the means for age groups 15–19, 20–29 and 30–39 is significantly higher than for age group 10–14 ($p < 0.01$). The IgM levels show a gradual decrease after age 40 and remain stable in women 60 years of age and older. For all the age groups between 5 and 49 years of age the means are significantly higher in females than in males ($p < 0.02$ and smaller). However, the means are not significantly different for the children aged 2–4 and also not for the age groups 50 years of age and older ($p > 0.05$). As the figure shows, the sex difference seems to have disappeared completely in individuals 60 years of age and older.

The foregoing results clearly show that IgM levels are elevated in girls and younger women but that this elevation disappears in older women. The time of the highest elevation, from 15 to 40 years, coincides roughly with the reproductive phase in women. The question arises whether the increased IgM levels did evolve to afford the women increased immunologic protection during pregnancy because it is difficult to imagine that such a marked sex difference would have arisen just by chance alone. Girls are more resistant to certain types of infection than boys are[7], indicating that the difference in IgM is of biological importance.

Sex hormones associated with adult gonades have been suggested to be concerned with certain aspects of resistance. The decrease of IgM in women after 40 shows some similarity to the decrease in estrogen secretion[8]. However, in girls the IgM increase is quite different from the rapid preadolescent increase in estrogen secretion. Also, the difference in resistance in children seems to long precede the marked difference in hormone secretions between the sexes[9].

Although the marked changes in females from early childhood to old age have not previously been demonstrated, evidence supporting the present findings does exist in the literature. For children, the data of Allansmith et al.[1] show much higher IgM levels in girls aged 15–16 and 17–18 than younger girls, while IgM levels in males remained stable after 2 years of age. Data showing a significant decrease of IgM in women over 40 years of age were published in 2 reports[10,11]. As in our study, the sex difference had disappeared by about 60 years.

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Morphology of the carnation-light synthetic lethal focus in *Drosophila melanogaster*

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Summary. A histological study of the carnation-light lethal focus revealed morphological abnormalities in brain tissue. The ratio of core width to total brain width and brain texture consistently differed between lethal *(car-lt)* and their non-lethal sibs.

2 questions fundamental to an understanding of developmental mechanisms relate to the time and anatomical site of gene activity. Because of their high frequency of occurrence, lethal mutations provide a rich source of experimental material since each lethal mutant reveals a specific development action for a mutated chromosomal region. *Drosophila* lethals are generally classified as to phase specificity (larval, pupal, adult) and morphologic abnormality thereby indicating the temporal and spatial requirements for a normal gene product. We used sex mosaic fate mapping[1-3] to determine that nerve tissue is the anatomical site (focus) at which the *carnation* (*car:* position 62.5 on the X chromosome) and *light* (*lt:* position 55.0 on the 2nd chromosome) loci exert their lethal interaction[4]. More precisely, the focus was located in the ventral region of the blastoderm surface approximately 7 sturts from the blastodermal origins of the legs and 17 sturts from the midline.

In this paper we reveal the primary anatomical lesion at the lethal focus as well as other anatomical sites which may represent secondary areas of damage. Focus determination in conjunction with histological studies has been used in *Drosophila* mutants such as *wings-up* and *drop-dead.* The *wings-up* mutant mapped to presumptive mesoderm, and histological examination of flight muscles showed myofibril defects and muscle atrophy. The *drop-dead* focus was located in the brain which showed extensive degeneration upon histological examination[3].

Penetrance of the *car-lt* lethal interaction is complete such that all double mutants *(car/car; lt/lt* and *car/Y; lt/lt)* die before ecolosion. This synthetic lethal is unique in that the lethal phase (3rd instar larva, prepupa, midpupa, late pupa) is specified by the number of maternal car^+ and/or lt^+ genes[5]. All strains of *D. melanogaster* were reared at 25 °C in half-pint milk bottles containing standard cornmeal, yeast, molasses, sucrose, agar medium except that riboflavin was added to the medium to intensify Malpighian tube color and therefore allow a sharper distinction between the lt^+/lt and lt/lt larvae[6]. This intensification occurs even in crosses where a maternal effect influences pigmentation of the Malpighian tubes[7]. Age-controlled larvae were obtained by the method previously described[8]. Larvae were prepared for histological examination by fixation in Dietrich's solution[9], alcohol dehydration, and toluene clearing[10]. 7-µm sections were stained with Delafield's hematoxylin and counter-stained with aqueous eosin[11]. Histological data were collected from tissues deemed significant from

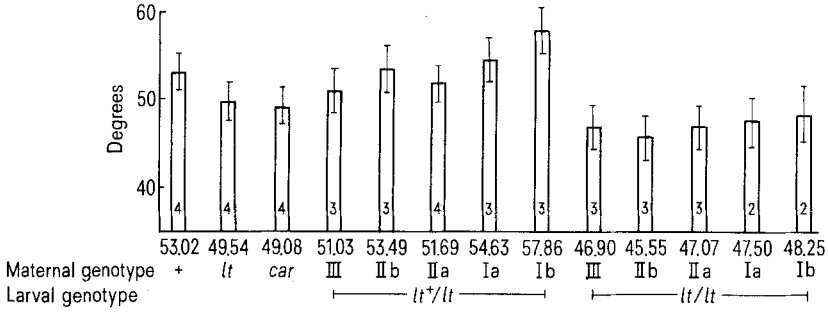

Fig. 1. Means (with 95% confidence limits) of the arcsin values (transformed core/total width) for the brain measurements.

