sis, and carcinoma of the pancreas with metastasis to the liver. The elevation in SLAP appears to be an increase in all LAP components, rather than the appearance, *de novo*, of other components in cases of hepatobiliary disease.

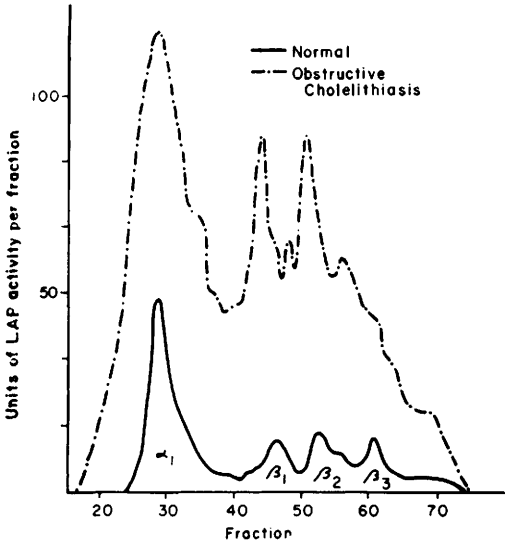

FIG. 1. LAP activity in fractions of typical serum samples from (1) a normal person and (2) a person with obstructive cholelithiasis.

TABLE I. Average and Range of Concentrations of SLAP Components in Serum of Normal Persons.*

Component	Avg level (units/ml)	Extreme levels (units/ml)
α_1	130	124-135
β_1	33	25-42
β^2	30	22-33
β_3	23	23-25

* These data are from 10 normal adult persons.

These findings of several SLAP components in normal persons are in direct contrast to those of Kowlessar(5), and Rutenburg(6), who report only one component in normal persons. The nature of these SLAP components and factors influencing their elaboration are being actively investigated.

Summary. Four distinct leucylaminopeptidase components have been found in normal human sera by DEAE Cellulose chromatography. In cases of hepatobiliary disease, there is apparently an increase in all components rather than the appearance of new components.

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Received November 16, 1961. P.S.E.B.M., 1962, v109.

Effects of Amine Oxidase Inhibition on *E. coli* Endotoxin Mortality in Mice.** (27222)

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The role of vasoactive amines in shock due to bacterial endotoxin has received increasing attention recently. The observation of Gordon and Lipton(1) that pretreatment of mice with serotonin (5-hydroxytryptamine) reduced endotoxin mortality suggested that inhibition of endogenous serotonin catabolism by inhibition of monoamine oxidase (MAO) might also be effective in protecting against endotoxin. Such an effect was demonstrated

** This work supported by U.S.P.H.S. grant and Minnesota Heart Assn.

* U.S.P.H.S. Special Research Fellow.

† U.S.P.H.S. Post Doctoral Fellow.

TABLE I. Mortality Following Intraperitoneal *E. coli* Endotoxin Injection.

	P.I.H. group		Nialamide group		S.K.F. 556 group	
Dose of endotoxin (mg/kg)	P.I.H. treated	Saline controls	Nialamide treated	Saline controls	S.K.F. 556 treated	Saline controls
2	0/21	0/20	—	—	—	—
5	4/20	5/20	—	1/14	—	1/14
10	4/20	14/20	4/13	6/14	2/13	6/14
20	12/20	14/20	8/13	12/14	6/13	12/14
30	—	—	10/13	—	12/13	—
40	16/20	19/20	11/13	14/14	13/13	14/14
60	—	—	10/13	—	12/12	—

Numerator: No. of animals dead at end of 72 hr. Denominator: Total animals in each group.

(2) although other workers failed to show protection under similar conditions(3). Recently it has been reported that pretreatment with the M.A.O. inhibitor beta-phenyl isopropyl hydrazine increased mortality to endotoxin in mice(4).

Materials and methods. Albino A strain inbred mice, weighing 15 to 25 g, and about 2 months old, were used in this study. All mice were randomized prior to receiving intraperitoneal injections of the M.A.O. inhibitor or of 0.2 ml of isotonic saline at the indicated time prior to challenge with endotoxin. Mice in all groups received endotoxin at essentially the same time of day to exclude diurnal variations in sensitivity. Endotoxin was prepared by the method of Braude and associates(5)‡. Mortality was tabulated at 12-hour intervals for 72 hours. MAO inhibitors used were beta phenyl isopropyl hydrazine (P.I.H.)§, 1 - (2 - [benzylcarbamyl] ethyl) - 2 - isonicotinoyl - hydrazine (Nialamide)‖ and N,N-dimethyl-2-phenylcyclo-propylamine hydrochloride (S.K.F. 556).¶ Nialamide and S.K.F. 556 were given on successive days to one-half of the animals used in each case, to confirm the reproducibility of the experiment. The results were pooled for statistical purposes. P.I.H. was given in a dose of 10 mg/kg two hours before endotoxin, Nialamide was given in a dose of 20 mg/kg eighteen hours before endotoxin, and S.K.F. 556 in a dose of 10 mg/kg 8 hours before endotoxin. All animals were weighed individually prior to treatment with a MAO inhibitor, and prior to administration of endotoxin. The data were analyzed by computing Spearman-Karber estimates(6) of LD_{50}'s and the corresponding potency estimates.

