tion of parakeratosis. This also indicates that the basic condition of the skin in a zinc deficiency is the same throughout the body. Reducing the total amount of feed consumed, either by zinc deficiency or by limited feeding, substantially retarded the rate of generation of new skin following surgical removal of the skin. The effects of zinc deficiency and dietary restriction were reversible.

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Effect of 3-Aminopropanol on Choline-Deficiency in Rats.* (29866)

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We reported(1) that addition of ethanolamine to low-choline diets containing either 18 or 42% casein increased the incidence of both hemorrhagic kidneys and hemorrhagic eyes in weanling male rats consuming these diets for 7 days. In the same animals the liver fat accumulation was reduced by addition of ethanolamine. Addition of choline to the diet containing added ethanolamine markedly decreased the incidence of both hemorrhagic kidneys and hemorrhagic eyes.

Recently we have studied the effect of 3-aminopropanol (3AP), the homologue of ethanolamine, in choline-deficient rats. The present communication shows that 3-aminopropanol increased the severity of kidney hemorrhagic degeneration, and unlike ethanolamine, markedly elevated the liver fat. The results reported here suggest that 3AP behaves very much like 2-amino-2-methylpropanol (2A2MP) which has been shown to increase not only the severity of kidney hemorrhagic degeneration(2,3) but also the liver fat(4) in rats consuming a choline-deficient diet.

Experimental and results. Weanling male rats (18 to 22 days of age; 35 to 55 g) derived from the Sprague-Dawley strain and born to mothers fed Laboratory Chow (Ralston-Purina Co., St. Louis, Mo.) were placed in raised cages and fed experimental diets *ad libitum* for 7 days. Water was available to the animals at all times. Food consumption and body weights were recorded each day. At the end of the 7-day period the rats were sacrificed by decapitation and the kidneys and eyes were examined for hemorrhage.

The composition of the diet (diet A) used in these experiments and the method for measuring the liver fat as shown in the following Tables have been described earlier (4).

Table I shows that when either 3AP or 2A2MP was incorporated into diets and fed to rats, the incidence of hemorrhagic kidneys

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TABLE I. Effect of 2-Amino-2-Methylpropanol and 3-Aminopropanol in Rats Consuming Low-Choline Diets.

Inhibitor (μmoles/g food)		No. of rats*	Avg wt of liver fat (mg)	Liver fat as % of body wt†	Avg daily food intake (g)	Avg daily wt increase (g)
0		146 (6)	494	.62 ± .049	6.3	4.2
11.2	2A2MP‡	760 (32)	841	1.24 ± .014	6.2	3.5
22.4	2A2MP	108 (58)	557	.86 ± .029	5.6	3.1
33.6	2A2MP	36 (75)	384	.62 ± .017	5.1	2.4
11.2	3AP‡	159 (30)	919	1.32 ± .032	5.8	3.9
39.9	3AP	298 (52)	970	1.42 ± .023	6.1	3.7
66.5	3AP	72 (69)	934	1.45 ± .030	5.9	3.6

* Number in parentheses represents percentage of animals having kidney lesions.
† Mean ± standard error.
‡ 2A2MP = 2-amino-2-methylpropanol; 3AP = 3-aminopropanol.

TABLE II. Effect of Methyl Donors and N-Methyl Derivatives of Ethanolamine in Rats Consuming Low-Choline Diets Containing 11.2 μmoles of Either 2-Amino-2-Methylpropanol or 3-Aminopropanol per g of Food.

Supplement (μmoles/g food)	Inhibitor	No. of rats*	Avg wt of liver fat (mg)	Liver fat as % of body wt†	Avg daily food intake (g)	Avg daily wt increase (g)
52 Bet‡	0	60 (0)	182	.26 ± .024	6.5	3.7
52 Bet	2A2MP‡	144 (3)	543	.76 ± .027	6.7	4.0
52 Bet	3AP‡	23 (0)	347	.50 ± .044	5.5	4.0
52 Meth‡	0	36 (0)	200	.30 ± .025	6.0	3.3
52 Meth	2A2MP	36 (0)	709	1.04 ± .074	6.3	3.5
52 Meth	3AP	24 (0)	628	.94 ± .089	5.5	3.6
7 Chol‡	0	84 (0)	95	.14 ± .012	5.9	3.6
7 Chol	2A2MP	120 (0)	154	.23 ± .022	5.9	3.7
7 Chol	3AP	27 (0)	92	.13 ± .014	5.9	4.4
7 DME‡	0	72 (0)	142	.21 ± .029	6.1	3.7
7 DME	2A2MP	120 (0)	283	.41 ± .049	6.1	3.8
7 DME	3AP	27 (0)	144	.21 ± .017	6.0	4.7
7 MME‡	0	60 (0)	198	.29 ± .050	5.7	3.4
7 MME	2A2MP	108 (8)	283	.44 ± .036	5.8	3.5
7 MME	3AP	26 (0)	195	.27 ± .034	5.9	4.3

