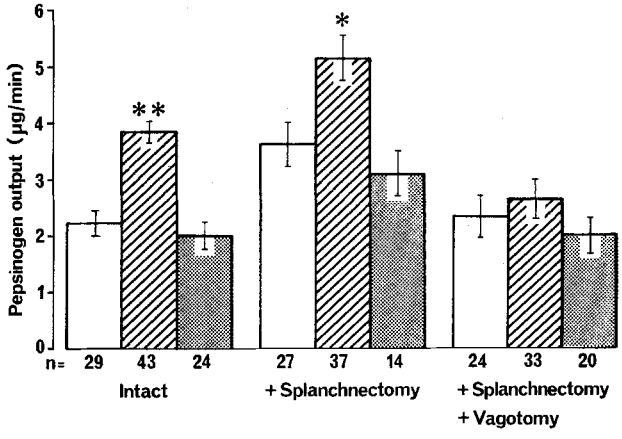
alter this response. This was despite the slightly raised basal values following sympathectomy, as has been previously observed[11]. The sympathetic nervous supply is recognized as having inhibitory actions on gastric secretion[12]. However, the similarity between the pepsin increases before and after splanchnectomy suggests that the splanchnic nerves play no part in the regulation of the response to acid. Bilateral vagotomy virtually abolished the response, suggesting that a vagal pathway is in operation. It is worth noting that pepsin secretion, unlike acid, is not totally abolished by vagotomy[13,14].



Gastric pepsin output induced by acidified saline perfusion of the intact, splanchnectomized and vagotomized (totally denervated) stomach in anaesthetized rats. Mean values (± SEM) before (□), during (▨) and after (▩) perfusion with acidified saline. n = Number of estimations of pepsin activity in 9 rats. Significant difference between pepsinogen secretion during acidified saline perfusion, and pepsinogen secretion into normal saline is shown by * ($p < 0.01$) and ** ($p < 0.001$).

The substantial pepsin secretion in response to acid instillation previously reported by Johnson[2] and Bynum and Johnson[3] could not be duplicated using the present preparation. The instillate pH employed by these authors (pH 1-2) was lower than ours, and may not represent physiological norms. Although these pH values may be obtained by stimulation of the parietal cells in the fasted animal, it is unlikely that such large amounts of acid occur normally in the empty stomach. Furthermore, these authors used a phosphate buffer, pH 7.4, for control instillations. Pepsin is readily inactivated by weak alkali and at pH 7.4 only a fraction of the true pepsin concentration would be detected[15]. This could lead to exaggeration of any true increase that occurred when the pH was lowered. It is clear, therefore, that normal pepsinogen secretion in the rat stomach is not simply the result of initial acid secretion, and stimuli of pepsin and acid secretion can be considered to act on each cell type independently.

1 Present address: Department of Medicine, Royal Veterinary College, North Mymms, Hatfield, Herts. AL9 7TA (England).
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Potassium transfer from brain to blood during sustained hyponatraemia in the newborn calf[1]

R.M. Gardiner and A.G. Wilkinson[2]

Physiological Laboratory, University of Cambridge, Cambridge CB2 3EG (England), 2 November 1979

Summary. The effect of dilutional hyponatraemia on cerebral blood flow and oxygen consumption, and net transfer of K^+ to the circulation from brain tissue drained by the sagittal sinus was investigated in anaesthetized calves. Cerebral blood flow decreased, and net transfer of K^+ to the circulation increased during hyponatraemia.

The K^+ content of brain tissue is reduced after prolonged hyponatraemia and it has been suggested that this loss of intracellular electrolyte represents the means by which brain swelling is mitigated in hyposmolar conditions[3]. However, the route, mechanism and time course of brain K^+ loss during hyponatraemia remain uncertain. These experiments were undertaken to quantify net transfer of K^+ to the circulation from brain tissue drained by the sagittal sinus during normonatraemia and during sustained hyposmolar hyponatramia.

The animals were anaesthetized with i.v. sodium pentobarbitone (30 mg/kg b.wt), paralyzed with gallamine triethiodide and ventilated via a tracheostomy. Cerebral blood flow was measured using an intra-arterial injection technique, in which the clearance of H_2 from cerebral venous blood is determined by a platinum anode located in the sagittal dural sinus[4]. Cerebro-spinal fluid (CSF) was sampled and its pressure recorded from a needle placed p.c. in the cisterna magna. Estimations were performed in duplicate on paired samples withdrawn simultaneously from the aorta and sagittal dural sinus at the beginning and end of each flow determination. Plasma and CSF electrolyte concentrations were determined with a Corning 455 Flame Photometer after dilution 1 in 200, and whole blood oxygen content by a polarographic technique[5]. Osmolality was determined by freezing point depression. Cerebral oxygen consumption and net K^+ transfer were calculated from the blood or plasma flow and arterio-cerebral venous concentration difference. Arterial blood gas tensions, pH, blood pressure and EEG were also monitored. The experiments were carried out on 12 pedigree Jersey calves aged between 10 and 46 days. Measurements were made

