	Number	Body weight (g)	Dose remaining 6 h following intragastric administration (%) Stomach	Small intestine	Cecum and colon	Absorption[b] (%)
Germfree	8	218.0 ± 16.0[a]	11.3 ± 4.9[a]	6.0 ± 1.5[a]	17.7 ± 4.6[a]	74.3 ± 4.6[a]
Conventionalized	8	222.1 ± 19.4	3.8 ± 1.8	6.0 ± 1.3	5.7 ± 2.0	87.8 ± 2.5
P value[c]			$<0.2->0.1$	>0.9	<0.025	<0.025

[a] Mean ± S.E. of mean. [b] Corrections were made for differences in gastric emptying by considering only the amount of D-xylose which actually left the stomach was available for absorption[9]. [c] Student's *t*-test.

and BISHOP[11] have shown that the time necessary for intestinal transit is acutally longer in germfree mice, and a similar observation has been made in germfree rats[6]. Degradation of D-xylose by intestinal bacteria is negligible under the condition of our studies[12,13] and could not have been responsible for the differences observed. We believe that the differences in D-xylose absorption are most likely related to differences in mucosal absorption per se. This interpretation suggests a functional correlation with previously reported morphologic studies in which germfree rats were shown to have significantly less mucosal surface area than conventional controls[1].

Résumé. Les observations faites sur les rats gnotobiotiques et les rats normaux montrent que l'absorption de D-xylose est beaucoup plus elevée chez les rats normaux que chez les rats gnotobiotiques. Cette différence est attribuée au changement de transport muqueux produit par la présence de microrganismes intestinaux.

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Kallikrein-Like Activity in the Urine of Renal Hypertensive Rats

Since evidence has been given that kinins produce changes in the renal blood flow and sodium excretion[1-3], it was considered of interest to study the enzymatic systems which might be involved in the production or in the release of kinins in the kidneys. This communication describes the results obtained in measurements of the kallikrein-like activity (KA) found in the urine of rats in which different reductions in renal functional mass were produced. Interest was focused on groups of rats which after manipulation of the kidneys developed renal hypertension. The study was undertaken in 114 Wistar and 30 Sprague Dawley male rats distributed in different groups: a) 42 normal; b) 35 uninephrectomized; c) 17 figure-of-8-ligature in one kidney; d) 50 uninephrectomized and with figure-of-8-ligature in the remnant kidney. In the latter group the operation was carried out according to the GROLLMAN[4] procedure to induce the development of renal hypertension. Blood pressure was measured in the rat tail at weekly intervals beginning 10 days after kidney removal. The microphone technique described by FRIEDMAN and FREED[5] was used. During blood pressure determinations the animals were kept quiet with light ether anesthesia. Every week or fortnight, the urine was collected by placing the animals in metabolic cages in the morning for 3–9 h. No food was given but they had free access to drinking water during the collection period. In many experiments only the freshly voided urine was used for testing, but in some of the cases the urine was collected for several hours in order to carry out purification procedures. Toluene, as antiseptic, was added (2%) when the collection period lasted more than 4 h. Each sample of urine was measured, centrifuged and kept frozen in the refrigerator when not immediately assayed.

The KA was tested either in dialyzed or non-dialyzed urine using 2 bioassays: the contraction of an isolated rat uterus and the depressor effect on the blood pressure of an anesthetized rat. According to BERALDO et al.[6] and CROXATTO et al.[7] urinary kallikrein induces a direct oxytocic effect upon isolated rat uterus and its effect is dose dependant. This effect is inhibited by Trasylol (Bayer) and carboxypeptidase B. The urine keeps its kallikrein activity after prolonged dialysis against distilled water in the cold room. The responsible substance releases kinins very rapidly in the presence of kininogen. A standard bradykinin solution was used to quantificate the urine effect upon the isolated rat uterus and blood pressure. The KA was expressed in ng of bradykinin which produces equivalent oxytocic effect induced by 1 ml of urine. No significant differences were found between a dialyzed or non-dialyzed fraction of the same urine sample.

