Breathing of Uremic Rats

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Dear Sir,

Previous investigations in rats 24 and 48 h after nephrectomy revealed normal or even increased cardiac output and arterial blood pressure, normal arterial and tissue oxygen partial pressures, and decreased PaCO₂ [1]. The whole body oxygen consumption was depressed by about 40 and 60%, respectively, whereas BUN was in the range of 140–280 mg/dl, and serum potassium between 7 and 12 mmol/l [1–3]. During these studies, we occasionally observed respiratory arrest about 48 h after surgery. As there is no study on breathing in this model of acute uremia, the present investigations were performed.

We used 24 male Wistar rats weighing 160–212 g. The rats were randomly divided into two groups which were either bilaterally nephrectomized or sham operated under ether anesthesia [2]. After surgery, the animals were deprived of water. In a body plethysmograph for unanesthetized animals [4], tidal volume, the rate of breathing, and colonic temperature were measured before, and 24 and 48 h after surgery. Then the animals were anesthetized with urethane (1.3 g/kg i.p.), their trachea cannulated, and their ventilation monitored in a body plethysmograph [5] until respiratory arrest occurred. Minute ventilation was calculated and related to body weight.

It is obvious from figure 1 that during 2 days after nephrectomy or sham operation, minute ventilation as well as tidal volume are maintained at the same levels. There is a higher rate of breathing in nephrectomized rats 48 h after surgery. In both groups (minute) ventilation drops to about 70% under urethane anesthesia. Within 0.5–4 h of anesthesia, a decline in ventilation occurs in all uremic rats, leading to acute respiratory arrest within 1 h.

1 This work was supported by the Dreher Gedächtnisschenkung, Vienna, Austria.

Control 24 h 45 h Anesthesia

Fig. 1. Time courses of rate of breathing (f), tidal volume (V_T), and minute ventilation (VE) in nephrectomized (•) and sham-operated (O) rats. Parameters were measured before (control), and 24 and 48 h after nephrectomy or sham operation in awake rats, and during urethane anesthesia. Four uremic animals were monitored until the last breath. In 1 of them, larger and smaller tidal volumes alternated during this period, in the others, tidal volume and respiratory frequency

decreased continuously (fig. 2). After cessation of breathing, the heart was still beating for about 5–30 min at low frequencies of about 20/min.

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In man, respiratory failure due to hyperkalemia is rare [6] but may be more common in rats [7]. The constant level of respiration during the 2 days after nephrectomy results, with respect to decreased oxidative metabolism, in low PaCO₂ [3], as it was also observed in chronically uremic patients [8].

Fig. 2. Breathing of nephrectomized rats. Time marks in seconds; volume calibration indicated by the vertical bar=1 ml. a Normal tidal volume and normal respiratory frequency (left); alternating smaller and larger tidal volumes 2 h later (right), b Small tidal volumes and slow breathing frequency until final respiratory arrest (about 52 h after surgery).

Already 1 day following nephrectomy, the oxidative metabolism is reduced and further decreases on the second day [1–3]. At the same time, the level of substances normally excreted by the kidneys continuously increases. Until the second day, however, minute ventilation remains constant, as do the circulatory parameters [1]. The following rapid decline in ventilation resulting in acute respiratory arrest occurs within 1 h before death. It is possible that after surpassing a certain level of retained substances, ventilation is suddenly and severely disturbed. Whether serum potassium or other ‘uremic toxins’ are involved remains unclear.

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