higher glucuronosyl and glucosyl transferase activities. Increases also occur in the hepatic concentration of UDP-glucose which, in the rabbit, constitute an important conjugating substrate for bilirubin[10].

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Intraluminal bile salt increases rate of firing in afferent fibers from the small intestine of the rat[1]

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Summary. Perfusion of a rat intestinal segment with a solution containing sodium deoxycholate (8 mM) increases the rate of firing in periarterial afferent nerves from the gut. This observation indirectly supports our earlier proposal that bile salt evokes a net fluid secretion in the small intestine via an activation of the enteric nervous system.
Key words. Bile salt; intestinal afferent nerves.

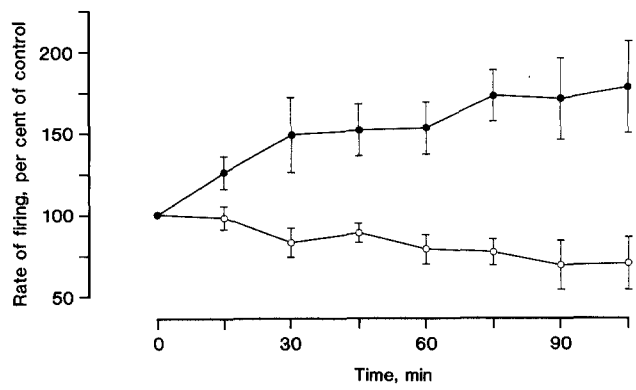
In an earlier series of experiments we provided evidence for the view that the intestinal net fluid secretion evoked by an increased concentration of a bile salt, sodium deoxycholate, in the intestinal lumen is at least in part caused by an activation of the enteric nervous system[2-5]. The present study was undertaken to obtain further evidence for the view that this bile salt can activate nerves, by recording afferent activity in periarterial nerves from the small intestine before and after exposing the intestinal lumen to a solution containing sodium deoxycholate.

Methods. The experiments were carried out on male Sprague-Dawley rats (Anticimex, Stockholm, Sweden), weighing 250–350 g. The animals were kept in the animal quarters under constant environmental conditions (22 °C, 50–60% relative air humidity, artificial lighting 06.00–18.00 h) for at least 7 days before the experiment. The animals were fasted 12 h before the experiment. Anesthesia was induced by i.p. injection of sodium methohexital (Bricanyl, Lilly Inc; 75 mg/kg b. wt) and maintained throughout the experiment by a continuous i.a. infusion of chloralose (1.25 mg/ml; 0.02 ml/min). The chloralose was administered in a glucose-bicarbonate solution via a catheter in the right femoral artery. Additional amounts of chloralose were administered through a catheter in the femoral vein if needed. The total dose of chloralose during an 8-h experiment did not exceed 150 mg/kg b.wt. Arterial pressure was measured in the femoral artery with a pressure transducer (Statham P23 DC).

After a tracheotomy, a midline abdominal incision was performed and a 15–20 cm long intestinal segment was selected and cannulated both proximally and distally. The proximal cannula was connected to a T-shaped tube which permitted the simultaneous perfusion of fluid and measurement of luminal pressure via a pressure transducer (Statham P23 AC). The perfusion was maintained at a constant rate of about 1 ml/min by means of a roller pump (Ismatec, Switzerland). The perfusate was heated to about 38 °C before entering the intestinal segment. After passing the segment, the perfusate was drained through the distal cannula into a beaker. The body temperature of the animal was kept at 38 °C by a lamp and a heating pad. The former was connected to a thermocouple thermometer in the mouth of the animal.

Bundles of periarterial nerve fibers around the superior mesenteric artery were dissected free from the surrounding adipose tissue distal to the coeliac ganglion. The proximal end of the bundle used for registration was ligated in order to eliminate the recording of efferent impulses. Afferent impulses were recorded via a bipolar platinum electrode that was kept in place with silicone rubber (Wacker Sil Gel 601). After amplification the signal was displayed on an oscilloscope (Tektronic Type 502). Two types of recordings were performed. In one the signal was rectified and the average response above base line (including background noise activity) was recorded. In another only signals greater than a certain preset magnitude were counted and recorded by means of a spike counter. The fact that the activity recorded was increased in response to a distension produced by clamping the drainage while introducing fluid into the segment was taken as evidence for the recording of afferent impulse traffic from the segment selected. All recordings were made on a Grass polygraph.

The modified Krebs-Henseleit solution used to perfuse the segment contained (mM): NaCl 122; KCl 4.7; KH_2PO_4 1.2; $NaHCO_3$ 25; mannitol 30. The pH of this solution was 7.7. In the



The effect of perfusing a rat intestinal segment with an isotonic solution containing sodium deoxycholate (8 mM) on the rate of firing in afferent fibers from the gut (n = 8). Bile salt (●——●) perfusion was started at time 0 which represents the control value. As a comparison is shown the corresponding results from control (○——○) experiments in which the intestinal perfusate contained no bile salt (n = 6). Bars indicate SE.

test solution 8 mM sodium deoxycholate was added. The pH of this solution was 8.0.

