Laboratory mouse (strain MF1) was used as a model to investigate the effects of high protein intake on daily energy expenditure and lactation performance. The specific dynamic action (SDA) for high protein (HP: 60% energy as protein) and high carbohydrate (HC: 70% energy as carbohydrate) diets was measured using open-flow respirometry at 9.4% and 6.1%, respectively. The same two diets were fed ad libitum to mice during lactation. Mice fed on HP and HC diets at 21 °C reached an asymptote in their daily food intake at 12.29±0.2 g day-1 and 16.57±0.2 g day-1, respectively between days 12-17 of lactation. HP-fed mice had a significantly higher daily energy expenditure (DEE) measured by doubly labelled water (133.4±4.8 kJ day-1) and higher water turnover (41.1±6.2 g day-1) than HC-fed mice (DEE: 102.1 ±14.2 kJ day-1 and water turnover: 26.7±6.5 g day-1) but the energy they exported as milk was significantly lower (84.2±31.4 kJ day-1) than that of HC-fed mice (164.6±30.5 kJ day-1) and therefore resulted in poor growth rate of their offspring. The urea production of HP-fed mice from their daily protein intake of 7.1 g was estimated at 1994 mg which required 10.2 ml of water per day to be cleared. The mice increased their urine production by 14.4 ml probably to eliminate this urea. In conclusion, the MF1 mice fed HP diet at 21 °C and the HC-fed mice reached an asymptote in their daily food intake at 12.29 g day-1 and 16.57 g day-1 respectively, between days 12-17 of lactation. HP diet had negative effects on lactation performance at 21 °C when compared with the HC diet. The negative effects of the HP diet were due to the higher DEE which resulted from the heat production consequent of digestion and milk production by the HP-fed mice. Therefore, the higher DEE greatly reduced the energy available for milk production. This probably explains the reduction in growth of the pups/offspring from the HP-fed mothers because they did not get sufficient energy for growth. Key words: Laboratory mouse, Lactation, High protein, Specific dynamic action, Asymptotic food intake, Daily energy expenditure