

4) Serum Sodium Chloride: In two of four cases belonging to the group to which 10 mg per kg NaF had been administered, a slight decrease of the serum NaCl was observed. In one of four cases of the 50 mg/kg group, however, the NaCl values were elevated.

The above results of urine and blood suggest that renal damage occurs in fluorosis.

Part II

INFLUENCE OF SODIUM FLUORIDE ON RENAL CLEARANCE IN RABBITS

by

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(Abstracted from *Shikoku Acta Medica* 8:273-282, 1956)

In previous papers the author reported disturbances of renal function, especially changes in the urine, serum NPN, serum creatinine and serum chlor-natrium of rabbits due to ingestion of fluoride. The current investigation deals with the effect of sodium fluoride on renal clearance, particularly on plasma urea clearance, on renal plasma flow (RPF) and glomerular filtration rate (GFR) in rabbits.

Method

1) Plasma urea clearance: Twelve healthy male rabbits weighing from 1800 to 3000 grams were given orally 10 mg, 30 mg and 50 mg per kilogram body weight of an aqueous solution of sodium fluoride daily for 2 weeks to 2 months. During the course of this experiment, plasma urea clearance was measured by the Van Slyke method at intervals of 7 to 10 days.

Urine was collected by catheter every half hour and blood samples were taken twice between the urine collections. Plasma and urinary urea concentrations were determined by the bi-acetylmonoxime method.

2) Renal Plasma Flow and Glomerular Filtration Rate: For this study 15 adult rabbits weighing from 2100 to 2600 grams received intravenous injections of 10 mg, 30 mg and 50 mg per kg of a 1% NaF isotonic saline solution. The glo-

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merular filtration rate was measured by exogenous creatinine clearance the the renal plasma flow by p-aminohippuric acid clearance (Table 1).

Urine collections varied from 15 to 30 minutes depending upon the urinary flow. The blood samples were taken from the jugular vein. Creatinine was determined by the Folin's method and p-aminohippuric acid by the technique of Smith et al.

Results

Plasma urea clearance was significantly below normal in nine of twelve animals; in one animal it was above normal and in two it was unchanged. The low values were most marked in the group which had received 50 mg per kg (Table 1).

TABLE 1

Plasma Urea Clearance: Continuous Oral Administration of
10 mg NaF per Kilo of Body Weight - Rabbit No. 25

Days	Body Weight (gr)	cc of Urine		Urea Concentration (cc/m)		Urea Clearance	
		per hour	per minute	Plasma	Urine	(cc/m)	(average) (cc/m)
Before	2340	20.4	0.34	17.2	157.0	3.10	3.18 ± 0.12
		18.2	0.303	18.0	194.5	3.27	
8	2320	31.5	0.525	22.9	131.2	3.14	3.51
		50.8	0.846	22.9	105.0	3.88	
14	2330	32.0	0.533	28.5	220.0	4.08	4.03
		31.5	0.525	29.7	225.0	3.98	
20	2180	22.5	0.375	28.3	273.7	3.62	3.56
		22.0	0.367	29.2	278.2	3.50	
31	2140	18.0	0.3	30.9	285.0	2.73	3.05
		27.2	0.453	30.0	236.2	3.37	
38	2060	18.0	0.3	22.0	230.6	3.14	3.52
		29.4	0.49	24.7	196.8	3.91	

The renal plasma flow increased in 1 of 4 animals which were given 10 mg NaF per kg. No decrease occurred in any of them. A marked reduction was observed however in all animals which had received 50 mg NaF/kg. In the 30 mg group no change was noted.

No significant changes in the glomerular filtration rate were observed in the 10 mg/kg group whereas in 3 out of 4 animals, which had received 30 mg/kg, a tendency to lower values was found.

In the 50 mg/kg group, all animals showed a marked decrease in the glomerular filtration rate. A slight increase in filtration fraction was noted in two of four animals which had received 10 mg/kg. There were no other significant changes in the other groups.

No consistent changes whatsoever in the percentage of renal tubular re-sorption were observed in any cases.

