for instance, ^{14}C-edrophonium was eliminated via the biliary canaliculus, its concentration in bile should be reduced (and its rate of excretion unaffected) during choleresis induced by agents acting on ductal or ductular mechanisms. In fact, circumstantial evidence[2] suggests that all the quaternary amine that gains access to parenchymal liver cells is rapidly metabolized to a 3-oxyglucuronide prior to excretion by the canaliculus.

In the present experiments, the influence of secretin on the elimination of ^{14}C-edrophonium in bile was most marked during the first 5 min. The initial increase in biliary elimination may be due to the transient high concentration of the drug in the periductal and periductular capillaries immediately after its injection into the hepatic arterial tree (i.e., before equilibration throughout extracellular fluid has occurred). In general, the biliary excretion pattern in both control and secretin-infused animals appears to accurately reflect the rapid removal of ^{14}C-edrophonium from the circulation, since the drug is almost completely cleared from extracellular fluid within 20 min of i.v. administration[8].

In previous experiments[2], it was shown that the biliary elimination of unchanged ^{14}C-edrophonium was significantly greater after injection into the hepatic artery than after infusion into the portal vein. Both these studies and the results of the present experiments support the hypothesis that unchanged ^{14}C-edrophonium is directly transferred from plasma to bile across the ductal or ductular epithelium.

Résumé. On a étudié l'effet de la sécrétine sur l'élimination biliare de ^{14}C-edrophonium et montré que cette excrétion est significativement plus élevée pendant l'injection de la sécrétine.

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18 May 1972.

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Effect of Sodium Deoxycholate on Net Transintestinal Movement in the Uraemic Rat: Acute Experiments[1]

Bile salts were reported to increase intestinal absorption of various hydrophilic substances[2,3]. It has been suggested that the mechanism of action consists of an alteration of membrane structure[4,5]. If increased solute lumen-to-blood (l-b) transfer is the result of an altered membrane permeability, then increased solute transfer in the opposite direction should also be possible.

The purpose of the present investigation was to determine the effects of an unconjugated bile salt, sodium deoxycholate (NaDC), on net solute blood-to-lumen (b-l) transfer in the uraemic rat. Increased intestinal elimination of uraemic waste products could be helpful in the management of uraemia.

Materials and methods. Male WC albino rats (450 to 600 g body weight) were binephrectomized by bilateral lumbar incision 36 h prior to experiments and fasted (with water allowed ad libitum). The experiments were carried out using in situ single loop preparations under light ether anesthaesia. A midline incision was made to locate the small intestine. A segment of 35 cm of the proximal small intestine (approximately 3 cm from the ligament of Treitz) was carefully ligated at its two ends. No major blood vessels were occluded by these ties. 3 ml of a prewarmed mannitol-NaCl solution in the presence or

[1] This work has been supported in part by a research grant from the Deutsche Forschungsgemeinschaft Nr. Dr 74/2.
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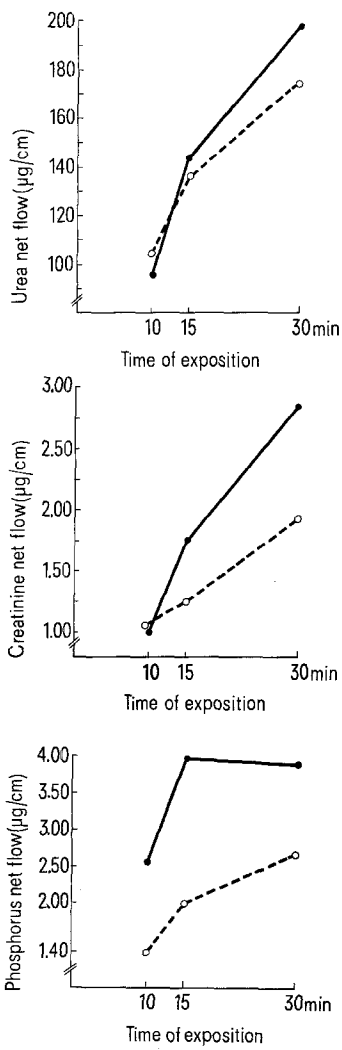
Net transintestinal solute and water flow with control solution A (no NaDC) and with solution B containing 2 m*M* NaDC (mean ± S.D.)

