Serotonin analyses. Tissues analyzed were stomach fundus (SF), pyloric antrum (PA) and mid-jejunum (MJ). These were prepared as described previously[13] and serotonin assayed spectrophoto-fluorometrically[14]. Data in μg/g mucosa, wet weight, are presented as mean values ± S.E.M. Student's *t*-test was used to determine differences between groups.

Results. Serotonin was reduced approximately 50% in SF and MJ, and about 70% in PA following PCPA; no additional changes, however, were noticed after PGE_1 injection (Table I). In reserpinized rats no significant changes in total mucosal serotonin were noted following PGE_1 injected subcutaneously (Table II) or i.v. (Table III); reserpine reduced MJ serotonin stores about 20% (Tables II and III).

Discussion. The data presented confirm that PGE_1 apparently has no major releasing action on gastrointestinal serotonin. KOE[7] has indicated that PCPA reduces conversion of tryptophan to serotonin by inhibiting the activity of tryptophan hydroxylase, the rate limiting enzyme. The precise mode of action of reserpine is unknown, but it probably acts mainly by blocking amine re-uptake[15]. One might expect, therefore, that serotonin release, for example by PG, would be detectable in animals adequately pretreated with either PCPA or reserpine. Such was not the case, and data obtained following PG administration gave similar results when compared to control rats.

Gastrointestinal serotonin is mainly present in enterochromaffin cells[16] and enterochromaffin-like cells[17] with small quantities located in the myenteric plexus[18]. The cell of PG origin is not known but prostaglandins are liberated from the stomach and intestine[19–21] and recently they have been isolated from amine-peptide secreting tumours of the gut in man[22].

The close similarity between the actions of serotonin and prostaglandins may thus relate either to the liberation of undetectable quantities of serotonin by prostaglandins; the release of some third substance, for example a polypeptide, or the release or activation of prostaglandins by serotonin. This latter seems most likely since PG have been shown to interfere with the formation of cyclic AMP[23–25] and be intermediates in the action of hormones in a variety of tissues[26, 27].

Zusammenfassung. Bei Ratten wurde die Gesamtmenge von Serotonin in der Fundus- und Atriumschleimhaut sowie im mittleren Jejunum bestimmt. Prostaglandin E_1 (200 μg/kg, s.c. oder i.v.) reduzierte den Serotoninspiegel weder in den Kontrolltieren noch in mit *p*-Chlorophenylalanin (150 oder 300 mg/kg) oder mit Reserpin (5 mg/kg) vorbehandelten Tieren.

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Intrarenal Circulation in Mercuric Chloride-Induced Renal Failure

Intravenous or oral administration of suitable mercuric chloride doses brings about death due to acute anuria and consecutive uraemia. Because of the oligo-anuria the various parameters of renal function such as renal blood flow (RBF) etc. cannot be determined by the usual clearance technique. By applying some direct method RBF was found to be only slightly diminished, in moderate cases even renal hyperaemia could be observed (EPPINGER et al.[1], CONN et al.[2], BÁLINT[3]). SAPIRSTEIN's method[4] of ^{86}Rb fractionation (as modified by HÁRSING and PELLEY[5]) is suitable for the investigation of the intrarenal distribution of blood flow. In this study we aimed at the evaluation of total renal blood flow (RBF_{total}) by measuring directly the renal venous effluent and at the assessment of its intrarenal distribution by applying SAPIRSTEIN's method in mercuric chloride-induced renal failure.

The further aim of this study was to clarify the possible existence and role of renal vascular shunts in sublimate intoxication. According to the SAPIRSTEIN principle (based on fractional distribution of ^{86}Rb) only the blood flowing through capillaries (so-called nutrient flow: RBF_{nutr}) is to be determined. If the differences between simultaneously determined total and nutrient flow values

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were significant, we should be forced to the conclusion that part of the blood is flowing through bypasses avoiding the peritubular capillaries ($RBF_{non\text{-}nutr}$).

Our observations were made on mongrel dogs of either sex. 2 mg/kg of mercuric chloride dissolved in 20 ml saline were administered i.v. The acute experiment was made on the third day following the injection. Details of the surgical and experimental techniques are published elsewhere[6]. The main points are as follows.

