tor of toxemia, possibly arising from the stromal substance of the lysed red blood cells, undoubtedly plays an important part in the fatal outcome in these cases. The manifestations of such a toxemia are found in kernicterus and in the evidences of kidney and liver damage that may exist. It was felt that the mere administration of Rh– blood did not meet the problem in all cases. It did seem desirable to remove the known Rh+ blood of the infant and to replace it with Rh– blood. Such a procedure would either minimize or entirely prevent the action of the hemolytic end products upon the liver, kidneys, and brain ganglia.

A technique has been evolved to carry out this purpose to a considerable degree, without subjecting the child to the hazard of shock due to exsanguination. This is accomplished by the simultaneous withdrawal of the Rh+ blood from the sagittal sinus and the administration of Rh– blood through a cannulated vein.

It can be shown mathematically that if a continuous transfusion and withdrawal is carried out for 60 minutes, if the mixing is considered the equivalent of instantaneous, and if the baby's blood volume is approximately 250 cc., only 36.7 per cent of the original blood will remain. To test this hypothesis, we duplicated the conditions by the use of an aspirator bottle containing 250 cc. of tenth normal HCl with a pipette for the constant admission of distilled water, at a rate which was equal to the loss of the HCl in the aspirator bottle, into a measuring cylinder. A stirrer was kept within the aspirator bottle. When 250 cc. of fluid from the aspirator bottle was collected in the cylinder, a sample of the liquid remaining in the aspirator bottle was titrated and showed .0367 normal HCl.

A variation of this procedure, whereby 50 cc. of blood are removed from the baby and then an equivalent amount administered in alternation, can be shown arithmetically to permit of an exchange that leaves behind 80 cc. of the original 250 cc. Inasmuch as the child is given approximately 100 cc. of Rh– blood over and above that withdrawn, the dilution factor permits of a reduction of the original Rh+ blood to 25 per cent of the original volume. The typing of the blood cells removed at the start and at the end of the exchange confirms the fact that only 25 per cent of the original Rh+ cells remain after such a procedure.

On the basis of the above, this technique has been carried out on three separate infants since May 1945, with immediate improvement in their conditions and eventual recovery without further therapy. It will be understood that, because of the dramatic nature of the procedure, only infants who were most severely ill with erythroblastosis were submitted to this routine. These included a twelfth pregnancy of a mother with eight previous erythroblastotic babies and stillbirths, a second case with an icterus index of 625, and a third infant showing marked toxicity and spasm.

The results to date justify a more widespread use of this method in the combating of the severe cases of erythroblastosis fetalis.

The Apparent Antagonism Between Vitamin A and Carotenoids in the Fowl

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Hammond and Harshaw (*2*), working at the Beltsville Research Center, showed that there was some material in fortified cod-liver oil which interfered with the deposition of xanthophyll in the shanks and skin of chicks. Mattson and Deuel (*5*) reported that there was interference in the carotenoid metabolism of growing chickens when they were given daily doses of shark-liver oil to supply 9,300 I.U. of vitamin A. Deuel, *et al.* (*1*) fed 0.01 per cent to 2.42 per cent of shark-liver oil to hens to supply from 1,000 to 200,000 I.U. of vitamin A per pound of feed. There was a progressively decreasing quantity of pigment in the

TABLE 1

Supplement to basal diet	Approx. I.U. of vitamin A per 100 grams of diet	Av. pigment score	Range of scores
First Experiment			
(1) None	.....	16.0	15.0–17.0
(2) 0.045 per cent vitamin A concentrate	9,000	6.4	3.0–10.0
(3) 5.4 mg. crystalline carotene per 100 grams of diet	9,000	15.2	14.0–16.0
(4) 3.0 per cent vitamin A and D oil No. 1	9,000	7.0	4.0–12.0
(5) 0.140 per cent shark-liver oil	3,000	12.2	7.0–16.0
(6) 3.0 per cent vitamin A and D oil No. 2	3,000	13.4	8.0–16.0
(7) 3.0 per cent irradiated* A and D oil No. 2	.....	14.2	10.0–16.0
(8) 3.0 per cent shark-liver oil	60,000	4.6	4.0– 6.0
Second Experiment			
(1) None	.....	15.7	15.0–17.0
(2) 0.4 per cent ethyl laurate	.....	16.4	16.0–17.0
(3) 0.4 per cent ethyl laurate and 3.51 mg. crystalline vitamin A alcohol per 100 grams	9,000	11.4	6.0–16.0
(4) 0.053 per cent vitamin A concentrate	9,000	11.0	3.0–16.0
(5) 0.492 per cent shark-liver oil	9,000	10.2	4.0–17.0

* Irradiated with ultraviolet light for 16 hours to destroy vitamin A.

egg yolks as the shark-oil content of the diet was increased. These workers concluded that the vitamin A interfered with the carotenoid metabolism in both growing chickens and laying hens. It seemed desirable to subject this conclusion to a more critical test by feeding, respectively, crystalline vitamin A and fish oil in which the vitamin A had been destroyed.

