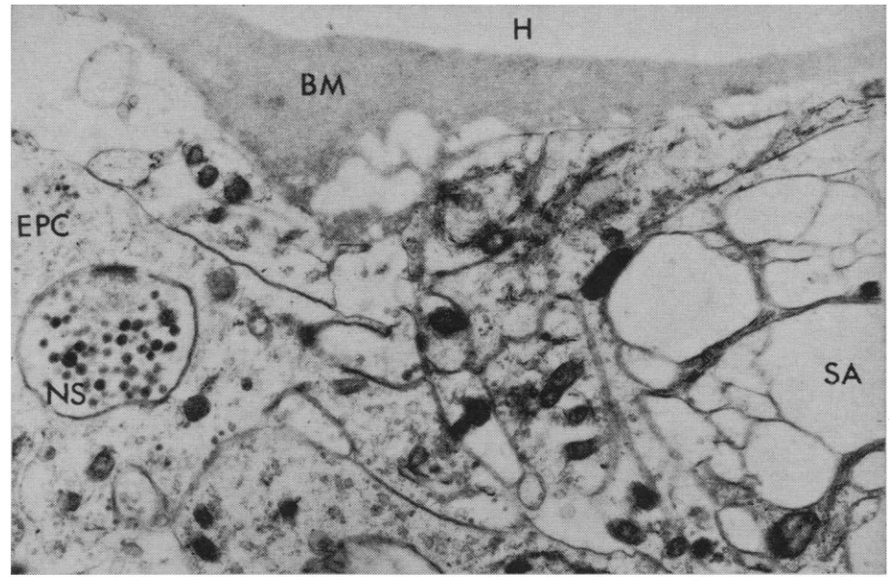
Neurosecretory Supply to the Epidermis of an Insect

Abstract. *Electron microscopy of the abdominal nerves of* Rhodnius *reveals neurosecretory axons which supply the abdominal epidermis. This suggests that the epidermal cells of insects are under more localized endocrine control than has previously been supposed.*

The nerves which supply the abdominal wall of the larva of *Rhodnius prolixus* contain axons, all of which were thought to be sensory and each of them terminating in a primary sensory cell in the epidermis (*1*). However, with the use of the electron microscope, a few of these axons are in fact neurosecretory; they contain membrane-bound electron-opaque granules (Figs. 1 and 2), whose size and appearance are characteristic of elementary neurosecretory granules (*2*). Since there are no neurosecretory cell bodies in the epidermis, these axons constitute an efferent supply to the epidermis. Figure 2 shows a bundle of sensory axons and a neurosecretory axon in a nerve at the point where it runs into the abdominal wall. Serial sections have shown that these neurosecretory axons run into the epidermis and can be found among the epider-



