Difference in Intestinal Absorption Between Vitamin A Alcohol and Ester.* (17621)

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Vitamin A is transported from the intestinal tract to the liver in ester form and is stored as such in the liver(1). It is presumed to pass through the intestine wall as the free alcohol even if given in esterified form. However, it has been observed in normal children that the administration of free vitamin A results often in lower blood levels than that of an equal dose of the esters(2). The contrary was seen in the newborn or in children with pancreatic diseases or with other pathologic conditions which do not necessarily influence intestinal absorption(2,3,4). Recently(5), fluorescence microscopic studies of the intestinal absorption of vitamin A in rats revealed that vitamin A alcohol is less efficiently absorbed than are the vitamin A esters. It appeared, therefore, pertinent to compare the absorption of free vitamin A with that of vitamin A esters as measured by the response of the plasma vitamin A level to a test dose of vitamin A. This was done in a group of adult patients including cases of liver diseases in which the intestinal vitamin A absorption is known to be impaired. It appeared also interesting to study the influence of dispersion upon both vitamin A preparations and furthermore to establish what percentage of vitamin A is esterified in the blood after administration of any of the different preparations used.

Material and Method. The blood vitamin A level of 16 hospital controls and 14 patients with liver diseases including acute hepatitis, cirrhosis and obstructive jaundice was determined according to the method of Kimble(6) (using the Coleman spectrophotometer) after an intake of a test dose of 75,000 units of vitamin A unless otherwise specified. In 4 cases, in addition, the vitamin A esters were determined according to a slight modification(7) of the procedure of Gillam and Senior(8). The alcohol vitamin A was calculated by subtraction of the vitamin A esters from the total vitamin A level. Vitamin A was given (usually with some lemon juice) in preparations containing 25,000 units per cc either as the alcohol in the form of a vitamin concentrate (unsaponifiable fraction of fish liver oil) or as an especially prepared vitamin A palmitate or acetate. Both preparations were either dissolved in corn oil or dispersed in water with an appropriate nonionic emulsifier (fatty acid polyoxyalkylene derivative).† In an additional series, the amount of vitamin A administered was slightly varied.

Results. In hospital controls, equal amounts of vitamin A palmitate in aqueous menstruum raised the blood vitamin A level slightly more than those of vitamin A alcohol. This difference was not marked in all instances and appeared reversed in 2 out of 16. Similarly, vitamin A palmitate in oily solution produced, as a rule, a more marked response of the plasma vitamin A than vitamin A alcohol (Fig. 1). On the average, vitamin A alcohol in aqueous menstruum produced approximate-

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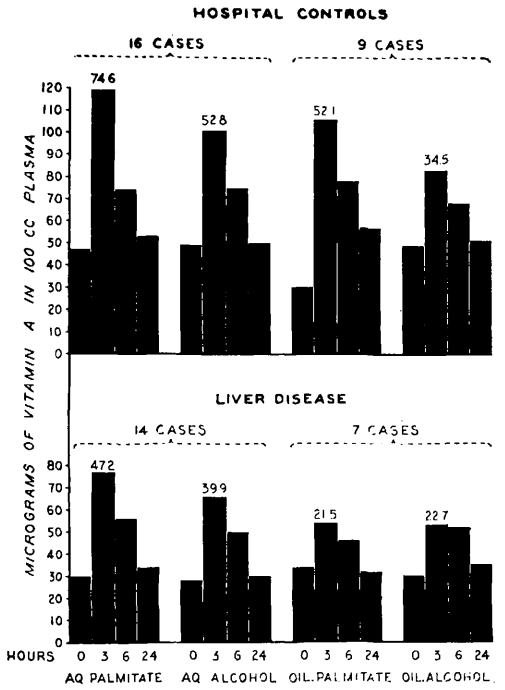

FIG. 1.
Average of plasma vitamin A level before, 3, 6, and 24 hours after administration of 75,000 units of vitamin A as palmitate or as alcohol in aqueous and oily menstruum in hospital controls and patients with liver diseases. The figure over the highest bar indicates the average maximal difference between the plasma vitamin A level before and after intake of the test dose of vitamin A.

ly the same rise of the plasma vitamin A level as vitamin A palmitate in oily solution. None of the differences, however, were statistically significant. Thus, the T value of the difference between aqueous emulsion of vitamin A alcohol and palmitate was 1.8, the lower limit of statistical significance being 2.5. In patients with liver diseases, an almost similar behaviour was noted except that the response of the plasma vitamin A level to the same dose of vitamin A was significantly lower than in the hospital controls. This is more apparent with the oily preparations which hardly produced any difference in plasma levels of vitamin A after ingestion of vitamin A alcohol or palmitate.

