EFFECT OF FLUORINE ON THE NUTRITION OF SWINE, WITH SPECIAL REFERENCE TO BONE AND TOOTH COMPOSITION[1]

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INTRODUCTION

Numerous reports have appeared in the literature purporting to show the value of phosphoritic minerals as calcium and phosphorus supplements in animal nutrition. A great variance exists between the results obtained by different investigators. Forbes and others (*9*)[2] have inferred that the fluorine content of these naturally occurring products was the cause of the harmful and variable results obtained when these minerals were fed to livestock. Such an assumption seems to be fairly well grounded, since there is some correlation between the fluorine content of various grades of these minerals and the poor results obtained. However, the majority of the investigators have made no attempt to determine whether the feeding of fluorine salts would produce results comparable to those produced when the natural minerals were fed. In the present investigations a study was made of the comparative effects of flourine, in the forms of chemically pure sodium fluoride and the natural phosphate mineral, in the nutrition of swine, with special reference to the effect on bone and tooth composition.

REVIEW OF LITERATURE

Different investigators have shown that fluorine in one form or another may prove to be extremely toxic and very often fatal. Baldwin (*2*) and McNally (*24*) reported several cases of fluorine poisoning in man. Blaizot (*5*), Wieland and Kurtzahn (*39*) and Marcovitch (*25*) studied the lethal doses of different forms of fluorine for rabbits, while Heidenhain (*16*) reported on the lethal effects of sodium fluoride in dogs. Using sublethal doses of fluorine in different forms, Schulz and Lamb (*30*), Bergara (*3*), Sollmann, Schettler, and Wetzel (*32*), and McClure and Mitchell (*19*) observed an impairment of growth and feed consumption in rats.

The effects of fluorine on the various organs and tissues of the body have been studied by numerous investigators. Brandl and Tappeiner (*6*) could find no histological changes in the blood, liver, kidneys, or muscles of a dog fed varying amounts of sodium fluoride. The same investigators found no evidence of histological change in

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[2] Reference is made by number (italic) to Literature Cited, p. 1035.

the bones, but reported the presence of crystals—presumably calcium fluoride—in the Haversian canals and in the porous bone near the epiphysis of the long bones. Sollmann, Schettler, and Wetzel (*33*) reported that they were unable to find histological lesions in rats fed 8 mg of sodium fluoride per kilogram of body weight daily for 9 weeks. Pitotti (*27*) observed a degeneration of the epithelium of the kidneys and a cloudy swelling of the liver in rabbits and guinea pigs fed lethal doses of sodium fluoride. Siegfried (*31*) noted that sodium fluoride and sodium fluosilicate caused a destruction of the epithelium of the intestines, even though these salts had been introduced into the body through other channels. Weinland (*38*) reported that the mucous membrane from the throat of a frog was killed by a 2.1 per cent solution of sodium fluoride. Grützner (*13*) noted that nerves were equally sensitive. Maumene (*26*) and Goldemberg (*11*) each reported that the feeding of sodium fluoride caused an increase in the size of the thyroid glands of dogs and rats, whereas Chaneles (*7*), and Tolle and Maynard (*36*) were unable to verify these findings.

The specific effect of fluorine on the teeth of rats has been shown by Schulz and Lamb (*30*), McCollum, Simmonds, Becker, and Bunting (*21*), Bergara (*3*), and Tolle and Maynard (*36*). The incisors became soft, elongated, and lost their normal pigmentation. Taylor (*35*), Huffman and Reed (*17*), and Bohstedt and his coworkers, as reported by Christensen (*8*) also reported that the teeth of dairy cattle became soft and showed excessive wear when rock phosphate containing fluorine was fed. The latter investigators also reported similar teeth changes in brood sows fed rations containing fairly liberal amounts of rock phosphate. The effect of fluorine ingestion on human teeth has been reported by Smith, Lantz, and Smith (*32*). These investigators found that children who drank water containing large amounts of fluorine developed soft teeth with mottled enamel. Similar observations were made by the California State Department of Health (*1*). The only known reference to any change in the chemical composition of the teeth due to fluorine ingestion is that of Sonntag (*34*), who reported an increase in the fluorine content.