The authors concluded from the experimental data presented here that the administration of fluoride in the above doses impairs the kidney function.

Part III

MORPHOLOGICAL STUDIES ON THE CHANGES OF THE KIDNEY OF RABBITS AND GROWING ALBINO RATS DUE TO SODIUM FLUORIDE

by

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(Abstracted from *Shikoku Acta Medica*, 8:283-288, May 1956)

In previous papers (Part I and II), the author reported impairment of renal function in rabbits due to fluorosis. The current study presents morphological renal changes of rabbits and young albino rats due to fluorosis.

Method

1) After the experiments reported in the first and the second report, all rabbits were sacrificed and their kidneys examined.

2) Young albino rats 30 to 50 days after birth were fed with Scherman's standard ration mixed with sodium fluoride which contained 375, 100, 50, 10, 5 ppm of sodium fluoride respectively. The animals were killed at various periods extending from 16 to 234 days and their kidneys were compared with those of control littermates.

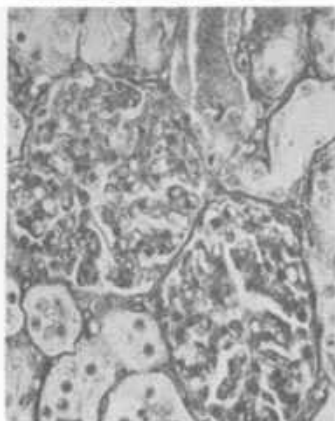
Results1. Changes in Rabbits

Macroscopic and histological changes of kidneys of RABBITS receiving NaF orally for 14 to 150 days (Fig. 1-3):

On gross examination, no marked changes were observed. However, in both groups which had been given 30 and 50 mg of NaF per kg of body weight, inflammatory changes in the glomeruli with increased cellularity, capillary hyperemia, exudation, hypertrophy or atrophy, tubular degeneration with cloudy swelling, vascular degeneration and protein casts or blood in the tubular lumens were seen microscopically.

Fig. 1

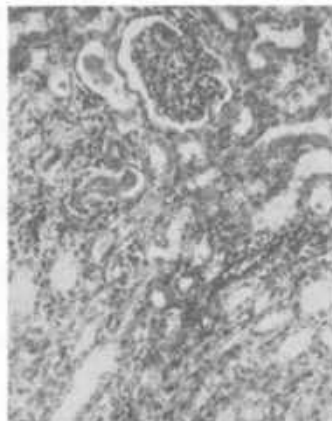
Rabbit No. 6 - Kidney (400x)
30 mg/kg NaF; 120 Days



Capillary hyperemia and hypertrophy of glomeruli, protein casts in tubules.

Fig. 2

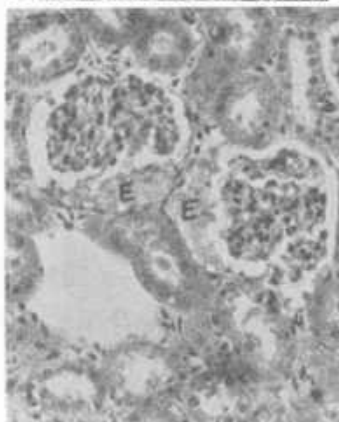
Rabbit No. 36 - Kidney (140x)
50 mg/kg NaF; 14 Days



Round cells infiltration in interstitium and protein casts in tubules.

Fig. 3

Rabbit No. 60 - Kidney (200x)
30 mg/kg NaF; Intravenously



Exudate (E) in glomeruli, cloudy swelling of tubules.

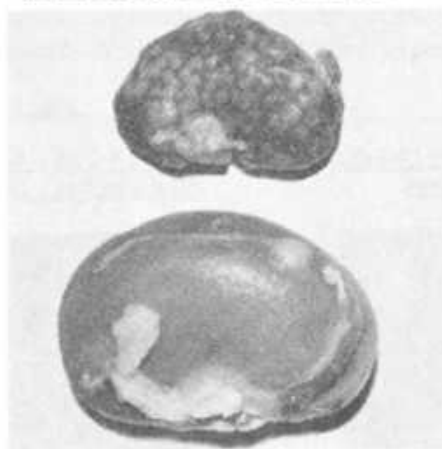
2. Changes in Rats

Similar histological changes occurred in animals which received intravenous injections of 30 and 50 mg/kg NaF.

