creased capacity for destroying solid carcinomata *in vivo*, producing characteristic histological changes. The oncolytic Coxsackie B_3 virus produced by rat-HeLa tumor passage *in vivo*, compared to the same strain passed in HeLa cells grown in tissue culture, revealed marked differences in oncolytic capacity. Use of this method illustrates the possibility of virus adaptation by tumor to tumor passage; that this principle has been successfully employed to destroy solid tumor transplants of human origin, suggests its possible application for future clinical studies.

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Utilization of Vitamin A and Carotene by Selenium Poisoned Rats.* (22932)

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A previous study has shown that aqueous dispersions of carotene given intravenously to rats are readily converted to vit. A(1). In further experiments designed to obtain information about the site of conversion of carotene injected intravenously, attempts were made to block the reticuloendothelial system and also to damage the liver.

Methods. Weanling male rats of Holtzman strain were placed on synthetic, vit. A-free diet as follows: purified casein 18, salts 4(2), sucrose 74, cottonseed oil‡ 2, vit. mixture in sucrose 2(3). Half of the animals in each experiment received 12

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‡ Wesson oil.

TABLE I. Storage of Vitamin A by Normal and Selenium Poisoned Rats (Mean Values ± Stand. Error).

Exp.	No. rats	Days on selenium	Avg wt	Supplement	Time interval, hr*	Liver + kidney: Carotene Total, μg	Carotene μg/g	Vit. A Total, μg	Vit. A μg/g
1	5	0	147 ± 3.6	100 μg carotene orally	65	0		26.4 ± 1.3	3.9 ± .3
	5	8	129 ± 3.0		65	0		13.6 ± 2.7	2.3 ± .4
2	6	0	100 ± 4.0	95 μg carotene inj.	6	28.2 ± 1.2	6.0 ± .2	9.0 ± 1.5	2.6 ± .4
	6	22	96.1 ± 3.0		6	26.3 ± .9	6.0 ± .3	5.8 ± .2	1.1 ± .1
3	3	0	84.7 ± 6.0	68 μg carotene inj.	6	20.8 ± .7	4.7 ± .4	7.7 ± .5	2.2 ± .2
	4	14	80.0 ± 3.5		6	20.5 ± .9	4.2 ± .2	2.6 ± .8	1.0 ± .3
4	5	0	97.6 ± 5.6	100 μg vit. A orally	24	0		31.6 ± 3.7	5.8 ±1.0
	8	7	80.0 ± 2.5		24	0		13.8 ± 1.7	2.9 ± .3
5	5	0	83.0 ± 1.6	100 μg vit. A + 0.3 mg vit. E orally	24	0		32.9 ± 2.6	7.5 ± .5
	8	7	77.1 ± 2.1		24	0		12.9 ± 1.4	3.2 ± .4

* Interval animal was permitted to survive after giving the supplement.

ppm of selenium, as sodium selenite, in the diet. Due to differences in maternal diet, some groups became depleted of vit. A in 17-21 days while others required 30-35 days. Selenium did not affect rate of depletion. Food intake of control rats was restricted to the amount consumed by the selenium-fed group. Animals were caged singly in air-conditioned room at 75 ± 1°F. Supplements of crystalline carotene (85% β–, 15% α–) dispersed in water with 20% Tween 40 or of vit. A acetate dissolved in cottonseed oil,‡ were administered by tail vein or by stomach tube when vit. A deficiency was apparent. The rats were sacrificed 6 hours after injection, or 33-65 hours after stomach-tubing. In the latter groups, selenium was removed from diet 18 hours prior to giving carotene or vit. A supplement. All animals were fasted at least 8 hours prior to death. Vit. A in combined kidneys and livers was determined with antimony trichloride on an aliquot of the hexane extract of the unsaponifiable fraction, using correction for color due to carotene. Analyses of deficient rats revealed no detectable vit. A in livers and kidneys. Rats depleted of vit. A as described above were injected with trypan blue or carbon tetrachloride prior to administering carotene, and the tissues analyzed for vit. A. The conditions are given in Table II.