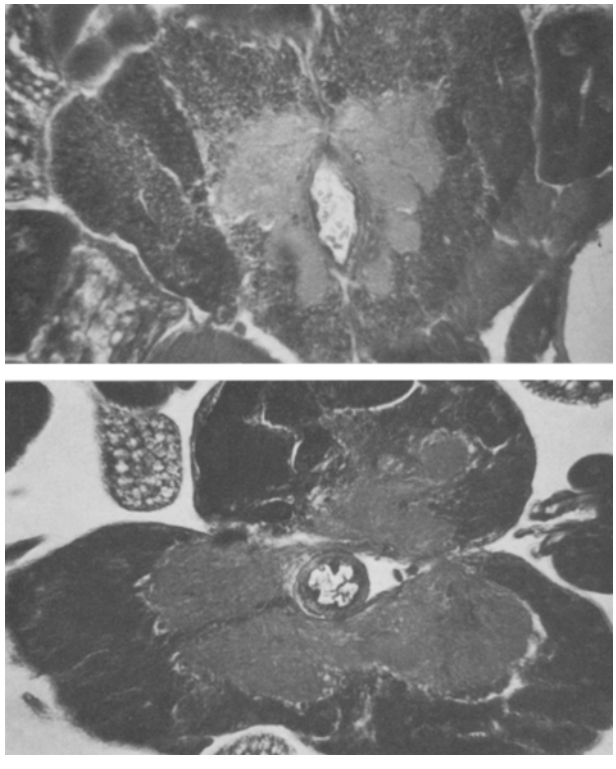

Fig. 2. Photomicrographs of 3rd-instar, lethal (top) and non-lethal (bottom) brains (level I).

focus-mapping; the nervous system[4], and those areas which may represent significant patterns of damage caused by the *car-lt* interaction (fat body, Malpighian tubes). In addition, such data were also collected from those areas not perceived as directly related to *car-lt* lethality (gut cell thickness, number of gut loops).

The following 4 levels (cross sections) were selected for histological examination: Level I consisted of the cross section in which the cerebral hemispheres possess their greatest diameter. Here, measurements were made of brain core and total brain width. Brain texture was also noted. Level II was the 5th section posterior to level I. Measurements of ganglion core width and total ganglion width were made. Ganglion texture was noted. Level III was the cross section which passed through the middle of the larva's right gonad. Here the number of gut loops and gut wall thickness were determined. Malpighian tubule width and lumen diameter were also measured. Level IV was at the first appearance of a hind intestine. Measurements of cell wall thickness were taken.

In addition, fat-body measurements were taken at all 4 levels. A fat cell was randomly chosen by assigning numbers to each quadrant of an ocular grid, and randomly selecting a corresponding quadrant number. Measurements of fat body size and fat globule diameter were made.

Age-controlled specimens of the following genotypes were examined: Wild (Urbana), *car, lt, car-lt* double mutants and non-lethal sibs obtained as offspring from the following parents: (III) car^+/Y: $Cy(lt^+)/lt \times y$ *car*/Y; $Cy(lt^+)/lt$, (IIa) $FM6(car^+)/y$ *car;* $Cy(lt^+)/lt \times y$ *car*/Y; $Cy(lt^+)/lt$, (IIb) car^+/Y; $lt/lt \times y$ *car*/Y; $Cy(lt^+)/lt$, (Ia) *y car/y car;* $Cy(lt^+)lt \times y$ *car*/Y $Cy(lt^+)/lt$, $FM6(car^+)/y$ *car;* $lt/lt \times y$ *car*/Y; $Cy(lt^+)/lt$ (car^+ represents the attached $-X$ *v tu-l* chromosome). A complete description of the strains and symbols used is given in Lindsley and Grell[12]. Larval sex has a minor but statistically significant influence on certain measurements from the vertral ganglion, diameters of Malpighian tubule, and globule diameters of the middle fat body. Such influences are appropriately accounted for in the interpretation of results.

Of those parameters examined (see above), 2, ratio of core width to total brain width (figure 1) and brain texture (figure 2), consistently differed between lethal *(car-lt)* larvae and their non-lethal sibs. Core width in brains of lethal larvae is less than in their non-lethal sibs. Brains of larvae having a non-lethal genotype have a compact cortex with no intercellular spaces, while brains of larvae having the lethal genotype possess intercellular spaces and various cell sizes in the cortex. In addition, the overall shapes of the brain cores differ. Larvae having the lethal genotype exhibited an irregular, lobulated core outline as compared to a smooth, even outline in wild type and non-lethal sibs *(lt^+/lt).*

The precise nature of car^+ and/or lt^+ gene products is not known. While considerable information exists regarding the influence these loci exert on eye colour pigmentation, such pleiotropic effects such as lethal interaction are at best poorly understood. It is clear however that both the car^+ and lt^+ gene products exert considerable influence on the structure and function of nerve tissue.

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