beling and isolation of nuclear RNA that administration of cortisone stimulated precursor incorporation into nuclear RNA. Furthermore, Kenney (*13*) showed that corticosteroid administration resulted in an actual increase in the rate of synthesis of tyrosine transaminase, in complete analogy to enzyme induction in microorganisms. Since this process is so like that in microorganisms where both ultraviolet radiation and x-rays cause an inhibition of enzyme induction, it is not clear why high-energy radiation does not inhibit the steroid induction of this enzyme in mammals. An interesting possibility in view of the resistance of serine dehydrase and ornithine transaminase induction during periods of template stability (actinomycin D resistance) is that tyrosine transaminase is also synthesized on a stable template and that the steroid actually alters the rate of enzyme synthesis at the mRNA stage rather than the stage of DNA-dependent RNA production. The effect of actinomycin in inhibiting corticosteroid induction of tyrosine transaminase may be related to some other action of the antibiotic, such as that reported by Revel and Hiatt (*14*).

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22 July 1965

Evolution of Fitness in Experimental Populations of *Drosophila serrata*

Abstract. *Changes which enhance adaptedness to the environment occur in experimental populations of* Drosophila serrata *which are acted upon by strong natural selection. The improvement is greater in hybrid than in single-strain populations because genetic variability is greater in the former.*

Evolutionary changes can be observed not only on the geological time scale. Rapid adaptive changes have been found in both natural and experimental populations. Among insects, adaptive changes in the genetic constitution of natural populations, caused by natural selection in changing environments, have been recorded in several species (*1*); in some cases these genetic changes have also been reproduced experimentally (*2*). With *Drosophila*, improvements in fitness in carriers of certain chromosomal arrangements have also been observed in the laboratory (*2, 3*). Experiments devised to observe and measure improvements in the ability of a population to exploit the resources of a particular environment are nevertheless rare (*4*). The experiments reported here were designed to study changes of this kind.

Two strains of *Drosophila serrata*, derived from impregnated females collected in nature, were used. One was collected near Popondetta, New Guinea, and had been maintained in the laboratory by mass culture for 1½ years before the beginning of the experiment. The other one was collected in Bulahdelah, about 130 miles north of Sydney, Australia, and had been maintained by mass culture for about 3 years. Six experimental populations were used. Two of the populations were derived from the Popondetta strain and two from the Sydney strain; the other two populations were started with F_1 descendents of mass crosses between the Popondetta and the Sydney strains.

One population of each pair was maintained at 25° ± 0.5°C and the other at 19° ± 0.5°C. Each population was started with 150 pairs of flies. The populations were maintained in ½-pint milk bottles, with a ¾-inch layer of medium (cream of wheat and molasses) and with a double piece of toweling, 2 by 7 inches, partially pressed into the medium. The technique has been described in detail elsewhere (*5*). In short, the adult flies are introduced into a bottle with

