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Studies in Vitamin A

14. THE ALLEGED MOBILIZATION OF VITAMIN A BY ADRENALINE

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In 1940 Young & Wald reported that the injection of adrenaline into a rabbit was followed by a very marked increase in the blood vitamin A level, which reached a maximum approximately 30 min. after injection. In view of its possible importance in helping to elucidate the mode of action of vitamin A and the possible clinical implications, the effect has been reinvestigated using both rats and rabbits as experimental animals.

EXPERIMENTAL

Animals. Rabbits were kept in a constant environment and given an unvarying diet of Lever's cubes and outer leaves of cabbage; rats were maintained similarly except that they were not given cabbage.

Dosing. The required dose of adrenaline was injected intraperitoneally into rats and intravenously into a marginal ear vein of rabbits.

Collection and examination of blood. The samples of rat blood were withdrawn by cardiac puncture using a method previously described (Glover, Goodwin & Morton, 1946). The samples of rabbit blood (approx. 10 ml.) were withdrawn without anaesthesia from a marginal vein of the ear not used for the injection of adrenaline.

In most experiments the plasma was separated from the red cells and examined for vitamin A using the method

developed in this laboratory (Glover *et al.* 1946; Goodwin & Gregory, 1948). In some experiments whole blood was used and extracted according to the method of Young & Wald (1940), but the extract was examined for vitamin A using our method.

RESULTS

Rabbits. The results of the rabbit experiments are collected in Table 1. It will be seen that adrenaline has no appreciable effect on the vitamin A plasma levels of rabbit, and an analysis of the data using the *t* test indicated that the differences are not significant.

Young & Wald (1940) used whole blood for their vitamin A tests, but as it is now well established that under normal circumstances no vitamin A exists in the red cells, most of our experiments were carried out on blood plasma. There was, however, a possibility that adrenaline mobilized vitamin A into the red cells and that this would account for Young & Wald's results. To check this, two experiments were carried out in which whole blood instead of plasma was examined for vitamin A; again no mobilization was apparent.

Rats. When rats were used the experimental approach had to be altered slightly. The volume of

Table 1. *The action of adrenaline on the blood levels of vitamin A in rabbits*

Animal no.	Dose of 1/1000 adrenaline (ml.)	Interval between injection and withdrawal of blood (min.)	Vitamin A plasma values (i.u./100 ml.)	
			Before injection	After injection
C	1.0	120	215	226
120	1.0	30	213	211
120	0.5	30	213	193
134	1.0	10	224	221
81	1.0	35	221	252
113	1.0	10	218	234
161	0.5	30	204	180
167	0.5	30	82	71*
130	0.5	30	55	46*

* The values in these two experiments are those obtained using whole blood instead of plasma only.

blood required for each test was more than it was possible to draw from the same animal before and after injection of adrenaline. Consequently, groups of rats (about six per group) of the same sex, age and nutritional background were used; one group was injected with adrenaline and the other served as a control. The vitamin A plasma level of each rat was determined separately and the mean values for the two groups compared. It will be seen from Table 2 that no significant differences could be demonstrated between the control groups and those treated with

of vitamin A (Glover *et al.* 1946); thus any substance which can mobilize vitamin A alcohol into the blood from the mainly esterified liver reserves might be of considerable importance clinically. Clausen, Baum, McCoord, Rydeen & Breese (1940) claimed that ethanol mobilized vitamin A in dogs and later the same group of workers (Clausen, Breese, Baum, McCoord & Rydeen, 1941) stated that drinking liquor to the extent of 'the usual "social" evening common in this country' (U.S.A.) raised the vitamin A plasma levels of humans. Brenner & Roberts (1943) also found a rise in humans. However, not only have British investigators failed to observe any rise after administration of ethanol (Yudkin, 1941; Hume & Krebs, 1949), but the increase recorded by the American investigators was almost entirely due to esterified vitamin A (Clausen, Baum, McCoord, Rydeen & Breese, 1942), so that any such rise would apparently serve no useful therapeutic purpose. This raised the question whether the surprisingly large increase in the vitamin A level of plasma after adrenaline injections reported by Young & Wald (1940)—a doubling within 30 min.—was in the alcohol or the ester fraction.

We could not test this point, however, as we were unable to reproduce Young & Wald's results; no mobilization of vitamin A was apparent in either plasma or red cells. It is impossible at the moment to offer any explanation of these contradictory results.

Table 2. *The action of adrenaline on the plasma levels of vitamin A in rats*

Exp. no.	Dose of 1/1000 adrenaline (ml./rat)	No. of rats		Interval between injection and withdrawal of blood (min.)	Mean vitamin A plasma levels (i.u./100 ml.)	
		Control group	Test group		Control group	Test group
1	0.5	7	7	30	49.9	49.8
2	0.5	10	3	60	35.8	40.4
3	0.5	8	4	15	38.0	45.7
4	0.5	4	4	14	61.7 64.3 66.3 57.1	61.7* 66.8 68.8 61.7
					Mean 62.3	64.7

* The results of Exp. 4 are recorded in detail to illustrate the usual variations found between plasma levels of rats of the same group.

adrenaline. It should be noted that the variations between the values obtained on rats in a single group are quite small, and could thus in no way mask an effect as large as that encountered by Young & Wald (1940); to illustrate this the individual results are quoted for Exp. 4 (Table 2).

DISCUSSION

Owing to the existence of a blood-liver equilibrium the plasma levels of vitamin A alcohol (the functional form) are only slightly raised even after large doses

SUMMARY

1. The claim that intravenous injection of adrenaline into rabbits mobilizes liver vitamin A into the blood has not been confirmed.

2. Similar negative results were obtained with rats.

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