output to the control values was often observed (Figure 2, B). Inactivation or transport processes of these 2 substances might account for the observed recovery in the ACh values.

Discussion. GABA is the inhibitory transmitter at the crustacean neuromuscular junction[8] where it increases membrane conductance to Cl^-[11], and it is suggested as a mediator of presynaptic inhibition in the amphibian spinal cord[15,16]; therefore in the latter a reduction in ACh output after the administration of GABA may be the result of increased inhibitory influences on motor neurones which are the main source of the ACh released from this preparation[9]. Baclofen (10^{-4} to 10^{-2} *M*) did not act in a similar way to GABA at the lobster neuromuscular junction, and at the dose of 2×10^{-4} *M* had a weaker and shorter action than GABA (10^{-4} *M*) in the frog spinal cord. This accords with previous findings on the cat CNS[6,7] where baclofen is less potent than GABA and seems to have a different mechanism of action. In the spinal cord, however, the administration of baclofen depresses the neuronal firing[6] and the ACh release; two findings which might account for its antispastic action. CURTIS et al.[6] and DAVIES and WATKINS[7] suggested that the effect of baclofen might derive from an interaction with catecholamine receptors. It seems therefore that baclofen does not act via GABA mechanisms. The precise mechanism of action of this drug remains yet to be elucidated.

Riassunto. Il Baclofen (acido β-clorofenil-γ-aminobutirrico), a differenza del GABA, non modifica la conduttanza di membrana della fibra muscolare di aragosta. Il Baclofen riduce la liberazione di acetilcolina dal midollo spinale di rana; tale effetto è minore di quello prodotto dal GABA. Le due sostanze sembrano agire attraverso differenti meccanismi.

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Renal Effects of the Prostaglandins A_1 and E_2 in Hydrated and Hydropenic Dogs

Differences between prostaglandin A_1 and E_2 (PGA_1, PGE_2), with respect to their effects on renal blood flow and fluid and electrolyte excretion by the dog kidney, have been reported recently[1-3]. PGA_1 increases renal blood flow in maximally effective doses by approximately $^1/_3$ with only weak effects on excretory parameters, whereas PGE_2 increases blood flow by up to 80% and urine output by more than 400%. Since these experiments were performed in dogs with their fluid metabolism in steady state undergoing a slight NaCl-diuresis, no evidence could by obtained on the effects of the prostaglandins on the renal handling of free water. On the other hand, effects on free water excretion can be expected, since it is well known that prostaglandins can stimulate the formation of cAMP and that PGE_2 inhibits the effects of ADH in isolated collecting ducts[4]. In the study reported here, we infused PGA_1 and PGE_2 at the maximally effective rate[2] of 1 µg/min into 1 renal artery of dogs which were either in hydropenic state or undergoing water diuresis to evaluate the effects on free water reabsorption and excretion. In addition, the urinary excretion of cAMP was determined in the antidiuresis experiments.

Methods. The experiments were performed in 5 mongrel dogs of either sex weighing 17–20 kg. 3 'hydropenic' dogs were deprived of water 36 h prior to the experiments with free access to dry food. They received 20 U vasopressin after the induction of anesthesia, and an infusion at 3.5 ml/min during the surgical procedure and at 1.5 ml/min throughout the experiment which contained 147 mEq/l Na^+, 4 mEq/l K^+, 140 mEq/l Cl^- and 11 mEq/l HCO_3^-. The experiment was not begun unless urinary osmolality was at least 1000 mosmol/l. 2 'hydrated' dogs were deprived of food 24 h prior to the experiments with free access to water. They received an infusion of 0.3 *M* glucose at 10–12 ml/min after induction of anesthesia for 90 min during the surgical procedures and an infusion of 0.15 *M* glucose, 73.5 mEq/l Na^+, 2 mEq/l K^+, 70 mEq/l Cl^- and 5.5 mEq/l HCO_3^- at 10 ml/min throughout the experiment. The experiment was not begun unless urinary sodium concentration was below 15 mEq/l.

Anesthesia, surgical procedure, infusion of prostaglandins[5] into the left renal artery, general protocol of the experiments, and determination of renal blood flow with an electromagnetic flow meter, of glomerular filtration rate (GFR) as clearance of creatinine and of the excretion of fluid and electrolytes were carried out as described previously[1,2]. The concentration of cAMP in the urine of the infused kidney was determined by a radio isotope dilution test using the test kit of Boehringer/Mannheim. To discriminate effects by the prostaglandins from changes of other variables, all parameters from the experimental kidney except blood flow and C_{H_2O} or Tc_{H_2O}, were related to the control kidney. The ratios of experimental (left) kidney/control (right) kidney during the infusion of one of the prostaglandins were expressed in percent of the ratios during the corresponding control periods.