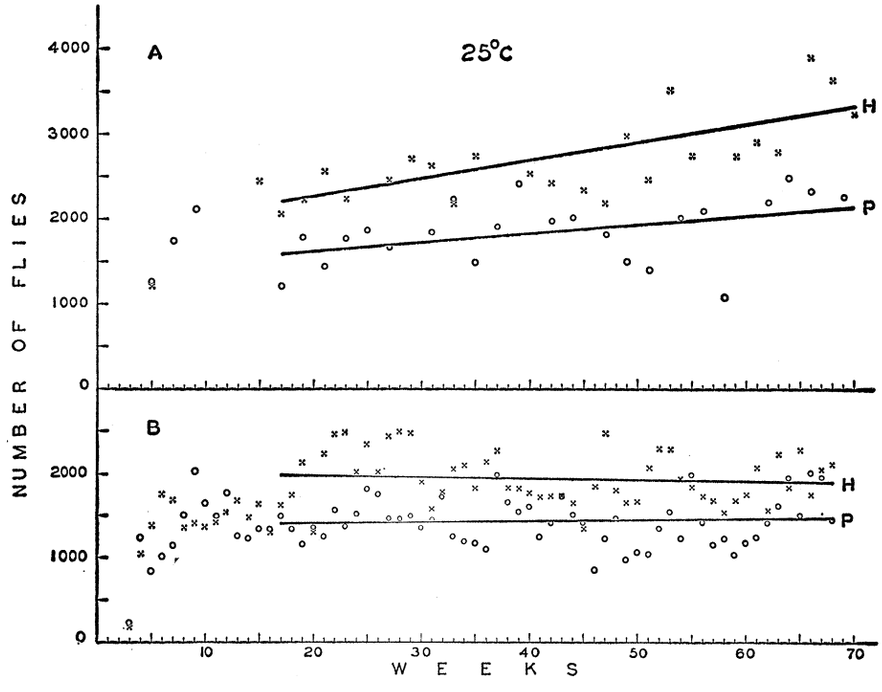

Fig. 1. Population size (*A*) and weekly production (*B*) of two experimental populations of *Drosophila serrata* at 25°C. *H*, Hybrid population; *P*, single-strain (Popondetta) population.

fresh medium and transferred to a new bottle at regular intervals. For flies maintained at 25°C, transfer is made on Mondays, Wednesdays, and Fridays; for the others, on Mondays and Fridays. The bottles containing eggs are also kept in the constant-temperature incubators. At 25°C, adult flies start to emerge about the 12th day; at 19°C, about the 16th day. The newly hatched flies are collected and counted on the same days on which the populations are transferred to new bottles and then are added to the bottle with the adult flies. The adult, ovipositing flies are thus always in a single bottle with fresh food, while some 13 other bottles in each series contain eggs, larvae, pupae, and hatching adults. Every second week, on Friday, the adult populations are anesthetized with ether, counted, and weighed; the newborn flies are also weighed on that day before they are added to the adult population.

The adult populations increase in numbers very rapidly because of continuous addition of newly hatched flies. In 5 to 8 weeks they reach a size of about 2000 individuals; then they oscillate around that number during the rest of the experiment. The action of natural selection is very strong, both among the adults and during the immature stages. The number of eggs laid in each bottle is at least 10 times, and perhaps 100 times, larger than the number of flies which can develop on the amount of food available. The adult flies are extremely crowded in the bottle. The surface of the food is covered with several layers of flies attempting to feed and to lay eggs.

Table 1. Mean population size, $\bar{Y}$, of four experimental populations of *Drosophila serrata* from weeks 17 to 70, and regression coefficients, *b*, of population size on time (weeks as time units), with *t* and *P* values for significance of regression.

$\bar{Y}$	*b*	*t*	*P*
	Single strain at 25°C		
1862	+10.5	2.27	<.05
	Hybrid at 25°C		
2750	+19.5	3.36	<.01
	Single strain at 19°C		
1724	+ 8.4	2.58	<.02
	Hybrid at 19°C		
2677	+20.4	4.46	<.001

The two Sydney populations were discarded after 51 weeks. Their performance is not reported here since it was similar to that of the Popondetta populations and has been reported elsewhere (*5*). The other four populations were maintained for 70 weeks. The sizes of the adult populations and the numbers of flies hatching per week are shown in Figs. 1 and 2. A trend toward increasing population size is quite apparent. This trend was examined statistically by the regression of population size on time between weeks 17 and 70. During the first 5 to 8 weeks the populations grew in size until they reached the limits imposed by food and space. To dissociate the increase in population size due to the natural growth of the population from the increase caused by the genetic improvement in fitness, the occasional counts made during the first 16 weeks of the experiment were not used in the regression analysis. About five generations must have elapsed during that period at 25°C, and about three generations at 19°C (*5*). A regression analysis on time for the number of flies hatched per week was also done for the interval of weeks 16 to 68. The regression lines are drawn in Figs. 1 and 2. Table 1 shows, for the adult flies, the mean population size, $\bar{Y}$, and the regression coefficient of population size on time; time units are weeks. The same parameters for the newborn flies are presented in Table 2. Student's *t* was used to test the significance of the coefficients of regression. The *t* values and the probability that such values are due to chance are also included in Tables 1 and 2.

