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.
5. Correlational data are now available on 107 separated pairs of monozygotic twins from four series: H. H. Newman, F. N. Freeman, K. J. Holzinger, *Twins: A Study of Heredity and Environment* (Univ. of Chicago Press, Chicago, 1937); J. Conway, *Brit. J. Stat. Psychol.* **11**, 171 (1958); N. Juel-Nielsen and A. Mogensen, cited by E. Strömgren, in *Expanding Goals of Genetics in Psychiatry*, F. J. Kallmann, Ed. (Grune and Stratton, New York, 1962), p. 231; J. Shields, *Monozygotic Twins Brought Up Apart and Brought Up Together* (Oxford Univ. Press, London, 1962).
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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 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 ± 0.92 (S.E.) per 1000 cells; that of

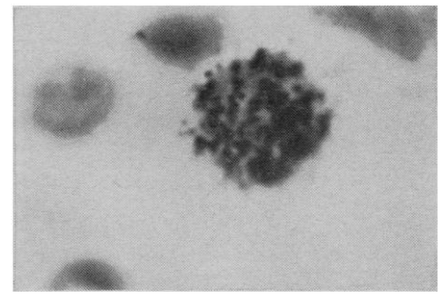

Fig. 1. Autoradiograph of a cell labeled with tritiated thymidine, from a rat with compensatory hyperplasia. (× 1450)

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 ± standard error		
12.10 ± 0.92	6.56 ± 0.57	20.33 ±2.5

the rats who received control serum 6.56 ± 0.57 per 1000 cells. These two results are significantly different from each other ($p < .02$). The average number of labeled cells in the kidneys of rats who had a uninephrectomy was 20.33 ± 2.5 per 1000 cells. This figure is significantly different from that of the rats receiving nephrectomy serum ($p < .05$).

The medullas of the kidneys from each rat contained less than one labeled cell per 1000 cells, and there was no significant difference in the counts among the three groups. The livers of the rats in all three groups contained between 1 and 2.4 labeled cells per 1000 cells, there being no significant differences between each group.

The results indicate that a substance in the serum of uninephrectomized rats may be responsible for the increase in cell division that occurs during renal compensatory hyperplasia. It is indicated that the substance is not a general growth-promoting factor, since the liver showed no increase in cell division.

The increase in cell division in the kidneys of rats that received nephrectomy serum was significantly smaller than that in the remaining kidney of uninephrectomized rats. This may be due to the fact that the amount of serum was not large enough or injected often enough for maximum growth, or it may mean that factors other than a serum factor are implicated in renal compensatory hyperplasia. Other hypotheses that have been advanced to explain the hyperplasia include an increase in renal blood supply (*8*), increase in excretory load (*9*), and the local stretching of areas of the kidney (*10*). Also the administration of pituitary hormones, thyroxin, testosterone, progesterone, and desoxycorticosterone acetate are each known to increase renal size (*11*).

Williams has reported that an injection of nephrectomy serum into recipient rats did not increase the incidence of mitosis in the kidney (*12*). However, he gave only one injection of the serum which may have been an insufficient amount to cause an increase in cell division.

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Long-Term Stability of Visually Evoked Potentials in Man

Abstract. *Although the variability of averaged evoked potentials as recorded from cortex in man has been a constant source of concern among investigators, the degree of variability has not received systematic treatment. The authors have accordingly undertaken an exploratory study of reliable differences that may occur in the first 300 msec of the averaged evoked response over long periods of time. Computer analysis of visually evoked responses in seven subjects over several weeks indicated stability of the response of each individual, with reliable intra-individual correlations. Inter-individual differences, however, were large. The evoked responses of different individuals were found to be unique.*

The electrocortical response to a brief stimulus, such as a flash of light or a click, is a complex wave made up of a number of components, frequently referred to as an evoked potential or an evoked response. Increased interest in the study of evoked potentials has resulted from the development of electronic instruments that can extract the wave pattern of brief, minute electrical changes, that follow a stimulus, from ongoing random electrical activity of the brain (*1*). Constructed electronically from many responses, the averaged evoked potential that emerges contains components which were previously invisible. Such a procedure has caused some to question the reliability of the averaged evoked response (*2*). Some measure of reliability is needed if the averaged evoked response is to become a useful tool in neurophysiology.

Shagass and Schwartz demonstrated that the pattern during the first 40-msec period of somatosensory-evoked potentials was reliable, or stable, over intervals of from 1 to 3 hours. Correlations between evoked potentials recorded at these intervals averaged .87 (*3*). A question remains, however, regarding the stability of the averaged evoked potential over much longer periods of time, intervals separated by days or weeks. Equally important is the question of the stability of the later components of the response, those components following the stimulus by 50 or 100 or even 300 msec. The present study was designed to investigate these questions.

Seven subjects, normal male adults, reclined comfortably in a padded chair facing a reflecting hemisphere 70 cm in diameter. The hemisphere was illuminated by a PS-1 Grass photic stimulator lamp, positioned immediately behind and to the left of the subject and aimed at the center of the hemisphere, at a distance of 70 cm. The PS lamp was housed in a fiberboard box to muffle the clicks accompanying light flashes. None of the subjects queried reported that they could hear the clicks. The light flash was of relatively low intensity (2 on the PS intensity range of 1 to 16). The calculated illuminance at the center of the hemisphere was 0.7 lu/7m^2. The duration of the flash was 10 μsec. The center of the hemisphere at eye level was 40 cm from the subject's eyes. The flash produced a uniform surround completely enveloping the subject's face. The visual angle subtended by the reflected flash was approximately 165°.

Subjects were fitted with electrodes attached to 3-mm^2 scratched patches of scalp with collodion. Placements were bilateral, 4 cm anterior and lateral to the inion. All were monopolar to insure knowledge of electrical polarity, with cortical electrodes referred to earground leads.

A Mnemotron computer of average transients (CAT), a multipurpose digital computer, was employed to extract cortical responses to the light flash. Inked plots of the evoked response patterns were made by a Mosley X-Y plotter.

One hundred flashes, 2 to 3 seconds apart, were delivered to each subject during a recording session. The CAT was set to analyze the brain activity from the left visual cortex for a period of 2 seconds after each flash.

The subjects presented a variety of