Attempts to study the effect of fluorine feeding on bone formation have for the major part dealt with the use of rock phosphate as a mineral supplement in animal nutrition. Hart and his associates (*15*) reported improved bone formation when floats (rock phosphate) were used to supplement low phosphorus rations for pigs. Forbes and his coworkers (*9*), on the contrary, found that the feeding of rock phosphate to pigs produced less dense and weaker bones than when no minerals, or minerals practically free from fluorine, were fed. The weaker bones were characterized by maximum magnesium and phosphorus content and minimum calcium and carbon dioxide percentages. Reed and Huffman (*28*) demonstrated that the feeding of rock phosphate resulted in a thickening of the jaw and the metatarsal bones of dairy cattle. McClure and Mitchell (*19*) observed an increase in the ash percentage of bones, accompanied by a slight decrease in the calcium content of the ash, in rats on high fluorine rations. Tolle and Maynard (*36*), on the contrary, reported a decrease in the percentage of bone ash in rats fed a ration containing 1.8 per cent rock phosphate. The last-named investigators also reported that phosphatic limestone, containing approximately 1 per cent fluorine, was equal to a mixture of limestone and steamed bone meal for growth and bone formation in the pig.

McClure and Mitchell (*20*) found that fluorine, in the form of rock phosphate or calcium fluoride, depressed calcium metabolism in the pig and that excessive fluorine intake also decreased growth and feed consumption.

That fluorine is a normal constituent of body tissues has been shown by Zdarek (*41*), Gautier (*10*), Wrampelmeyer (*40*), Jodlbauer (*18*), Harmes (*14*), Sonntag (*34*) and others. Sonntag (*34*) found that whereas normal teeth and bones of dogs contained not over 0.3 per cent fluorine, the bones of dogs fed sodium fluoride contained 1.73 per cent on the moisture-free and the fat-free basis, and the teeth 1.29 per cent on the dry basis.

EXPERIMENTAL PROCEDURE

Two separate experiments were carried out with growing pigs, housed indoors in concrete paved pens. Straw was used as bedding. At the termination of the experiment the animals were slaughtered and subjected to a routine post-mortem examination. The femurs and mandibles were removed for physical and chemical examinations. They were cleaned of adhering flesh and subjected to certain physical measurements, prior to the removal of the teeth for analytical purposes and the crushing and extraction of the femurs for chemical analysis. All the physical measurements and chemical determinations were made on the same femur from each animal in any particular experiment. The kidneys were fixed in 4 per cent formalin and subsequently examined histologically.

The maximum length and smallest diameter of the femurs were obtained by means of vernier micrometers. The volume of the femurs was determined by difference in the weights of the green, cleaned bone in air and when completely immersed in distilled water. Breaking strength determinations were made with an Olsen dynamometer. Calcium and magnesium were determined by McCrudden's (*22*, *23*) method, and phosphorus by the official gravimetric procedure. The carbon dioxide in the dry, fat-free bones was determined by the Van Slyke (*37*) method, and the volatilization method of Reynolds, Ross, and Jacobs (*29*) was used for the estimation on fluorine.

The same basal rations were used in the two experiments. Previous studies in this laboratory had shown that these rations were satisfactory for growing pigs when properly supplemented with calcium. The starting ration consisted of 55 parts yellow corn, 25 parts wheat middlings, 19 parts linseed meal, 0.5 part sodium chloride, and 0.5 part cod-liver oil. When the animals had attained a weight of approximately 125 pounds, the basal ration of all lots was changed at the same time to one consisting of 75 parts yellow corn, 14 parts wheat middlings, 10 parts linseed meal, 0.5 part sodium chloride, and 0.5 part cod-liver oil. The change in ration was made to widen the nutritive ratio, and conforms to good animal-husbandry procedure. The rations were hand-fed twice daily. The pigs were weighed individually every two weeks.

In the first experiment, which ran for 144 days, eight lots of eight pigs each, weighing at the start approximately 50 pounds each, were used. Four lots of pigs received the basal rations supplemented with 908 g of ground limestone, and 0, 30, 60, and 100 g of sodium fluoride per 100 pounds of ration. Two more lots were fed the basal rations supplemented with 2 parts of different rock phosphates. Rock phosphate A was of Tennessee origin and analyzed 3.34 per cent fluorine, while rock phosphate B represented a pebble rock phosphate mined in Florida and contained 3.61 per cent fluorine. The pigs in another lot had their ration supplemented with equal parts of ground limestone and rock phosphate A, and the remaining lot received a ration that included 2 parts of steamed bone meal.

