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

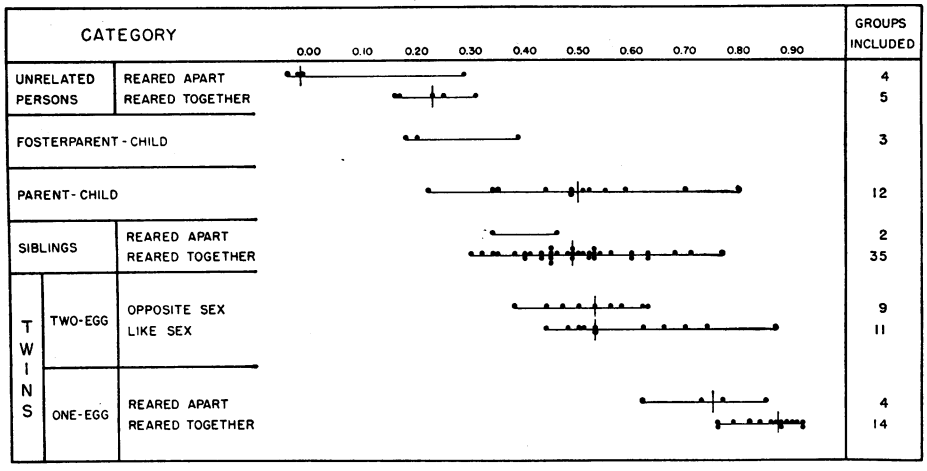

Fig. 1. Correlation coefficients for "intelligence" test scores from 52 studies. Some studies reported data for more than one relationship category; some included more than one sample per category, giving a total of 99 groups. Over two-thirds of the correlation coefficients were derived from I.Q.'s, the remainder from special tests (for example, Primary Mental Abilities). Midparent-child correlation was used when available, otherwise mother-child correlation. Correlation coefficients obtained in each study are indicated by dark circles; medians are shown by vertical lines intersecting the horizontal lines which represent the ranges.

child, as well as that between siblings (including dizygotic twins) is 0.50. The median correlations actually observed on tests of intellectual functioning are: 0.50 for parent-child, 0.49 for siblings reared together, and 0.53 for dizygotic twins, both the opposite-sex and like-sex pairs. Although twins are presumably exposed to more similar environmental conditions than are siblings spaced apart in age, the correlations for mental ability do not indicate a sizable difference between the groups. Since only two studies dealt with siblings reared *apart*, it is possible to state only that the reported correlations for that group fall within the range of values obtained for siblings reared together and exceed those for unrelated children living *together*.

For unrelated persons in a large random-mating population, the theoretical genetic correlation is usually considered to be zero; for smaller populations, or those that deviate substantially from panmixia, however, the genetic correlation between presumably unrelated individuals in fact may be considerably higher. The observed median for unrelated persons reared apart is −0.01. Medians for unrelated individuals reared together (children reared in the same orphanage or foster home from an early age) and for the fosterparent-child group are 0.23 and 0.20, respectively. The relative contributions made by environmental similarity and sample selection to these deviations from zero are still to be analyzed.

At the other end of the relationship scale, where monozygotic twins theoretically have 100 percent genetic correlation, medians of the observed correlations in intellectual functioning are 0.87 for the twins brought up together, and 0.75 for those brought up apart (*5*). The correlations obtained for monozygotic twins reared together are generally in line with the intra-individual reliabilities of the tests. The median for the separated twins is somewhat lower, but clearly exceeds those for all other relationship groups.

In further reference to twin studies, our survey (*2*) shows that mean intrapair differences on tests of mental abilities for dizygotic twins generally are between 1½ to 2 times as great as those between monozygotic twins reared together. Such a relationship appears to hold also for the upper age groups, as suggested by a longitudinal study of senescent twins (*6*).

