technic,[5] was employed. In addition some tests were run by placing either 5-grain or 7.5-grain sulfanilamide tablets in the center of a sterile petri plate and pouring agar inoculated with a milliliter of an 18-hour broth culture of bacteria or 48-hour broth culture of yeast. Depending on the organism, the tablet or agar cup filled with sulfanilamide was surrounded by a zone of no growth or partial growth. At the edge of the area of inhibited growth stimulation was indicated by the appearance of a zone of growth heavier than elsewhere in the plate. Control plates were poured to check the distribution of inoculum in the agar and the possible influence of technique. For the bacteria, a beef infusion to which was added 2 per cent. sodium chloride, 1 per cent. Difco-peptone and 0.05 per cent. glucose was used. This was adjusted to pH 7.6. Czepak's medium was employed for the yeasts studied.

The following bacteria from our stock culture collection showed no zone of stimulation: *Lactobacillus acidophilus, Streptococcus fecalis, S. zymogenes* (both a proteolytic and non-proteolytic strain), *S. durans, S. mastiditis, S. pyogenes group A* (strains Dochez, J 17A4), two strains of *S. lactis, Escherichia coli, Aerobacter cloacae, Salmonella schottmulleri, S. paratyphi, Shigella gallinarum, Klebsiella ozaenae, Staphylococcus citreus, S. albus, Sarcina ventriculi, Micrococcus nitrificans.* Irregular results were given by *Aerobacter aerogenes* and two strains of *Eberthella typhi.*

Stimulation was exhibited by a strain of *Pseudomonas aeruginosae* and *Alkaligenes fecalis.*

Of 29 strains of aerobic spore-forming bacteria tested, 12 which represented strains of *Bacillus vulgatus, B. mesentericus* and *B. mycoides,* showed zones of stimulation. Gram stains prepared from cells in the stimulation zone and from normal growth revealed no obvious or systematic differences. In one case cells from the stimulation zone showed a greater number of chain formations. In another case the cells were larger.

Of 12 strains of *Bacillus vulgatus* (identified according to published criteria[6]) 7 showed a zone of stimulation. Thus the effect seems to be an intra-species one rather than related to the species.

The zone of stimulation did not always appear in the early stages of growth. Often it became visible only after 72 hours of growth.

In the case of the yeasts, an unidentified strain of *Torulaspora* showed a zone of slight stimulation. The following were not stimulated: *Torula glutinis, T. cremoris, Saccharomyces cerevisiae, S. ellipsoideus, Willia anomala, Zygosaccharomyces bailii, Oidium lactis, Monilia nigra.* The yeasts were incubated at room temperature and observed at the end of 72 hours and 7 days.

Will an organism manifest stimulation by one toxic substance and not another? Apparently it will, as tests run on *Escherichia coli, Bacillus subtilis, Willia anomala* and a few others gave a stimulation zone with bichloride of mercury and not with sulfanilamide.

Of late there has been renewed interest in the therapeutic efficacy of anti-bacterial substances produced by microorganisms. It would be informative to know whether they too exhibit a stimulative action in low concentrations. Waksman[7] in a review of the subject of bacterial antagonism makes no mention that the question has been considered. Yet it is evident that for one of these substances, actinomycin, a stimulative effect is exerted on *Bacillus mycoides* and *Sarcina lutea* as photos published in a paper[8] describing *Actinomyces antibioticus* clearly show zones of stimulation.

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narcosis, and possibly bring some of the biologically produced antagonistic substances within the ken of narcotic mechanisms.

[5] U. S. Department of Agriculture Circular No. 198, 1931.

[6] C. Lamanna, *Jour. Inf. Dis.*, 67: 193, 1940.

INCREASED LIVER ARGINASE ON ADMINISTRATION OF ADRENOCORTICAL AND CORTICOTROPIC HORMONES[1]

IT has been shown in recent years that dietary conditions may affect the arginase content of the liver of rats. Thus, as would perhaps be expected, factors leading to increased deamination and gluconeogenesis, such as high protein diets or fasting, were found to increase liver arginase.[2] An investigation of the action on liver arginase of hormones known to control the rate of gluconeogenesis appeared indicated.

Liver arginase was determined in several groups of hypophysectomized rats which had received 15 daily injections of pituitary extracts high in adrenocorticotropic activity (ACT H),[3] and in one group which had been similarly treated with cortin (Adrenal Cortical Extract, Upjohn).[4] In each case a considerable

[7] S. A. Waksman, *Bact. Rev.*, 5: 231, 1941.

[8] S. A. Waksman and H. B. Woodruff, *Jour. Bact.*, 42: 231 (fig. 1), 1941.

[1] Aided by grants from the Board of Research of the University of California and the Rockefeller Foundation, New York City, and Parke Davis and Company, Detroit, Michigan. We wish to acknowledge assistance from the Work Projects Administration, Project No. OP-65-1-08, Unit A-5.

[2] D. H. Lightbody and A. Kleinman, *Jour. Biol. Chem.*, 129: 71, 1939; *Proc. Soc. Exp. Biol. and Med.*, 45: 25, 1940.

[3] Prepared according to an as yet unpublished method of C. H. Li, of this laboratory.