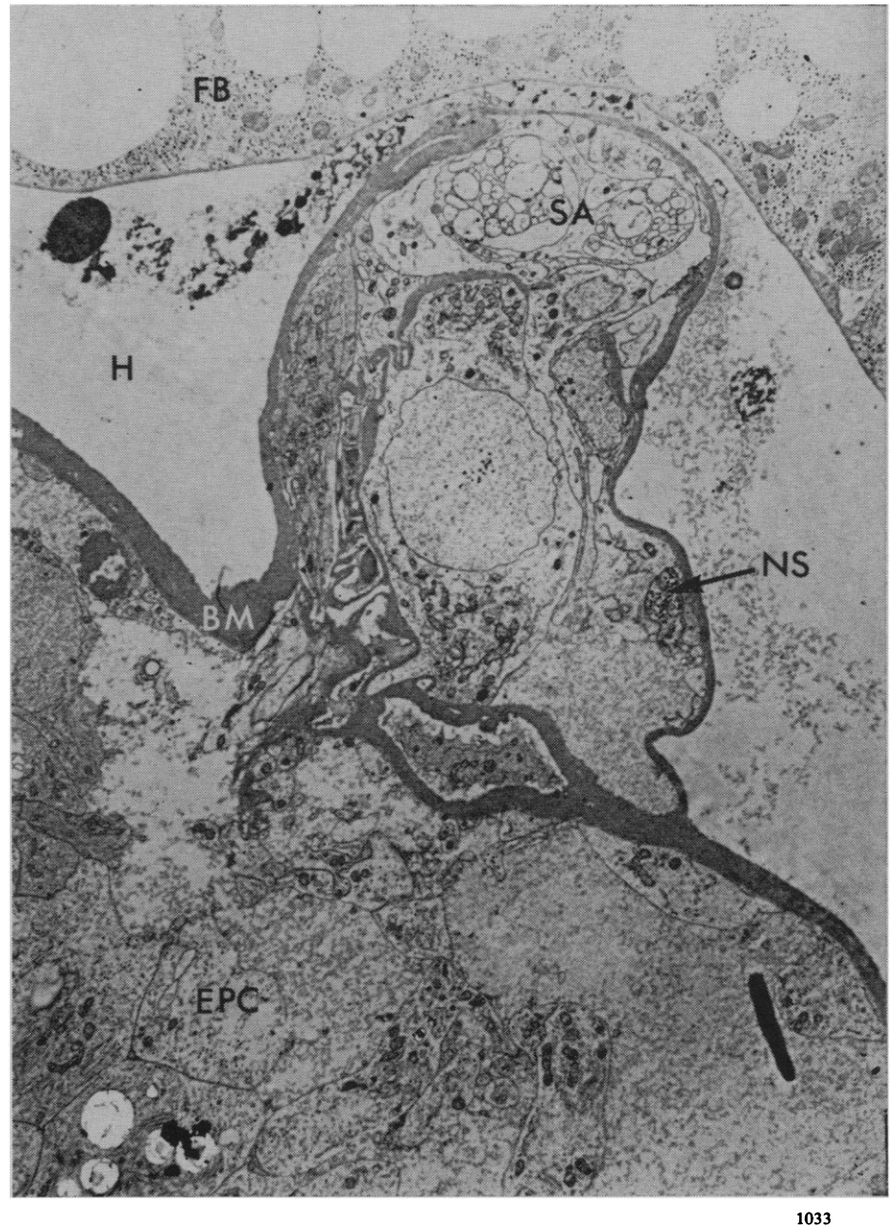


Fig. 1 (top right). Section through the epidermis of the fourth abdominal sternite of a fifth stage larva of *Rhodnius*. The tissue was fixed in osmium tetroxide and embedded in Araldite. The section was stained with Reynolds' lead stain. In this section a neurosecretory axon (*NS*) is running through or into an epidermal cell (*EPC*). The axon contains elementary neurosecretory granules which vary in diameter betwen 1000 and 1600 Å; some of them are clearly membrane-bound. Also in the section are a bundle of sensory axons (*SA*) which has also penetrated the basement membrane of the epidermis (*BM*). The hemocoel (*H*) lies outside the basement membrane (× 14,250).

Fig. 2 (bottom right). Transverse section through a peripheral abdominal nerve of *Rhodnius* at the point where it runs into the fourth abdominal sternite. The tissue was fixed in osmium tetroxide and embedded in Araldite. The section was stained with Reynolds' lead stain. The nerve includes a neurosecretory axon (*NS*) and several sensory axons (*SA*). The section also includes a part of the fat body (*FB*), hemocoel (*H*), epidermal cells (*EPC*) and the basement membrane of the epidermis (*BM*) which is continuous with the nerve sheath (× 2900).

mal cells under the basement membrane (Fig. 1).

In larvae of *Rhodnius* at least part of this neurosecretory supply is probably concerned in directing the change in the mechanical properties of the abdominal cuticle which occurs when the insect feeds (*3*). However, this discovery opens up the possibility that the epidermal cells of insects can be under much more localized endocrine control than that afforded by the established basis of blood-borne hormones.

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References and Notes

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Histamine Synthesis and Gastric Secretion after Portacaval Shunt

Abstract. *In man there is an increased incidence of peptic ulcer after portacaval shunt. In the rat, 2 months after portacaval anastomosis, there is a generalized increase in the histamine content of the soft tissues, and the increase is most marked in the acid-secreting portion of the stomach. This appears to be secondary to increased activity of the histamine-synthesizing enzyme, histidine decarboxylase. A histidine decarboxylase inhibitor can prevent such hypersecretion of acid in the stomach of these animals.*

An increased incidence of duodenal ulcer has been noted in man after portacaval shunt (*1*). Gastric hypersecretion of acid occurs in experimental animals in which portal venous blood flow has been diverted from the liver (*2*, *3*) and might account for the increased incidence of peptic ulceration. The hypersecretion may be due to a secretagogue, such as histamine or gastrin, which escapes inactivation by the liver (*3*, *4*). Histamine content of the stomach is increased in rats after portacaval shunt (*5*); this suggests that some change in the storage or metabolism of histamine occurs after portacaval anastomosis. In our study, the metabolism of histamine in rats subjected to portacaval shunt has been examined.