The plasma vitamin A level of 6 patients who received vitamin A palmitate in significantly smaller amounts than vitamin A acetate or alcohol (all in aqueous emulsion) rose, on the average, almost equally; it rose more after acetate given in the same amount as the alcohol (Table I). In the two controls and the two patients with hepatic cirrhosis in whom the plasma vitamin A was partitioned into alcohol and esters, the rise following the intake of alcohol or palmitate in both aqueous or oily menstruum was almost entirely due to an elevation of the esters (Table II).

Discussion. The present study indicates that in normal adults as well as in patients with liver diseases esterified vitamin A is not only as well absorbed by the intestine as the free vitamin A but slightly better. The difference in the absorption of the two forms however is not statistically significant. Superiority of vitamin A ester to alcohol(9,10) or of alpha tocopherol ester to free alpha tocopherol(10) in bioassays has been reported. If vitamin A passes the intestinal tract only in the free form, the necessary lipolytic process does not seem to retard the absorption of esterified vitamin A. Vitamin A is transported in the blood from the intestinal tract to the liver in the ester form. If at least some vitamin A passes the intestinal wall in the esterified form (not requiring subsequent esterification in the intestinal wall) the trend for better absorption of the esterified form would be explained. However, it has been shown that in pancreatic disorders the free form is better absorbed and it has even been claimed that a characteristic difference between celiac disease and pancreatic disorders lies in the poor absorption of the esters in the latter(2). In hepatic diseases in which the

TABLE I.
Average Maximal Difference Between Plasma Vitamin A Level Before and After Intake of Various Doses of Vitamin A Alcohol, Palmitate, and Acetate in Aqueous Emulsion in 6 Patients.

Form of vit. A admin.	Amt in units	Avg max. rise of plasma vit. A level in μm per 100 cc
Alcohol	82,500	56.5
Palmitate	69,300	61.8
Acetate	83,800	73.3

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TABLE II.

Mean Plasma Levels of Total and Ester Vitamin A in 2 Normals and 2 Patients with Hepatic Cirrhosis Before and at the Peak After Administration of 75,000 Units of Vitamin A as Palmitate or as Alcohol in Aqueous or Oily Menstruum.

Vit. A preparation administered	Mean Plasma vitamin A in μm per 100 cc in two Controls				Patients with cirrhosis			
	Prevalue		Peak		Prevalue		Peak	
	Total	Esters	Total	Esters	Total	Esters	Total	Esters
Aqueous palmitate	44.2	13.8	120.1	79.3	15.2	7.3	44.0	32.0
" alcohol	46.0	8.7	89.9	42.7	9.6	3.3	23.9	14.2
Oily palmitate	44.9	11.4	66.8	47.6	8.0	3.8	22.4	15.9
" alcohol	44.7	4.9	57.7	21.9	7.7	3.7	13.5	3.4

deficiency of bile acids usually impairs lipolysis, this difference does not exist. The findings can be explained either by a better stability of the esters protecting them from oxidative destruction in the intestine(10) or by the assumption that vitamin A is absorbed partially as alcohol and partially as esters. While in normals the esters are slightly better absorbed, in pancreatic disorders the defect in lipolysis outweighs this advantage. Against the hypothesis that the higher blood levels following the administration of the esters are the result of a delayed uptake by the liver speaks the fact that the absorbed vitamin A in the blood stream is in the ester form independent of the form it was originally fed(7). Moreover, the microscopically observed better absorption of vitamin A in the gut of animals following administration of the esters does not support that hypothesis. From a practical point of view, the state of esterification appears of less significance for the absorption of vitamin A, despite the slight advantage of the ester, than the degree of dispersion which is equally important for the absorption of ester as of alcohol. Recently, ample evidence has been presented for the better absorption of aqueous preparations of vitamin A in comparison to the oily ones(11,12,5).

Summary. The plasma vitamin A level of hospital controls and patients with liver diseases was, as a rule, slightly more elevated after the intake of equal doses of vitamin A esters than of the alcohol. This difference was noted if the preparations were given in oily as well as in aqueous menstruum. Equal amounts of vitamin A in aqueous medium produced regularly a higher plasma level than in oil. The rise of the plasma level was mainly due to elevation of vitamin A esters whether vitamin A was administered as alcohol or as ester. Lipolytic processes, therefore, do not retard the absorption of vitamin A and it is suggested that part of vitamin A may be absorbed as ester. The greater stability of the esters may be an alternative explanation.

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