uracil therapy with an initial small dose of 0.2 g daily but the leucocyte count fell within a week to 3,600 with 18% polys.

The appearance of the normal number of granulocytes in the blood stream is dependent on two factors: a hypothetical and as yet undemonstrated substance which regulates the orderly maturation of the myeloblast into the completely segmented granulocyte and the second which governs the entrance of the mature cell into the peripheral blood stream. The rapidity of action of the pyridoxine would seem to indicate that the primary action must be on the release mechanism. However, the possibility of a direct stimulation of the myelocytic elements of the bone marrow is a question which can only be answered by extensive bone marrow studies.

Summary. Our results would seem to indicate that pyridoxine can bring about a rapid and significant rise in the number of circulating granulocytes in the blood in human subjects after a depression caused by thiouracil. Although there is a large element of self recovery after removal of the toxic agent there seems to be no doubt that the recovery process is much accelerated by pyridoxine.

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Experimental Tumors after Nerve Section in an Insect.*

BERTA SCHARRER. (Introduced by Ernst Scharrer.)

From the Department of Anatomy, School of Medicine, Western Reserve University, Cleveland, Ohio.

In the course of a study of the endocrine functions of the corpora cardiaca and allata in insects the occurrence of tumors was noted. The corpora cardiaca in the species used (*Leucophaea maderae,* Orthoptera) are elongate structures behind the brain which continue postero-laterally into the corpora allata. In a series of experiments both corpora allata together with the posterior part of the corpora cardiaca were removed (Fig. 3, b). Following these operations tumors developed predominantly in 2 locations, namely, in the anterior portion of the alimentary canal and in the salivary reservoir. In rarer instances the salivary glands were involved (Fig. 1).

The appearance of these tumors was first suspected to be due to an endocrine disturbance resulting from the removal of the corpora allata or cardiaca. Such an interpretation would be supported by the fact that in young nymphs of another Orthopteran (Dixippus) allatectomy was followed by abnormal tissue growth and degeneration.[1] Furthermore, endocrine factors play a role in the origin of certain mammalian tumors.[2,3] Of the two endocrine glands here under consideration the corpora allata seemed by far more likely to be connected with the formation of neoplasms, since tumors developed also in such operations where a major portion or almost all of the corpus cardiacum tissue had been left intact (Fig. 3, c). Furthermore, the known hormonal actions of the corpora allata include the regulation of the rate of tissue growth and maturation, metabolism, and egg development.[4-8]

If the tumors to be described are caused by the lack of a corpus allatum hormone, it should be possible to prevent their occurrence by reimplantation of corpora allata into allatec-

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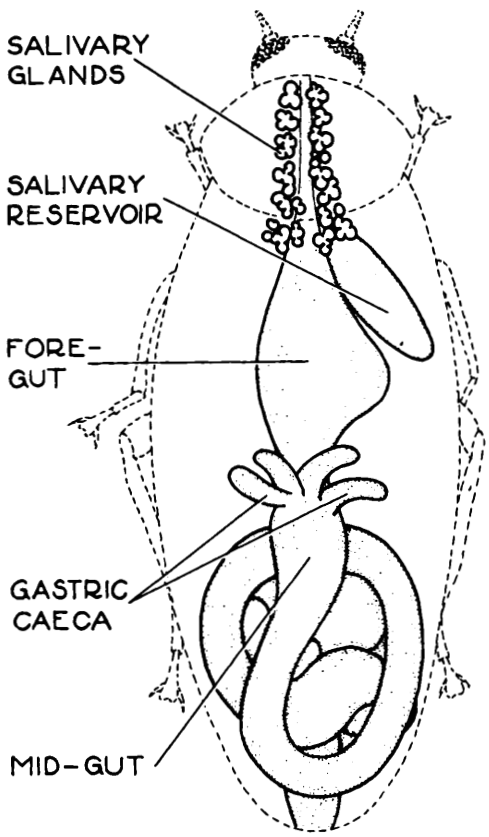

FIG. 1.