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Kallikrein like activity in 1 ml of urine expressed in ng bradykinin oxytocic equivalent effect

No. of experiment	Days after operation	Strain	Group of rats							
			Normal		Uninephrectomized		Fig of 8 in one kidney		Fig of 8 uninephrectomized hypertensive	
										Blood pressure
I	48	Wistar	745 ± 113	(4)	300 ± 48	(4)	280 ± 83	(4)	40 ± 10	(5) 158
II	90	Wistar	950 ± 103	(4)			480 ± 112	(11)	27 ± 14	(6) 165
III	101	Wistar	520 ± 82	(8)	355 ± 70	(6)	370 ± 92	(8)	30 ± 12	(6) 155
IV	70	Sprague Dawley	450 ± 72	(10)	310 ± 88	(6)			< 10	(8) 192 ± 18
	75	Sprague Dawley			285 ± 81	(4)			< 10	(9) 188 ± 15.5
	84	Sprague Dawley			200 ± 53	(9)			< 10	(10) 188 ± 15.5
	108	Sprague Dawley	420 ± 83	(10)	270 ± 78	(9)			< 10	(8) 190 ± 15

Mean values and S.D. of the KA found in 1 ml of urine, expressed in ng of bradykinin. Figures in parenthesis correspond to the number of animals used in each group. Different series of animals were used for the experiments I, II and III. The figures for the KA were obtained in a single experiment carried out after the kidney removal, on the day shown in the second column. The experiment IV correspond to one serie of Sprague-Dawley rats, studied at different intervals (days) after the kidney extirpation.

The results shown in the Table provide the mean value and standard deviation of the KA per ml of urine of the different groups of animals. In the normal Wistar and Sprague-Dawley rats, the average of the KA was equivalent to 725 ng and 435 ng of bradykinin respectively. The reduction of the renal tissue or a figure-in-8-ligature in one kidney induce a decrease in the KA shortly after the operation. After one kidney removal KA diminishes by 65% (Wistar) and 45% (Sprague Dawley). The group c) of animals which had figure-of-8-ligature in one kidney but the other one was left untouched, showed similar diminution to that found in the uninephrectomized (350 ng). All the animals of the groups a), b) and c) exhibited normal blood pressure through the experimental period. The group d) of uninephrectomized rats with a figure-of-8-ligature in the remnant kidney which developed high levels of arterial blood pressure, showed an invariably striking fall in the KA which persisted until death ensued. The lowest KA, less than 50 to 10 ng bradykinin per ml, was found in those rats whose arterial blood pressure was constantly high, 155 Hg or higher (Table). The rats of this group which did not develop hypertension, had in their urine a significantly higher titer of KA as compared to the hypertensive ones. A few animals of group d) whose blood pressure remained stabilized at normal level had KA similar or somewhat less than that found in the uninephrectomized rat. When the animal showed a moderate or fluctuating blood pressure, the KA changed from one week to the other. In general, rats with moderate hypertension exhibited KA which was 20–30% below that found in the uninephrectomized but much above the low values constantly recorded in the severe hypertensive rats. In rats with a transient elevation in the blood pressure, low KA was found during the hypertension period, whereas it increased very much, approaching the levels found in uninephrectomized rats, as soon as the blood pressure was spontaneously restored to normal.

The data support the concept that in general there is an inverse correlation between the blood pressure and the KA in the urine. The same differences in the KA found in the freshly voided urine of the different groups of rats were confirmed on testing the purified materials obtained from the corresponding pooled urine. On the other hand, parallel results using the blood pressure assay were gained either with urine or purified fractions. In order to purify the active substance, further dialysis, acetone precipitation, gel filtration on Sephadex G 100 and Sephadex G 200 were used.

Although the experiments do not provide evidence that KA in the urine is involved in the mechanism of renal hypertension, it is of paramount importance that this activity is inversely correlated with arterial blood pressure. It is possible to assume that KA in the urine reflects the kidney impairment which leads to the renal hypertension development.

Résumé. La ligature «en figure huit» d'un rein suivie de l'ablation de l'organ contrelatéral, est accompagnée d'une remarquable amoindrissement de l'activité kallikreine urinaire pourvu que les animaux développent une pression artérielle permanente et élevée.

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Action de différents mélanges gazeux sur l'artère mésentérique de l'embryon de poulet explantée in vitro[1]

Au cours d'expériences précédentes nous avions cultivé l'artère mésentérique d'embryon de poulet avec la méthode de culture organo-typique selon Wolff et Haffen[2–4]. Avec cette méthode les explants manifestaient, déjà après 1 jour de culture, des signes manifestes de souffrance: dégénérescence lipidique, dédifférentiation de la musculature, fibrose de la paroi. Nous avons pensé qu'à l'origine de ces phénomènes il pouvait y avoir un apport inadéquat d'oxygène, empêchant une bonne survie de la paroi artérielle.