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Comparative Threonine, Valine, Histidine, and Glucose Oxidation in Chicks.* (25221)

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There are very few reports of comparative studies on relative amounts of different essential amino acids which will be catabolized and oxidized, or synthesized into protein after ingestion by an animal. Mice injected intravenously with 0.7 to 2 mg of labeled amino acids(1) oxidized 28% of injected activity from glycine-1-C^{14}, 45% of that from L-histidine-2-imidazole-C^{14}, 55% of that from L-leucine-1-C^{14}, and 25% of that from L-lysine-1-C^{14} to expired CO_2 within 4 hours. Peak $C^{14}O_2$ production occurred within 30 minutes after injection. Fasted rats fed 25 mg of glycine-1-C^{14}(2) oxidized 50% of activity to CO_2 within 18 hours. Young turkey poults(3) had a maximum $C^{14}O_2$ production within 2 hours after subcutaneous administration of DL-lysine-2-C^{14} with total recovery of 20% of administered activity within 24 hours. Fasted phlorizinized rats given DL-lysine-6-C^{14} orally(4) oxidized 40% of activity to CO_2 in 8 hours. In a comparison of phenylalanine, tyrosine, and tryptophan metabolism(5), tracer doses of uniformly labeled amino acids administered orally to fasted rats showed a maximum $C^{14}O_2$ production during the first hour after administration. Within 8 hours, 45% of the C^{14} in tyrosine had appeared as CO_2, 20% of that from phenylalanine, and 25% of that from tryptophan. Tumorous mice injected intravenously with DL-tyrosine-3-C^{14}(6) oxidized 40% of the activity to CO_2 within 24 hours. Phenylalanine-deficient mice fed meals containing uniformly labeled L-phenylalanine(7) converted a smaller percentage of tracer doses to CO_2 than did normal mice when the meal contained a deficient level of phenylalanine, but a larger percentage when the meal contained a normal level of phenylalanine. This suggests that an animal tends to conserve an amino acid if it is deficient in its diet. This is also shown in the report that rats fed diets rich in methionine(8) oxidized 25% of methyl-C^{14} to CO_2 in 24 hours, but when diets contained a marginal level of methionine, only 6% of methyl-C^{14} appeared in CO_2 in the same time. Peak $C^{14}O_2$ production was reached 2 to 3 hours after oral administration of labeled amino acid in both cases. Since these reports involved various experimental animals, fed or fasted, with amino

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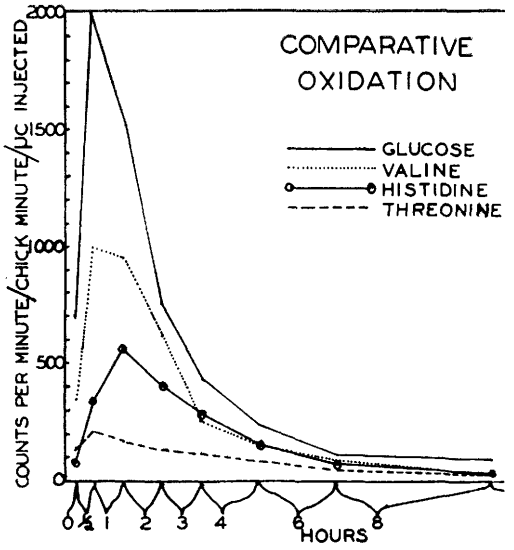

FIG. 1. Avg recovery of $C^{14}O_2$ from chicks after intraper. injections of uniformly labeled amino acids and glucose.

acids labeled in various positions, and administered by different methods, it is difficult to compare the data critically.

Methods. In this study of oxidation of essential amino acids, intraperitoneal injections of different amounts of solutions of L-threonine, L-valine, L-histidine, and glucose uniformly labeled with carbon-14 were given young chicks weighing 80 to 150 g. They had been previously fed either a complete purified diet based on crystalline amino acids, a diet lacking the amino acid injected, or a diet lacking all essential amino acids. The chicks were fed before being injected and feed and water were available in the metabolism chamber in which they were placed immediately after being injected. Respiratory CO_2 was trapped in NaOH, precipitated as $BaCO_3$ by addition of $BaCl_2$, collected on filter paper circles by filtration, dried, and activity determined by counting in a windowless, gas-flow counter (Tracerlab). The counts obtained were corrected for self-absorption, aliquot volumes used, and length of collection periods. They are expressed as counts/minute for each minute of collection time/microcurie administered. Validity of the intraperitoneal method of administration was checked by oral forced feeding of diet mixed with labeled threonine. Oral and intraperitoneal administration gave similar results.