Diagram of *Leucophaea maderæ*. The organs indicated are sites of tumor formation. × 2¼.

tomized animals. This type of operation was performed in 231 male and female adults with, however, no apparent effect on the incidence of tumors. At least a certain percentage of these implants must have taken because egg development occurred in 56 females of this group. Tumors were also found after unilateral allatectomy (49 cases). This operation, however, did not prevent normal egg development which fact shows that one corpus allatum can fulfill the endocrine function of both glands.

These results suggested that the extirpation of the corpora allata may not have been the cause of tumor formation. The destruction of or interference with the normal function of some neighboring structure occurring accidentally during allatectomy was, therefore, suspected. Consequently pains were taken to improve the technic of allatectomy so that damage to neighboring structures was reduced as much as possible. The incidence of tumors after these improved operations decreased appreciably. The question arose which structures in the immediate proximity of the corpora allata and cardiaca could be involved.

Of such structures the recurrent nerve was given special attention, because its distribution, as traced in methylene blue preparations, showed a relationship to the sites of tumor formation.

The recurrent nerve belongs to the stomatogastric, *i.e.*, sympathetic nervous system, and takes its origin from the frontal ganglion (Fig. 2, 3). After passing between brain and pharynx the nerve becomes most intimately connected with the corpora cardiaca. Here is located a second sympathetic ganglion (hypocerebral ganglion) which in Leucophaea is represented by an inconspicuous group of

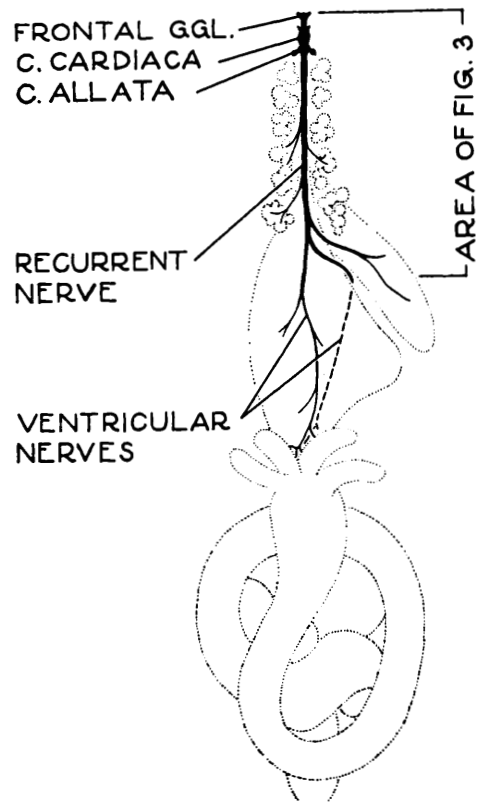

FIG. 2.

Diagram of innervation of salivary glands, salivary reservoir, and anterior portion of alimentary canal by branches of the recurrent nerve. × 2¼.