Taken individually, many of the 52 studies reviewed here are subject to various types of criticism (for example, methodological). Nevertheless, the overall orderliness of the results is particularly impressive if one considers that the investigators had different backgrounds and contrasting views regarding the importance of heredity. Not all of them used the same measures of intelligence (see caption, Fig. 1), and they derived their data from samples which were unequal in size, age structure, ethnic composition, and socioeconomic stratification; the data were collected in eight countries on four continents during a time span covering more than two generations of individuals. Against this pronounced heterogeneity, which should have clouded the picture, and is reflected by the wide range of correlations, a clearly definitive consistency emerges from the data.

The composite data are compatible with the polygenic hypothesis which is generally favored in accounting for inherited differences in mental ability. Sex-linkage is not supported by these data (for example, under a hypothesis of sex-linkage the correlations for like-sex dizygotic twins should be higher than those for opposite-sex twins), although the possible effects of sex-linked genes are not precluded for some specific factors of ability.

We do not imply that environment is without effect upon intellectual functioning; the intellectual level is *not* unalterably fixed by the genetic constitution. Rather, its expression in the phenotype results from the patterns laid down by the genotype under given environmental conditions. Two illustrations of the "norm of reaction" concept in relation to intellectual variability are seen in early total deafness and in phenylketonuria. Early deafness makes its stamp upon intellectual development, in that it lowers I.Q. by an estimated 20 score points (*7*). Phenylketonuria is ordinarily associated with an even greater degree of intellectual impairment. However, early alteration of the nutritional environment of the affected child changes the phenotypic expression of this genetic defect (*8*). Individual differences in behavioral *potential* reflect genotypic differences; individual differences in behavioral *performance* result from the nonuniform recording of environmental stimuli by intrinsically nonuniform organisms.

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2. This material was included in a report presented at the XVII International Congress of Psychology, Washington, D.C., 1963 (L. Erlenmeyer-Kimling, L. F. Jarvik, and F. J. Kallmann). Detailed information about the data presented here is available upon request and is in preparation for publication.
3. This survey does include reports on opposite-sex (hence dizygotic) twin pairs from these studies.
4. Correlational pairings refer to the number of individual pairs used in deriving the correlation coefficients. Some investigators constructed a large number of pairings on the

basis of a relatively small number of individuals. Altogether, we have been able to identify the following minimum numbers: twins, 3134 pairs (1082 monozygotic and 2052 dizygotic); sibs apart, 125 pairs plus 131 individuals; sibs together, 8288 pairs plus 7225 individuals; parent-child, 371 pairs plus 6812 individuals; fosterparent-child, 537 individuals; unrelated apart, 15,086 pairings; unrelated together, 195 pairings plus 287 individuals.

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27 October 1963

Serum Factor in Renal Compensatory Hyperplasia

Abstract. *Serum from uninephrectomized rats was injected into normal recipient rats. This led to an increased incorporation of tritiated thymidine in the kidney cells, but not in the liver cells of the recipients. The results suggest that there is a humoral substance acting specifically on the kidney that promotes renal compensatory hyperplasia.*

Renal compensatory hyperplasia, the increase in the number of cells in one kidney when the other kidney is removed, has been documented by an increase in the mitotic index (*1*), an increase in desoxyribonucleic acid synthesis (*2*) and an increase in the number of cells incorporating thymidine (see *3*). This paper reports a test of the theory that there is a specific humoral substance that causes the hyperplasia. A group of normal rats were injected with serum obtained from uninephrectomized rats. It was found that the incorporation of tritiated thymidine into renal cells was greater in this group than in a second group of rats injected with control serum.

