ity that death will occur increases if the concentration of DDT in the brain exceeds 500 ppm in otherwise healthy rats, or exceeds 200 ppm in debilitated rats.

These data confirm the known fact that the concentration of DDT in the fat is not related to acute toxicity.

The appearance of measurable amounts of DDE in the plasma before other tissues parallels the results of Rothe *et al.* (*6*) who found that DDE appeared in chyle collected from the ductus lymphaticus during the absorption of DDT from the intestine. Values for DDE in brain, liver, kidneys, and fat are not shown in the table, because the concentrations were all below the experimental limits of the method.

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Actinomycin D: Its Effect on Antibody Formation in vitro

Abstract. *The formation of antibodies to bacteriophage T_2 in vitro was inhibited by 5×10^{-8}M actinomycin D. This result is consistent with the concept that antibody formation depends upon DNA-dependent RNA synthesis.*

The polypeptide antibiotic actinomycin D, at low concentrations, has been shown to inhibit cellular RNA synthesis while having little or no effect on DNA synthesis (*1*). It was therefore of considerable interest to test the effect of this antibiotic on antibody formation. In the studies reported here, it has been shown that $5 \times 10^{-8}M$ actinomycin D can inhibit completely both the continuation of primary antibody formation and the secondary antibody response induced in vitro to T_2 bacteriophage.

Lymph nodes were obtained from rabbits and cultivated in vitro according to the technique described by Michaelides and Coons (*2*). The rabbits were immunized twice, at a 2-week interval, with 2×10^{11} T_2 phage in saline distributed in the four footpads. After 6 to 34 weeks, both popliteal lymph nodes were removed and were cut into 1-mm^2 fragments. About 15 fragments were placed in each tube. The fragments were "fixed" to the glass by addition of one drop of heparinized plasma, and 1 ml of medium 1066 (*3*) containing 20 percent rabbit serum was added, followed by T_2 phage (2×10^{10}/ml) or actinomycin D (*4*), or both, as indicated. The tubes were placed in an incubator at 37°C with 5 percent CO_2. After 24 hours and, subsequently, every 3 to 4 days, the medium was replaced with fresh medium with or without actinomycin D. Antibody determinations were made by the standard titration for phage antibody (5). (Results are expressed as k, the inactivation constant of the rate of neutralization of phage by a given antiserum.)

The results of a representative experiment are depicted in Figs. 1 and 2. The antibody concentration (k) of each tube is plotted on a logarithmic ordinate against time on the abscissa. As can be seen in Fig. 1, the maintenance of antibody concentration in tubes to which T_2 had not been added, was prevented by $3 \times 10^{-7}M$ actinomycin D (0.3 μg/ml). The evidence that antibody is synthesized in vitro and is not formed in vivo and merely released during incubation is: (i) before incubation, only small amounts of antibody could be demonstrated in washed lymph node cells after repeated freeze-thawing; and (ii) the actinomycin D effect as described here. Figure 2 shows that larger amounts of antibody were usually formed in tubes to which T_2 had been added, indicating that a secondary response was stimulated in vitro; this response was also prevented by actinomycin D.

Thus actinomycin D can prevent the secondary response induced in vitro and the continuation of primary antibody formation in vitro. Additional experiments have revealed the following. (i) At a concentration of $5 \times 10^{-8}M$, actinomycin D completely inhibited both types of antibody formation; the effect on continuation of primary synthesis was detected as early as 72 hours after addition of actinomycin D to the medium. (ii) Antibody formation during the second week of culture was also

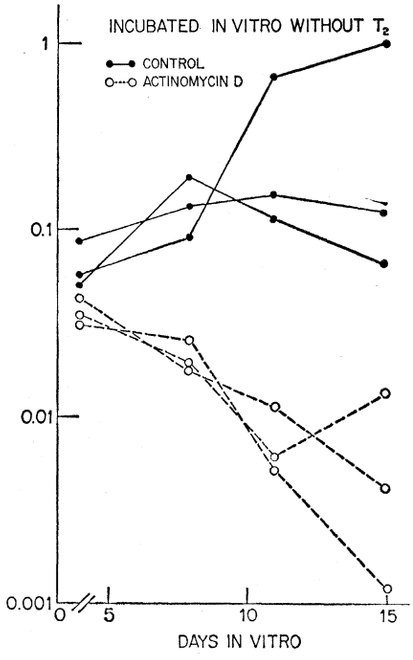

Fig. 1. The concentration of antibody to bacteriophage T_2 in each of six tubes. The culture medium was changed every 3 to 4 days; actinomycin D ($3 \times 10^{-7}M$) was added to three of the tubes.