The mineral composition of these rations are presented in Table 1. The calcium: phosphorus ratios of the rations of the different lots were variable. However, other work in this laboratory indicates that the variations fall within the range of maximum performance and that the percentages of calcium and phosphorus, or the proportion in which they were present in the ration, were not limiting factors in the growth, or in the bone and tooth formation of these animals.

TABLE 1.—*Mineral composition of rations used for each of eight lots of pigs in Experiment 1*

[Upper figures represent starting ration; lower figures represent finishing ration]

Lot No.	Mineral additions to 100-pound basal ration	Calcium	Phosphorus	Magnesium	Fluorine	Ca:P ratio
		Per cent	*Per cent*	*Per cent*	*Per cent*	*Per cent*
1	908 g ground limestone	0.802 .766	0.527 .422	0.269 .212	([a]) ([a])	1.5 1.8
2	908 g ground limestone; 30 g sodium fluoride	.802 .766	.527 .422	.269 .212	0.029 .029	1.5 1.8
3	908 g ground limestone; 60 g sodium fluoride	.802 .766	.527 .422	.269 .212	.058 .058	1.5 1.8
4	908 g ground limestone; 100 g sodium fluoride	.802 .766	.527 .421	.268 .211	.097 .097	1.5 1.8
5	454 g ground limestone; 454 g rock phosphate, A	.786 .751	.676 .570	.254 .197	.033 .033	1.2 1.3
6	908 g rock phosphate B	.772 .736	.827 .721	.236 .180	.070 .070	.9 1.0
7	908 g rock phosphate A	.770 .734	.824 .719	.240 .183	.065 .065	.9 1.0
8	908 g steamed bone meal	.735 .700	.822 .717	.240 .183	([a]) ([a])	.9 1.0

[a] Trace.

From the growth and feed-utilization data presented in Table 2, it is obvious that as the percentage of fluorine in the ration increased, the feed intake, the daily gains, and the feed utilization of the animals were materially reduced. These reductions occurred irrespective of whether the fluorine in the ration was derived from rock phosphate or sodium fluoride. The data, in general, substantiate the observations of other investigators that an excess of fluorine in the ration retards growth and feed consumption in various classes of animals.

TABLE 2.—*Gains and feed requirements of various lots of pigs in Experiment 1*

Lot No.	Fluorine in ration	Average initial weight	Average final weight	Average daily gain per pig	Average daily feed per pig	Feed required per 100 pounds of gain
	Per cent	*Pounds*	*Pounds*	*Pounds*	*Pounds*	*Pounds*
1	([a])	54.6	204.6	1.04	4.92	472.4
2	0.029	52.0	192.0	.97	4.48	461.3
3	.058	54.0	182.6	.89	4.31	483.1
4	.097	52.5	138.0	.59	3.62	610.5
5	.033	54.0	196.0	.99	4.84	491.7
6 [b]	.070	51.1	139.4	.59	3.89	635.8
7	.065	53.1	130.3	.54	3.48	650.1
8	([a])	52.1	217.0	1.14	5.02	438.7

[a] Trace. [b] 1 pig in lot 6 died at 103 days.

Daily observations of the different lots revealed that the pigs in the lots on high-fluorine rations, particularly lots 6 and 7 (2 parts rock phosphate) were consuming considerably more water than were those in the other lots. No attempts were made to record the comparative water consumption of the different lots in this experiment. It was also noted that several of the animals in the fluorine-fed lots manifested signs of stiffness and were rather reluctant to move. This was especially true in the higher fluorine lots. One pig in lot 6 (2 parts rock phosphate B) died at 103 days. Post-mortem examination showed a contracted, roughened, firm, pale kidney.

