whether other factors are involved remains to be determined.

Summary. Of 18 compounds studied, only protoporphyrin significantly protected mice injected with lethal doses of "hematoporphyrin." Results of separate experiments with 277 mice showed (a) 14% survival in 76 mice which received "Hp" and vehicle alone, (b) 47% survival in 90 mice injected with protoporphyrin in addition to the "Hp" and kept in the dark, and (c) 30% survival in 109 mice injected with both porphyrins and kept in a room illuminated with fluorescent lights. The marked fall in total body oxygen uptake associated with "Hp" administration was decreased considerably by administration of protoporphyrin.

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On the Mechanism of Emesis Induced by 5-Hydroxytryptamine. (29260)

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The author(1) has reported that intravenous injection of catecholamines induces emesis in cats and dogs. Recently, Peng(2), has confirmed these results. Studies of a similar nature with 5-hydroxytryptamine (5HT) have yielded seemingly contradictory results. Bogdanski *et al*(3) demonstrated that injection of 5-hydroxytryptophan (5HTP), the precursor of 5 HT, produces vomiting in dogs; on the other hand, Feldberg and Sherwood(4) reported that 5HT introduced into the ventricles of cats does not elicit this effect.

The experiments described here were carried out to determine whether 5HTP-induced emesis in cats might be mediated through the release of brain norepinephrine (NE).

Materials and methods. Experiments were carried out in nonfasted cats of either sex, weighing 1.5-4.0 kg. The animals received 50 ml of lukewarm water by stomach tube and 20 minutes later were given various doses of 5HTP (1% solution in isotonic saline). The emetic effects of 5HTP were determined in control cats and in cats pretreated with various monoamine oxidase (MAO) inhibitors (iproniazid, nialamide and isocarboxazid), with central depressants (pentobarbital and chlorpromazine) and with various NE-depleting agents (α-methyl-3-4 dihydroxyphenylalanine [α-methyl DOPA], α-methyl-m-tyrosine [α-MMT] and reserpine)(5,6). The results are expressed as the proportion of cats that showed an emetic effect. All drugs were administered intraperitoneally unless otherwise noted.

Results. Emesis produced by 5HTP. Table I shows that the emetic effect of 5HTP (10 to 50 mg/kg, i.p.) was related to the dosage; in doses of 50 mg/kg, 5HTP produced vomiting in 5 of 5 cats. No vomiting occurred in 8 cats given saline alone. Tolerance to 5HTP did not occur, for an almost identical dose-response curve was obtained when the amino acid was given to the animals 5 days later. In contrast to the catecholamines which in-

TABLE I. Effect of Various Drugs on 5HTP-Induced Emesis in Cats. Cats were pretreated with various drugs and then given 5HTP. Results are expressed as: No. of cats vomiting/total of cats (n).

Pretreatment (mg/kg, i.p.)	Dose of 5HTP (mg/kg, i.p.) 10	15	20	50
None	0/4	3/9	3/5	5/5
Iproniazid, 10	—	4/5	—	—
" 20	—	6/6	—	—
Nialamide, .5	—	4/6	—	—
" 1.0	—	6/6	—	—
Isocarboxazid, .5	—	1/4	—	—
" 1.0	—	5/6	—	—
Pentobarbital, 32.5	—	—	0/8	—
Chlorpromazine, .25	—	—	3/6	—
" .50	—	—	1/5	—
Reserpine, 0.1	—	—	0/11	—
α-Methyl DOPA, 50	—	—	1/5	—
α-MMT, 50	—	—	1/5	—
" 75	—	—	0/3	—

duce emesis rapidly(1), 5HTP had a latent period of 15 to 75 minutes.

Effect of MAO inhibitors on emesis produced by 5HTP. To show whether the emetic effect is associated with formation of a biogenic amine, the various MAO inhibitors were administered to cats 90 minutes before the injection of 5HTP (15 mg/kg, i.p.). The MAO inhibitors markedly increased the incidence of vomiting, the higher dose of each inhibitor producing an emetic effect in virtually 100% of the animals (Table I),

Effect of central depressants. Pentobarbital in anesthetic doses (32.5 mg/kg) prevented the emetic action of 5HTP (20 mg/kg). Chlorpromazine given one hour before 5HTP also appeared to exert an antiemetic effect in nonsedative doses (0.5 mg/kg) (Table I).

