For the time being, American science is apparently receiving more support for basic research than ever before. We have part of a National Science Foundation after all, and we are gaining experience[16] which will be invaluable in further planning for a permanent Foundation. At this point it must be remembered, however, that the easiest thing for Congress to do is nothing. The Army, as well as the Navy, has officially[17] supported a National Science Foundation, and if scientists, educators, and others throughout the country fail to support this view, thereby failing to assume responsibility for encouraging the promotion of science for peaceful purposes, then there is another question to be faced: *Is the primary end of free American science to be the national defense—free because of the necessity of fundamental discoveries leading to novel weapons of war?*

[16] For example, with admittedly less than a year's experience in contracting for basic research, the Office of Naval Research has not had a single patentable discovery brought to its attention. This suggests that last year's controversy over patents was all out of proportion to its importance. Indeed, this is not surprising because the fundamental knowledge resulting from basic research is rarely patentable.

[17] Except for the patent provisions, S. 1850 was supported by the War and Navy Departments in letters to the Chairman of the Senate Committee on Military Affairs during April 1946.

Technical Papers

The Role of the Liver in Guanidoacetic Acid Metabolism in Man

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The experimental production of pathologic changes in the liver of rats, rabbits, and dogs by the restriction of dietary methyl (*1*) groups suggests that a study of methylation processes in patients with cirrhosis may yield information of value. Najjar, *et al.* (*7*) claim that there is a reduction of the excretion of N^1 methylnicotinamide (F2) in patients with liver disease after the administration of nicotinamide. However, Perlzweig and Huff (*8*) have shown that the excretion of F2 is the resultant of two or more metabolic reactions involving nicotinamide, methylation, and the conversion of F2 to products the natures of which are unknown. McKibbin, *et al.* (*6*) were unable to demonstrate decreased excretion of F2 in dogs after the production of fatty livers by a choline-free diet.

It is probable that this problem could be approached more directly by studying the methylation of guanidoacetic acid to creatine. It is now presumed that guanidoacetic acid is synthesized in the kidney from arginine and glycine (*2, 3*), and that its methylation to creatine occurs in the liver with methionine, or with the system of choline + homocystine (*5*) acting as methyl donors. Creatinine containing a deuteriomethyl group has been isolated from normal human urine after the administration of methionine containing a deuteriomethyl group (*9*).

From the observations of Block and Schoenheimer (*2*) the conclusion is drawn that approximately 2 per cent of the creatine depot of the rat undergoes daily turnover. This value corresponds well with the amount of creatinine excreted in the urine per day. It was also demonstrated that, as far as is known, there is but a single pathway in the metabolism of guanidoacetic acid, namely, its conversion to creatine and thence to creatinine. Therefore, if it is assumed that in man the amount of creatinine excreted daily is replaced in the body by an equimolar amount of creatine, synthesized from equimolar amounts of guanidoacetic acid and methyl groups, a quantitative estimation of the urinary excretion of guanidoacetic acid and total creatinine should be informative in determining the extent of this transmethylation reaction. This process has the significant advantage that the transformation of guanidoacetic acid to creatine normally reaches 95 per cent of completion in man, *i.e.* the amount of guanidoacetic acid in the urine is equal to approximately 5 per cent of the sum of the total amount of creatinine + guanidoacetic acid (see below). Therefore, small deficiencies in the conversion of guanidoacetic acid to creatine should be reflected by relatively large increases in the excretion of guanidoacetic acid in the urine.

We have found in 15 determinations (*4*) on 8 men that the ratio $\frac{\text{mg. guanidoacetic acid}}{\text{mg. total creatinine + guanidoacetic acid mg.}}$ (guanidoacetic acid index) in the urine of normal male adults on an unrestricted diet is in the range 0.03–0.05, with an average value of 0.043 + 0.006. The excretion of guanidoacetic acid by the normal female

[1] The authors are very grateful for the aid given by Mrs. Gloria K. Peacock.

has been found to be related to the menstrual cycle, with maximum excretion in the urine occurring at midcycle. The guanidoacetic acid index of 10 male patients with cirrhosis of the liver was found to be between 0.040 and 0.17, and appears to be related to the degree of cirrhosis as approximated by the usual clinical criteria.