Results and discussion. None of the 2 prostaglandins A_1 and E_2 affected systemic blood pressure or GFR at the doses applied here. The effects of the 2 prostaglandins on blood flow (BF), urinary flow rate (UV) and osmolar clearance (C_{osm}) are demonstrated in the Figure. PGA_1

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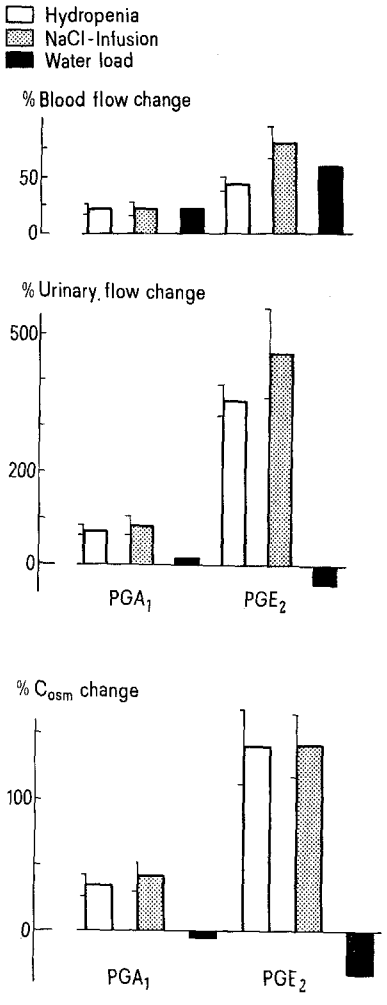
increased renal blood flow by approximately 25% independent of the water balance. This increase is higher under the influence of PGE_2 as expected from previous experiments[1], but the difference is less marked in hydropenia than in the other two states, possibly as consequence of the reduced available circulating blood volume.



Effects of PGA_1 and PGE_2 on renal blood flow (BF), urinary flow rate (UV) and C_{osm} in dogs undergoing hydropenia, NaCl-infusion, and water-load. The scale on the ordinate indicates % change related to control periods previous to the infusion of the prostaglandins into the renal artery (see methods). The data 'NaCl-infusion' are taken from [2] and added for comparison.

Effects of PGA_1 and PGE_2 on urinary concentration and excretion of cyclic AMP ($\bar{x} \pm s\bar{x}$; $n = 6$) during hydropenia

	cAMP concentration (pM/ml)	cAMP excretion (pM/min)
Control	1780 ± 200	724 ± 90
PGA_1	1640 ± 230	1108 ± 194
PGE_2	740 ± 80	1386 ± 136

In hydropenia, the effect of PGE_2 on urinary flow rate is 3–4 times higher than that of PGA_1, whereas during water-load urine volume was not affected by PGA_1 and decreased to 60% of the control by PGE_2. Na^+ and Cl^- excretion parallelled urine flow: In hydropenia a slightly increased excretion with PGA_1 and an approximately 500% increase with PGE_2, in water-load no effect with PGA_1 and a 20% decrease with PGE_2 were observed. Likewise, the effects of both prostaglandins on C_{osm} and UV correspond in hydropenia as well as in water-load (Figure). In water-load, the decrease of UV after PGE_2 outweighs absolutely the change of C_{osm} causing a decrease of C_{H_2O} from an average of 1.5 ml/min in controls to 0.5 ml/min under PGE_2. The influence of PGA_1 on C_{H_2O} is not marked (1.7 versus 1.9 ml/min in controls). In hydropenia, the absolute increment of C_{osm} is slightly higher than that of UV, thereby increasing Tc_{H_2O}. This increase is quantitatively poor with mean values for Tc_{H_2O} of 1.0 ml/min before and 1.2 with PGA_1, and 1.0 before and 1.4 ml/min with PGE_2, but it is a constant and reproducible event.

The excretion of cAMP in control periods during hydropenia which is summarized in the Table is more than twice as high compared with control periods during water-load where we found an average concentration of 80 pM/ml and an urinary excretion of 320 pM/min. Both prostaglandins, but PGE_2 more than PGA_1, increased the excretion of cAMP significantly and markedly.

In conclusion: 1. Both, PGA_1 and PGE_2, increase renal blood flow independently of the fluid balance, indicating that they can be involved in the likewise independent renal autoregulation. 2. Only PGE_2 influences markedly renal fluid and electrolyte excretion in all three states of fluid balance, which supports the view that, if a prostaglandin is involved in the regulation of the renal fluid or electrolyte excretion, it has to be of the E-type. 3. The 2 prostaglandins and again especially PGE_2 act ADH-like in water-load and have at least no ADH antagonistic effect during antidiuresis. This is in agreement with micropuncture studies in rats[3], but inconsistent with in vitro results in collecting ducts[4]. 4. The high cAMP excretion during hydropenia and antidiuresis is increased by the 2 prostaglandins PGE_2 and PGA_1. If this is an indication of an enhanced renal formation of cAMP, it is not likely that prostaglandins antagonize the effects of ADH in vivo.

Zusammenfassung. PGA_1 und PGE_2 erhöhen die Nierendurchblutung sowohl im Zustand des Wassermangels als auch der Überwässerung, während PGE_2 nicht aber PGA_1 unabhängig vom Flüssigkeitsgleichgewicht die renale Wasser- und Elektrolytexkretion steigert. Beide PGs erhöhen die Ausscheidung von cAMP. Sie wirken ADH-ähnlich während einer Wasserdiurese und nicht antagonistisch gegen ADH während der Antidiurese.

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