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Effect of Fasting on Urinary Excretion of Water and Nitrogen in the Rat *

J. Codina and E. Herrera

Cátedra de Fisiología General
Facultad de Biología
Universidad de Barcelona
and Departamento de Investigación
Centro «Ramón y Cajal»
Madrid (Spain)

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Rats housed in metabolic cages undergoing 48 h fasting showed reduced daily intake of drinking water and increased urinary volume. Both the daily amount of urinary creatinine and urea excreted were diminished with fasting, while that of ammonia was augmented. Besides demonstrating metabolic water loss under fasting, results suggest that ammonia derived from glutamine in the kidney, rather than urea formed in the liver, is the main nitrogenous catabolic product of amino acids in fasting.

The endogenous metabolic changes which occur during fasting may be assessed by urinary excretion patterns of different metabolites. In preliminary studies we observed significant changes in the amount of urine per day during fasting in the rat. In addition to its intrinsic weaning action, this effect may alter the interpretation of urinary parameters whether expressed per unit of volume or per total daily excretion. In the present study we have quantified the daily urinary volume and nitrogenous compound in fed rats and during two different periods of fasting.

Materials and Methods

Female Wistar rats were individually housed in metabolic cages and fed *ad libitum* for the continuous collection of urine for 24 h periods. The animal quarters were maintained under automatically controlled temperature (23 ± 1° C) and light cycles (12 h on and 12 h off). The amount of food and water intake and the body weight of each animal were determined daily. During the two fasting periods of

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Reprint request to: Prof. E. Herrera. Departamento de Investigación. Centro «Ramón y Cajal». Ctra. de Colmenar, Km. 9. Madrid-34 (Spain).

48 h, the rats were allowed drinking water *ad libitum*.

Urine specimens were collected in graduated receptacles containing 0.5 ml 6N HCl and light mineral oil to maximize recovery of ammonia (4), and processed as described elsewhere (14). Creatinine (21), urea (6, 12) and ammonia (12) were determined by colorimetric methods. Recovery of the compounds initially added to urine exceeded 95.6 % for creatinine, 99.0 for urea and 83.5 % for ammonia. Recuperation of ammonia levels was very constant and the values were corrected accordingly.

Results and Discussion

The body weights of individually housed rats increased progressively during the experiment (fig. 1), although the rate of change was less than in age and sex matched animals housed collectively (data not shown), indicating that social communication is required for normal development in the adult rat. Fasting for 48 h produced an intense reduction in body weight (fig. 1) which was not completely recovered until the 5th day of re-feeding. This delay in recuperation on body weight was not caused by smaller food intake, that actually enhanced immediately after fasting (fig. 1). It is known that refeeding allows the rapid recuperation of the lipogenetic and glucogenetic capacities in animals (2, 3, 9) suggesting that other factors require prolonged periods of time in order for the animal to regain its normal metabolic state. During the two periods of fasting studied, water intake was significantly reduced in comparison with values on the day prior to food deprivation (figure 1).

Re-feeding produced a rebound effect in the amount of water intake which paralleled the increased food intake. The amount of drinking water was, however, inversely related to the urine volume which rose significantly during the two fasting periods (fig. 1). Thus the loss of urinary liquid during deprivation was due not to an enhanced water intake but to internal dehydration. It is known that fasting produces an intense loss of water in certain organs, especially the liver (13, 15). The urine volume increase indicates that quantitatively the internal water loss during fasting was the most important factor determining the body weight loss.