Gross examination of the femurs showed that those from lots 1 and 8 (2 parts limestone and 2 parts steamed bone meal, respectively) were smooth and dense in appearance, with a normal yellowish color and a definite luster, while those of the other lots were rough, lusterless, white in color, and with some exostoses. These conditions became more pronounced as the amount of fluorine in the ration increased. It is apparent from the data in Table 3 that the breaking strength of the bone is affected by high fluorine intake. Those rations that contained approximately 0.06 per cent of fluorine or more, either in the form of rock phosphate or sodium fluoride, significantly decreased the tensile strength of the femur. The data also indicate that excessive fluorine ingestion increases the diameter of the femur. This is particularly evident when the comparative length and weight of the bone are taken into account. The ash content of the femurs (Table 3) shows some variation. In general, the percentage of ash is lowest in the highest fluorine-fed lots. The difference in ash values are, however, only statistically significant in the case of lots 1 and 4 (control, and 100 g of sodium fluoride, respectively). Further experimental work is required before it can be stated with certainty whether or not excessive fluorine feeding will significantly lower the percentage of bone ash in pigs during short or long feeding periods.

TABLE 3.—*Physical measurements and ash analyses of the femurs of pigs in various lots in Experiment 1*

Lot No.	Fluorine in ration	Weight	Volume	Length	Smallest diameter	Breaking strength	Ratio of breaking strength to weight of bone	Ash	Grams of ash/cc volume
	Per cent	*Grams*	*Cubic centimeters*	*Centimeters*	*Centimeters*	*Pounds*		*Per cent*	
1	([a])	177	135	18.4	2.00	690±62	3.94	61.33±0.39	0.805
2	0.029	164	124	17.5	2.06	733±29	4.51	62.34± .27	.825
3	.058	167	131	16.8	2.21	647±34	3.92	60.50± .31	.770
4	.097	135	111	16.3	2.03	393±19	2.93	58.03± .29	.708
5	.033	160	126	17.1	2.12	766±31	4.81	61.86± .51	.760
6	.070	133	111	16.3	2.05	407±34	3.21	59.42± .68	.707
7	.065	134	109	16.1	2.01	456±40	3.34	60.78± .54	.743
8	([a])	177	134	18.3	1.95	841±55	4.80	61.61± .32	.816

[a] Trace.

The close correlation between the amount of ash per unit volume of bone and the breaking strength is of special interest. Apparently the ash-volume ratio is a more critical factor in determining the tensile strength of the femur than is the percentage of ash in the dry extracted bone.

The chemical analyses of the bone ash and dry extracted femurs, presented in Table 4, show that increasing percentages of fluorine in the ration had no significant effect on the percentage of calcium and phosphorus in the ash, whereas the percentage of magnesium tended to increase with increased fluorine intake, irrespective of the magnesium content of the ration. The carbonate content of the fat-free bones tended to decrease with increased fluorine intake, while the percentage of fluorine in the bone was directly proportional to the amount ingested.

TABLE 4.—*Chemical analyses*[a] *(per cent) of the femurs of pigs in various lots in Experiment 1*

Lot No.	Fluorine in ration	Calcium	Phosphorus	Magnesium	Carbon dioxide	Fluorine
1	([b])	38.39	17.48	0.790	2.76	0.039
2	0.029	38.50	17.99	.959	2.72	.534
3	.058	38.27	17.68	.972	2.37	.775
4	.097	38.43	17.62	1.141	2.34	1.108
5	.033	38.10	17.89	1.036	2.57	.594
6	.070	37.79	17.91	1.167	1.92	1.037
7	.065	37.92	18.14	1.137	2.06	1.093
8	([b])	38.31	17.75	.823	2.81	.036

[a] The calcium, phosphorus, and magnesium percentages are based on the bone ash; those of the carbon dioxide and fluorine are based on the dry, fat-free bone.
[b] Trace.

The mandibles of the fluorine-fed pigs showed the same thickened condition and rough, white, lusterless appearance that was noted in the femurs. Enlargement of the body of the bone and the appearance of exostoses became more evident with increased fluorine intake. No differences in the amount of wear of the teeth from the various lots were noted. However, there was a tendency for the teeth from the higher fluorine lots to chip more easily than those from the controls. Chemical analysis of the teeth did not show any significant difference in the percentage of ash or in the calcium, phosphorus, and magnesium content of the ash. (Table 5.) The carbon dioxide content of the teeth was not affected, except in lots 6 and 7 (2 parts rock phosphates A and B), which gave evidence of a slight decrease. The percentage of fluorine in the teeth was directly proportional to the amount present in the ration.

