seconds before they moved away. While standing, they appeared to be very excited and commonly made slight pecking movements.

In testing sessions, the drug or control water dose was administered intramuscularly 10 minutes before the experimental session began. The results of a series of sessions with two birds are shown in Fig. 1. Dose-response curves for chlorpromazine, a widely used tranquilizer, and pentobarbital, a hypnotic, appear together, with their associated water controls. The average response times during three sessions at each dosage are connected by lines, while individual sessions appear as separate dots. Dosage, in milligrams per kilogram, is shown on the abscissa.

It is evident that chlorpromazine substantially lengthened the response time that these birds were able to sustain, while pentobarbital reduced the response time (*5*). Since the birds were highly excited, one may appreciate at a common-sense level why a "tranquilizer" might enable the bird to "stand still" for an extended time. Neither drug, it should be noted, was given in doses large enough to produce gross behavioral effects such as ataxia. The difference in the direction of effect of the two drugs is of some interest, because these drugs have produced effects in the same direction (though of different magnitude) both in conditioned avoidance and in discrimination experiments (*1, 3*). It remains to be seen whether other tranquilizers will produce effects similar to those of chlorpromazine, or whether such effects will be matched by drugs not ordinarily classed as tranquilizers. If the promise of the initial results is borne out, it may prove profitable to study other varieties of "continuous" responding and perhaps to investigate the effects of tranquilizers in other areas that do not involve "anxiety" or "fear."

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Hormone-Induced Ovarian Development in Mosquitoes

The common house mosquito, *Culex pipiens* L., is said to be anautogenous in that the adult female requires a blood meal to form eggs. A closely related form, referred to as *Culex molestus,* is autogenous; these females are able to produce a small batch of eggs without having imbibed blood or any other food.

It has been stated that a blood meal or some blood fraction is necessary to initiate egg formation in some mosquitoes (*1*).

Twohy and Rozeboom (*2*) have shown that *C. molestus* contains more nutritional reserves than *C. pipiens* if the two species are reared under comparable conditions, but they agree with Clements (*3*) that nutritive conditions per se are not responsible for initiation of autogenous ovarian development. However, the possibility that the ovarian development of mosquitoes, like that of some other insects, is controlled by hormones has been suggested. The experiments that are reported here (*4*) were specifically designed to clarify this issue.

The undeveloped ovaries of *C. pipiens* were removed 5 to 7 days after the females had emerged [Fig. 1 (3)] and were transplanted into recently emerged *C. molestus* females. Four days later the *C. molestus* females were dissected, at which time the transplanted ovaries were seen to be fully developed [Fig. 1 (4)]. Undeveloped ovaries of *Aedes aegypti* (also an anautogenous mosquito) which had been transplanted into recently emerged *C. molestus* females also were shown, on dissection, to have become completely developed after 4 days. On the other hand, ovaries of *C. pipiens* or *C. molestus,* when transplanted into *C. pipiens* females, do not develop if the hosts are denied a blood meal. Hence, the factors responsible for initiation of development are not inherent in the ovary.

It has been shown for a number of insects that ovarian development is controlled by hormones and that a hormone produced by the corpora allata is involved (*5*). In the light of these findings, the corpora allata were removed from *C. molestus* females within 24 hours after emergence and transplanted into 5- to 7-day-old female *C. pipiens.* This operation is technically rather difficult but was successful on five occasions. These females were dissected 5 days after the transplantation and, in each case, contained fully developed eggs [Fig. 1 (1, 2)]. The evidence thus suggests that ovarian development is induced by a gonadotropic hormone secreted by the corpora allata. The young *C. molestus* female is apparently able to release this hormone without taking a blood meal, while *C. pipiens* needs to ingest blood for the release of the allatum hormone.

Ligature experiments by Detinova (*6*), Clements (*3*), and Gillette (*7*) and by me have provided evidence that a factor in the brain, presumably hormonal in nature, is also involved in the maturation of the ovary. The evidence presented here indicates that the corpora

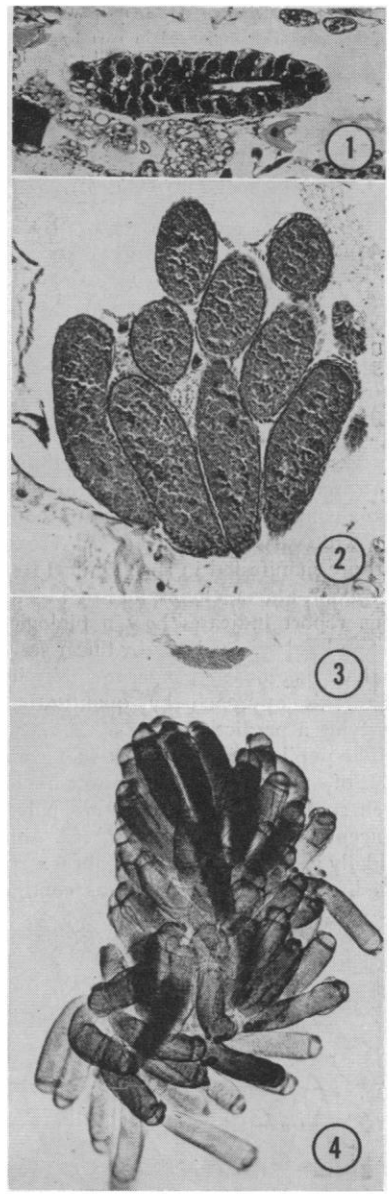

Fig. 1. (1) Section through ovary of a 2-day-old adult *C. pipiens,* showing condition of resting ovary in adult mosquito not fed on blood. (2) Section through part of adult *C. pipiens* ovary, showing fully developed eggs 5 days after corpora allata transplantation. (3) Total mount of ovary of a 5-day-old adult *C. pipiens* not fed on blood, showing size of ovary at time of transplantation. (4) *Culex pipiens* ovary 4 days after transplantation into a 24-hour-old *C. molestus* host. Note fully developed eggs. Compare with ovary in (3).