The impression gained above, namely, that in human cirrhosis a deficiency of methylation of guanidoacetic acid may exist, was confirmed by comparing guanidoacetic acid indices of normal men and men with cirrhosis after either the oral or intravenous administration of guanidoacetic acid. Patients with cirrhosis tended to show significantly higher elevations of the guanidoacetic acid index than did the normal controls. The administration of methionine before giving guanidoacetic acid has, as yet, given only equivocal results.

Results of these investigations will be submitted in detail in a future publication.

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An "Invisible" Chromosome [1]

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Males of *Drosophila melanogaster* were X-rayed with a dose of 4,000 r, and their offspring investigated genetically for the presence of induced chromosomal rearrangements. Among such rearrangements one called $R^3(+)$ originated in consequence of at least four breaks in the left arms of chromosomes 2 and 3 and in the right arm of chromosome 4 (*2*). These breaks and the resulting rearrangements will not concern us here. In addition, two more breaks occurred in the right arm of chromosome 3, causing a deficiency for the region 95D/E–97C1, as defined in Bridges' map of the salivary gland chromosomes. As a result of the deficiency, the region 95D/E–97C1, present in the normal homologue of the deficient chromosome, forms a typical unpaired loop (Fig. 1). No flies have been found which are genetically deficient for this region, since every individual carrying a deficient chromosome also contains the excised fragment. Larvae carrying one or two 95D/E–97C1 fragments, in addition to one or two undeleted chromosomes 3, are viable. In the salivary gland nucleus the fragment is found deeply imbedded in the chromocenter with its 95D/E end, and the other 97C1 end often likewise attached to the chromocenter. In this case the fragment forms a short loop; otherwise it ends freely.

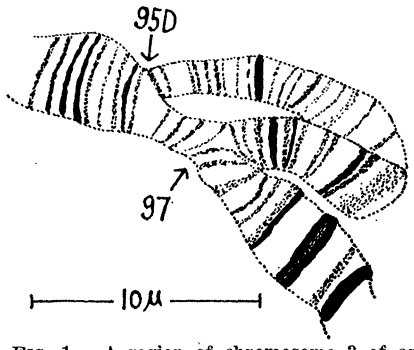

Fig. 1. A region of chromosome 3 of an individual heterozygous for a normal chromosome and one deficient for section 95D/E–97C1.

The rearrangement, including the fragment, is distributed independently of sex, *i.e.* the fragment is not linked with either the X- or Y-chromosome. Cytogenetic studies show further that the fragment is distributed at random with respect to the autosomes, *i.e.* it represents an independent chromosome. Clearest proof for this statement is seen in the following results: A male heterozygous for the $R^3(+)$ rearrangement and a set of normal chromosomes was crossed to a female with normal chromosomes. Salivary gland nuclei of six F_1-larvae from this cross were shown to contain three of the four possible viable combinations of the $R^3(+)$ rearranged large autosomes, the normal large autosomes, and the fragment. Of the six larvae, two had obtained from the P ♂ the rearranged autosomes plus the fragment; three, the rearranged autosomes without the fragment; and one, the normal autosomes without the fragment. Among the offspring of a normal female and another male which itself had received the $R^3(+)$ rearrangement from one of its parents, and, from its other parent, a chromosome 2 carrying an inversion as well as a normal chromosome 3, the following types of constitutions were found: two larvae without the $R^3(+)$ rearrangement but with the 95D/E–97C1 fragment, and one larva likewise without the $R^3(+)$ rearrangement and lacking the fragment.

The origin of the kinetochore to which the fragment presumably has been joined is not known with cer-

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