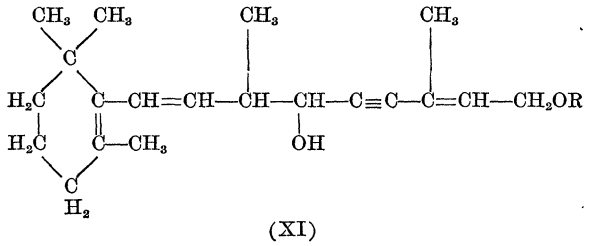
was produced in very good yields. This carbinol was easily dehydrated to the polyvinyl acetylene (VI),



(XI)

from which the vitamin A ethers were obtained by selective hydrogenation. The acetylene carbinol (XI) has also been selectively hydrogenated to the corresponding polyene carbinol (XII), which was advantageously dehydrated to give good yields of vitamin A ethers.

The final products produced by the three synthetic routes outlined above are identical whenever R is the same. Ultimate analysis, unsaturation, and molecular weight determinations agreed well with the expected values for the structural formula (VI). The absorption spectrum in the ultra-violet has a well-defined maximum similar to that observed for the corresponding natural vitamin A substances, except that it is slightly displaced towards the ultraviolet region by about 30 to 50 A. The synthetic ethers of vitamin A give a purplish blue color with antimony trichloride which exhibits both the 6,200-A. and the 5,800-A. bands characteristic of natural vitamin A. The vitamin A esters and the alcohol itself give a deep blue color exhibiting the same bands.

Biologically, all the synthetic products which are represented by the final structure (VI) have been found active by Prof. Harris, of the Nutritional Laboratories of this Institute. Furthermore, the biological effect on rats has been found to be identical with that produced by cod-liver oil. The potency, however, was much lower than that generally accepted for the purest sample of natural crystalline vitamin A (3,500,000 U.S.P. vitamin A units per gram). For the synthetic vitamin A methyl ether, for example, Prof. Harris reported indications of activity in the order of 500,000 to 1,000,000 U.S.P. vitamin A units per gram and reproducible activity of the order of 50,000 to 100,000 U.S.P. units per gram. Several other laboratories have tested our synthetic products and confirmed, within certain limits of variation, the lower potencies reported by Prof. Harris. Although the potency of the synthetic products is much lower than that of the purest natural crystalline vitamin A, the biological activity cannot be disputed and, if compared to commercial products, it is of the order of 50 to 100 times that of ordinary cod-liver oil, one of the chief sources of vitamin A.

If the biological potency of the synthetic products is much lower than that of the corresponding natural products, one can raise the question whether they are identical. We have devoted a considerable amount of our time in an attempt to answer this question. Our most recent results seem to indicate that the synthetic products are mixtures of stereoisomers of the *cis-* and *trans-* type, exceedingly difficult to separate and some of which are probably completely devoid of biological activity. This is not surprising, for even the natural vitamin A, when first isolated by Karrer (1931), presumably in a chemically "pure" form, had a considerably lower potency than the crystalline vitamin A recently prepared by Baxter and Robson (*1*). Was Karrer's sample a mixture of stereoisomeric forms, some of which were biologically inactive? This question cannot be answered until the stereochemical configuration of vitamin A is known. Merely speculating from analogies with certain carotenoids may lead to a false conclusion. Some organic chemists are unwilling to admit that *cis-* and *trans-*isomerism is even present in molecules which have more than three double bonds in conjugation. Work along these lines is exceedingly difficult and time-consuming, but it is quite essential because of its connection to the important problem of specificity of vitamin A.

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Treatment of Severe Erythroblastosis by Simultaneous Removal and Replacement of the Blood of the Newborn Infant[1]

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Although considerable information has been accumulated concerning the mechanisms involved in the causation of erythroblastosis fetalis, the established treatment by repeated transfusions of Rh– blood has thus far not been entirely successful. Many babies with erythroblastosis have died of the disease, though no evidence of severe anemia existed. A fac-

[1] Preliminary report from the Laboratories of the Queens General Hospital, Jamaica, Long Island, and from the Department of Hematology, Jewish Memorial Hospital, New York City.

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.