The coefficients of regression of population size on time vary from 8.4 to 20.4, and in all the populations they are significantly different from zero. The populations have evolved toward a superior adaptation to the experimental environment. This evolution occurs gradually during the 54 weeks of the experiment. The improvement during this period seems to be due exclusively to the increased ability of the flies to survive the crowding in the bottles, and their average longevity is constantly increasing. The coefficients of regression for the number of newborn flies per week are not significantly different from zero, so that no improvement is apparent in the ability of the populations to transform the available food into living flies. Moreover, the differences between the regression coefficients of population size and newborn flies are statistically significant ($P < .05$) for all four populations. Two considerations, not mutually exclusive, may account for this result. During their past history drosophila flies have probably been exposed quite frequently to conditions in which a limited amount of food was available for the number of eggs and larvae present in a particular ecological niche. Under these con-

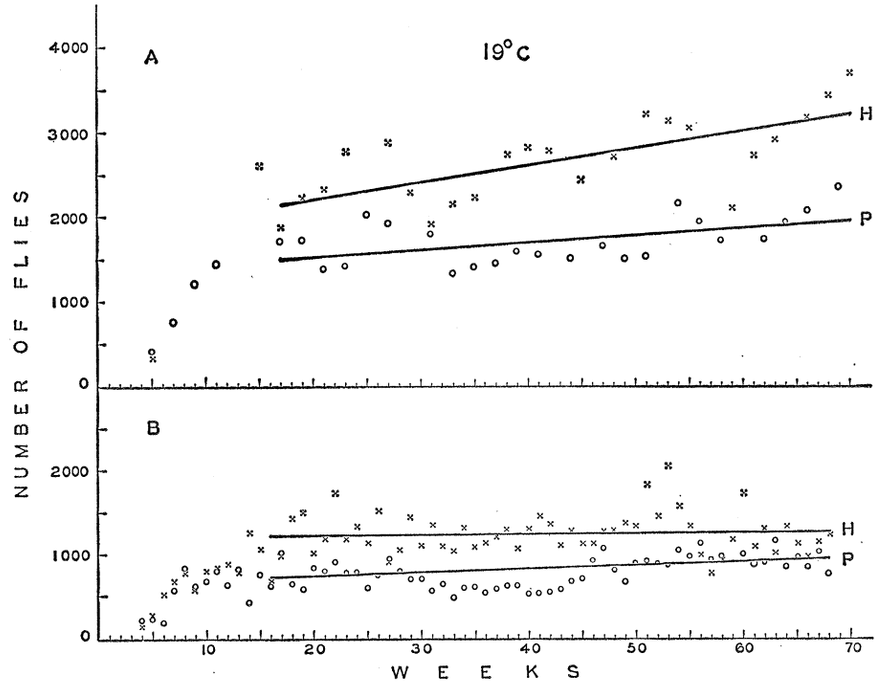

Fig. 2. Population size (*A*) and weekly production (*B*) of two experimental populations of *Drosophila serrata* at 19°C. *H*, Hybrid population; *P*, single-strain (Popondetta) population.

Table 2. Mean number of flies, Y, produced per week between weeks 16 to 68 by four experimental populations of *Drosophila serrata*, and regression coefficients, b, of the number of flies produced on time (weeks as time units) with t and P values for significance of regression.

Y	b	t	P
	Single strain at 25°C		
1434	+1.05	0.43	>.50
	Hybrid at 25°C		
1939	−2.08	0.64	>.50
	Single strain at 19°C		
795	+1.87	1.20	>.20
	Hybrid at 19°C		
1244	+0.69	0.30	>.50

ditions, natural selection is expected to produce and to maintain genetic constitutions which allow the populations to exploit maximally the available food sources. Any mutation arising in the experimental populations which would increase their ability to transform food into living matter had probably originated in the past and had been incorporated into the genetic endowment of the population. The second hypothesis is that competition for food during the immature stages was so strong that the maximum genetic improvement had already been achieved during the first three to five generations of the experiment, which are not included in the regression analysis. The higher productivity of the hybrid populations seems to support this hypothesis.