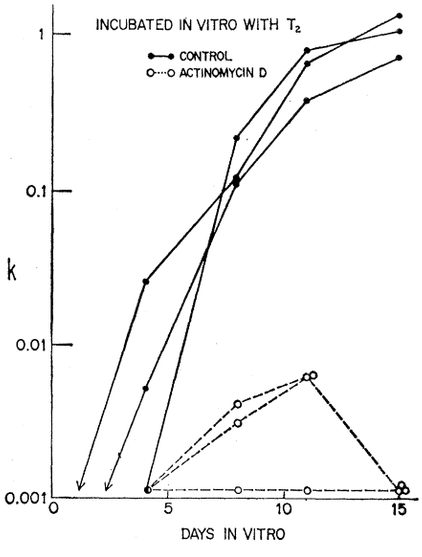

Fig. 2. The concentration of antibody to bacteriophage T_2 in each of six tubes. Actinomycin D ($3 \times 10^{-7}M$) was added to three of the tubes. Bacteriophage T_2 (10^{10}/ml) was added at the start of the experiment; the medium was changed on day 1 and every 3 to 4 days thereafter.

prevented when actinomycin D was added 4 days after the addition of T_2. (iii) Antibody formation was only partially suppressed when secondary immunization with T_2 was effected 4 days before the nodes were removed and cultivated with actinomycin D.

Ambrose and Coons (*6*) found that the secondary antibody response was also inhibited in vitro by low concentrations of actinomycin D; and Jerne has shown that actinomycin D injected into mice inhibits antibody formation in vivo (*7*).

The interpretation of our results depends upon the mechanism of action of actinomycin D on those cells involved in specific antibody formation to bacteriophage T_2. Since no information is available at present on this relatively small and possibly heterogeneous cell population (*8*) within the lymph node, a tentative explanation must rely on results obtained from studies of other systems. In this respect there has recently accumulated considerable evidence to indicate that, at the concentrations of actinomycin D used in this study ($5 \times 10^{-8} M$), cellular RNA synthesis is specifically inhibited, while DNA synthesis remains relatively unaffected in bacterial (*9*) liver (*10*) hela (*11*) and mouse L cells (*12*). The basis for this specificity has been elucidated recently by Kahan *et al.* (*13*) who have shown that actinomycin D binds specifically to the deoxyguanosine residue of native DNA, but has a poor affinity for denatured DNA. Actinomycin D also blocks the protein synthesis initiated in vitro by T_2 DNA and RNA polymerase (*14*). In this system, the effect of actinomycin is probably due to the prevention of messenger RNA (mRNA) formation, since protein synthesis is not inhibited if a messenger such as polyU, G (uridylak, guanilak) is added.

Our results suggest, therefore, that antibody formation depends upon a DNA-dependent RNA synthesis, and, in particular, upon mRNA formation. The prompt and complete inhibition of already established antibody synthesis by actinomycin D is also consistent with an effect on messenger RNA rather than on the other, more stable classes of cytoplasmic RNA, and suggests that this messenger has a half-life of less than several days. This explanation leaves unanswered, however, the crucial question of whether or not the messenger carries information for immunological specificity. In addition, our data do not exclude the possibility that actinomycin D has damaged antibody-producing cells, possibly by interfering with cell division (*12*). We are therefore trying to determine whether mRNA, synthesized in vitro by DNA obtained from lymphoid cells of hyperimmunized animals, and RNA polymerase, can stimulate specific antibody formation by unimmunized lymphoid cells (*15*).

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Genetics and Intelligence: A Review

Abstract. *A survey of the literature of the past 50 years reveals remarkable consistency in the accumulated data relating mental functioning to genetic potentials. Intragroup resemblance in intellectual abilities increases in proportion to the degree of genetic relationship.*

Nomothetic psychological theories have been distinguished by the tendency to disregard the individual variability which is characteristic of all behavior. A parallel between genetic individuality and psychologic individuality has rarely been drawn because the usual assumption has been, as recently noted in these pages (*1*), that the organisms intervening between stimulus and response are equivalent "black boxes," which react in uniform ways to given stimuli.

While behavior theory and its analytic methods as yet make few provisions for modern genetic concepts, the literature contains more information than is generally realized about the relationship between genotypic similarity and similarity of performance on mental tests. In a search for order among the published data on intellectual ability, we have recently summarized the work of the past half century (*2*). By using the most commonly reported statistical measure, namely, the correlation coefficient, it has been possible to assemble comparative figures from the majority of the investigations.

Certain studies giving correlations had to be excluded from this compilation for one of the following reasons: (i) type of test used (for example, achievement tests, scholastic performance, or subjective rating of intelligence); (ii) type of subject used (for example, mental defectives); (iii) inadequate information about zygosity diagnosis in twin studies (*3*); (iv) reports on too few special twin pairs.

The 52 studies (*2*) remaining after these exclusions yield over 30,000 correlational pairings (*4*) for the genetic relationship categories shown in Fig. 1. The data, in aggregate, provide a broad basis for the comparison of genotypic and phenotypic correlations. Considering only *ranges* of the observed measures, a marked trend is seen toward an increasing degree of intellectual resemblance in direct proportion to an increasing degree of genetic relationship, regardless of environmental communality.

Furthermore, for most relationship categories, the *median* of the empirical correlations closely approaches the theoretical value predicted on the basis of genetic relationship alone. The average genetic correlation between parent and