not synthesize virus antigen as judged by either complement-fixation or immunofluorescence techniques (Table 1; Fig. 1*d*). However, iododeoxyuridine (50 μg/ml) did not halt synthesis of viral antigen, although the titer of the antigen was lower than that of the controls (Table 1). These results were confirmed in tests with other concentrations of the inhibitors. Additional confirmation was obtained by examining the antigens used in the complement-fixation test by electron microscopy after staining with uranyl acetate (*8*). No virus particles were observed in preparations from cultures treated with cytosine arabinoside, although virus particles (*8*) were readily observed in antigens prepared from control cultures and from cultures maintained in the presence of iododeoxyuridine.

A preparation of adenovirus 7, shown to induce SV40 tumor but not virus antigen (*9*), was also tested for SV40 genome activity in the presence of cytosine arabinoside and iododeoxyuridine. The SV40 tumor antigen was synthesized in the presence of both inhibitors in the same way that it was produced in cells inoculated with SV40 itself.

Both iododeoxyuridine and cytosine arabinoside inhibit the replication of the DNA-containing vaccinia and herpes viruses (*6*, *10*) but cytosine arabinoside appeared to be more potent than iododeoxyuridine as an inhibitor of the replication of herpes viruses. Like fluorouracil (*7*), iododeoxyuridine also prevents replication of infectious SV40 (*11*). Our observations suggest that the DNA antagonists tested differ in the manner in which they inhibit the replication of DNA viruses. Apparently the portion of the genome coding for the synthesis of SV40 tumor antigen is less sensitive to the action of cytosine arabinoside than the genome responsible for coding for virus antigen. The inhibition of the synthesis of viral antigen in a system allowing the elaboration of SV40 tumor antigen will greatly aid both the separation and the purification of the tumor antigen.

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Adrenal Response to Fighting in Mice: Separation of Physical and Psychological Causes

Abstract. *The concentration of unbound corticosterone in mice exposed to the presence of a trained fighter is much greater if the mice have previously experienced physical defeat than if they have not. There is little difference in the concentration of the hormone between mice placed in the presence of a fighter, given a background of physical defeat, and mice actually attacked and defeated. Two possible categories of stimuli which could be responsible for hyperactivity of the adrenal cortex following defeat by another mouse are psychological and physical (for example, bite wounds); the former is apparently by far the more important under the conditions of these experiments.*

Crowding of mice and its resulting "social stress" (*1*) have become important variables in many areas of biological experimentation. Among those effects attributed to social stress are decreased resistance to disease (*2*) and endoparasitism (*3*), lowered reproductive performance (*4*), and altered behavior of offspring of crowded mothers (*5*). Such varied effects are thought to be, directly or indirectly, due to increased activity along the adenohypophyseal-adrenocortical axis.

Many investigators (*6*) have thought the actual stimuli which elicit the adrenal and pituitary responses among crowded mice to be primarily psychological rather than physical (for example, systemic effects due to bite wounds), but experimental evidence is inconclusive. It is known that fighting among males contributes heavily to the degree of adrenal response occurring among grouped mice. However, the results of two studies concerned with crowding were somewhat conflicting with respect to the relative importance of wounding as opposed to sociopsychological stimulation (*7*). We have therefore investigated adrenal responses (unbound corticosterone in the plasma) in mice placed in the presence of a trained fighter. Mice which had previously experienced physical defeat by a fighter showed a much greater adrenal response to the fighter's presence than did mice not having experienced defeat, thus demonstrating a psychological component and yielding a basis for comparing the relative roles of psychological and physical stimulation.

All mice (180 C57BL/6J) were weaned at 21 to 28 days and reared in isolation (in stainless steel boxes, 15 by 30 by 15 cm) until used in the experiment at 85 to 95 days of age. All mice remained in isolation during the 6- to 9-day experimental period except for 15 minutes each day. The basic experimental treatment consisted of placing a mouse in the home cage of a trained fighter of the same strain; but the subject was physically separated from the fighter by a removable partition consisting of two layers of 0.6-cm wire mesh mounted on each side of a wooden frame. Procedures following such initial separation from the fighter varied among three experimental groups of 60 mice each; in group 1 the partition was always removed after 10 minutes, allowing the fighter to attack the subject for 5 minutes; in group 2 the partition was removed as in group 1 for the first 5 days, but remained in place for the entire 15-minute period after day 5; and in group 3 the partition was never removed. Twenty mice from each of the three groups were killed for blood collection on each of days 6, 7, and 9 of the experiment. Two of the groups, therefore, were physically exposed to the fighter on each of 5 days. In one of these groups (group 1) physical exposure continued on each of days 6 to 9 when blood was collected, and the other (group 2) was exposed to only the presence of a fighter during the period of blood collection. Group 3 served as a control group. Physical exposure of an untrained mouse to a trained fighter invariably results in almost instantaneous attack by the fighter, defeat of the un-

Table 1. Mean concentrations of unbound corticosterone (micrograms per 100 milliliters of plasma) in mice which were exposed to physical defeat by a fighter for 6 to 9 days (group 1), similarly treated for 5 days and then placed only in the fighter's presence on days 6 to 9 (group 2), or continually exposed to only the fighter's presence (group 3). The results are shown for four samples of plasma (each pooled from five mice) per daily average per group (12 samples when days pooled for each treatment).