TABLE 5.—*Chemical composition*[a] *(per cent) of the teeth of pigs in various lots in Experiment 1*

Lot No.	Fluorine in ration	Ash	Calcium	Phosphorus	Magnesium	Carbon dioxide	Fluorine
1	([b])	74.04	35.83	17.48	1.45	2.03	0.083
2	0.029	74.96	36.32	17.77	1.54	2.09	.181
3	.058	74.17	36.83	17.86	1.63	2.07	.281
4	.097	74.69	36.99	17.88	1.53	2.15	.361
5	.033	74.84	36.67	17.66	1.51	2.11	.228
6	.070	74.44	36.70	17.57	1.50	1.83	.331
7	.065	75.17	37.02	17.35	1.56	1.95	.375
8	([b])	75.80	36.88	17.33	1.79	2.12	.092

[a] Calcium, phosphorus, and magnesium percentages are based on tooth ash; those of carbon dioxide and fluorine on dry, fat-free teeth.
[b] Trace.

Gross examination of the various organs at the time of slaughter revealed no abnormalities, with the exception of the kidneys from the pigs that had been fed rock phosphate. The kidneys were pale in color, contracted, and firm in texture, and their surfaces were roughened by numerous small nodules and depressions. (Fig. 1, A.) The capsules were slightly thickened, and in some instances firmly adherent to the surface. Occasionally small cysts containing a clear or amber-colored fluid protruded above the surface of, or were more

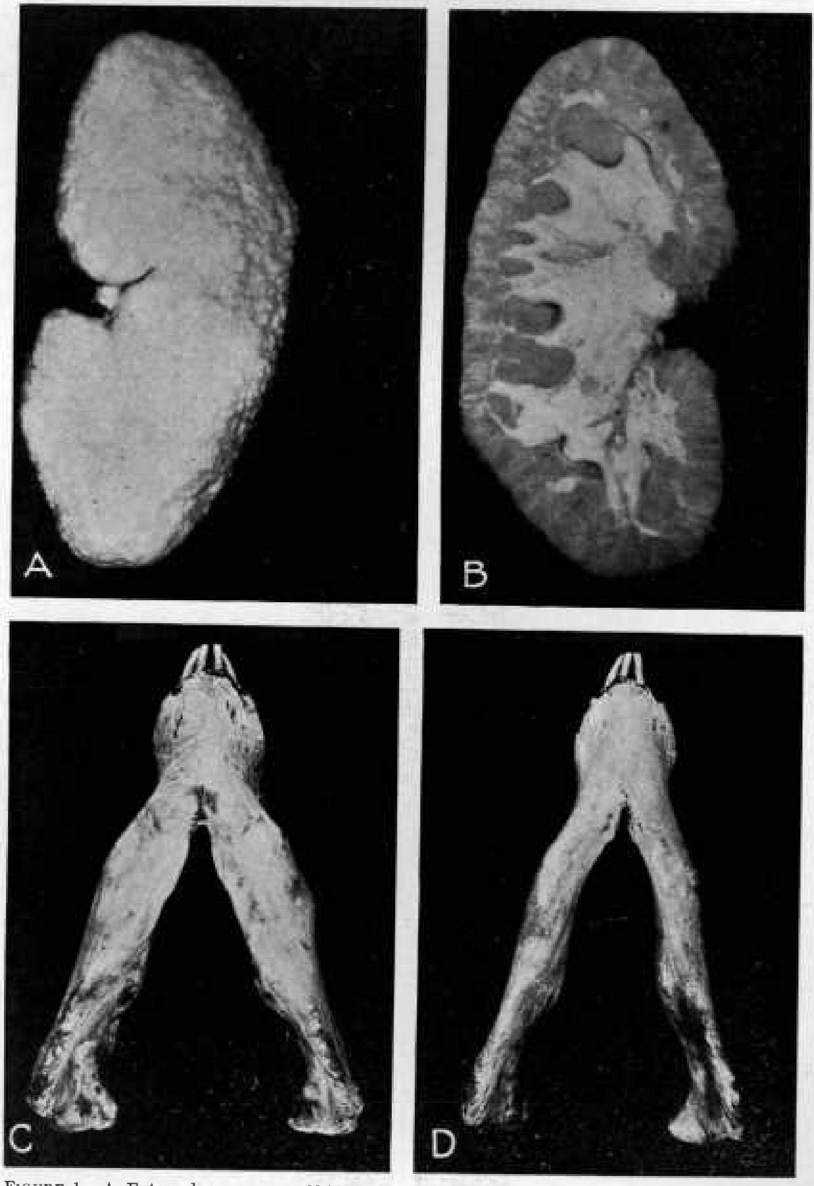


FIGURE 1.—A, External appearance of kidney from a pig that was fed 2 per cent rock phosphate; B, cross section of kidney from a pig that was fed 2 per cent rock phosphate; C, D, mandibles of pigs No. 76 of lot 4 and No. 58 of lot 1, showing increased thickness caused by the ingestion of fluorine