Male Sprague-Dawley rats aged 5 weeks were used. Each weighed 100 g, and all were kept on a normal diet. Serum, called nephrectomy serum, was prepared from blood drawn from the aorta of some of these rats 48 hours after one kidney was removed. This time period was selected because the greatest mitotic activity of the remaining kidney was found to occur 48 to 60 hours after nephrectomy (*1*). Control serum was obtained 48 hours after a sham nephrectomy. The serums were frozen until used. The recipient rats were divided into three groups. The first group received an intraperitoneal injection of 0.5 ml of nephrectomy serum twice daily for 4 days. The second group received 0.5 ml of control serum according to the same schedule. The third group had one kidney removed and received saline according to the same schedule. The rats were weighed 96 hours later, and only those rats which had gained 8 to 12 g during the experimental period were selected. This helped to eliminate variations in mitotic activity due to food intake (*4*). The final numbers of animals in each group were seven in the first group, and eight each in the second and third groups. One microcurie of tritiated thymidine (*5*) (specific activity 6.7 c/mmole) per gram of body weight was injected intraperitoneally into each rat. One-half hour later the animals were killed. The animals were operated on quickly on one day and killed in quick succession at the same time of the 4th day to minimize the variation in mitotic activity that occurs diurnally (*6*). The animals were all killed on the same day.

Kidneys and livers were fixed in formalin, dehydrated with alcohol, embedded in paraffin, and cut into sections 6 μ thick. Autoradiographs were prepared by the method of Doniach and Pelc (*7*), with Kodak AR 10 stripping film. The slides were exposed in the dark at 4°C for 4 weeks. They were then developed with Kodak D19 developer for 7 minutes and fixed with acid fixative for 4 minutes in the dark. After several washes with tap water, they were stained with hematoxylin for 2 minutes.

The number of labeled cells in 200 microscopic fields from each kidney (400 fields for the two kidneys of each rat) were counted at a magnification of 1450 times (oil immersion). A typical labeled cell is shown in Fig. 1. Only those sections with a background of less than one radioactive grain per unlabeled cell were counted. On these sections, the labeled cells contained over 15 grains. The number of cells in ten microscopic fields were counted, and the final results expressed as the number of radioactive cells per 1000 cells. The

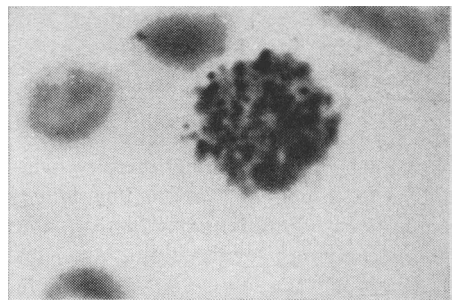

Fig. 1. Autoradiograph of a cell labeled with tritiated thymidine, from a rat with compensatory hyperplasia. ($\times$ 1450)

types of cells that were labeled were also determined by counting the labeled cells in successive microscopic fields from the capsule to the tip of the papilla. For each kidney section, 50 such fields were counted. Most of the labeled cells occurred in the cortex (Table 1). Sixty-one percent of the labeled cells were proximal tubule cells and 17 percent distal tubule cells. Very little uptake occurred in the glomeruli and the medulla. The types of cells that were radioactive were similar in the kidney sections of all three groups of rats. In the cortex, the average number of labeled cells in the kidneys of rats who received nephrectomy serum was 12.1 $\pm$ 0.92 (S.E.) per 1000 cells; that of

Table 1. Types of cells labeled with tritiated thymidine in the kidneys of rats with renal compensatory hyperplasia.

Type of cell	Total No. of radioactive-labeled cells counted (%)
Proximal tubule cells	61
Distal tubule cells	17
Collecting duct and loop of Henle cells	10
Miscellaneous*	12

* The cells examined included glomerular, capillary, and capsular cells.

Table 2. Thymidine incorporation into the kidneys of rats with renal compensatory hyperplasia. Group 1, normal rats injected with nephrectomy serum; group 2, normal rats injected with control serum; group 3, uninephrectomized rats injected with saline. Results expressed as the number of labeled cells per 1000 cortical cells.

Group 1	Group 2	Group 3
9.12	4.32	9.96
9.16	4.44	11.72
10.12	5.32	14.40
12.00	6.60	19.76
13.48	6.92	24.40
15.40	7.12	26.72
15.44	7.36	27.00
	10.44	28.72
Mean $\pm$ standard error		
12.10 $\pm$ 0.92	6.56 $\pm$ 0.57	20.33 $\pm$2.5