Day	Group		
	1	2	3
6	9.0	11.1	3.8
7	9.5	11.2	1.2
9	3.5	10.9	4.5
	Mean ± standard error		
	7.3±1.6	11.1±1.1	3.2±0.9

trained mouse, and, within a few days, all of the behavioral symptoms of severe subordination on the part of the untrained, attacked mouse (*8*).

Mice were killed by decapitation 1 hour after the end of daily sessions with the trained fighter and within 15 seconds after their home cages were removed from the rack. Mice treated in each different way were divided into groups of five, the blood from each group being pooled. The plasma was then analyzed fluorimetrically for unbound (not precipitated by zinc) corticosterone (*9*).

Two-way analysis of variance revealed large differences which could be attributed to the experimental procedures ($p < .001$), but no significant differences which could be attributed to the days when blood was collected or to a possible interaction. Mice which had never been physically defeated by a fighter (group 3) had generally low concentrations of unbound hormone (Table 1). Those which had been exposed to the fighter's presence on the days of blood collection and which had experienced physical defeat (group 2) had continually high concentrations. Group 1, which was physically exposed to a fighter every day throughout the experiment, had relatively high concentrations, at least initially. Since variance analysis revealed no difference between results obtained on the 3 days on which blood was collected, the data within each type of treatment were pooled and the resulting means tested against each other by *t*-tests. The mean for group 3 was significantly lower than that for group 2 ($p < .001$) and, despite the overlap on day 9, was significantly lower than the mean for group 1 ($p < .05$. Group 1 was not significantly different from group 2.

The amount of unbound corticosterone is well suited as the measure of adrenal response in this type of experimentation because: (i) unbound corticosterone is present only in trace amounts in isolated controls; (ii) short daily exposures to fighters have little, if any, effect on bound corticosterone; (iii) the peak concentration of unbound corticosterone in the plasma is reached about 1 hour after exposure to the fighter; and (iv) after the 4th day of exposure to fighters, the concentrations return to trace amounts by 3 hours after each exposure (*10*). This last point is particularly important in the present experiment since differences in concentrations of unbound hormone which were found among the mice killed on days 6, 7, or 9 cannot be considered as having been carried over from the treatment on previous days.

The significant increase in the concentration of unbound corticosterone in mice placed in the presence of a trained fighter, given a background of physical defeat, when compared with those which had never experienced defeat, adequately demonstrates the reality of a psychological component in the adrenocortical response to defeat in a fighting situation. It is important that mice which had experienced defeat actually had somewhat higher concentrations of unbound hormone when exposed to a fighter's presence than did mice actively attacked by the fighter on the days of blood collection. This difference was not significant but does attest to the relative importance of psychological, as opposed to physical, stimuli. These data may, in addition, indicate that much the same type of stimuli could be responsible for hyperactivity of the adrenal cortex among crowded mice; that is, neurotropic stimuli elicited by the presence of the dominant animal in the group. Socially subordinate mice are known to have heavier adrenals than those which are dominants (*11*).

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Feeding Stimulants for the Female House Fly, *Musca domestica* Linneaus

Abstract. *Both casein and yeast hydrolysate contain feeding stimulants for the adult female house fly. Guanosine monophosphate is the major active component in yeast hydrolysate. Several amino acids, including leucine, methionine, lysine, and isoleucine, are also effective feeding stimulants and are presumed to be the active components in the casein hydrolysate. Solution in phosphate buffer is necessary in all instances to obtain maximum activity with the stimulants.*

During experiments on nutrition and reproduction in the house fly, the addition of yeast hydrolysate (*1*) to a dry semidefined adult diet appeared to make the diet more attractive to the flies, since both the incidence of feeding and the amount of food taken up increased. To determine whether this effect was due to an attractant or a feeding stimulant, or both, filter-paper discs were impregnated with solutions of the yeast hydrolysate and placed in cages of 4- to 7-day-old house flies which had fed on dry granular sucrose and water since emergence. Attraction from a distance could not be demonstrated by a variety of techniques (*2*); however, flies which came in contact with the disc extended