Solution	A (control)	B (NaDC)	A (control)	B (NaDC)	A (control)	B (NaDC)
No. of segments	7	6	6	8	6	6
Time of exposition	10 min	10 min	15 min	15 min	30 min	30 min
Sodium (μEq/cm)	[a]1.41 ± 0.90 (p = NS)	[a]1.18 ± 0.61	[a]1.36 ± 0.30 ($p < 0.05$)	[a]2.45 ± 0.97	[a]3.77 ± 1.66 (p = NS)	[a]4.15 ± 2.16
Potassium (μEq/cm)	[a]0.31 ± 0.07 (p = NS)	[a]0.38 ± 0.06	[a]0.39 ± 0.04 ($p < 0.01$)	[a]0.52 ± 0.08	[a]0.48 ± 0.09 (p = NS)	[a]0.58 ± 0.09
Calcium (μg/cm)	[a]2.05 ± 0.87 (p = NS)	[a]2.74 ± 1.37	[a]2.26 ± 1.44 (p = NS)	[a]2.36 ± 1.04	[a]2.75 ± 0.91 (p = NS)	[a]3.41 ± 1.75
Water (μl/cm)	[b]8.5 ± 9.1 (p = NS)	[b]11.1 ± 6.8	[b]8.2 ± 2.6 (p = NS)	[b]8.9 ± 4.8	[a]8.8 ± 12.1 (p = NS)	[a]15.8 ± 10.3

[a] net b-l transfer. [b] net l-b transfer.

absence of 2 m*M* NaDC were injected into the intestinal loop, by means of a syringe and needle. The loops were excised 10, 15 or 30 min after injection, the solution in the loops was withdrawn as completely as possible, and the animals were sacrificed. Mean plasma urea level during the experiments was 280 mg/100 ml, mean plasma creatinine level was 9 mg/100 ml. Two types of solution of identical osmolality (320 mOsm/kg) were used. Control solution A contained 220 m*M* mannitol and 50 m*M* NaCl. Solution B contained 220 m*M* mannitol, 48 m*M* NaCl, and 2 m*M* NaDC. Both solutions were adjusted to pH 7.0 by small amounts of NaOH. No significant change in the pH of the solutions occurred during the experiments. Urea, creatinine, phosphorus and calcium were determined with the Technicon Auto Analyzer (model SMA 12/60), sodium and potassium by flame photometry. Net water movement was calculated from the weight difference of injected and withdrawn solution.

Results. The Figure illustrates an increase in net b-l transfer of creatinine after 15 and 30 min and of phosphorus after 10, 15 and 30 min with 2 m*M* NaDC in the lumen. These increases were probably significant for creatinine ($p < 0.05$) and significant for phosphorus ($p < 0.01$) when compared to values of control solution containing no NaDC. Net creatinine b-l transfer after 10 min did not differ from control. The increase in net urea b-l flow was not statistically significant. Mean values per cm of loop are indicated. 12 instillations were performed in each period.



Net urea, creatinine and phophorus b-l flow with control solution A (no NaDC) in the lumen and with solution B containing 2 m*M* NaDC. ○, solution A; ●, solution B.

The Table shows significantly increased net sodium ($p < 0.05$) and potassium ($p < 0.01$) b-l transfer (mean ± S.D.) with 2 m*M* NaDC in the lumen for 15 min. Net sodium, potassium, calcium and water fluxes were not significantly different from control after the 10 and the 30 min instillation periods.

Discussion. Bile salts act on intermediate metabolism of the small intestine in a complex manner. Besides the emulsifying effect on lipophilic substances and the increase of their absorption, inhibition of intestinal absorption by blocking various enzymatic processes[6,7] and enhancement of intestinal absorption of hydrophilic substances[2,3] have been reported. Increased small intestine permeability to hydrophilic substances has been attributed to direct action of bile salts on mucosal structure. If the alteration of the membrane resulted in increased absorption by increased passive l-b movement, then passive b-l movement could be equally increased.

The present investigation shows that net creatinine, phosphorus, sodium and potassium b-l fluxes were significantly increased when 2 m*M* NaDC were present in the lumen of the proximal half of uraemic rat intestine. This increase could be due to increased membrane permeability and/or to inhibited active l-b transport. Since creatinine transintestinal movement seems to involve no active transport system[8] increased membrane permeability could play a role. Increased permeability due to irreversible, toxic changes of the mucosa must be considered[9–11]. In an experimental series in non-uraemic rats, solutions identical to control solution A but containing 0.6, 1.0, 2.0 or 5.0 m*M* NaDC were injected into isolated chronic jejunal loops, on 3 consecutive days during 5 h. No lesions were observed in light microscopy when NaDC concentration was 2 m*M* or less (unpublished work). The results of increased jejunal permeability with 2 m*M* NaDC in the lumen accord with data obtained by the perfusion of chronic jejunal loops in the uraemic rat (in preparation).

Increased membrane permeability to nitrogenous substances and electrolytes could be interesting in the management of chronic uraemia in the human.

Zusammenfassung. In vivo gelingt der Nachweis, dass der Transport von Kreatinin, Phosphor, Natrium und Kalium vom Blut in das Lumen des Dünndarms bei urämischen Ratten durch Natriumdesoxycholat gesteigert wird.

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