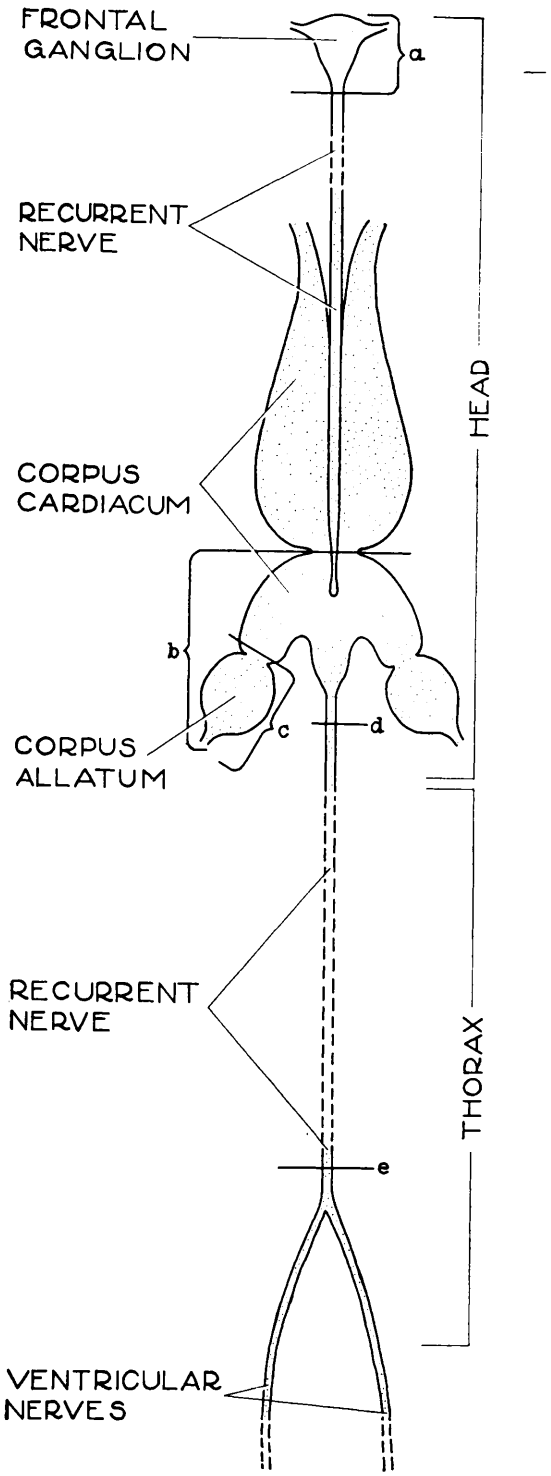

FIG. 3.
Diagram of stomatogastric nervous system and corpora cardiaca and allata of *Leucophaea maderæ*. a-e indicate the following operations: a, Extirpation of frontal ganglion. b, Removal of corpora allata and posterior corpora cardiaca. c, Allatectomy. d, Section of recurrent nerve close to corpora cardiaca. e, Section of recurrent nerve near bifurcation.

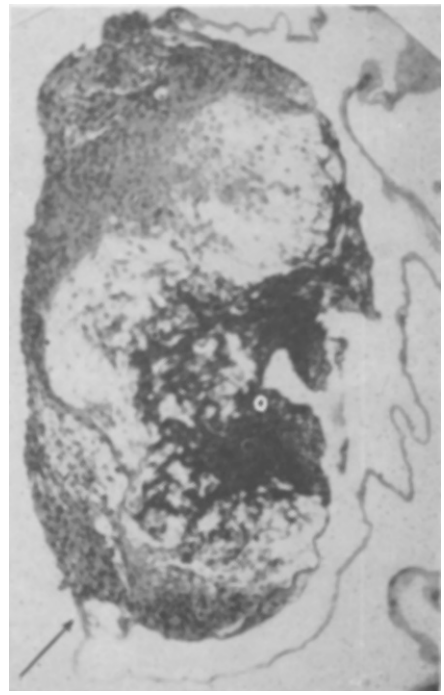

FIG. 4.
Tumor in wall of salivary reservoir. × 35.

FIG. 5.
Tumor in wall of salivary reservoir. The border between the thin wall of the salivary reservoir and the tumor is well marked (arrow). Three layers can be distinguished. An outer layer consists of small cells, a middle layer of swollen, vesiculated cells, an inner layer facing the lumen of the reservoir consists of brown cell debris. × 80.

ganglion cells associated with the recurrent nerve. In the thoracic region the recurrent nerve divides into 2 rami (ventricular nerves), and gives off branches to the salivary glands and to the wall of the salivary reservoir. The ventricular nerves continue to follow the alimentary canal which they innervate (Fig. 2). In Leucophaea they could be traced as far caudad as the gastric caeca which mark the beginning of the mid-gut (ventriculus). In this region the nerves ramify into thin branches whose actual termination could not be ascertained.

From this description it is obvious that during an operation in the region of the corpora cardiaca and allata the recurrent nerve may easily be severed (Fig. 3, b, c). In fact, this was demonstrated to have occurred in a considerable number of cases available for post mortem dissection or histological study. There was good agreement between the incidence of nerve injury and tumor development. It seemed not unlikely, therefore, that the accidental cutting of the recurrent nerve during cardiac- and allatectomy was the cause of the formation of tumors.

FIG. 6.
Tumor in salivary gland. Normal glandular tissue and salivary ducts (at right) above arrow. Tumor mass with remnants of glandular tissue beneath arrow. The tumor cells show whorl formation with degeneration in center. × 80.

This possibility was investigated in 3 series of experiments.