Diminished excretion of both creatinine and urea were consistently observed dur-

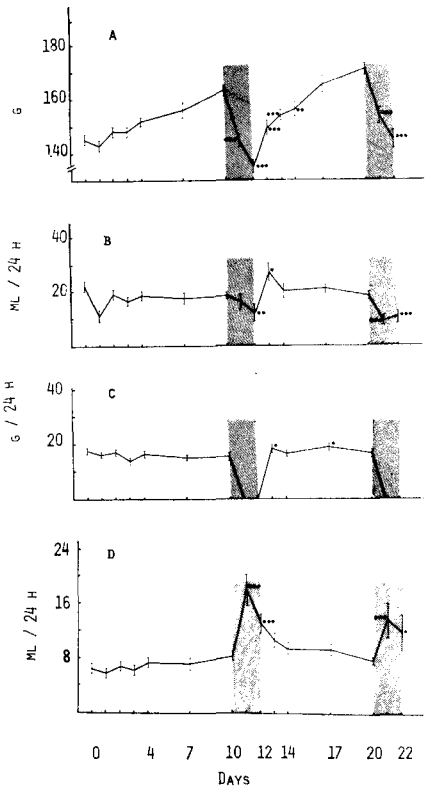

Fig. 1. *Effect of two periods of 48 h fasting (shadowed area) on body weight (A), water intake (B), food intake (C) and daily urine volume (D) in the rat.*
Asterisks correspond to the statistical comparison versus the values at each day previous to the fasting periods: * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$.

ing the two fasting periods (fig. 2), in agreement with previous results (17). As neither of these nitrogenous compounds is altered in plasma during deprivation (15), the present finding indicates their reduced renal clearance in the fasting state as well as decreased internal production. The reduced daily excretion of creatinine during fasting invalidates the use of its casual concentration to derive the amount of daily urinary parameters (5, 7, 8, 16, 23) when food is withheld.

Ammonia excretion was the only nitrogenous compound enhanced during fasting (fig. 2). The integrated values of urea and ammonia indicate that the augmented catabolism of amino acids during deprivation is not followed by an increased production of urea by the liver, but by an augmented production of ammonia by the kidney. These considerations agree with the need of more prolonged starvation periods (up to 7 days) than those used in the present study to obtain a significant enhancement in the activity of the urea-cycle enzymes in the rat's liver (1, 20). The enhanced ammonia excretion may be the result of an active catabolism of glutamine by the kidney, as it is well known that this amino acid is the major substrate utilized by the kidney for the production of ammonia (18, 19, 22). This enhanced renal ammoniogenesis with fasting may be triggered by acids (10, 11) which would correspond to the augmented ketonemia observed with this period of food deprivation in the rat (13, 15).

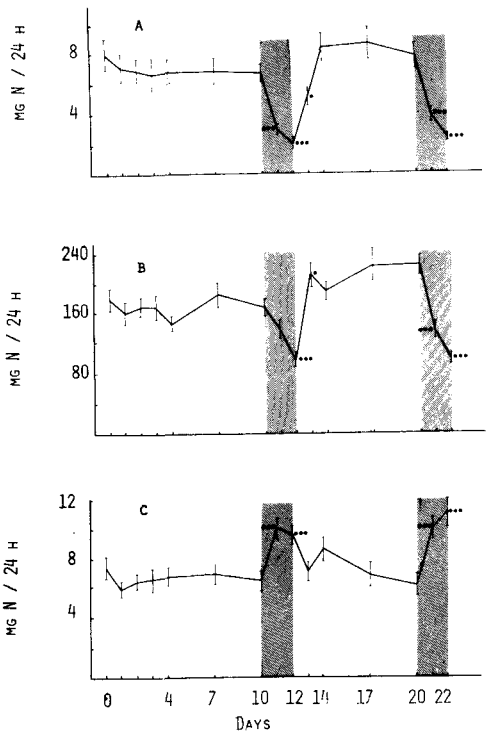

Fig. 2. *Effect of two periodic of 48 h fasting (shadowed area) on the daily urinary excretion of creatinine (A), urea (B) and ammonia (C) nitrogen.*
Asterisks correspond to the statistical comparison versus the values at the day previous to the fasting periods: * = $p < 0.05$; *** = $p < 0.001$.

Resumen

El ayuno de 48 h produjo en ratas, mantenidas en jaulas metabólicas, una disminución en la cantidad de agua bebida y aumento del volumen de orina excretada. Tanto la cantidad de creatinina como de urea excretada al día disminuyeron con el ayuno, mientras que la de amoníaco aumentó. Además de demostrar la pérdida de agua metabólica con el ayuno, los resultados indican que el principal producto del catabolismo de aminoácidos con el ayuno es el amoníaco derivado del metabolismo de la glutamina en el riñón más que la urea formada en el hígado.

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