The left kidney was approached by laparatomy and the left renal vein was connected by means of a plastic catheter to the external jugular vein. A T-extension of the tube made the direct measurement of total RBF possible. A suitable dose of ^{86}Rb was rapidly injected i.v. Cardiac output and nutrient blood flow of the whole kidney (RBF_{nutr}) and of the cortex (RBF_{cort}), outer medulla ($RBF_{o.m.}$) and inner medulla ($RBF_{i.m.}$) were assessed by considering the ^{86}Rb activities of the blood and kidney tissue, respectively. Nutrient flow values are calculated for 100 g of the respective tissues. The nutrient flows for 100 g kidney are calculated under the assumption that cortex, outer medulla and inner medulla weigh 70 g, 20 g and 10 g, respectively, in 100 g kidney. Our findings that $RBF_{cort} + RBF_{o.m.} + RBF_{i.m.} \approx RBF_{nutr}$ prove that our assumptions concerning the relative weight of the various zones are essentially correct. The difference RBF_{total}-RBF_{nutr} is called non-nutrient flow and is supposed to bypass the peritubular capillaries.

i.e. the fraction bypassing the capillaries. Nutrient flows through the various parts of the kidney are identical in the control and moderate series.

In the severe group RBF_{total} averages the same value as in the control set of experiments. Nutrient flow, however, drops to very low values, i.e. about $^2/_3$ of the total blood flow bypass the capillaries. The decrease of nutrient flows in the various kidney zones is nearly proportional.

It is assumed that the microcirculation of the kidney includes an arteriovenous capillary the proximal contractile portion of which is called metarteriole. The true capillaries which provide the tubular cells with blood branch off the metarterioles; the term precapillary sphincter designates the muscular investment at the origin of the outflowing branches. The number and patency of the true capillaries is regulated by the tone of the precapillary sphincters as described by ZWEIFACH[7]. In the normal kidney, the arteriovenous capillaries are contracted and the precapillary sphincters are relaxed.

After mercuric chloride administration, muscular elements of the arteriovenous capillaries relax (toxic effect?) and non-nutrient flow increases. In moderate cases the precapillary sphincter tone remains unaltered and the true capillaries are normally perfused. In severe cases a significant number of true capillaries is bypassed and postglomerular circulation is maintained chiefly through the arteriovenous capillaries. It should be stressed that, in lack of direct morphological evidence, our view concerning renal vascular structure is entirely hypothetical.

Intrarenal distribution of blood flow $\bar{x} \pm s_{\bar{x}}$

	Control conditions ml/min per 100 g kidney $n = 12$	ml/min per 100 ml RBF_{total}	Moderate failure ml/min per 100 g kidney $n = 9$	ml/min per 100 ml RBF_{total}	Severe failure ml/min per 100 g kidney $n = 9$	ml/min per 100 ml RBF_{total}
Arterial pressure mm Hg	133 ± 4	–	122 ± 6	–	119 ± 5	
RBF_{total}	421 ± 37	100.0	736 ± 75	100.0	447 ± 58	100.0
RBF_{nutr}	*400 ± 34*	*95.0*	*469 ± 54*	*63.7*	*153 ± 21*	*34.2*
RBF_{cort}	338 ± 29	80.3	406 ± 47	55.2	125 ± 19	27.9
$RBF_{o.m.}$	56 ± 8	13.3	56 ± 4	7.6	21 ± 4	4.7
$RBF_{i.m.}$	8 ± 1	1.9	11 ± 1	1.5	6 ± 1	1.3
$RBF_{non\text{-}nutr}$	*21 ± 18*	*5.0*	*264 ± 53*	*35.8*	*289 ± 66*	*64.6*
	423	100.5	737	100.1	441	98.5

The intrarenal distribution of blood flow in control conditions is shown in the left columns of the Table. The difference between RBF_{total} and RBF_{nutr} is *not* significant, i.e. practically the whole blood of the normal kidney flows through the capillaries.

It was found in previous experiments (BÁLINT[3]) on dogs in mercuric chloride-induced renal failure that, if on the third day after the sublimate administration, NPN exceeds about 150 mg/100 ml the animals die with uraemia; if, on the other hand, NPN remains below about 150 mg/100 ml they usually survive. Thus our experiments were divided into moderate (NPN below 150 mg/100 ml) and severe (NPN over 150 mg/100 ml) groups.

As shown in the Table, RBF_{total} of the moderate group highly exceeds that of the control series. Nutrient flows, however, do not differ significantly, thus 'hyperaemia' is entirely due to an increase of $RBF_{non\text{-}nutr}$,

Zusammenfassung. Durch simultane Ermittlung der totalen und der nutritiven Nierendurchblutung wurde festgestellt, dass 1. in der normalen Hundeniere die gesamte Durchblutung durch die Kapillaren strömt; 2. 3 Tage nach i.v. Verabreichung von 2 mg/kg Sublimat etwa $^1/_3$–$^2/_3$ der totalen Durchblutung durch arteriovenöse Anastomosen geleitet werden und 3. die kapillare Durchblutung umso mehr abnimmt, je schwerer die Symptome der Sublimatvergiftung sind.

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