($p < 0.01$). Urinary calcium excretion remained unchanged or decreased in acidotic or alkalotic animals that did not receive fluorocitrate.

These studies demonstrate that administration of fluorocitrate, an aconitase inhibitor known to increase blood and tissue citrate content by inhibiting the conversion of citrate to isocitrate[7], is associated with an increased urinary calcium excretion. In contrast to the present study, Karam et al.[6] reported that fluoroacetate administration was associated with decreased urinary calcium excretion. These conflicting results, however, may be related to a divergent action of fluoroacetate and fluorocitrate as inhibitors of metabolism, since fluorocitrate, unlike fluoroacetate, causes striking increases in urinary citrate excretion despite similarly elevated blood and tissue citrate levels[10].

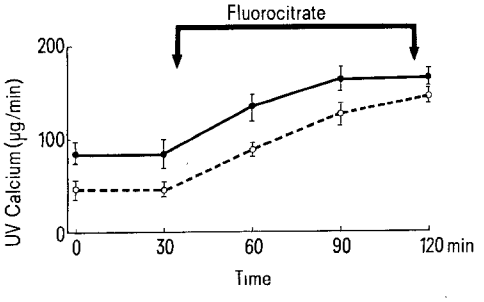

Fig. 2. Urinary calcium excretion in 5 acidotic (closed circles) and 5 alkalotic (open circles) dogs before and during the infusion of fluorocitrate. The vertical bars represent SEM. In both groups of animals the increments at 60 and 90 min were statistically significant with the paired t-test (acidosis: $p < 0.05$; alkalosis: $p < 0.01$) urinary calcium excretion decreased or remained unchanged in control animals.

The hypocalcemia produced by fluorocitrate administration would have been expected to stimulate parathormone release. Although this hormone increases tissue and urinary citrate excretion recent studies indicate that it lowers urinary calcium probably by stimulating distal tubular reabsorption[11]. The hypercalciuria previously reported after administration of parathyroid hormone[3] is probably related to the fact that crude extracts increase the filtered load of calcium, thereby, obscuring enhanced fractional reabsorption[12]. 2 main conditions enhance urinary citrate excretion: alkalosis and the administration of substrates of the Kreb's cycle, including citrate, presumably by inhibition of tubular reabsorption of citrate[13]. In the present study, fluorocitrate increased the urinary excretion of citrate to exceed the quantity filtered. Although the method used to measure glomerular filtration rate slightly underestimates the inulin clearance[14], the error of the method is too small to alter our results. Net citrate secretion has not been reported before, except during the infusion of malate[13]. Kook and Lotspeich[15], however, found ^{14}C-citrate in the urine of dogs given labelled precursors in stop-flow experiments.

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Arterial and mixed venous blood gases following DNP infusions in rabbits

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Summary. Hypocapnia and respiratory alkalosis was found in arterial and mixed venous blood after i.v. administration of DNP. Stimulation of ventilation resulted in steady P_aO_2, when PvO_2 decreased, and seemed to be independent on CO_2.

Ramsay[1] and Huch et al.[2] have shown an increase in body oxygen consumption following i.v. infusions of 2,4-dinitrophenol, an uncoupler of oxidative phosphorylation in mitochondria. This effect was accompanied by an increase in lung ventilation, with arterial blood gases remaining close to control values.

The mechanism of respiratory response in the case of DNP-induced hypermetabolism is uncertain. The influence of the drug itself on respiration by direct central action, and/or action on carotid baro- and chemoreceptors, seems to be negligible, when compared with the total effect, as was shown by cross-perfusion experiments of Levine and Huckabee[3]. Therefore 2 possible sources of enhanced respiratory drive should be taken into account: tissue metaboreceptors, detecting rate of metabolism in muscles[4], and venous or pulmonary chemoreceptors, responding to changes in mixed venous blood composition[5]. In the present study, arterial and mixed venous pH, PCO_2 and PO_2 were measured in 6 rabbits (2.5–3.5 kg b.wt), lightly anaesthetized with sodium pentobarbitone (45 mg/kg, small supplementary doses added when signs of arousal were observed), and treated with DNP. Up to 6 infusions of 5 mg/kg DNP (1% solution in 1.5% $NaHCO_3$) were performed every 15–20 min. Blood samples (arterial – from right femoral artery, and mixed venous – from right atrium via right jugular vein) were taken prior to each infusion and analyzed for pH, PO_2 and PCO_2 with the Radiometer BMS-3 blood analyzer.

