INTESTINAL RECYCLING AND SUBSTITUTION OF HAEMOFILTRATE IN DOGS

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Summary

Haemofiltrate was administered into the duodenum of 5 ambulatory dogs through an implanted silastic catheter at a rate of 5–10ml/min. None of the dogs presented signs of discomfort or suffered from regurgitation or diarrhoea. All 5 dogs had solid stools, enhanced diuresis and no change in body weight over a time period of 8 hours.

Filtration rates between 5 and 10ml/min were obtained in 7 dogs after connecting an Amicon in-line Ultrafilter with an external a.v. shunt. The intestinal recycling rate via the duodenal tube as a rule was 2ml/min lower than the free flow ultrafiltration. Recirculation of autologous haemofiltrate in 5 uraemic dogs indicated unselective reabsorption of all electrolytes and small molecules. In 5 experiments with intestinal substitution of ultrafiltrate by a potassium-free Ringer's lactate solution, correction of acidosis and decrease in plasma potassium, creatinine and BUN was achieved.

Objectives and Aims

The investigation of intestinal recycling and substitution of haemofiltrate aims at further development in the field of haemofiltration. The overall objective is the development of a wearable filtration artificial kidney (W·FAK) without pumps, operated solely by the arteriovenous pressure gradient. Ultrafiltrate is obtained continuously as in the natural kidney, and the small intestine is used as a renal tubule for absorption of the substitution fluid or a processed haemofiltrate. The anticipated advantages of this method are:
a) administration of non-sterile (inexpensive) fluid
b) pumps for operation are not needed
c) detoxification and fluid balancing are performed continuously.

The details of the experimental device we are working on are demonstrated in Figure 1.

We are not yet in the position to present longterm survival data of uraemic dogs with the W·FAK, but based on short-term experiments we are able to
answer some important questions about this project.

**Methods and Results**

*Intestinal Administration of Human Haemofiltrate*

The first question which had to be answered in this project was whether haemofiltrate may be administered into the intestine of dogs at a sufficiently high rate without causing discomfort, intestinal sequestration of fluid, regurgitation of fluid or diarrhoea. In order to answer this question for ambulatory dogs, it was necessary to implant a catheter, the end of which terminates in the small intestine. After evaluation of various methods we decided on the following: a silastic tube is introduced into the stomach through a small incision in the anterior gastric wall and advanced through the pylorus into the duodenum. The tube is conducted through an intercostal space and then subcutaneously to the posterior neck region of the dog, where it perforates the skin. Infection was prevented by the use of ‘skin buttons’ which are short silastic tubes with sealed endings, one of which perforates the skin [1]. The buttons are fixed subcutaneously by means of a dacron-velour collar and are implanted 10 days prior to implantation of the duodenal catheter. After the ‘skin buttons’ have healed completely without infection, the subcutaneous and the external endings are cut off and the silastic tube is conducted through the button and sealed in with sterile silicone rubber. With these skin buttons we have been able to keep the silastic catheters free of
infection for as long as 2 months. With the first successfully implanted catheters we have administered human haemofiltrate at a rate of 5 to 10ml/min over 8 hours while walking with the dogs through the woods, and carrying the haemofiltrate in a backpack. None of the dogs presented signs of discomfort or suffered from regurgitation or diarrhoea. All 5 dogs had solid stool, enhanced diuresis and no change in body weight.

*Arterio-venous Haemofiltration* [2]

The next question to be answered was whether the filtration rate and filtration pressure obtained with arterio-venous haemofiltration are high enough to maintain an intestinal recycling rate of more than 0.1ml/hr/kg. As shown in Figure 2, filtration rates between 5 and 10ml/min were obtained in 7 dogs one hour after connecting an Amicon In-Line- Ultrafilter with the external shunt. The maximum filtration pressure depended mainly on the venous flow-back pressure, but it had very little influence on the ultrafiltrate recycling rate. As a rule the intestinal recycling rate was 2ml/min lower (3—7ml/min) than the free-flow ultrafiltration rate (5—10ml/min). These results indicate that arteriovenous haemofiltration may be a useful method for low-rate and longterm recycling of autologous haemofiltrate.

