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DIFFERENCES IN RENAL CLEARANCES MEASURED IN DANISH PIGS

by

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Previously published reports of the examination of renal clearances in Danish Landrace pigs have given somewhat divergent results. *Dalgaard-Mikkelsen et al.* (1953) found the clearance of inulin to be 36.5 ml/min./10 kg, whilst *Lassen & Nielsen* (1963) determined the clearances of inulin and PAH to be 41 ± 18 and 126 ± 28 ml/min./10 kg, respectively. *Nielsen* (1968) reported the clearances of inulin to be 35.7 ± 11.6, endogenous creatinine 36.3 ± 13.2, and PAH 121 ± 24 ml/min./10 kg. The values found by *Gyrd-Hansen* (1968) for clearances of inulin, endogenous creatinine, urea and PAH were 21 (18—25), 22 (15—34), 12 (9—18) and 64 (52—84) ml/min./10 kg, respectively. However, the experimental conditions under which these clearance determinations were carried out were not identical. *Dalgaard-Mikkelsen et al.* used the subcutaneous injection method on pigs sedated with urethane, while in the other works the continuous infusion method was employed on pigs anaesthetized with pentobarbitone (mebumalum NFN) (*Lassen & Nielsen; Nielsen*) or on unanaesthetized pigs (*Gyrd-Hansen* 1968). Another possible reason for the divergencies between the clearance values found might be different intensity of feeding with its consequent effect on growth rate and perhaps the relative kidney weight. There was also the possibility that different strains of pigs might have varying renal clearances, since the pigs used by *Gyrd-Hansen* (1968) originated from one farm (A), while all the three other examinations were carried out on pigs from another farm (B). It was the aim of this study to elucidate whether any of these factors might influence renal clearances.

MATERIAL AND METHODS

Fifteen female pigs of the Danish Landrace breed were studied, 10 of these being from farm A and five from farm B. The pigs, which weighed from 17 to 80 kg, were fed as described by *Gyrd-Hansen* (1969) and had free access to water.

Fifteen experiments were carried out on six pigs to investigate the effect of urethane and pentobarbitone on the clearance of inulin, endogenous creatinine, urea and PAH. The animals were starved for 12 hrs. before the experiments. The experiments commenced with three periods of 20 min. without anaesthesia, after which the animals were given either urethane (eight experiments) or pentobarbitone (seven experiments), followed 30 min. later by three clearance periods of 20 min. In the experiments with urethane, 250 mg/kg was administered by stomach tube. In the pentobarbitone experiments 30 mg/kg was injected intraperitoneally initially, supplemented by 2—3 mg/kg given intravenously repeatedly during the experiment. The clearance technique used was as described by *Gyrd-Hansen* (1968).

In order to compare the clearances determined by the subcutaneous injection method and the continuous infusion method, eight experiments were carried out on four pigs. The experiments with continuous infusion (3 ml 0.6 % sodium chloride per min.) were performed as described previously (*Gyrd-Hansen* 1968). The method used in the experiments with subcutaneous injection was that of *Ramsay & Coxon* (1967), except that 4.8 g PAH per 100 ml solution was employed.

The effect of feeding intensity on the renal clearances of the pigs was examined in 16 experiments on six pigs. Two animals were used for determining the renal clearances after they had been given 50 % of the normal ration for one and two months, respectively (*Gyrd-Hansen* 1969). The renal clearance of four pigs was determined while they were given a normal ration, after which the ration administered to two of the pigs was reduced by half, while the other two remained on the normal ration. Renal clearances were determined on all four pigs one and two months after the two of them had been put on half ration. At the end of the experiments the pigs were killed and the kidneys weighed.

The five pigs from farm B were fed according to the normal schedule (*Gyrd-Hansen* 1969) for at least a week before the first experiment. The investigation included determination of the clearance of inulin, endogenous creatinine, urea and PAH. At the

end of the experimental period, the pigs were killed and the kidneys weighed.

The analytical methods used were: Inulin (*Brun* 1946), creatinine (*Bonsnes & Taussky* 1945), urea (*Conway* 1950), PAH (*Bratton & Marshall* 1939).

RESULTS

Renal clearances in conscious, sedated and anaesthetized pigs

The doses of urethane and pentobarbitone used produced deep sedation and surgical anaesthesia, respectively. The results of the experiments are given in Tables 1 and 2. These show that

Table 1. Renal clearances in pigs in conscious and urethane-sedated state.

