

USE OF 3-METHYLHISTIDINE EXCRETION AS AN INDEX
OF MUSCLE PROTEIN BREAKDOWN IN MICE

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The excretion of 3-methylhistidine has been shown to be a valid measure of the rate of muscle myofibrillar protein breakdown in humans, rats, chickens, and cattle but it is not valid for sheep or pigs (Young and Munro 1978; Harris and Milne 1981). The method has been applied to the measurement of muscle protein breakdown rates in humans with muscle wasting conditions to assess the efficacy of therapeutic treatments (Tomas and Ballard 1979). One possible mode of treatment is through nutritional intervention. The branched chain amino acid leucine, for example, is known to increase muscle protein accretion by both stimulation of synthesis and inhibition of breakdown (Buse and Weigand 1977).

The dystrophic mouse (129 Re J, dy/dy) is a useful model for human muscular dystrophy. Thus the metabolism and excretion of 3-methylhistidine by these mice was examined to determine its suitability as a marker for myofibrillar protein breakdown.

Male and female non-dystrophic mice were injected i/v with a known quantity of 3-¹⁴C methylhistidine and the urine collected for 5 d. Urine samples were fractionated on an ion exchange column and the amount of recovered radioactivity associated with 3-methylhistidine and other substances was determined. Male mice excreted 85 per cent of the injected dose recovered in the first 2 days (83%) in the form of 3-methylhistidine or the N-acetylated derivative. Female mice, however, metabolised half of the injected 3-methylhistidine to non-acid labile compounds. Thus 3-methylhistidine excretion may provide a qualified indication of muscle protein breakdown in male mice but is of no value in female mice.

Three groups of male mice (normals aged 22 d; dystrophic aged 21 d, and 35 d) were given diets which contained 1.75 (basal), 3.50 or 5.25 g leucine/100 g in a Latin Square design experiment. The 3-methylhistidine/creatinine ratio (mmol/mol) was unaffected by treatment in normal or older dystrophic mice but was significantly ($P < 0.01$) reduced from 24.5 ± 0.62 (SEM) to 22.2 ± 0.80 and 19.7 ± 0.44 for increasing levels of leucine intake respectively in the young dystrophics. This reduction is unlikely to have been due to altered metabolism of 3-methylhistidine in these male mice and indicates that significant reductions in muscle protein breakdown in dystrophy may be achieved by nutritional means.

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