**Figure 2.** Blood flow rate, arterial pressure, maximum filtration pressure, filtration and recycling rate and venous backflow pressure under free-flow conditions in 7 dogs one hour after connection of an Amicon In-line Ultrafilter with the external shunt.
**Intestinal Recycling and Substitution of Autologous Haemofiltrate in Uraemic Dogs**

The third question to be answered was whether absorption of electrolytes and other substances of low molecular weight, which are contained in the haemofiltrate or in the substitution fluid, is selective or total and unselective. In dogs rendered uraemic by transarterial embolisation of the renal arteries, recirculation and substitution of haemofiltrate via the intestinal tube did not cause haemoconcentration, as indicated by the haematocrit and total protein concentration, which decreased rather than increased as a result of blood sampling. As demonstrated in Figure 3, plasma concentrations of BUN, creatinine, and potassium showed an increase in 5 dogs with recirculation of haemofiltrate, but a decrease of these parameters in 5 dogs with intestinal substitution of the haemofiltrate. (Composition of the substitution fluid: Na+ 142mEq/l, Cl− 103mEq/l, Ca++ 4mEq/l, Mg+ 1.5mEq/l, lactate− 44.5mEq/l, HCO₃− 6.5mEq/l and glucose 265mEq/l). Thereby the correction of azotaemia was dependent on the recycling rate, the initial values and whether steady-state uraemia had been obtained before onset of intestinal substitution. The effect of intestinal haemofiltrate substitution is convincingly demonstrated (Figure 4) by the change of

![Image](https://via.placeholder.com/150)

**Figure 3.** Change of plasma concentration of various parameters in uraemic dogs by recirculation and substitution of haemofiltrate, expressed in per cent of the initial value.
Figure 4. The effect of intestinal haemofiltrate substitution on haemodynamic and plasma parameters

plasma parameters observed in the dog with the highest substitution rate. A total fluid substitution of 11.1 L during 19 hours in the 26 kg dog resulted in a complete correction of acidosis, decrease of urea, creatinine and potassium concentrations by more than 60%. Only phosphate concentration increased, which was also seen in the other 4 dogs.
Conclusions

1. Intestinal capacity for absorption of haemofiltrate in dogs is 10ml/min.
2. Gastrointestinal recycling or substitution of haemofiltrate has to take place beyond the pylorus.
3. Long-term arterio-venous haemofiltration seems practicable.
4. All electrolytes, particularly Cl⁻ and HCO₃⁻ and small molecules are reabsorbed unselectively by the small intestine if administered into the duodenum.
5. Intestinal substitution of ultrafiltrate by a none-sterile Ringer's lactate solution for compensating uraemia seems to be more simple, more effective and less costly than processing and recycling of haemofiltrate.

Future Clinical Application of Intestinal Substitution

3. Arterio-venous haemofiltration with intestinal substitution via an implanted intestinal tube during sleep, in patients with chronic renal failure.

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References

1. Reinhardt, WU Personal communication

Open Discussion

FUNCK—BRENTANO (Paris) You have shown us the dog who was uraemic and treated in this way. How uraemic was he and how long did the treatment last in this particular dog?

KRAMER We are not yet in the position to show you long-term survival in these dogs.

FUNCK—BRENTANO Just in terms of hours.

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KRAMER In these dogs in which we do the first embolisation of the renal arteries the creatinine goes up 5–8mg%. And then we do a second embolisation. And this makes the dogs anuric. So with the first embolisation they get a steady state uraemia; after the second embolisation they will die.

We have not tried a long term survival with this method yet.

DRUKKER (Amsterdam) The results are significant in lowering of creatinine and urea, but how long was the treatment? Something like 19 hours? The efficiency is much less than, let us say, in ordinary haemofiltration with replacement intravenously. Is that true?

KRAMER Yes, that is true. I think that we have to think from another perspective with low rate haemofiltration and substitution. This gives a decrease of creatinine and other uraemic substances comparable to a glomerular filtration rate of, in this case, 10ml/min. That is a slow decrease and this makes it difficult to prove that it is effective.