End-to-side portacaval anastomoses were performed by a modification of the technique described by Lee and Fisher (*6*) in Osborne-Mendel rats (300 g). The patency of the shunts was verified by splenoportography in intact rats and at autopsy.

Day *et al.* (*5*), using a bioassay, noted a marked increase in the histamine activity of stomachs of rats 6 months after portacaval shunt. Increased concentration of substances that contract smooth muscle may be present in subjects with liver disease (*7*). Possibly the elevated histamine activity noted by Day *et al.* (*5*) may have been due to some other substance with the same activity. Therefore, our study included the assay by a fluorometric method (*8*) of histamine in the stomachs of rats 2 months after portacaval shunt. There was a fourfold increase in the histamine content of the fundi of these animals over that in sham operated controls (shunted 44.62 $\pm$ 4.85, controls 11.69 $\pm$ 1.51 μg of histamine per gram of stomach, $P <$ .001). There was a smaller increase in histamine content in the cardia, the thin-walled portion of the stomach (shunted 7.76 $\pm$ 0.75, controls 4.12 $\pm$ 0.38 μg of histamine per gram of stomach, $P <$ .01).

There are several possible mechanisms which could account for an accumulation of histamine after portacaval shunt. Histamine absorbed from the gastrointestinal tract might bypass the liver and thereby escape enzymatic inactivation and accumulate in tissues (*4*). Decreased activity of enzymes that destroy histamine in the stomach or intestine—namely, histamine methyltransferase and diamine oxidase—could explain a local accumulation of this amine. Finally, an increase in histamine synthesis may be responsible for its greater concentration in the stomach.

To examine the possibility that after portacaval anastomosis, histamine liberated from the intestine might escape inactivation by the liver and accumulate in tissues (*5*), the disposition of exogenous histamine was studied after oral and parenteral administration. Two months after operation, groups of shunted rats and sham-operated controls received 15 mc of histamine-C^{14} by stomach tube or subcutaneous injection. Rats were killed 3 hours later by cervical fracture, and stomachs, spleens, hearts and livers were assayed for histamine-C^{14} and its metabolites, imidazolacetic acid-C^{14} and imidazolacetic acid-C^{14} riboside (*9*). After either subcutaneous or oral administration, the concentration of histamine-C^{14}, imidazolacetic acid-C^{14}, and imidazolacetic acid-C^{14} riboside in shunted rats did not differ from that of control animals. It is therefore unlikely that a diminished hepatic destruction of circulating histamine could account for the accumulation of this amine.

Table 1. Histidine decarboxylase activity in stomach wall of rats 2 months after portacaval shunt operation. Results are given as the mean $\pm$ the standard error of the mean (S.E.M.) for groups of 12 animals.

Operation	C^{14}-histamine formed ($m\mu$mole g^{-1} hr^{-1})	
	Fundic stomach	Cardiac stomach
Sham	4.23 $\pm$ 0.42	0.63 $\pm$ 0.04
Portacaval shunt	17.57* $\pm$ 2.94	2.02* $\pm$ 0.32

* $P <$ .001.

The biogenic amine, serotonin, is largely inactivated by monoamine oxidase in the liver. If accumulation of the amine were secondary to its escaping destruction by the liver, one might expect an increase in serotonin as well as in histamine. However, serotonin, measured by the technique of Bogdanski *et al.* (*10*), was normal in animals with a portacaval shunt. From these data we conclude that there is a specific alteration in histamine metabolism.

Histamine is primarily catabolized either by *N*-methylation of the 4-nitrogen of the ring by histamine methyltransferase, or by oxidative deamination of the side chain by diamine oxidase. Decreased activity of these enzymes in the gastrointestinal tract might allow the local accumulation of histamine. Histamine methyltransferase activity in the stomach (*11*) and diamine oxidase activity of stomach and small intestine (*12*) were not altered in rats with portacaval shunts.

To examine the possibility that histamine synthesis is altered after portacaval shunt, the activity of histidine decarboxylase, the histamine-synthesizing enzyme, was measured by a modification (*13*) of the technique of Schayer (*14*). Histidine decarboxylase activity in the fundus, the acid-secreting portion of the stomach, was increased