other hand, injection of dihydroxyphenylalanine (Dopa) was followed by a very marked increase of chromogenicity of the brain extracts which reached its maximum within one hour and was on the decline after two hours. Whether this phenomenon is due to mere temporary deposition of Dopa in the brain or to a conversion into encephalin, is a question which deserves further study with the aid of paper chromatography.

Summary. Colorimetric assay of a large number of human and animal brains for "encephalin" revealed a rather uniform pattern of intracerebral distribution in various species. There was no appreciable difference between the encephalin content and its distribution in the brains of "normal" and "psychotic" humans. No major changes were observed under the influence of various hormones, adrenalectomy, hypophysectomy, convulsive drugs, electrical stimulation of the brain, narcotics, conditions of stress, acetylcholine, and N-free diet. Only the injection of dihydroxyphenylalanine was followed by a very marked temporary increase of the colorimetric readings, which suggests either a selective absorption of this substance by the brain or its conversion into encephalin.

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Metabolism of Isomers of Linoleic and Linolenic Acids.* (18399)

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It has been repeatedly shown that the rigid exclusion of fat from the diet of rats and other animals results in cessation of growth and appearance of skin symptoms which are prevented or cured by either linoleic or arachidonic acid(1). However, either linolenic acid or hexaenoic acid permits growth, but does not cure the skin symptoms. The administration of linoleate to fat deficient rats causes the deposition of predominantly arachidonic acid (tetraenoate), and the administration of linolenic acid causes deposition of predominantly hexaenoate in certain tissues(2). However, the conversion of linoleate to hexaenoate and linolenate to tetraenoate has been demonstrated in the whole animal. Reiser has recently shown the conversion of linoleate to tetraenoate and pentaenoate, and of linolenate to hexaenoate in the chick(3). To attempt to learn something of the nature of the highly unsaturated acids deposited as the result of linoleate or linolenate feeding, a study was made of the deposition of polyunsaturated fatty acids in the rat as the result of administration of unnatural isomers of the essential fatty acids.

Experimental. Rats which had been kept on a fat deficient diet(2) for 10-12 months after weaning were given daily oral doses of 40 mg of ethyl esters of the various fatty acids under study for a period of 2 months. At the end of this time, the animals were killed, the total fatty acids were isolated, the polyunsaturates were estimated spectrophotometrically(4), and the total quantities of 4, 5 and 6 double bond acids were estimated as described previously(2). Ethyl linoleate and ethyl linolenate were prepared by the usual bromination-debromination procedures. Ethyl linolelaidate was prepared by selenium iso-

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TABLE I. Deposition of Polyunsaturated Fatty Acids as the Result of Supplementation.

Supplement	Animals	Avg wt gain, g	Total fatty acids, g/rat	Hexaenoic acid, mg/rat	Pentaenoic acid, mg/rat	Tetraenoic acid, mg/rat
None	2	0	3.2	35		9
Linoleate	4	96	10.4	155		78
Linolelaidate	5	2	4.4	67		27
Conj. linoleate	2	—36	0.5	15		7
Linolenate	4	69	7.2	164	22	88
Elaidolinolenate	3	33	13.8	288		
Arachidonate(10)	4	77	8.3	126	8	217

merization of linoleate(5). Ethyl elaidolinolenate was prepared by the method of Kass, Nichols and Burr(6). Conjugated linoleic acid, (m.p. 8°), was prepared from linoleic acid by alkaline isomerization(7).

Results of the investigation, shown in Table I, indicate that both linoleate and linolenate cause increases in total tetraenoate and hexaenoate in the whole animal. These results at first glance disagree with earlier conclusions (2,8) which were based on analyses of selected tissues, and in which the conversions of linoleate to hexaenoate and linolenate to tetraenoate escaped notice. The present data, however, in partial agreement with Reiser's data obtained on chickens(3) raise the question why tetraenoate formed from linolenate is inactive in curing the skin symptoms of fat deficiency.

Trans isomers of linoleate and linolenate, although not active in alleviating fat deficiency symptoms, are converted to spectrophotometrically detectable polyunsaturated forms. Linolelaidate (*trans, trans*-linoleate) is converted to both tetraenoate and hexaenoate, but to a lesser degree than is natural linoleate. Likewise, elaidolinolenate (*trans, trans, trans*-linolenate) is converted to hexaenoate and pentaenoate. However, these polyunsaturated fatty acids formed from the unnatural isomers of linoleate and linolenate are probably themselves unnatural isomers containing *trans* double bonds, which although detectable by alkaline isomerization and spectrophotometric technic, are biologically inactive forms.

