Experiment 2: *Effect of semicarbazide on larval development.* This substance is known to inhibit a variety of enzymes of which decarboxylase and also histaminase. It is possibly for this reason that the rate of excretion of histamine in mammals is not greatly modified. In other words both the rate of histamine formation and destruction would be lowered so that the available histamine would remain relatively unchanged. In Figure 2 we see that semicarbazide has very little effect on growth. However at higher doses, i.e. at 1%, it was found to be 100% toxic to larvae.

Experiment 3: *Effect of deoxypyridoxine on larval growth.* This substance is known to be potent antimetabolite of pyridoxine. Its presence in a diet would inhibit all decarboxylase including the one for histidine and would therefore interfere with the formation of amines such as histamine, serotonine, etc. Figure 3 shows that deoxypyridoxine has some effect on larval growth but that this effect is not independent of a simultaneous toxic action contrary to aminoguanidine. Indeed at 2%, deoxypyridoxine retards growth but at the same time it is lethal to about 66% of the larvae as shown in Figure 3.

Experiment 4: *Effect of aminoguanidine combined with semicarbazide or deoxypyridoxine on larval growth.* The purpose of this study was to find out if the effect of aminoguanidine on larval growth, which is presumably due to histamine accumulation, could be prevented by inhibiting simultaneously the transformation of histidine into histamine. Figure 4 shows that semicarbazide almost completely prevents the effect of aminoguanidine on pupation and deoxypyridoxine exerts a similar action. It should also be mentioned that both these substances are slightly more toxic when used in association with aminoguanidine than when used alone as may be seen by comparing Figure 3 and 4.

Experiment 5: *Effect of semicarbazide combined with deoxypyridoxine on larval growth.* As shown in Figure 2 semicarbazide and deoxypyridoxine potentiate one-another and retard pupation at doses where used separately these substances are relatively inactive. This result in the light of the above mentioned experiments would seem to indicate that interference with amine formation results in inhibition of larval growth.

Discussion. In mammals histamine has marked effect on smooth muscles and exerts strong actions on the cardiovascular system. GILMOUR believes that this amine cannot have much effect on insects[12]. However since both histidine, the immediate precursor of histamine, and pyridoxine, the coenzyme of decarboxylase, are essential in *Tribolium confusum* and since as postulated by KAHLSON histamine could be involved in all growth processes, its importance in larval growth was investigated. Two methods of approach were used in this study which consisted first in interfering with histamine destruction by using aminoguanidine and in the second case in preventing histamine formation by decarboxylase inhibitors such as deoxypyridoxine or semicarbazide. Our results show that aminoguanidine, possibly by inhibiting histaminase and consequently increasing histamine concentration[13], has a marked effect on larval growth. This effect is non toxic since even at quantities 400 times higher than the minimum required effective dose for slowing of larval growth, the larvae are all transformed eventually into pupae. It seems then that excess histamine retards larval growth. When attemps were made to inhibit histamine formation it was found that this procedure did not affect growth significantly without becoming toxic. KAHLSON found that interference with histamine formation in mammals prevents fetus development[8]. Our study shows the same phenomenon to be true in insects. It would be interesting to see if excess histamine would retard growth in mammals as it does in insects.

It was shown recently that reserpine inhibits histaminase activity to the same extend than aminoguanidine[14]. On the other hand two of us have shown recently that reserpine inhibits larval growth[11]. When the effective concentration of reserpine and aminoguanidine needed for retardation of larval growth are compared it is found that both substances are active at the same concentration, i.e. approxymately 0,01% in diet. It is then possible that both reserpine and aminoguanidine retard larval growth because they increase histamine concentrations.

Résumé. Le rôle possible de l'histamine au cours de la croissance larvaire a été étudié. L'inhibition de l'oxydase des diamines au moyen de l'aminoguanidine, a fortement ralenti la croissance larvaire du *Tribolium confusum*. Cette substance, cependant, ne s'est pas avérée toxique. D'autre part l'inhibition des décarboxylases par le semicarbazide ou le deoxypyridoxine ne modifie pas la croissance sans devenir toxique.

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[12] D. GILMOUR, *The Biochemistry of Insects* (Academic Press, New York 1961).

[13] O. ARUNLAKSHANA, J. L. MONGAR, and H. O. SCHILD, J. Physiol. *123*, 32 (1954).

[14] K. S. SACHDEW, R. AIMAN, and M. V. RAJAPURKAR, Brit. J. Pharm. *16*, 146 (1961).

Adrenergic Blocking Action of Cysteamine

It had been found previously that cysteamine protects rats subjected to extreme hypoxia (barometric pressure 141 mm Hg, pO_2 = 30 mm Hg) and prolongs the survival time (unpublished data). In the present experiments, evidence is presented that cysteamine has an adrenergic blocking action and causes a rise in blood pressure of the rat by itself.

Rats of both sexes (170 to 210 g) were used and anaesthetized with urethane. The blood pressure was recorded through a cannula which was inserted into the carotid artery and connected with a mercury manometer. A small polythene cannula, 0.5 mm in diameter, was inserted into the jugular vein and was used for injecting drugs. In another group of animals, cysteamine was injected intravenously in a dose of 120 mg/kg, and 1 h later these animals were sacrificed. The adrenals were taken out and the amount of catecholamines in the adrenals was estimated biologically by rat blood pressure. The action of cysteamine on the hyperglycemic effect of adrenaline was studied in rabbits. For producing hyperglycemia, adren-