deeply situated in, the kidney. On section the cortex appeared reduced in width, and frequently the medulla contained considerable amount of fat. (Fig. 1, B.)

Microscopically the kidneys showed a nephritis with a varying degree of degeneration of the tubular epithelium and, as a terminal result, the replacement of many tubules and glomeruli with fibrous tissue. (Pl. 1.) None of the animals in the control or sodium fluoride-fed lots exhibited this condition.

In an attempt to confirm the results of the previous trial, and to study the effects of smaller amounts of fluorine in the ration, a second experiment, using six lots of eight pigs each, was started. The basal rations were the same as those used in the first test. The experiment ran for 160 days and was conducted under conditions similar to those in the first experiment. The mineral composition of the rations are presented in Table 6. The amounts of the phosphatic minerals and limestone were so adjusted that the percentages of calcium and phosphorus were the same in the rations of all lots. Fluorine was supplied in varying amounts in the form of sodium fluoride or rock phosphate.

TABLE 6.—*Mineral composition of rations used for each of six lots of pigs in Experiment 2*

[Upper figures represent starting ration; lower figures finishing ration]

Lot No.	Mineral additions to 100-pound basal ration	Calcium	Phosphorus	Magnesium	Fluorine	Ca:P ratio
		Per cent	*Per cent*	*Per cent*	*Per cent*	
1	454 g ground limestone; 454 g steamed bone meal	0.714 .672	0.654 .556	0.348 .260	([a]) ([a])	1.1 1.2
2	454 g ground limestone; 454 g steamed bone meal; 10 g sodium fluoride.	.714 .672	.654 .556	.348 .260	0.010 .010	1.1 1.2
3	454 g ground limestone; 454 g steamed bone meal; 30 g sodium fluoride.	.714 .672	.654 .556	.348 .260	.029 .029	1.1 1.2
4	454 g ground limestone; 454 g steamed bone meal; 60 g sodium fluoride.	.714 .672	.654 .556	.348 .260	.058 .058	1.1 1.2
5	429 g ground limestone; 227 g steamed bone meal; 222 g rock phosphate.	.714 .671	.654 .557	.346 .258	.016 .016	1.1 1.2
6	404 g ground limestone; 444 g rock phosphate	.714 .672	.654 .557	.343 .255	.032 .032	1.1 1.2

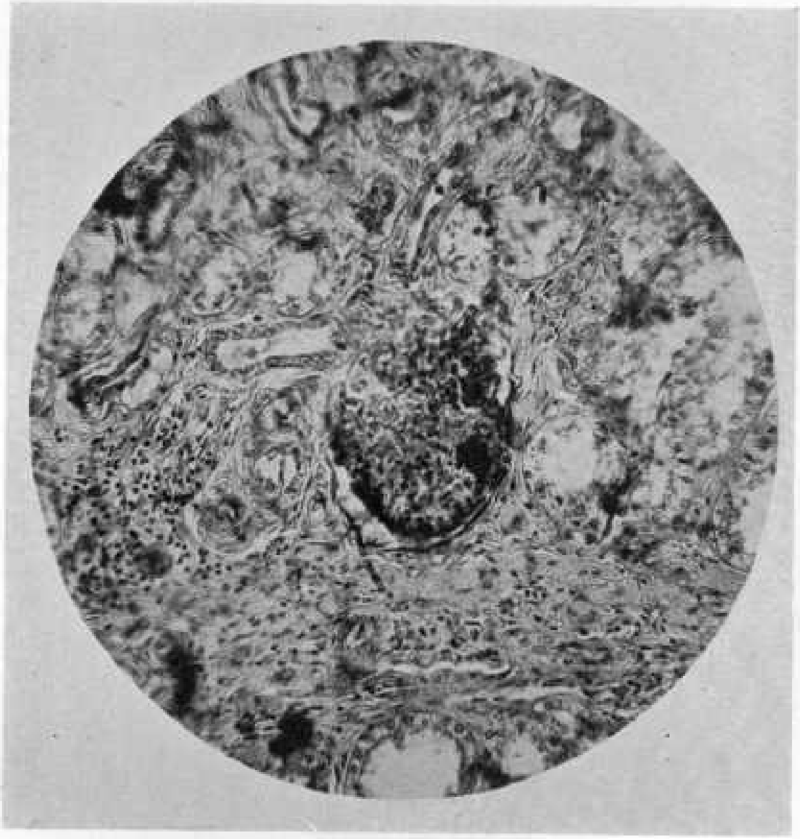
[a] Trace.