Results. Comparison of average rates of $C^{14}O_2$ production by chicks after injection of labeled compounds is given in Fig. 1. The curves are averages for 4 or 5 chicks for each compound. Total recovery of administered activity during the 14 hour periods averaged 10% for threonine, 25% for histidine, 40% for valine, and 50% for glucose. In addition, peak $C^{14}O_2$ production varied among the 3 amino acids. Peak production from valine and threonine occurred close to one hour after injection, but peak production from histidine did not occur until nearly 2 hours after injection.

Different diets previously fed had little effect on oxidation of each amino acid or glucose. A diet lacking the labeled amino acid administered had little effect on the fraction of amino acid oxidized except possibly in the case of one lacking all essential amino acids. Even 10-fold differences in amounts injected from less than one mg to amounts above the daily requirements did not affect the fraction oxidized to CO_2. There was no apparent conservation of an amino acid lacking in the diet. Activity remaining in chicks at end of experimental period was much higher in blood, liver, and muscle picric acid-precipitable proteins of chicks given threonine than of those given histidine, whose activity was higher than that of those given valine. Almost all activity remaining in the chicks was in picric acid-precipitable proteins; only limited amounts were found in free amino acids or other compounds. Most activity in proteins was in the form of injected amino acids, only limited activity appearing in non-essential amino acids.

Discussion. The percentage of each administered amino acid which is rapidly oxidized was consistent even when the level of the amino acid in the diet was varied from very low to high levels. It was typical for individual amino acids. The low percentage of labeled threonine oxidized to $C^{14}O_2$ raises the possibility that oxidation of an amino acid is not a result of a "spillover" of an excessive level of the free amino acid pool into oxidative pathways. In these experiments, the amount of threonine administered was varied enough

so that it should have affected the level of the free threonine pool but the percentage of administered threonine which was oxidized was not changed. The rapid appearance of radioactivity in the picric acid-precipitable proteins points to the possibility, at least in the case of threonine, of some metabolic route from administered amino acids to bound amino acids to the oxidative pathways possibly without participation in free amino acid pools.

Summary. When different amounts of uniformly labeled L-threonine, L-valine, L-histidine, or glucose were administered intraperitoneally to young chicks previously fed complete purified diets or diets lacking different essential amino acids, the total percentage of administered activity recovered as $C^{14}O_2$ during 14 hour experimental periods averaged 10% for threonine, 25% for histidine, 40% for valine, and 50% for glucose. There were large differences in the fraction of each amino acid incorporated into picric acid-precipitable protein. Peak $C^{14}O_2$ production occurred about one hour after administration of glucose, threonine, or valine; 2 hours after administration of histidine. Neither previous diet (complete or lacking the amino acid injected) nor 10-fold variations in amounts of amino acids administered appeared to affect fractions oxidized or synthesized into proteins.

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Comparative Passage of Calcium and Strontium from Plasma into Cerebrospinal Fluid in Man.* (25222)

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Comparative passage of strontium and calcium through various membranes is of importance in determining distribution of Sr^{90} in the body. *In vitro* ultrafiltration experiments with serum using Sr^{85} and Ca^{45} as tracers have shown that filtration of strontium is greater than that of calcium and that strontium is less completely bound to plasma proteins than calcium(1). Since passage of these ions through various membranes *in vivo* may differ from that *in vitro*, the relative transfer rates from plasma into different body fluids were studied. This report deals with passage of Sr^{85} and Ca^{45} from plasma into cerebrospinal fluid in man. The question whether cerebrospinal fluid is formed by ultrafiltration or secretion has been much argued(2). It was hoped that these tracer studies might also help clarify this point.

Materials and methods. Tracer doses of Sr^{85} (approximately 0.2 μc/kg body weight) or of Sr^{85} and Ca^{45} (approximately 0.2 μc/kg body weight of each) were administered as chlorides in single intravenous injections to 17 patients in whom lumbar puncture was to be performed for medical reasons. The intervals between injection of the tracers and lumbar puncture ranged from 5½ to 47 hours, at

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