Results. The 'resting' discharge rate recorded while perfusing the segment with the modified Krebs-Henseleit solution was increased when perfusing the segment with the solution containing bile salt as illustrated in the figure summarizing 8 technically successful experiments. Rate of discharge (spike counter) increased throughout the experiments lasting for more than 100 min. In the figure the rate of nervous firing is expressed as a percentage of the control rate, since 'resting' rate of discharge varied between experiments.

Sustained increases of nerve fiber activity were poorly correlated with changes in intraluminal pressure as recorded by the pressure transducer located at the proximal end of the intestinal segment. However, transient intestinal contractions were accompanied by small transient increases of rate of signalling. Administration of atropine (0.25 mg/kg b.wt) did not influence the sustained rate of discharge. This dose of atropine has earlier been shown to inhibit the vagally induced decreases of heart rate in rats[6]. In control experiments with a solution devoid of bile salt no change of discharge rate was observed (fig.).

In all experiments the recorded nerve fiber activity decreased markedly after application of lidocaine hydrochloride onto the intestinal serosa and onto the mesentery.

Discussion. In a rather extensive series of experiments by Karlström and collaborators[2–5] evidence was provided for the view that the net fluid secretion from the small intestine evoked by sodium deoxycholate was in part produced by the activation of the enteric nervous system. This conclusion may indirectly be supported in the present series of experiments, which showed that the afferent nervous activity recorded from periarterial nerves was significantly increased when the intestinal mucosa was exposed to a solution containing 8 mM sodium deoxycholate.

It is not known whether the increased nervous activity is secondary to a direct action of the bile salt on nerve endings in the small intestinal mucosa, or whether sodium deoxycholate acts via some other endogenous compound. Karlström et al were unable to block the effects of bile salt on net fluid transport by indomethacin or histamin-1 blocking agents. They proposed that the bile salt itself might acts as a calcium ionophore on sensory nerve endings[7].

The sensory modality reflected in the increased afferent firing in the periarterial nerves can of course not be determined from the present study. However, it has been reported that perfusing the small intestine with a 10 mM bile salt solution causes abdominal pains in humans[8].

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Selective blockade of components of potassium activation in *Myxicola* axons

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Summary. The K^+ conductance in *Myxicola* giant axons activates in two phases which are pharmacologically separable. The fast phase of K^+ activation is specifically inhibited by 4-aminopyridine and by the substitution of D_2O for H_2O. We suggest *Myxicola* giant axons, like the amphibian node of Ranvier, may possess more than one variety of K^+ channel.

Key words. Potassium conductance; *Myxicola* axons; neuronal cell bodies; multiple K^+ channels.

A variety of K^+ channels has been characterized in axons and neuronal cell bodies. In addition to the classical delayed rectifier K^+ channels first described by Hodgkin and Huxley[1] in squid giant axons other K^+ channels include an anomalous rectifier[2], a Ca^{++}-dependent K^+ channel[3], a rapidly-inactivating K^+ channel[4], and a second-messenger-dependent K^+ channel[5]. Although many of these channels are only found in neuronal cell bodies, multiple K^+ channel types have also been identified in nodes of Ranvier[6–8]. The present study shows that K^+ activation in *Myxicola* axons occurs in two pharmacologically separate phases, suggesting that *Myxicola* may have more than one type of K^+ channel.

Methods. Myxicola axons were dialyzed and voltage-clamped by methods which included series resistance compensation and leak and capacity current subtraction[9]. The internal solution contained 450 mM K^+ glutamate; 50 mM KF; 30 mM K_2PO_4; pH = 7.30 ± 0.05. The external solution was Na^+ free and contained 10^{-6} M tetrodotoxin; 10 mM KCl; 10 mM $CaCl_2$; and 50 mM $MgCl_2$. The external substitute for Na^+ was Tris, also adjusted to pH 7.30 ± 0.05, and the temperature was 5.0 ± 0.5 °C. The time course of the K^+ conductance is distorted by K^+ accumulation in the Frankenhauser-Hodgkin space[8,10,11] but can be minimized either by using high K^+ solutions, or by calculating the K^+ conductance from simultaneous measurements of membrane current and the driving force, $(V\text{-}E_K)$. Both methods gave comparable results, but most of our experiments employed the second approach. Axons were held at −80 mV. Membrane currents were first recorded during 25-ms depolarizations to potentials between −60 mV and +100 mV (10-mV steps). Next, two-pulse protocols were applied in which axons were depolarized to a voltage V_1 for a time t_1; and then repolarized to a voltage V_2. For a given V_1 and t_1, V_2 was varied in steps (1-2 mV) small enough for determination of the reversal potential, $E_K(V_1, t_1)$. For each test voltage V_1, t_1 was increased from 0 to 25 ms and $E_K(V_1, t_1)$ redetermined for the same repolarization potentials V_2. Another test voltage V_1 was selected and the entire procedure repeated. We determined instantaneous I(V) curves for values of t_1 of 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 5.0, 6.0, 8.0, 10.0, 12.0, 14.0, 16.0, 18.0, 20.0 and 25.0 ms to accurately resolve changes in E_K. We monitored the K^+ current at +100 mV. Any deterioration caused us to terminate an experiment.

In all experiments the instantaneous $I_K(V)$ relationships were