[4] The determination and the calculation of arginase unitage were performed according to Edlbacher (S. Edlbacher and H. Röthler, *Zeits. physiol. chem.* (Hoppe-

increase in the arginase content of the livers of the treated rats was evident (see Table I). In a few

TABLE I

EFFECT OF ADRENOCORTICOTROPIC HORMONE (ACT H) AND OF CORTIN ON LIVER ARGINASE OF HYPOPHYSECTOMIZED RATS*

Exp. No.	Treatment	Liver Arginase Content		
		per g Liver (Units)	per 100 g Rat (Units)	Increase Per cent.
1	ACT H treated	2,700	8,400	+ 75
	controls	1,675	4,800	
2	ACT H treated	2,350	8,450	+220
	controls	800	2,640	
3	ACT H treated	2,000	7,200	+ 82
	controls	1,200	3,960	
4	Cortin treated	2,550	7,900	+193
	controls	925	2,700	

* All fasted 21 to 24 hours preceding autopsy, after an injection period of 15 days. Treated rats in expts. 1 to 3 received 3.9 mg of the hormone preparation daily and three times during the 24 hour fast. Rats in expt. 4 received 0.5 cc of Upjohn's Adrenal Cortical Extract twice daily, with three injections of 1 cc during the 24 hour fast. The rats in expts. 1 to 3 were males, approximately 50 days old at operation and injected from the first day p.o. on. Those of expt. 4 were females, operated when approximately 30 days and injected after a postoperative period of 1 to 2 weeks.
The ACT H preparation used contained about 5 to 10 per cent. lactogenic hormone and less than 1 per cent. of other known hormones. The adrenal weights of the treated animals average 51 mg, those of the controls 14 mg.

groups, liver arginase was determined after treatment with the same dose of ACT H in combination with lactogenic hormone; also after the same cortin treatment, combined with growth hormone. In each case increases were found, but these were somewhat less pronounced than those brought about by ACT H or cortin alone. Studies of the effect of various other purified pituitary hormones and of thyroxin are in progress. As was noted by Lightbody,[5] we find the hyperthyroid state, produced by high doses of thyroxin in normal rats, to be associated with a tendency to increases in liver arginase; physiological doses of thyroxin in hypophysectomized rats seem to have the opposite effect.

The striking increases in liver arginase produced by pituitary adrenocorticotropic preparations, as well as by an adrenal cortical extract, are in good agreement with the theory that the adrenal cortex plays a predominant role in the hormonal control of gluconeogenesis. It has been established through the work of Long[6] and others, that certain hormones of the adrenal cortex enable fasting animals to maintain or even increase their carbohydrate stores, at the expense of body proteins; a similar action of ACT H has been demonstrated by Bennet[7] and has since been amply confirmed by us. It is obvious that the action of these hormones in increasing liver arginase would favor gluconeogenesis.[8]

Studies are under way as to the effect on liver arginase of purified pituitary hormones under varied conditions in normal and hypophysectomized rats. The liver arginase increasing activity of various pure adrenocortical steroids should also be tested.

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THE EFFECT OF A PREPARATION OF AMINE OXIDASE ON EXPERIMENTAL HYPERTENSION

THERE is evidence that deamination but not decarboxylation of certain amino acids is incomplete in kidneys deficient in their supply of oxygen.[1,2] Since decarboxylation of amino acids leads in many instances to the formation of pressor amines, it was believed that this process might be responsible for some varieties of arterial hypertension. Because the enzyme tyrosinase lowers the blood pressure of hypertensive animals and human beings,[3,4] a phenolic compound is probably concerned in the existence of this condition. It was desirable that other enzymes with known activity be employed in arterial hypertension in order that something further be learned regarding the nature of the pressor substance or substances.

A preparation of hog liver containing active amine oxidase, an enzyme specific for certain amines,[5] was, therefore, given to animals. The intravenous injection of a small amount of this material consistently lowered the blood pressure of hypertensive rats, affecting that of normal ones to a less extent. When this preparation was mixed with a solution of angiotonin or tyramine the pressor response of these substances was abolished. Rats which had been injected

Seyler), 148: 264, 1925) and Takehara (H. Takehara, *Jour. Biochem.* (Tokyo), 28: 309, 1938), using xanthydrol for urea determinations. Since no activator was added to the crude liver extracts the determinations are regarded as indicating the amount of naturally activated arginase only. All rats were fasted 21 to 24 hours preceding autopsy.

5 D. H. Lightbody, E. Witt and A. Kleinman, *Proc. Soc. Exp. Biol. and Med.*, 46: 472, 1941.

6 C. N. H. Long, B. Katzin and E. G. Fry, *Endocrinology*, 26: 309, 1940.

7 L. L. Bennet, *Proc. Soc. Exp. Biol. and Med.*, 37: 50, 1937.

8 Liver and muscle glycogen and blood sugar were determined in all rats included in the table; nitrogen excretion during the 24-hour fasting period was determined in experiment 1. While these results will be presented elsewhere, it should be stated that they indicated a definitely increased rate of gluconeogenesis in the treated animals.

1 P. Holtz, K. Credner and H. Walter, *Zeits. physiol. Chem.*, 262: 111, 1939.

2 R. A. Bing, *Am. Jour. Physiol.*, 132: 497, 1941.

3 H. A. Schroeder and M. K. Adams, *Jour. Exp. Med.*, 73, 531, 1941.

4 H. A. Schroeder, SCIENCE, 93: 116, 1941.

5 H. Blaschko, D. Richter and H. Schlossman, *Biochem. Jour.*, 31: 2187, 1937.