Results. In Table I it can be seen that utilization of carotene, as measured by tissue storage of vit. A, was impaired in rats fed selenium. Regardless of whether carotene was given orally (Exp. 1) or intravenously (Exp. 2 and 3), the amount of vit. A was only about one half that of control animals. To determine if selenium might diminish utilization of pre-formed vit. A, 2 groups were dosed orally with vit. A acetate (Exp. 4). Tissues of selenium-treated animals again contained less than one-half as much vit. A as normal animals. In Exp. 5, dl,α-tocopherol was incorporated into the vit. A supplement to protect the vitamin against possible oxidation in the digestive tract. This failed to prevent decrease in storage of vitamin in selenium-fed animals.

Discussion. Rosenfeld and Beath(4) found that in selenium fed sheep a marked drop in vit. A content of blood and liver occurred, even though the diet contained an adequate amount of carotene. Ascorbic acid in these tissues was also significantly depressed by selenium.

In the present study, it is possible that selenium impaired intestinal absorption of vit. A. In view of the relatively efficient utilization of orally administered carotene, however, it appears that this factor was not of great significance. The effect of selenium on vit. A may be explicable by two different mechanisms, first, that seleniferous tissues destroy vit. A, but not carotene, and secondly, that poisoned liver may have decreased capacity for holding the vitamin. It has been shown *in vitro* that ascorbic acid is oxidized by se-

TABLE II. Carotene Utilization by Rats Injected with Trypan Blue or Carbon Tetrachloride.*

Treatment	No. rats	Avg wt	Carotene supplement	Vit. A, μg/g Liver	Vit. A, μg/g Kidneys
None	4	113 ± 6.5	120 μg, I.V.	2.7 ± .2	1.9 ± .1
Trypan blue†	6	107 ± 2.5	*Idem*	2.1 ± .6	2.3 ± .4
CCl_4‡	6	113 ± 2.7	"	2.4 ± .1	2.1 ± .3

* All rats were killed 6 hr after inj. with carotene.
† Inj. I.P. with 1 ml of 2% trypan blue; inj. with carotene 24 hr later.
‡ Inj. subcut. with 0.2 ml CCl_4 in cottonseed oil (50% w/vol) for 3 consecutive days; inj. with carotene on fourth day.

lenium salts and this mechanism was proposed as the cause of decreased ascorbic acid in livers from selenium-poisoned rats(5). However, we have not observed increased destruction of vit. A incubated in rat blood containing added sodium selenite (unpublished observation).

In support of the second possibility, that selenium alters storage capacity of the liver, the recent study of Krishnamurthy and Ganguly(6) may be quoted. They found that rats injected with India ink decreased liver storage of vit. A ester, but not of vit. A alcohol. This would support the theory previously proposed by these workers(7) that different proteins may specifically bind various carotenoids in blood. The fact that storage of carotene was not affected in our study, whereas storage of vit. A was, would lend further support to this theory. However, it should be pointed out that the 2 types of poisons (selenium and India ink) damage different structures in livers. In contrast to the results of Krishnamurthy and Ganguly, impairment of reticulo-endothelial system by trypan blue had no effect on carotene utilization in our study (Table II).

The observation that rats with selenium-poisoned livers could still convert carotene injected intravenously supports our previous conclusion(1) that this organ is not of significance in conversion of pro-vitamin. Recently, McGillivray *et al.*(8) have shown that injected carotene can be transformed to vit. A in the rat even when the entire liver has been removed.

Summary. Rats fed sodium selenite had impaired utilization of carotene given orally or intravenously. Storage of pre-formed vit. A was reduced, but not storage of injected carotene. Poisoning with trypan blue or carbon tetrachloride did not affect carotene conversion.

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