* Number in parentheses represents percentage of animals having kidney lesions.
† Mean ± standard error.
‡ Bet = betaine hydrochloride; Meth = L-methionine; Chol = choline chloride; DME = dimethylethanolamine; MME = monomethylethanolamine; 2A2MP = 2-amino-2-methylpropanol; 3AP = 3-aminopropanol.

and the level of liver fat were greater than in rats fed the control diet containing neither of these substances. When these substances were incorporated into diets at different levels, the incidence of damaged kidneys varied directly with the level of each fed. Ocular hemorrhages were present in a few animals consuming high levels of each amino alcohol. The decrease in liver fat due to increasing the level of 2A2MP perhaps can partially be explained by the decrease in both daily food intake and body weight gain.

The results of a study on the effect of methyl donors and N-methyl derivatives of ethanolamine in rats consuming the low-choline diet containing 11.2 μmoles of either 3AP or 2A2MP per gram of food are shown in Table II. When neither of the inhibitors was present, both added betaine and methionine maintained the liver fat at low levels. Addition of 2A2MP or 3AP markedly increased the liver fat when added betaine or methionine was present. In a separate experiment when animals were fed a 42% casein diet for 7 days, the liver fat was 0.26% of the body weight. Addition of 11.2 μmoles per gram of 3AP and 2A2MP increased the liver fat to 0.81 and 0.88% of the body weight, respectively. The 42% casein diet contains approximately the same amount of methio-

TABLE III. Effect of Ethanolamine in Rats Consuming Low-Choline Diets With and Without Added Methyl Donors Containing 11.2 μmoles of Either 2-Amino-2-Methylpropanol or 3-Aminopropanol per g of Food.

Methyl donor (μmoles/g food)	Ethanolamine (μmoles/g food)	Inhibitor	No. of rats*	Avg wt of liver fat (mg)	Liver fat as % of body wt†	Avg daily food intake (g)	Avg daily wt increase (g)
0	7	0	108 (12)	443	.66 ± .040	6.2	3.6
0	7	2A2MP‡	144 (30)	732	1.07 ± .036	6.1	3.4
0	7	3AP‡	90 (16)	636	.92 ± .042	5.6	3.9
0	14	0	84 (0)	319	.45 ± .021	6.5	4.0
0	14	2A2MP	60 (5)	732	1.03 ± .024	6.6	4.0
0	14	3AP	112 (18)	496	.72 ± .038	5.5	3.9
52 Bet‡	7	0	36 (0)	116	.15 ± .008	6.7	4.7
52 Bet	7	2A2MP	36 (0)	271	.38 ± .037	6.2	4.0
52 Bet	7	3AP	23 (0)	148	.21 ± .026	5.3	4.0
52 Bet	14	0	24 (0)	104	.15 ± .013	6.5	3.9
52 Meth‡	14	0	12 (0)	153	.21 ± .015	6.8	4.3
52 Bet	14	2A2MP	24 (0)	170	.26 ± .019	6.6	4.0
52 Meth	14	2A2MP	12 (0)	479	.67 ± .045	6.5	3.9
52 Bet	14	3AP	23 (0)	129	.20 ± .015	5.1	4.0
52 Meth	14	3AP	24 (0)	399	.62 ± .056	5.2	3.3

* Number in parentheses represents % of animals having kidney lesions.
† Mean ± standard error.
‡ Bet = betaine hydrochloride; Meth = L-methionine; 2A2MP = 2-amino-2-methylpropanol; 3AP = 3-aminopropanol.

nine as the 18% casein diet to which 52 μmoles of methionine have been added per gram.