Pig no.	Conscious periods				Urethane-sedated periods			
	inulin clearance ml/min./10 kg b.wt.	endogen. creatinine clearance ml/min./10 kg b.wt.	urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.	inulin clearance ml/min./10 kg b.wt.	endogen. creatinine clearance ml/min./10 kg b.wt.	urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.
6	24	23	26	100	23	23	29	88
7	21	22	18	84	25	26	21	97
8	18	21	22	63	18	22	18	74
9	18	17	11	58	19	17	11	66
9	22	22	12	65	19	19	13	62
10	20	22	13	76	20	22	14	80
11	21	19	16	71	22	18	15	71
11	17	20	20	62	14	15	12	47
average	20	21	17	73	20	20	17	73

Table 2. Renal clearances in pigs in conscious and pentobarbitone-anaesthetized state.

Pig no.	Conscious periods				Pentobarbitone-anaesthetized periods			
	inulin clearance ml/min./10 kg b.wt.	endogen. creatinine clearance ml/min./10 kg b.wt.	urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.	inulin clearance ml/min./10 kg b.wt.	endogen. creatinine clearance ml/min./10 kg b.wt.	urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.
6	29	27	17	67	32	29	24	68
7	25	25	21	94	29	28	23	92
8	23	17	11	54	23	20	11	51
8	21	19	14	68	27	27	21	78
9	27	20	14	72	28	21	15	67
10	23	20	18	74	25	21	15	71
11	28	21	18	68	26	21	19	56
average	25	21	16	71	27	24	18	69

Table 3. Renal clearances in pigs measured by the continuous infusion and by the subcutaneous injection method.

Pig no.	Continuous infusion method				Subcutaneous injection method			
	inulin clearance ml/min./10 kg b.wt.	endogen. creatinine clearance ml/min./10 kg b.wt.	urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.	inulin clearance ml/min./10 kg b.wt.	endogen. creatinine clearance ml/min./10 kg b.wt.	urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.
12	28	24	16	80	28	28	20	78
13	23	20	13	68	27	24	20	75
15	24	22	12	80	22	20	9	61
16	24	22	15	72	23	20	6	79
average	25	22	14	75	25	23	14	74

the clearance of inulin, endogenous creatinine, urea and PAH were not affected by urethane or pentobarbitone in the doses used.

Renal clearances measured by continuous infusion and subcutaneous injection methods. Table 3 shows that there is good correlation between the clearance values found by the two methods.

Influence of intensity of feeding on renal clearances. Table 4 shows the clearance of inulin, endogenous creatinine, urea and PAH of pigs fed normally and of pigs kept on half ration for one and two months. The Table also includes the average monthly increase in weight, together with the relative weight of the kidneys at death. It will be seen that neither the clearance of inulin, endogenous creatinine and PAH, nor the relative kidney weight were changed to any extent as the result of the reduced ration, but the clearance of urea seemed to be increased.

Renal clearances in two strains of pigs. The renal clearances and relative kidney weights of five pigs from farm B are shown in Table 5, together with the average clearance values for eight pigs from farm A and the clearance values for pigs from farm A found previously by *Gyrd-Hansen* (1968). It will be seen that the clearances of inulin, urea and PAH in four of the five pigs from farm B were considerably higher than the corresponding values for the pigs from farm A. However, the clearance of creatinine and the relative kidney weights of the pigs from farm B were of the same order of magnitude as found in the pigs from farm A.

Table 4. Average renal clearances in pigs under different intensities

Feeding intensity	Pig no.	Weight gain per month kg	Number of experiments	Urine flow ml/min.	Inulin clearance ml/min./10 kg b.wt.	Endogen. creatinine clearance ml/min./10 kg b.wt.	Urea clearance ml/min./1 kg b.wt
Normal	8, 9, 10, 11	18	8	0.7 (0.3—1.7)	22 (18—27)	19 (17—22)	14 (11—1
50 % of normal for 1 month	6, 7, 8, 11	7	4	3.7 (0.6—7.5)	24 (18—29)	23 (21—27)	19 (17—2
50 % of normal for 2 months	6, 7, 8, 11	5	4	3.9 (1.1—7.1)	22 (17—25)	22 (19—25)	20 (14—2

Table 5. Renal clearances in Danish Landrace pigs from two different farms.