(1) The recurrent nerve was severed in 42 males and 3 females behind the corpora cardiaca and allata, care being taken to leave the glandular complex itself intact (Fig. 3, d).

(2) The recurrent nerve or its 2 ventricular branches were cut in 9 males in the thoracic region, *i.e.*, in a region considerably distant from the corpora cardiaca and allata (Fig. 3, e).

(3) The frontal ganglion which contains part of the cells of origin of the recurrent nerve was extirpated in 36 males, 14 females, and 13 nymphs (Fig. 3, a).

All 3 types of operation resulted in tumor formation. In series 1 and 2 the incidence was particularly high (approximately 80%). This seems to furnish ample proof that the neoplasms observed in the anterior portion of the alimentary canal and in the salivary complex were caused by the interference with their innervation rather than by a disturbance of the endocrine balance.

A more detailed description of the mode of growth and of the histological characteristics of the tumors here under consideration will be given in another paper. For the present it may suffice to say that they are well defined conspicuous tissue masses which in advanced stages can be easily noticed with the naked eye.

In histological preparations the borderline between the normal tissue and the tumor is usually well marked. The tumors consist of layers of cells whose appearance becomes progressively abnormal as the tumor enlarges. The cells of consecutive layers differ in various respects. In one layer, for instance, a considerable percentage of nuclei may be pycnotic, while in another they may be irregularly vesicular containing little chromatin. Often, near the lumen, these cells break down into a debris of brownish color (Fig. 5). This description applies only in a general way to the various tumors mentioned. Differences are observed in accordance with the tissues in which the tumors develop as, for instance, in salivary glands (Fig. 6) or fore-gut (Fig. 7).

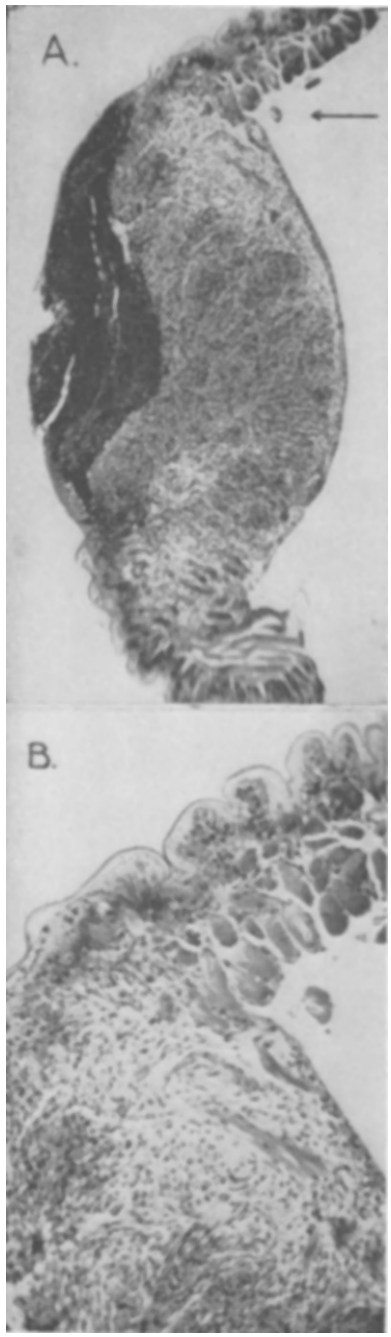

FIG. 7.

A. Tumor in wall of fore-gut. Above and beneath tumor the wall is normal consisting of a chitin-covered epithelium facing the lumen (to the left), and a muscularis. The stratification of the tumor is pronounced. × 35.

B. The tumorous transformation at the upper end (arrow) is shown at higher power. All components of the fore-gut wall are involved. × 80.

The part of the alimentary canal which is most commonly the site of extensive tumorous growth following the cutting of the recurrent nerve is the anterior portion of the mid-gut. At an early stage a ring-shaped thickening of the ventricular wall may be observed in the region of the gastric caeca. From there the neoplastic growth appears to proceed posteriorly for some distance. The intestinal wall, normally thin and more or less transparent, becomes thick and opaque. The columnar epithelium as well as part of the muscularis is replaced by multiple layers of cells. Examples are illustrated in Fig. 8 and 9. Fig. 8 shows the transition of the normal columnar epithelium of the mid-gut (left of arrow) into the irregular, multilayered tumor mass (above arrow). Fig. 9A illustrates the borderline between the epithelium of the esophageal valve (left of arrow) and the normal mid-gut epithelium (right of arrow) in an unoperated animal. In Fig. 9B a corresponding section through the alimentary canal of an animal in which the recurrent nerve had been cut is shown. The epithelium of the esophageal valve is unchanged, whereas the mid-gut epithelium is replaced by strati-

FIG. 8.