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Changes in arterial and mixed venous pH, PCO_2 and PO_2 following DNP injections

Total dose of DNP (mg/kg)	Arterial blood			Mixed venous blood		
	pH	pCO_2	pO_2	pH	pCO_2	pO_2
0 (control)	7.44 ± 0.05	26.5 ± 4.2	81.9 ± 6.9	7.40 ± 0.07	33.7 ± 6.4	42.0 ± 4.7
5	7.48 ± 0.04	24.3 ± 2.8	83.1 ± 10.7	7.43 ± 0.04	30.0 ± 4.5	37.5 ± 6.0
10	7.50 ± 0.05	21.8 ± 2.9*	80.9 ± 9.0	7.45 ± 0.03*	28.6 ± 4.8*	31.8 ± 5.0***
15	7.52 ± 0.06*	21.0 ± 1.6*	80.9 ± 4.5	7.44 ± 0.05	28.3 ± 3.0*	27.7 ± 4.2***
20	7.51 ± 0.03**	19.6 ± 2.3***	79.4 ± 14.4	7.44 ± 0.05	27.0 ± 4.4*	26.2 ± 4.5***

Statistical significance of changes from control by unpaired Student's t-test: *$0.90 < p < 0.95$; **$0.95 < p < 0.99$; *** $p > 0.99$.

The effect of the drug injections was found to be cummulative. Results are shown in the table.

Lung ventilation was not measured quantitatively, but a drastic rise in both tidal volume and breathing frequency was evident in every case. Rises in body (rectal) temperature were minimized by tracheotomy and never exceeded 1–1.5 °C (means: 37 °C ± 0.8 SD at the beginning, and 38.2 °C ± 0.6 SD at the end of experiments). Mean arterial blood pressure did not change.

Changes, observed in arterial and mixed venous blood composition suggest that in the case of DNP-induced ventilatory rise neither CO_2 nor pH is a respiratory stimulus. Gradual decrease in arterial PCO_2 accompanied by respiratory alkalosis were observed. Mixed venous PCO_2 and pH changes followed that of arterial PCO_2 and pH. Arterial and mixed venous hypocapnia could be explained by a shift in respiratory quotient; it is also possible that increase in cardiac output, which follows DNP infusions[6], together with increased lung ventilation, would favour CO_2 diffusion in lungs, because of substantial difference in diffusibility of CO_2 and O_2 across alveolar walls[7].

If perhaps CO_2 is more efficiently removed from blood than oxygen is dissolved, the possible mechanism might be suggested, which drives respiration to assure adequate supply of oxygen to the tissues rather than to stabilize arterial PCO_2. Therefore, in the condition of DNP-induced hypermetabolism, the role of carbon dioxide in the respiratory control would be of no essential importance. Both increase in cardiac output and lung ventilation were recently shown by Liang and Hood[8] to be related to mucsle afferents stimulation, resulting from DNP action. On the basis of those results it seems likely that muscle receptors play a substantial role in the ventilatory response to DNP. It is, however, uncertain whether increase in lung ventilation is directly related to the metabolic, i.e. chemical stimulus, or results from an increase in cardiac output[9]. If there is also an additional stimulation of ventilation, related to blood gas content, decrease in venous oxygen would be the only stimulus.

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Peritoneal dialysis in small laboratory animals[1]

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Summary. Healthy rats and guinea-pigs were treated with a simple method of continuous peritoneal dialysis for 12, 24 and 48 h. Increasing with time, both animal species developed severe hypoproteinemia and hemoconcentration due to protein loss into the dialyzate fluid. These changes were associated with a high mortality rate, when Sterofundin® was used for dialysis. Therefore, protein loss should be substituted and the type of dialyzate must be considered in experimental long-term dialysis using these small laboratory animals.

Peritoneal dialysis is widely used in the treatment of renal and non-renal diseases in man. As animal experiments were reported only in dogs[4,5] and rabbits[6] requiring difficult operative procedures, a simple experimental model was developed for small laboratory animals[7]. Our experiments show that prolonged peritoneal dialysis in these animals is associated with considerable protein loss requiring substitution in long-term experiments.

Material and methods. Peritoneal dialysis was carried out in 101 male Wistar rats (180–250 g) and 25 guinea-pigs (240–320 g). Operative procedure is described else-

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