Farm	Pig no.	Inulin clearance ml/min./10 kg b.wt.	Endogen. creatinine clearance ml/min./10 kg b.wt.	Urea clearance ml/min./10 kg b.wt.	PAH clearance ml/min./10 kg b.wt.	Relative kidney weight %
B	1	33	24	21	98	0.46
B	1	32	29	18	100	0.41
B	1	32	23	20	86	0.39
B	1	31	22	16	87	0.35
B	1	22	18	14	64	0.32
A	8	23(21—28)	20(17—24)	14(11—16)	71(54—80)	—
A	*)	21(18—25)	22(15—34)	12(9—18)	64(52—84)	0.36(0.31—0.43)

*) *Gyrd-Hansen* (1968)

DISCUSSION

The use of urethane and pentobarbitone for sedation purposes in experiments on pigs does not seem to affect the renal clearances (Tables 1 and 2). This is in agreement with the finding that anaesthesia with pentobarbitone in dogs has no influence on the glomerular filtration (*Glauser & Selkurt* 1952, *Corcoran & Page* 1943, *Gilmore & Michaelis* 1969), while the PAH clearance is unchanged (*Corcoran & Page*) or slightly decreased (*Glauser & Selkurt*). In contrast, when barbiturates or other anaesthetics are used in man, a considerable reduction takes place both in the glomerular filtration and in the renal blood flow (*Habif et al.* 1951; *Papper & Papper* 1964; *Deutsch et al.* 1967).

No change in the renal clearances could be demonstrated in pigs when using continuous infusion of 3 ml 0.6 % saline per min. (Table 3). In dogs *Dupré & Coxon* (1958) found that infusion of small amounts of physiological saline had no effect on renal clearance, while *Ramsay & Coxon* (1967) found that the infusion of 1.7 ml physiological saline per min. caused a 20—25 % increase in the clearance of inulin and PAH. However, a severe increase in the filtration clearance in pigs could be provoked by infusion of larger amounts of hypertonic (3—5 %) saline (*Nielsen* 1968).

A reduction in the feeding intensity, with consequent diminished growth rate, seemed to have only a slight effect on the renal clearances, even though the weight gain of the animals was

reduced to about 30 % of the normal (Table 4). The relative weight of the kidneys was not changed during the diminished growth of the pigs. The increase in urea clearance in the pigs on the low ration is probably due to the fact that these animals drank a great quantity of water and therefore had a high urine flow.

Comparison of the kidney function of pigs from two farms showed that the renal clearances of four of the five pigs from farm B were considerably higher than those of the pigs from farm A (Table 5). Furthermore, it will be seen that the inulin clearance of these four pigs is almost identical with what *Dalgaard-Mikkelsen et al.* in 1953 and *Nielsen* in 1968 found in pigs from the same farm. According to *Nielsen,* the very high clearance of inulin in *Lassen & Nielsen*'s study from 1963 is due to the infusion of larger amounts of 3 % saline.

A difference in the renal clearances of the two strains of pigs is probably the reason why *Dalgaard-Mikkelsen et al., Lassen & Nielsen,* and *Nielsen* found higher clearance values than *Gyrd-Hansen* (1968). There are apparently only rather small variations in the kidney function within the individual strains of pigs, but there seems to be considerable differences in the renal function of various strains within the Danish Landrace breed.

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SUMMARY

Measurements are reported of renal clearances of inulin, endogenous creatinine, urea and PAH in 15 pigs in order to elucidate (a) the effect of pentobarbitone and urethane on the renal clearances, (b) differences in clearances measured by continuous infusion and by subcutaneous injection, (c) the effect of the intensity of feeding on the renal clearances, and (d) the difference in the renal clearances between two strains of Danish Landrace pigs.

Sedation with pentobarbitone and urethane had no effect on the renal clearances of the pigs. Measurement of clearances by continuous infusion gave the same results as use of the subcutaneous injection method. Changes in the intensity of feeding and the consequent effect on growth had no influence on the renal clearances or on the relative kidney weight. Considerable differences were demonstrated in the renal function of pigs from two different strains of Danish Landrace pigs.

SAMMENDRAG

Forskelle i renale clearances målt på danske svin.

Der er udført renale clearance undersøgelser omfattende clearance for inulin, endogen kreatinin, urinstof og PAH på 15 svin til belysning af: a) mebumal og uretans indflydelse på de renale clearances, b) forskelle i clearances målt ved henholdsvis kontinuerlig infusion og ved subkutan injektion, c) fodringsintensitetens indflydelse på de renale clearances og d) forskellen i de renale clearances mellem to grisestammer indenfor Dansk Landrace.

Beroligelse med mebumal og uretan påvirkede ikke de renale clearances hos svin. Clearancemålinger udført med kontinuerlig infusion gav samme resultater som ved anvendelse af subkutan injektion. Ændret fodringsintensitet og dermed ændret tilvækst påvirkede hverken de renale clearances, eller den relative nyrevægt. Der påvistes betydelige forskelle i nyrefunktionen hos grise fra to forskellige grisestammer indenfor Dansk Landrace.

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