Results. The mortality due to endotoxin at the end of the 72-hour period is shown in Table I. The majority of animals were alive after 12 hours. Those that succumbed usually did so between 12 and 24 hours after endotoxin. An occasional animal died between 48 and 72 hours. All MAO inhibitors afforded protection. The LD_{50}'s estimated by the Spearman-Karber method are shown in Table II. All MAO inhibitors used showed a significant effect in protecting against endotoxin. There was no significant difference in the protective effect of the 3 drugs; statistically the protection of P.I.H. and S.K.F. 556 was seen at the 1% level, that of Nialamide at the 5% level. The effect of pretreatment was to reduce the potency of the endotoxin by about one-third.

Discussion. Under the given conditions the protective effect of MAO inhibitors was small, but statistically significant. These results are in accord with the protective action of pretreatment with serotonin(1) and of the serotonin precursor 5-hydroxytryptophan(4). The doses chosen in each case were those which gave significant inhibition of monoamine oxidase without side effects *in vivo*, and the endotoxin was given at a time when the pharmacologic action of the drug was maximal. When P.I.H. is used in larger amounts (c. 40 mg/kg) the lethal effect of endotoxin has been reported to be enhanced (4).

‡ Furnished through the kindness of Dr. Wesley W. Spink.

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‖ Pfizer Laboratories, Brooklyn, N. Y.

¶ Smith, Kline and French Laboratories, Philadelphia, Pa.

TABLE II. LD_{50} and Potency of M.A.O. Inhibitors in Protecting against *E. coli* Endotoxin.

	P.I.H.	Saline control	Nialamide	Saline control	S.K.F. 556	Saline control
LD_{50} (mg/kg)	15.85	9.12	17.38	10.72	17.38	10.72
Potency ratio	1.74 (1.74>1.00 at P ≤.01)		1.62 (1.62>1.00 at P ≤.05)		1.62 (1.62>1.00 at P ≤.01)	

P.I.H. and Nialamide both contain the hydrazine moiety and inhibit diamine oxidase (D.A.O.) as well as M.A.O., whereas S.K.F. 556 does not contain the hydrazine moiety and inhibits only M.A.O.(7). These data showed that when both M.A.O. and D.A.O. were inhibited, the effect was not one of simple potency reduction of the endotoxin effect, but also one of greater variation in tolerance to endotoxin, best shown in the wide dose range for Nialamide in which the mortality was between 0 and 100% (Table I).

Although a different mechanism of protection may be operative for animals given drugs which inhibit both M.A.O. and D.A.O., inhibition of M.A.O. alone is complex, affecting serotonin, tryptamine, dopamine, and catechol amine metabolism. Although inhibition of endogenous serotonin destruction alone may diminish the lethality of endotoxin, any protection afforded by serotonin may be mediated through adrenal corticoids, for serotonin administration has been shown to increase ACTH output(8) and adrenal corticoids are known to protect against endotoxin (9).

Summary. M.A.O. inhibitors P.I.H., Nialamide and S.K.F. 556 were shown to have a small but significant effect in reducing mortality to intraperitoneal injection of *E. coli* endotoxin. Inhibition of M.A.O. alone appeared to have an effect distinct from inhibition of both M.A.O. and D.A.O. though the 3 drugs were not of significantly different potency.

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Received November 16, 1961. P.S.E.B.M., 1962, v109.

Some Aspects of the Relationship Between Plasma and Urine Erythropoietin.* (27223)

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Anemia and hypoxia will induce elevated levels of erythropoietin (EPF) in plasma and/or urine(1,2). However, the relationship of EPF in plasma to that in urine is unclear. Systematic assays of EPF in plasma and urine taken during the same time interval from the same animals have not been reported. The present study deals with this aspect of the EPF problem, and reports data as to time of appearance and amounts of EPF present in plasma and urine after varying stimuli.

* This study was supported in part by U. S. Public Health Service and Atomic Energy Commission Grants.

Methods and materials. The experimental