Comparison of measurements made during normonatraemia and hyponatraemia in anaesthetized calves

	P_{ao_2} (mm Hg)	P_{aco_2} (mm Hg)	pH	PCV	MABP (mm Hg)	CSF pressure (mm Hg)	CBF $ml \cdot 100\ g^{-1}\ min^{-1}$	CMR_{O_2} $\mu m \cdot 100\ g^{-1}\ min^{-1}$	Arterial plasma osmolality (mosmole)	Arterial plasma Na^+ (mmole/l)	Plasma K^+ Arterial (mmole/l)	sag.sinus (mmole/l)	AVD (mmole/l)	$CPF \cdot AVD_{K^+}$ $\mu m \cdot 100\ g^{-1}\ min^{-1}$
Normo-natraemia	103±7 (22)	34±1 (22)	7.45 (22)	32±2 (15)	121±5 (12)	8±1 (9)	67±3 (26)	147±15 (18)	280±1 (42)	139.8±0.2 (86)	3.92±0.05	3.93±0.05	−0.01±0.00 (86)	−0.51±0.14 (22)
Hypo-natraemia	96±5 (47)	35±1 (47)	7.39 (47)	31±1 (41)	122±2 (56)	24±2 (20)	55±2 (82)	140±7 (41)	232±1 (100)	117.1±0.5 (247)	3.84±0.04	3.88±0.04	−0.04±0.00 (247)	−1.51±0.07 (71)

The values are mean±SEM. No. of observations in brackets. MABP: mean arterial blood pressure; PCV: packed cell volume; CMR: cerebral metabolic rate; AVD: arterio cerebral venous concentration difference; CBF: cerebral blood flow; CPF: cerebral plasma flow.

during normonatraemia, and during steady-state hyposmolar hyponatraemia produced by water loading after administration of a long acting anti-diuretic hormone analogue (Desmopressin; Ferring Pharmaceuticals; 16 µg). A total of 115±5 ml/kg b.wt 1% D-glucose solution was infused i.v. over about 4 h, and observations were made for up to 8 h following the end of the infusion (mean 4.2±0.3 h).

During normonatraemia (arterial plasma Na^+, 139.8±0.2 mmoles/l; plasma osmolality, 280±1 mosmole/kg) there was a small, statistically significant negative arterio-cerebral venous concentration difference for K^+ (−0.01±0.00 mmoles/l; $p < 0.001$). During hyposmolar hyponatraemia (arterial plasma Na^+, 117.1±0.5 mmoles/l; plasma osmolality, 232±1 mosmole/kg) there was a significant fall in cerebral blood flow ($p < 0.01$) and the arterio-cerebral venous concentration difference for K^+ increased to −0.04±0.00 mmoles/l ($p < 0.001$). The calculated net transfer of K^+ to the circulation increased from −0.51±0.14 to −1.51±0.07 $\mu mole \cdot 100\ g^{-1} \cdot min^{-1}$ (table).

During normonatraemia the electrolyte concentrations and osmolality of cisterna magna CSF were: Na^+, 146.3±1.1 mmoles/l; K^+, 2.9±0.04 mmoles/l; osmolality, 287 mosmole/kg. CSF was obtained during hyponatraemia in 5 experiments, and the corresponding values were: Na^+, 126.1±1.2 mmoles/l; K^+, 2.88±0.16 mmoles/l; and osmolality, 245±3 mosmole/kg. No changes were apparent in the EEG.

This experimental approach allows measurement of net transfer of K^+ to the circulation, only from that portion of brain which contributes venous blood to the sagittal sinus. It does not of course provide a measure of overall net cation exchange between the brain-CSF compartment and blood, which must be zero under normal conditions. The net efflux of K^+ observed during normonatraemia is consistent with the suggestion that the fall in CSF K^+ concentration which occurs in its passage from cisterna magna to cortical subarachnoid space[6] results from a continuous net efflux of K^+ from brain extracellular fluid to blood[7].

These results show that net transfer of K^+ to the circulation from brain tissue drained by the sagittal sinus increases during hyposmolar hyponatraemia. If influx of K^+ to the brain-CSF compartment (for example at the choroid-plexus) does not increase by a comparable amount, an overall net loss of K^+ to the circulation must ensue. No change in the measured rate of K^+ efflux was apparent over the time period examined. If this rate was sustained for 24 h, the calculated resulting reduction in brain tissue K^+ content (about 20%) is closely comparable to that which has been observed[8,9]. The fall in cerebral blood flow observed during hyposmolar hyponatraemia can probably be ascribed to the associated fall in perivascular osmolality[10]. No significant change occurred in any of the many other physiological variables which can alter cerebral blood flow (table).

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2 Present address: Westminster Hospital Medical School, 17 Horseferry Road, London SW1.

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