As for the adult flies, competition for space among them may not be so strong as competition for food among the larvae. On the other hand, it is unlikely that during their past history these populations have been living in their natural habitats with available space as limited as it is in the experimental environment. Adult crowding is a new environmental factor for these flies, and evolutionary adaptation is therefore more likely to occur. The genetic variability present in the populations, or arising by mutation and recombination, gives origin, under the action of natural selection, to new genotypes highly fit to survive under crowded conditions. In *The Origin of Species* Darwin wrote that natural selection "tends to the improvement of each creature in relation to its organic, and inorganic conditions of life." When drosophila flies are exposed to a novel condition of life, such as adult crowding, natural selection improves their genetic constitution in relation to that condition.

The conflict between adaptive fitness and genetic variability has been pointed out (*6*). The mutation process furnishes the raw materials from which adaptive changes are constructed, but it produces also a multitude of poorly adapted variants. Under the action of natural selection, those genetic variants in a population which increase the adaptation of the population to the environments in which it lives are preserved. Populations of the same species living in geographically widely separated regions are expected to have different genetic constitutions. Two such populations, one from New South Wales in Australia and the other from New Guinea, were used in these experiments to initiate hybrid populations. The hybrid populations may therefore carry larger amounts of genetic variability. The probability that highly adapted genotypes will be produced during exposure to new environments is greater in the hybrid than in the single-strain populations. Figures 1 and 2 show that the performance of the hybrid populations is superior for both the number of flies produced and the total population size. Similar results have been obtained in other cases (*3, 5, 7*). Moreover, Table 1 shows that the rate of increase in population size with time is considerably higher in the hybrid populations than in the single-strain populations. In other words, the hybrid populations are evolving faster. The rate of increase in the population size of the hybrid populations is approximately double that of the single-strain populations. The difference between the regression coefficients is statistically significant for flies maintained at 19°C ($t = 2.11$, $P < .05$), but not for flies maintained at 25°C ($t = 1.03$, $P > .20$).

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Collagen Defect Induced by Penicillamine

Abstract. *Collagen synthesis, as judged by the accumulation of collagen in a subcutaneous, induced granuloma, was significantly decreased by penicillamine. Penicillamine also caused a marked increase in the amount of soluble collagen in skin and a sharp drop in insoluble material. These findings, which reflect an abnormal pattern of collagen metabolism, are accompanied by an inhibition of wound-healing and by skin fragility.*

The resistance of penicillamine (β,β-dimethylcysteine) to metabolic degradation and its strong capacity to chelate metals suggested to Walsh (*1*) the possibility of using this compound in hepatolenticular degeneration (Wilson's disease), a disturbance accompanied by the accumulation of copper. It is presently under investigation for the treatment of macroglobulinemia, the cold-agglutinin syndrome, and in rheumatoid arthritis (*2*). It reduces the concentration of cystine in the plasma and urine of patients with cystinuria (*3*). The administration of penicillamine causes a number of side reactions which affect the connective tissue structures (*4*).

Subcutaneous granulomas were in-

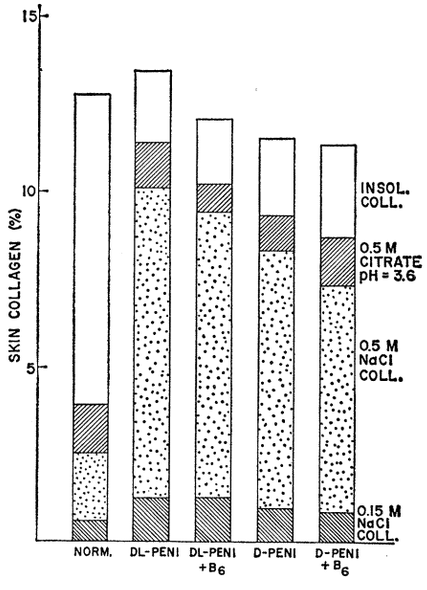

Fig. 1. Collagen distribution among the different soluble and insoluble fractions extracted from the skin of control rats and from those receiving DL or D-penicillamine, with or without additional supplements of pyridoxine. The height of the bars illustrates the percentage of each collagen fraction present in fresh skin.