Mid-gut tumor showing transition (arrow) from normal columnar epithelium to multilayered tumor mass, overlapping normal epithelium. × 80.

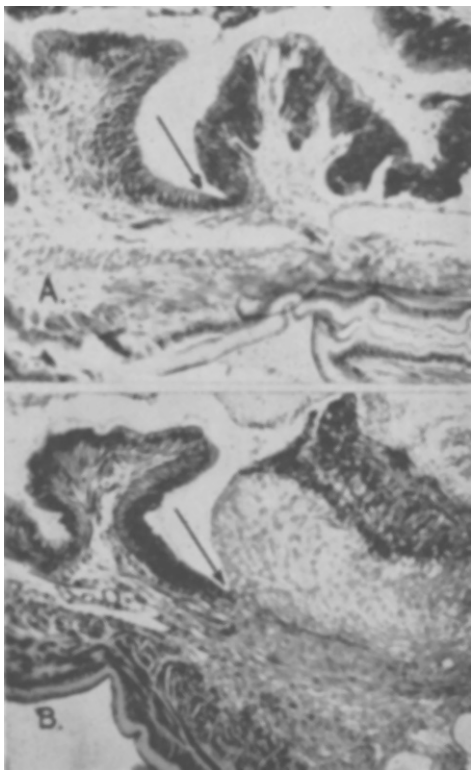

FIG. 9.
A. Intestinal wall at transition from esophageal valve (left of arrow) to mid-gut (right of arrow) in normal animal.
B. Corresponding section from an operated animal. Esophageal valve unchanged (left of arrow); tumor in mid-gut wall (right of arrow). × 80.

fied tumor tissue (right of arrow). Similar tissue changes as those described for the mid-gut may also be observed in the wall of the fore-gut (Fig. 7 A, B), but are, as a rule, less extensive and are less frequently encountered.

The severity of the tissue transformation makes it appear unlikely that the normal functions of the anterior portion of the alimentary canal can be maintained. In fact, animals with tumors of this kind died at intervals from 10 days to several months following the nerve lesion. The anterior portion of the alimentary canal was frequently filled with an abnormally large quantity of food, while at the same time the fat body was depleted. Death thus seems to be due to starvation.

Tumors growing from the thin, normally transparent wall of the salivary reservoir are conspicuous (Fig. 4 and 5). They may be round, oval, or irregularly shaped. The salivary reservoir may contain one large tumor (up to 10 mm in diameter) or several smaller ones. They consist of a thick layer of opaque tissue which, similar to that encountered in the mid-gut, appears to become gradually broken down into brown debris (Fig. 5).

The experimental tumors described were obtained in nymphs as well as in male and female adults ranging, at the time of operation, from shortly after emergence to 10 months of adult age. Altogether over 300 cases with tumors were studied.

In the literature reports on the occurrence of tumors in insects are rare. Brun[9] described a brain tumor in an ant, Stark[10-12] hereditary tumors in Drosophila. In view of the experimental findings in Leucophaea a search for spontaneously occurring tumors in this species was made. Among hundreds of unoperated animals, dissected at various ages, none had tumors in the salivary complex. However, a few specimens showed changes in the alimentary canal which, although of milder degree, were comparable to the tumors developing after the section of the recurrent nerve. Whether or not these tumors of the "normal" insect may be caused by some damage to the stomatogastric nervous system, or by irritation due to intestinal parasites cannot be decided.

Conclusion. (1) An insect is introduced as a suitable experimental animal offering new possibilities for the study of tumors.

(2) Interruption of a nerve has been shown to cause tumorous growth in organs which it supplies. Further experiments, already under way, must show whether this phenomenon occurs only in insects or applies also to vertebrates.

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