In young albino RATS, the following morphological kidney changes occurred (Fig. 4-8):

Fig. 4

Albino Rat No. 33 - Kidney
375 mg/kg NaF; 234 Days



Granular irregularity of the surface and atrophy.
Lower: Normal control kidney

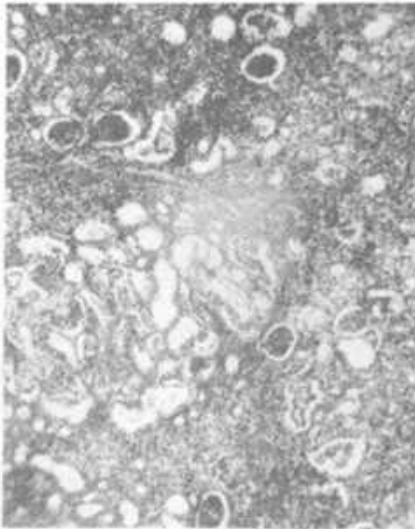
Marked nephrosclerosis and numerous granular irregularities of the kidney surface were observed macroscopically. In the group, which had received 375 ppm of fluoride, progressive fibrosis and round cell infiltration was detected in the interstitium.

Inflammatory changes in glomeruli and tubular degeneration were noticeable in the two groups which had received 100 ppm and 375 ppm.

The above-mentioned morphological changes, combined with impairment of renal function described in the previous reports, indicate that fluoride causes serious damage to kidneys.

Fig. 5

Albino Rat No. 33 - Kidney 375 ppm
NaF; 234 Days



Fibrosis and infiltration of round cells in the interstitium. Contraction and compensatory hypertrophy of the tubules.

Fig. 6

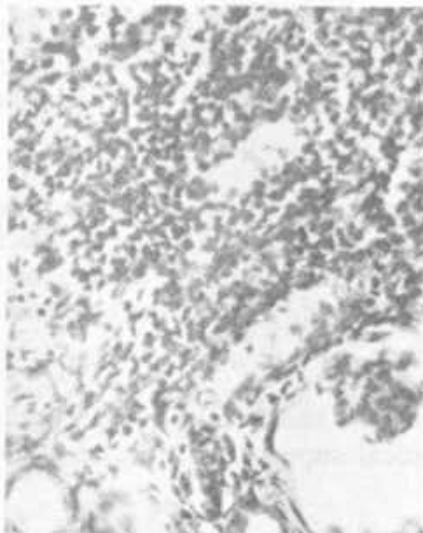
Albino Rat No. 33 - Kidney (400 x)
375 ppm NaF; 234 Days



Protein casts in the tubules(P).

Fig. 7

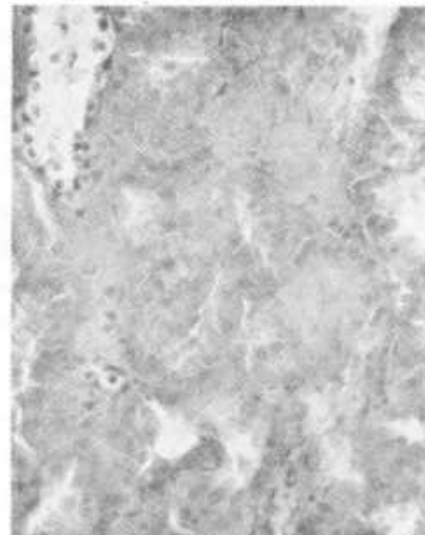
Albino Rat No. 34 - Kidney (280 x)
375 ppm NaF; 189 Days



Marked round cell infiltration in interstitium.

Fig. 8

Albino Rat No. 6 - Kidney (200 x)
10 ppm NaF; 120 Days



Severe cloudy swelling of tubules.