In the second experiment the average pigment scores of the chicks fed vitamin A supplements were not as low as in the previous test. However, it is evident that crystalline vitamin A alcohol suppressed pigmentation as effectively as did the vitamin A of the concentrate or of shark-liver oil.

Mattson and Deuel suggested that a high intake

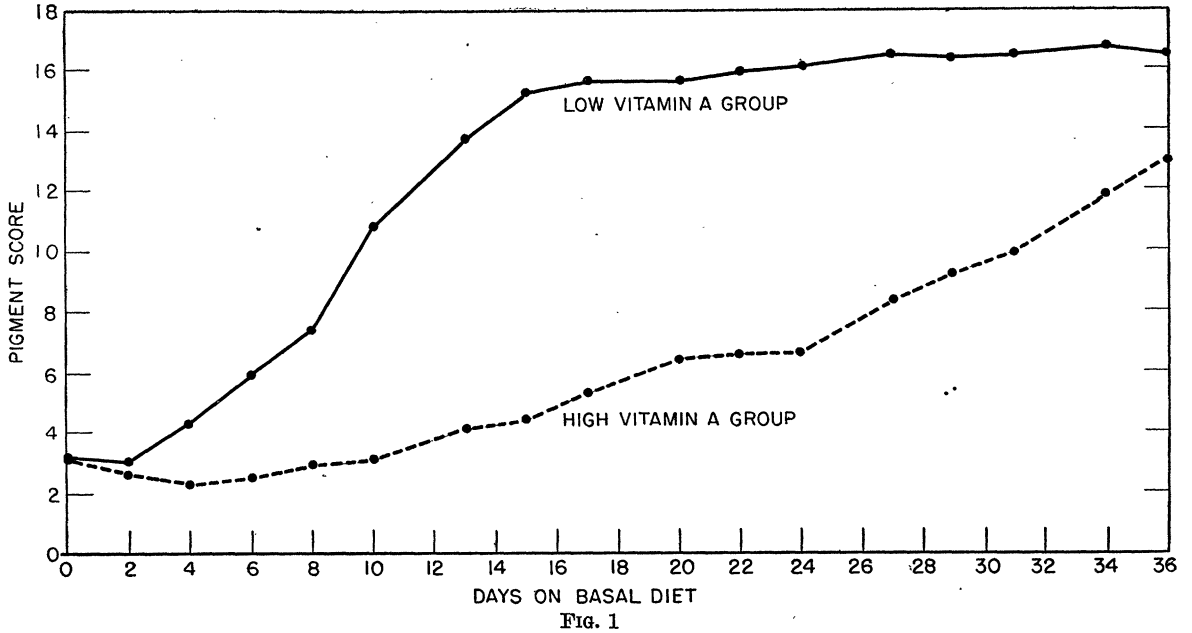

FIG. 1

Hammond and Harshaw suppressed pigmentation by feeding 3 per cent of fortified cod-liver oil which contributed 9,000 I.U. of vitamin A per 100 grams of diet. Therefore, two experiments were planned in which various supplements were fed to supply this level of vitamin A. These experiments are summarized in Table 1. The basal diet was Diet C of Hammond and Harshaw, containing 40 per cent yellow corn, 10 per cent corn gluten meal, and 3 per cent alfalfa leaf meal as sources of carotenoid pigments. The experimental diets were fed to groups of 25 chickens during the first six weeks of life, at the end of which time the degree of shank pigmentation was determined by matching the color of the shanks with the Heiman-Carver (*3*) color rotor.

In the first experiment, all groups fed 9,000 or more units of vitamin A per 100 grams of diet showed considerably less pigmentation than the control, except for the group fed carotene. The vitamin A concentrate fed to Group 2 was at least as effective as the vitamin A and D oil fed to Group 4. Compared to the effect of these two supplements the effect of the irradiated oil, which was free of vitamin A according to the antimony trichloride test, was very slight.

of vitamin A might lead to development of a nonspecific enzyme system capable of destroying not only vitamin A but also carotene and carotenoids. However, Hickman (*4*) has found that "*in vitro* experiments show that vitamin A is a specific pro-oxidant for beta-carotene, lycopene and probably zeaxanthin."

It was of interest to determine whether this pro-oxidant effect is largely confined to the intestinal tract in chickens or whether bodily stores of vitamin A are capable of exerting the same effect in the blood stream or tissues.