The gains and feed requirements of the different lots are recorded in Table 7. It is evident that when the fluorine content of the ration exceeded 0.029 per cent the rate of gain and the economy of gain were decreased. Smaller amounts of fluorine, either in the form of sodium fluoride or rock phosphate, appeared to be without effect on growth or feed utilization. These observations, in general, substantiate the results of the first trial and other unpublished data of this laboratory.

TABLE 7.—*Gains and feed requirements of various lots of pigs in Experiment 2*

Lot No.	Fluorine in ration	Average initial weight	Average final weight	Average daily gain per pig	Average daily ration per pig	Feed required per 100 pounds of gain
	Per cent	*Pounds*	*Pounds*	*Pounds*	*Pounds*	*Pounds*
1	([a])	39.3	243.4	1.28	5.08	398.4
2	0.010	37.7	244.6	1.29	4.92	380.2
3	.029	38.8	213.6	1.09	4.26	389.9
4	.058	39.4	161.3	.76	3.41	450.2
5	.016	40.4	246.0	1.29	5.06	394.7
6	.032	40.4	219.4	1.12	4.85	434.0

[a] Trace.



Photomicrograph of a section of a kidney from a pig fed 2 per cent rock phosphate, showing characteristic degeneration and presence of fibrous tissue.

Again, in this experiment it was observed that the pigs on the high-fluorine rations consumed larger quantities of water. To check this observation the water and feed consumption of all lots were carefully recorded for two weeks. The results (Table 8) show that a high-fluorine intake caused increased water consumption per unit of live weight.

TABLE 8.—*Effect of fluorine intake on water consumption of pigs in various lots in Experiment 2*

Lot No.	Fluorine in ration	Feed consumed	Water consumed	Average weight	Water consumed per 100 pounds of live weight
	Per cent	*Pounds*	*Gallons*	*Pounds*	*Gallons*
1	([a])	945	165	212	77.83
2	0.010	964	156	208	75.00
3	.029	767	153	188	81.38
4	.058	471	159	144	110.41
5	.016	927	165	212	77.83
6	.032	817	168	190	88.42

[a] Trace.

As in the previous experiment, the femurs of the pigs that had received 0.029 per cent or more of fluorine in their ration were rough, white, and lusterless, whereas the bones from the pigs on lower fluorine rations appeared normal. The data presented in Table 9 again show an increase in the diameter and a reduction in the breaking strength of the femurs of the pigs on the high-fluorine rations. The percentage of ash was not significantly affected by fluorine feeding. However, as in the first experiment, the amount of ash per unit volume of bone was decreased with higher levels of fluorine intake.

TABLE 9.—*Physical measurements and ash analyses of the femurs of pigs in various lots in Experiment 2*

Lot No.	Fluorine in ration	Weight	Volume	Length	Smallest diameter	Breaking strength	Ratio of breaking strength to weight of bone	Ash	Grams of ash/cc volume
	Per cent	*Grams*	*Cubic centimeters*	*Centimeters*	*Centimeters*	*Pounds*		*Per cent*	
1	([a])	178	139	18.4	1.96	1,013±38	6.06	61.75±0.34	0.801
2	0.010	182	140	18.3	2.04	976±55	5.33	62.85± .42	.826
3	.029	168	132	17.3	2.12	871±42	5.25	62.46± .41	.792
4	.058	157	131	17.1	2.22	550±23	3.49	60.74± .51	.732
5	.016	176	138	18.1	2.03	1,050±58	6.17	62.04± .25	.796
6	.032	179	142	18.3	2.10	827±37	4.76	62.62± .30	.792

[a] Trace.