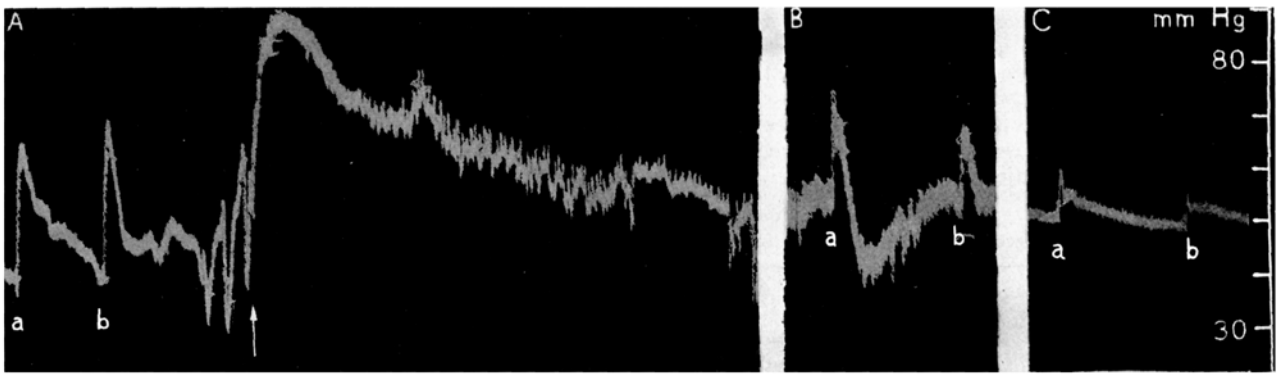

Fig. 1. The effect of cysteamine on the blood pressure of the rat. At the arrow in A, 100 mg/kg cysteamine intravenously. At a, 200 ng adrenaline i.v. At b, 300 ng noradrenaline i.v. B was taken 50 min after A, and C was taken 60 min after B. Time 1 min intervals.

aline was injected in a dose of 0.1 mg/kg subcutaneously.

It was found in all experiments that cysteamine in a dose of 100–120 mg/kg blocked completely the hypertensive effect both of adrenaline and noradrenaline (Figure 1). The reversal of the adrenaline hypertension was observed in one experiment only. The adrenergic blocking action of cysteamine was found to be slow in appearance. On the other hand, this effect was longlasting and it lasted until the end of the experiment. It was also found that cysteamine blocked the hyperglycemic effect of adrenaline in rabbit (Figure 2). Cysteamine by itself was found to cause a longlasting blood pressure rise in the rat. A tachyphylaxis was observed towards the hypertensive effect of cysteamine. In animals in which the brain was destroyed, cysteamine caused no increase of the blood pressure. Cysteamine is also found to decrease the amount of catecholamines in the adrenals of the rat.

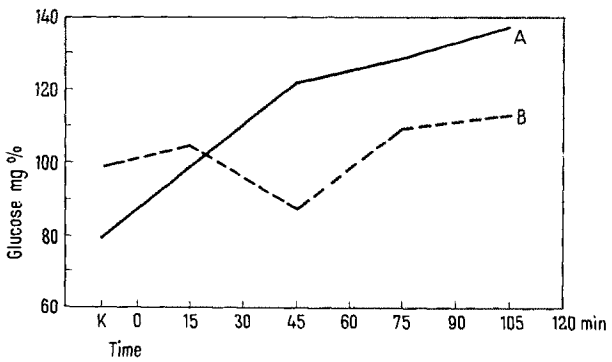

Fig. 2. The effect of cysteamine (150 mg/kg intravenously) on the hyperglycemic effect of adrenaline (0.1 mg/kg subcutaneously) in the rabbit. Full line (A) controls. Broken line (B) glycemia in animal treated by cysteamine.

It was therefore concluded that cysteamine by itself produces a central adrenergic activation accompanied by a release of catecholamines from the adrenals. Later this effect is succeeded by a peripheral blockade of the adrenergic receptors.

Résumé. Il a été démontré que la cystéamine provoque une activation centrale adrénergique accompagnée par une libération des catécholamines de la surrénale. Plus tard cet effet est suivi par un blocage périférique des recepteurs adrénergiques.

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Effect of Ferritin on Liver Catalase Activity

In a previous paper[1] it was shown that a variety of agents exhibited a depressing action on the activity of catalase in mouse liver. These agents were essentially protein in nature. These depressions in activity are similar to the well established phenomenon of the depression of liver catalase activity caused by the presence of a tumor in the body of the host.

The effects of iron and copper deficiencies on catalase activity have been studied by Schultze and Kuiken[2] and by Adams[3]. It has been shown that the depression of catalase activity in the liver of the tumor-bearing host can be offset by the administration of iron in various forms. Such forms include the feeding of liver powder, blood meal, or ferric chloride, and by injection of ferric chloride[4].

Fujii and Mizuno[5] fed rats a diet containing *p*-dimethylaminoazobenzene to induce carcinogenesis in the liver. Concurrently, they administered ferritin with the apparent expectation that ferritin would protect against the characteristic depression of liver catalase activity in such tumor-bearing hosts. Their results failed to show the expected protection and their paper fails to indicate that control animals were given ferritin. In this paper we are presenting the effects of ferritin on liver catalase in normal mice.

Adult C_3H/St mice were given 1 ml (1 mg) of ferritin[6] intraperitoneally. Catalase activity was determined by a method described earlier[1] on the 1st, 2nd, 3rd, 4th, and 7th day following the administration of the ferritin and compared with the activity of control mice.

[1] E. E. Riley, Jr., Cancer Res. *19*, 285 (1959).
[2] M. O. Schultze and K. A. Kuiken, J. biol. Chem. *137*, 727 (1941).
[3] D. H. Adams, Biochem. J. *51*, 328 (1952).
[4] F. Fukuoka and W. Nakahara, Gann *42*, 55 (1951).
[5] T. Fujii and T. Mizuno, J. Fac. Sci., Univ. Tokyo *7*, 41 (1954).