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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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

from 4.23 ± 0.42 mμmole of histamine-C^{14} formed per gram of stomach per hour to 17.57 ± 2.94 mμmole after portacaval shunt ($P < .001$). A similar increase was also noted in the cardiac stomach of these animals (Table 1). The activity of the serotonin-synthesizing enzyme, 5-hydroxytryptophan decarboxylase (*15*), was normal in stomachs of rats with portacaval shunts, an indication of specific alteration in histamine synthesis.

If hypersecretion of acid in our experimental rats is secondary to an increased activity of histidine decarboxylase, it should be possible to reduce this acid secretion by an inhibitor of this enzyme. Acid in the stomach was measured by the administration of a test meal (*16*). Two months after portacaval shunt, gastric secretion of acid rose from 26.80 ± 2.98 μeq of HCl per 30 minutes to 115.1 ± 16.4 μeq ($P < .001$). Treatment with NSD-1055 (4-bromo-3-hydroxybenzyloxyamine) (*17*), a potent inhibitor of histidine decarboxylase reduced acid secretion to 38.55 ± 3.08 μeq, nearly normal.

Our data suggest that the hypersecretion of acid after portacaval shunt may be secondary to increased histamine synthesis in the stomach. The mechanism of the activation of histidine decarboxylase is not clear.

Treatment with corticosteroids often results in hypersecretion of acids and an increased incidence of peptic ulcers (*18*). Telford and West (*19*) have noted an increase both in activity of histidine decarboxylase and histamine content in the stomachs of rats after administration of prednisolone. We have confirmed these observations and have been able to inhibit this hypersecretion by treatment with NSD-1055.

Histamine has been proposed as the final common pathway in secretion of gastric acid (*20*). Stimuli resulting in acid secretion do so by way of local release of histamine. If the content of histamine in the stomach is increased, as after portacaval shunt or steroid therapy, a given stimulus may result in greater histamine release, thereby resulting in greater acid secretion. Thus, an increase in synthesis of histamine in the stomach may play a part in hypersecretion of acid and subsequent peptic ulceration in these conditions and in a variety of pathological states.

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Crystal and Molecular Structure of a Phospholipid Component: L-α-Glycerophosphorylcholine Cadmium Chloride Trihydrate

Abstract. *The structure of* L-α-*glycerophosphorylcholine cadmium chloride trihydrate has been determined by the conventional, single-crystal, x-ray diffraction technique. The phospholipid component displays the characteristic* gauche *conformation for the choline residue and the* gauche-gauche *conformation for the glycerol moiety. Therefore, a possible model for the structures of phospholipids is similar to that proposed by Finean.*

The phospholipids form a major constituent of cell membranes. Their structures have never been studied by the method of single crystal x-ray techniques primarily because of the difficulty of obtaining adequate crystals. Any information on the molecular structure of the constituents would provide a useful basis for postulating probable structures for the phospholipids. We have determined the crystal and molecular structure of the trihydrate of the cadmium chloride complex of L-α-glycerophosphorylcholine (GPC). Figure 1 shows the chemical formula of GPC, which is a hydrolytic product of phosphotidyl choline (lecithin) and occurs in mammalian tissues and fluids.

The cadmium chloride complex of GPC crystallizes from aqueous solutions as the trihydrate, yielding colorless needles elongated in the *c* direction. The crystals have orthorhombic symmetry. Unit cell parameters measured with a diffractometer are: a = 9.452 ± 0.001 Å, b = 27.038 ± 0.004 Å, and c = 7.391 ± 0.002 Å. For four molecules, chemical composition $PO_6NC_8H_{20} \cdot CdCl_2 \cdot 3H_2O$, per unit cell, the calculated density is 1.739 g cm^{-3}, which is in agreement with the value of 1.731 g cm^{-3} measured by the flotation method in a mixture of CCl_4 and CHI_3.

The systematically absent reflections were $h00$, $0k0$ and $00l$ for h, k and l odd except for the very weak 100 and 500 reflections. The space group was assumed, therefore, to be $P22_12_1$. However, the three largest peaks in the Patterson function cannot be interpreted to give Cd positions consistent with the symmetry of this space group. It was assumed that reflections 100 and 500 were spurious, probably Renninger reflections, and that the space group is in fact $P2_12_12_1$.

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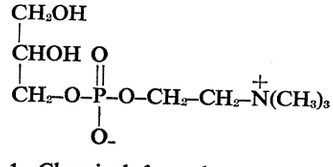

Fig. 1. Chemical formula of L-α-glycerophosphorylcholine.