During the first six weeks of life chicks were fed diets which were deficient in carotenoid pigment. The diet of the first group was supplemented with enough vitamin A to maintain good growth. The second group was supplied with 100,000 U.S.P. units of vitamin A per 100 grams of diet, a very large excess. Beginning at six weeks of age, and for 36 days thereafter, both groups were given the basal diet used in the previous experiments. Their shanks were judged for degree of pigmentation, and two chicks from each group were sacrificed for determination of carotenoid and vitamin A in the livers. The analyses for the low vitamin A group showed 1.5 μg. of xanthophyll and 1,112 B.U. of vitamin A per gram of liver, and

the analyses for the high vitamin A group showed 1.4 μg. of xanthophyll and 5,406 B.U. of vitamin A.

The shanks were scored three times each week, and the average pigment scores for each group were plotted against time (Fig. 1). The chicks with the lower vitamin A stores soon began to accumulate yellow pigment in their shanks. The group with larger vitamin A stores accumulated pigment in their shanks at a considerably slower rate, indicating that the effect of vitamin A is exerted in the blood stream or tissues or both.

It has also been observed that large quantities of vitamin A in the diet or stored in the body of the hen have an inhibiting effect on the pigmentation of egg yolk.

The results of some preliminary work on the liver analyses of chicks fed high levels of vitamin A indicate that there is a simultaneous destruction of the carotenoid pigment and vitamin A. This phase of the study is being continued.

Summary

These experiments show that the pigmentation-suppressing factor in fish-liver oils is vitamin A. Carotene fed at comparable levels does not exert a suppressing effect on pigmentation. Inhibition of pigmentation takes place when there is a sufficiently large bodily store of vitamin A; it is not exclusively an intestinal phenomenon.

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The Effect of Tocopherols in Preventing Gastric Ulcers in Rats[1]

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Although the anomalies encountered in vitamin A bio-assay have troubled investigators for many years, it has not been generally recognized that rats which are deficient in vitamin A are nearly always afflicted with stomach ulcers. In this note it is reported that inclusion of extra vitamin E in the diet has completely prevented the occurrence of such ulcers.

The experiments which revealed this relationship were undertaken to find out whether alcohol affected the utilization of vitamin A by the rat. In addition to a vitamin A-deficient diet, one group of rats was given a minimal dose of vitamin A daily (.57 μg.) and other groups, vitamin A plus either ethyl alcohol or vitamin E, as pure d,α-tocopherol, or both alcohol and vitamin E.

Table 1 shows the supplements given, the weight gains, and the percentage of rats having ulcers.

Severe gastric lesions were noticed upon autopsy of the vitamin A-deficient rats. The lesions, described as local circumscribed metaplasia of the surface epithelium,[3] were located in the fore-stomach and especially near the junction of the cardiac and pyloric portions. They ranged from pin-point size to craters 7 mm. in diameter, and some of them had been bleeding.

TABLE 1

Effect of Vitamin E, With and Without Alcohol, on Growth and Ulcer Production of Vitamin A-depleted Rats Receiving .57 μg. of Vitamin A Daily*

Group No.‡	Supplement†		Gain in body weight after 48 days	Incidence of gastric ulcers
	Alcohol as 95% C_2H_5OH	d,α-Tocopherol		
	(mg.)	(mg.)	(grams)	(%)
1	0	0	64	67
2	0	0.5	79	0
3	0	5.0	77	0
4	64	0	41	40
5	64	0.5	63	0
6	64	5.0	67	0
7	128	0	29	30
8	128	5.0	57	10

* The basal diet was fed ad libitum and contained: casein, vitamin-free, 18%; starch, 65%; salt mixture, U.S.P. #2, 4%; yeast, 8%; lard, 5%; vitamin D in the lard to furnish 30 units/10 grams of diet.

† In addition to .57 μg. vitamin A as a natural ester concentrate.

‡ The first group contained 15 rats; the others, 10 each.

Vitamin E fed to rats receiving minimal doses of vitamin A with and without alcohol supplementation protected the rats from ulcer formation, except those which were fed the larger dose of alcohol. Ulcers were present in many rats which did not receive the vitamin E supplement.

Since ulcers were prevalent among the vitamin A-deficient rats, and yet were nearly always absent when tocopherols were given, it may be tentatively assumed that the vitamin A-sparing action of the tocopherols was a factor in preventing the lesions. Alcohol, however, had an opposite effect on vitamin A utilization. The drop in weight gain from 64 to 29 grams (Groups 1 and 7) when comparing a diet without alcohol and one with alcohol may be used as a measure of the deleterious effect of alcohol on vitamin A. A larger tocopherol supplement for the group receiving the

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[3] Dr. Karl E. Mason, University of Rochester School of Medicine, very kindly examined some of these lesions grossly and microscopically.