When neither 3AP nor 2A2MP was added to the diet, choline, dimethylethanolamine and monomethylethanolamine maintained the liver fat at low levels. Addition of 3AP or 2A2MP to diets containing these amino alcohols resulted in only slight changes in liver fat. For the most part 11.2 μmoles per gram of food of 2A2MP or 3AP did not lead to the development of hemorrhagic kidneys in rats consuming diets containing added methyl donors or added N-methyl derivatives of ethanolamine at levels shown in Table II.

The effect of ethanolamine in rats consuming low-choline diets containing 11.2 μmoles of either 3AP or 2A2MP per gram of food is shown in Table III. In the absence of 3AP or 2A2MP added ethanolamine (14 μmoles/g) decreased the liver fat to a certain extent from that in animals consuming the unsupplemented basal diet (Table I). This decrease was not nearly as marked as that observed when the N-methyl derivatives of ethanolamine were fed (Table II). Addition of either 3AP or 2A2MP to the diet containing ethanolamine led to a significant increase in liver fat. Ethanolamine at the levels shown in Table III did not appear to have any marked influence on the incidence of hemorrhagic kidneys whether the inhibitors were present in the diet or not (Tables I and III).

Table III also shows the effect of ethanolamine in rats consuming low-choline diets containing 52 μmoles of either added betaine or methionine, plus 11.2 μmoles of either 3AP or 2A2MP per gram of food. The combination of ethanolamine and betaine was quite effective in reducing the liver fat of animals consuming either one of the inhibitors. The methionine-ethanolamine combination, although effective in decreasing the liver fat in the presence of the inhibitors, was not nearly as effective as the betaine-ethanolamine combination. The reduction of liver fat when added methionine and ethanolamine were fed together in the diet in the presence of 2A2MP was essentially the same as that obtained when they were fed in the presence of 3AP.

Discussion. Based on these results it would appear that 3-aminopropanol is similar to 2-amino-2-methylpropanol in its antilipotropic behavior in rats consuming low-choline diets. It has been shown (2,3,4) that N-methyl derivatives of ethanolamine markedly reduce the antilipotropic effects of 2-amino-2-methylpropanol, whereas betaine, methionine and ethanolamine reduce the effects only

slightly. Ethanolamine in the presence of added betaine is quite able to overcome the action of 2-amino-2-methylpropanol but in the presence of added methionine is unable to do so. Even though the inhibitory actions of 3AP and 2A2MP are quite similar in the rat, the latter substance appears to be the stronger inhibitor. An action difficult to explain is the decrease of liver fat when the level of 2A2MP is increased in the diet. Such is not observed when 3AP is increased.

Radioactive isotope studies(5) indicate that 2A2MP inhibits the incorporation of ethanolamine and dimethylethanolamine into rat liver phospholipids. Choline incorporation on the other hand is only slightly inhibited. Additional observations(6) indicate that 2A2MP itself is incorporated into liver phospholipid. It is suggested that ethanolamine and its N-methyl derivatives must first be incorporated into phospholipid before they are methylated to choline(7,8,9). It is postulated that 2A2MP and 3AP increase the severity of choline deficiency by inhibiting the incorporation of ethanolamine into phospholipid thus preventing its methylation to choline.

If it is demonstrated that 3AP is incorporated into phospholipid and is also an inhibitor of natural amino alcohol incorporation into phospholipid and thus methylation to choline (lecithin), it with 2A2MP should be of value in the study of phospholipid synthesis and metabolism. Further, they should be of value in studies involving the role of phospholipids in other biological mechanisms or systems.

Summary. 3-Aminopropanol, like 2-amino-2-methylpropanol, increased the incidence of hemorrhagic kidneys and the level of liver fat of weanling male rats consuming a low-choline diet. Choline, dimethylethanolamine and monomethylethanolamine prevented the antilipotropic action of 3-aminopropanol. In the presence of 3AP betaine and methionine prevented the occurrence of kidney hemorrhages but only partially reduced the liver fat. Ethanolamine had little influence on the occurrence of hemorrhagic kidneys and only partially reduced the liver fat. Betaine and ethanolamine together in the diet were quite effective, whereas, methionine and ethanolamine together were only moderately effective. The inhibitory action of 3-aminopropanol was not as great as that of 2-amino-2-methylpropanol.

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Plasma Bilirubin and Bromsulfophthalein Clearance During Simulated High Altitude in Unanesthetized Rats.* (29867)

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Recently Berendsohns(1) has reinvestigated the problem of bilirubinemia in residents of high altitude. There appeared to be a relationship to the degree of polycythemia. Though some tendency to parallel the bilirubin

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