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.

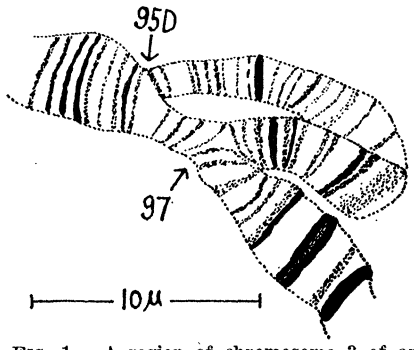

Fig. 1. A region of chromosome 3 of an individual heterozygous for a normal chromosome and one deficient for section 95D/E–97C1.

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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tainty. It may be assumed that the proximal end of the fragment is translocated to a base of chromosome 4. It is known that the origin of the $R^3(+)$ rearrangement involved at least one chromatid of chromosome 4R, breaking it near its base and translocating to it the tip of chromosome 3L. It is possible that the two bases of chromosome 4 required by the hypothesis originated as a result of breaks induced in the two chromatids of this chromosome which were transmitted by the irradiated sperm. It is not clear how the 97C1 end of the fragment terminates. Its tendency to synapse with the chromocenter brings to mind the capacity of chromosome 4R to join the chromocenter with both its ends. The possibility is suggested that the fragment became inserted in a chromatid of 4, which itself became deleted of nearly all of 4R excepting the base and very tip.

The most remarkable property of the chromosome fragment is its invisibility in metaphase plates of ordinary mitosis, either of ganglion cells, cells of imaginal discs, or oogonial cells. In order to prove simultaneously the presence of the fragment and its invisibility, nuclei of salivary glands and of mitotic ganglionic cells were studied from the same individual larvae. In two cases satisfactory preparations were obtained. One larva, in its salivary gland nuclei, exhibited normal chromosomes X, 2, and 3 in diploid condition, a single chromosome 4, plus the 95D/E–97C1 chromosome (Fig. 2a). In its ganglionic metaphases were visible two normal chromosomes each of X, 2, and 3 and a single chromosome 4, but no further element could be seen (Fig. 2b). In the second larva two X-chromosomes, a normal chromosome each of 2 and 3, and the rearranged chromosomes 2 and 3 were found both in salivary and ganglionic nuclei, as well as two normal chromosomes 4, and the base 4, tip 3L unit. The salivary cells showed, in addition, the presence of the 95D/E–97C1 chromosome. Again, the ganglionic nuclei did not exhibit an element corresponding to this chromosome.

Apparently the 95D/E–97C1 chromosome element is too small to be visible in mitotic divisions, at least with the aceto-orcein method used in both temporary and permanent preparations. The possibility of the existence of chromosome fragments beyond the limit of visibility in mitotic divisions had been considered before by Neuhaus (*1*), but correlated study of salivary nuclei was possible in his cases. Without the investigation of the giant nuclei of the salivary glands, the existence of the "invisible" chromosome in the $R^3(+)$ rearrangement likewise would have remained unknown.

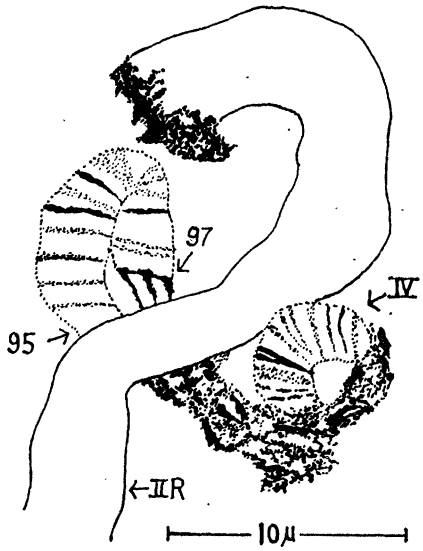

FIG. 2a. Part of the salivary chromosomes of a larva possessing normal diploid chromosomes X, 2, and 3, a single chromosome 4, and the 95D/E–97C1 element.

FIG. 2b. Metaphase figure from a ganglion cell of the same larva. No chromosome corresponding to the 95D/E–97C1 element is visible.

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