Control of amino acid uptake by the lactating mammary gland of the rat

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At the peak of lactation the mammary gland of the rat removes considerable amounts of amino acids (Viña et al., 1981). The increased demand for amino acids during this period is satisfied by an increase in dietary intake (Fell et al., 1963). As might be expected from a physiological standpoint, the major fate of amino acids taken up by the gland is the synthesis of milk proteins, but it has been observed that some are good precursors for lipid synthesis (Viña & Williamson, 1981).

We reported that γ-glutamyltransferase and glutathione are involved in amino acid uptake by the lactating mammary gland, thus providing evidence for the functioning of the γ-glutamyl cycle in the mammary gland in vivo (Viña et al., 1981).

We have studied the evolution of the arteriovenous differences of amino acids through the mammary gland during lactation, and found that in all cases the arteriovenous differences increase from day 0 to day 5 and from day 5 to day 10. They remain high between days 10 and 15 but fall sharply at day 20. These changes parallel those of the activity of γ-glutamyltransferase in mammary gland during lactation (Puente et al., 1979).

At the peak of lactation both the blood flow and the arteriovenous differences of amino acids are maximal. Thus the uptake of amino acids by the gland is maximal between days 10 and 15 after birth, when specific direction of blood metabolites to the gland is maximal (Williamson, 1980).

It has been shown that γ-glutamyltransferase is subject to hormonal control by oestrogens (Puente et al., 1979) and by prolactin (Pocius et al., 1980). The availability of bromocryptine, an inhibitor of prolactin secretion (Seki et al., 1974), was useful as a tool to investigate the role of prolactin in the regulation of amino acid uptake by the lactating mammary gland.

We compared the arteriovenous differences through the mammary gland under the following situations: (a) normal lactating rats at the peak of lactation; (b) rats at the peak of lactation with bromocryptine-induced prolactin deficiency (24 h); and (c) rats at the peak of lactation injected with bromocryptine and prolactin.

The arteriovenous differences of amino acids were significantly lower in prolactin-deficient rats than in untreated rats ($P < 0.05$ for threonine, serine, asparagine, cysteine, methionine, leucine, phenylalanine and lysine; $P < 0.005$ for glutamine, proline, glycine, alanine, isoleucine, tyrosine, histidine and arginine). However, when prolactin was injected together with bromocryptine, as described by Agius et al. (1979), the arteriovenous differences of amino acids were not significantly different from those of untreated rats.

Another model by which to study the regulation of amino acid uptake by the mammary gland is premature weaning. We measured the arteriovenous differences of amino acids through mammary glands in rats weaned for 2, 4, 5 and 24 h.

The arteriovenous differences of amino acids in rats weaned for 2 or 4 h were not significantly different from those of the controls. However, in rats weaned from 5 or 24 h the arteriovenous differences fell to values significantly lower than in the controls. Since after 5 h of weaning the blood flow through the mammary gland is decreased (Hanwell & Linzell, 1973), the amino acid uptake by the mammary gland, which depends on blood flow and on arteriovenous differences, will be decreased.

Injection of prolactin 2 h after removal of pups did not affect the fall in the removal of amino acids induced by 5 h of weaning.

In order to compare normal and 'weaned' glands in the same animal we used unilaterally weaned rats, i.e. normal lactating rats at the peak of lactation, with the teats of one side sealed with adhesive for 5 h to prevent the removal of milk by suckling. This model allowed us to compare normal and 'weaned' glands in the same animal, with the same hormonal environment and normal blood flow in both sides (Hanwell & Linzell, 1973).

Under these experimental conditions the arteriovenous differences of amino acids in the normal side were similar to those of the normal lactating rats. But those of the side which had the teats sealed were significantly lower than those of normal lactating rats ($P < 0.05$ for serine, proline, lysine and phenylalanine; $P < 0.005$ for the other amino acids). Thus milk accumulation plays an important role in amino acid uptake by mammary gland independently of the hormonal regulation and of the blood flow through the glands.

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