Conjugated linoleic acid is not converted to polyunsaturated acids. Its administration caused a decreased weight and the early death of the rats. Upon analysis, the polyunsaturated acid content of the animals was found to be less than in the deficient control animals. In as much as conjugated acids oxidize by a different mechanism than do the methylene-interrupted polyunsaturated acids (9), it would be expected that metabolism of conjugated linoleic acid would also be different. The possibility exists that the metabolic oxidation of conjugated linoleic acid has a wasting effect upon the structural polyunsaturated acids of the animal.

In these experiments classical symptoms of fat deficiency were cured only by ethyl linoleate. Arachidonate, fed in earlier parallel experiments(10) also cured symptoms and caused renewed growth. Data from the arachidonate experiment are included in Table I for comparison. Conjugated linoleic acid worsened the fat deficiency symptoms. Weight gains during the 2 months supplementation period were good for linoleate and linolenate. For linolelaidate no gain was made and for elaidolinolenate only a moderate gain was observed. Supplementation with linoleate, linolenate or elaidolinolenate caused significant increases in the total fatty acids of the rat, but the increases as the result of linolelaidate feeding were somewhat less. Feeding conjugated linoleic acid drastically

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reduced the total fatty acids of the animals.

Summary. From these experiments it is apparent that *trans* isomers of the "essential" fatty acids are converted to inactive forms of polyunsaturated acids which are, however, detectable spectrophotometrically. Conversely, the detection of polyunsaturated acid in a tissue does not imply that these substances are biologically active. However, this factor is not likely to affect studies of animals fed natural diets.

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The Effect of Acclimatization on the Propulsive Motility of the Small Intestine During Anoxia.* (18400)

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Only a relatively few objective criteria have been established for adaptation to oxygen want. Perhaps the two most widely recognized are the increases in the number of red blood cells and in the amount of hemoglobin. It is desirable to establish other criteria and it is always appropriate to study adaptation in different species of animals. In the present study albino rats were used.

We have shown(1) that the propulsive motility of the small intestine of rats is decreased by effective degrees of hypoxia. Actually a pressure of only 382 mm of Hg (simulated altitude of 18,000 ft.) is capable of producing a significant decrease of motility. If rats became acclimatized to a low oxygen tension, and then were exposed to altitude, the propulsive motility should not be affected to the same degree as it would in unacclimatized animals.

Methods. Seventeen albino rats (Wistar-strain) were acclimatized by placing them in a low-pressure chamber for three and one-half hours each day at a pressure of 303 mm Hg (simulated altitude of 24,000 ft.); 8 rats were exposed for 26 and 9 for 62 days. The temperature of the room in which the low-pressure chamber was located varied from 70° to 75° F. Forty-eight hours after the last acclimatization period the rats were paired with normal unacclimatized rats, which were similar in weight and age. They had been fasted for 24 hours. Each member of a pair of these rats was given 2 cc of a mixture of 10% powdered charcoal suspension in 10% gum acacia in water by stomach tube. After allowing 10 minutes for some of the material to enter the small intestine, both rats were placed in the low-pressure chamber at a pressure of 254 mm Hg (simulated altitude of 28,000 ft.) At the end of 30 minutes they were taken out of the chamber and decapitated. The small intestine was removed, slit open and the distance the charcoal had traversed measured.

In order to ascertain whether acclimatization alone affects normal propulsive motility of the small intestine 11 rats were acclimatized using the same general procedure as previously outlined. They were exposed to a low oxygen tension for four hours each day for 41 days. They were then paired with unacclimatized rats and the propulsive motility of the small intestine determined (at ground level) in the usual manner. No significant difference was found.

Results. The results are given in Table I. The latter shows that the propulsive motility of the small intestine of the acclimatized rats was less affected by hypoxia than the unacclimatized. The results were statistically significant at the 0.1% level (Fisher's t test). It was found, moreover, that those animals which had been exposed to hypoxia for 3.6 hours each day for 26 days were as well

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