Effect of drugs which block storage of brain amines. The possibility that 5HTP produces vomiting through the release of NE was investigated by determining whether 5HTP (20 mg/kg) caused emesis in cats when given after brain NE has been depleted by various agents. After pretreatment with reserpine, emesis occurred in 11 cats (Table I), and α-methyl DOPA (50 mg/kg, i.p.) decreased vomiting to 1 in 5 cats. Similarly, pretreatment with α-MMT (50 mg/kg) decreased the emetic effect of 5HTP to 1 of 5 cats while a larger dose of α-MMT (75 mg/kg) prevented vomiting in 3 of 3 cats.

A particularly definitive result was obtained in 3 cats that consistently vomited after intravenous injection of 50 mg/kg of 5HTP. Pretreatment with α-MMT (50 mg/kg, i.v.) prevented the emetic effect in all 3 animals.

Discussion. These results showing that 5HTP produces emesis in cats are in accord with those of Bogdanski *et al*(3) in dogs. Preliminary results (this laboratory, unpublished) indicate that cats are much more sensitive than dogs to the emetic action of 5HTP, perhaps because of the low activity of brain MAO and consequent slow disappearance of brain monoamines in this animal.

At first glance, the results presented here would suggest that emesis produced by 5HTP is mediated through 5HTP, since this amine is the decarboxylation product of the amino acid, and the emetic action is enhanced by MAO inhibitors. The time lapse between 5HTP administration and the emetic effect would correspond to the time required for accumulation of sufficient amounts of free 5HT in brain. These results would appear then to be contrary to the observations of Feldberg and Sherwood(4) who showed that intraventricular 5HT is not emetic. However, these authors have shown that catecholamines given by this route are effective emetics.

A number of biochemical and pharmacological data suggest that administration of 5HTP causes release of brain NE. For example, Bogdanski *et al*(3) have shown that 5HTP produces excitation in normal animals but not in animals previously depleted of brain NE; moreover, the excitation is antagonized by chlorpromazine, a drug believed to act mainly on central adrenergic mechanisms. These findings suggest that 5HT formed from 5HTP does not by itself produce excitation but through release of NE. Considerable biochemical evidence favors the view that 5HTP can result in release of NE. Since 5HTP and DOPA decarboxylase are one and the same enzyme(7), exogenous 5HTP will be decarboxylated in NE as well as in 5HT storage sites. Recent studies indicate that 5HT readily enters NE storage granules where it presumably displaces NE(8), and that the in-

fusion of 5HT through the heart *in vitro* causes the release of NE (unpublished work of Nash, Costa and Brodie).

The data presented here indicate that the emetic action of 5HTP is mediated through release of catecholamines; thus the emetic action is abolished by pretreatment with reserpine and is considerably reduced by pretreatment with α-MMT or α-methyl DOPA.

It is possible that the locus of action of NE is the hypothalamus, for Hess(9) caused emesis in cats after electrical stimulation of this brain area which is rich in NE. Alternatively, NE might also act at the area postrema for Borison(10) has demonstrated that ablation of this area abolishes the emetic action of catecholamines. However, other loci may also be involved in the action of 5HTP.

Summary. 1. 5-Hydroxytryptophan (5-HTP) given parenterally to cats exerts emesis. This effect is enhanced by various monoamine oxidase inhibitors and blocked by pentobarbital. 2. The emetic effect of 5HTP is antagonized by chlorpromazine and by compounds that deplete brain catecholamines (reserprine, α-methyl DOPA and α-methyl-m-tyrosine) suggesting that 5HTP acts through release of norepinephrine.

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Action of Isoimmune Serum on Peritoneal Cells *in vitro.** (29261)

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It has recently been shown that peritoneal macrophages from mice are capable of phagocytizing tumor cells *in vitro* in the presence of isoimmune serum(1,2). The isoimmune serum and peritoneal macrophages were invariably obtained from mice of the same inbred strain and the immune serum was directed against the isoantigens of the tumor cells. The isoantibody would therefore be expected to combine with the antigens on the surface of the tumor cells but not with those of the peritoneal cells. In this report experiments are described in which the isoimmune serum was directed against the peritoneal cells, and the properties of these cells were examined in both cytotoxic(3) and phagocytic tests(1,2). It was found that peritoneal macrophages when placed in tissue culture were characterized by a high resistance to the cytotoxic activity of isoantibody and complement under conditions where peritoneal lymphocytes, eosinophils, neutrophils and mast cells were readily lysed. Furthermore, in the presence of immune serum directed against the isoantigens of both the macrophages and the tumor cells, peritoneal macro-

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