The data on the chemical analysis of the femurs (Table 10) show no significant differences in the calcium and phosphorus contents of the bone ash from the different lots, while the percentage of magnesium increased with increased fluorine intake. Again, the carbonate content of the dry, fat-free femurs was reduced by high-fluorine feeding, whereas the percentage of fluorine in the bone was directly proportional to the amount ingested.

TABLE 10.—*Chemical analyses* [a] *(per cent) of the femurs of pigs in various lots in Experiment 2*

Lot No.	Fluorine in ration	Calcium	Phosphorus	Magnesium	Carbon dioxide	Fluorine
1	([b])	37.61	18.52	0.919	2.93	0.057
2	0.010	37.60	18.25	.968	3.01	.316
3	.029	37.64	18.33	1.001	2.71	.671
4	.058	37.74	18.23	1.211	2.31	1.077
5	.016	37.72	18.18	1.043	2.88	.409
6	.032	38.18	18.95	1.102	2.78	.624

[a] Calcium, phosphorus, and magnesium percentages are based on bone ash; those of carbon dioxide and fluorine on the dry, fat-free bone.
[b] Trace.

Gross examination of the mandibles revealed the same rough, white, lusterless condition in the high-fluorine lots, as noted in the previous trial. No difference could be detected in the amount of wear of the teeth from the various lots, although it was observed that the teeth of the high-fluorine lots had a tendency to chip more easily than those from the control or low-fluorine lots. The rami of the mandibles were increased in diameter as a result of high-fluorine intake. (Fig. 1, C, D.) This enlargement of the mandibles also caused an increase in the width of the dental arch at the point of the second molar. It was also found that the buccolingual dimensions, taken at the positions of the three molars, increased in direct proportion to the amount of fluorine in the ration. The vertical dimensions, taken at the same points, showed no significant differences

The analysis of the teeth (Table 11) showed no significant difference in the percentage of ash or carbon dioxide on the dry, fat-free basis. Neither did the tooth ash show any variation in the amount of calcium, phosphorus, or magnesium. The only variable noted was in the fluorine content of the dry, fat-free teeth. The amount present was directly correlated with the percentage in the ration.

TABLE 11.—*Chemical composition* [a] *(per cent) of the teeth of pigs in various lots in Experiment 2*

Lot No.	Fluorine in ration	Ash	Calcium	Phosphorus	Magnesium	Carbon dioxide	Fluorine
1	([b])	73.49	36.74	17.86	1.65	1.76	0.043
2	0.010	74.39	36.99	17.84	1.67	1.66	.127
3	.029	73.96	37.05	17.65	1.60	1.76	.262
4	.058	73.93	36.69	17.71	1.66	1.76	.373
5	.016	74.60	36.77	17.70	1.70	1.64	.124
6	.032	74.21	36.82	17.06	1.74	1.65	.228

[a] Calcium, phosphorus, and magnesium percentages are based on tooth ash; those of carbon dioxide and fluorine on dry, fat-free teeth.
[b] Trace.

A post-mortem examination revealed no abnormalities in the various organs, with the exception of the kidneys of the pigs from lot 6 (approximately 1 per cent rock phosphate). These organs showed the nephritis noted in the animals in the previous trial. None of the kidneys of the pigs from the other lots showed any pathological change.

In a third experiment pigs were fed rock phosphate at levels of 1 and 2 per cent of their ration and sodium fluoride at levels of 30 and

60 g per 100 pounds of ration for two years or more, extending through the complete reproduction cycle. Upon post-mortem these pigs showed bone and kidney changes similar to, but more extensive than, those observed in the experiments reported herein. The condition of, and changes in, the teeth of these long-time fluorine-fed pigs were much more marked than those of pigs in the short-time experiments. The detailed findings of the tooth changes have been reported elsewhere (*4*). Suffice it to state that frequently the teeth of the high-fluorine-fed pigs were worn to the gums, and the pulp cavities were exposed. This condition of the teeth was reflected in the manner in which the pigs consumed their feed. Upon taking a mouthful of feed the pigs would throw their heads backward in what appeared to be an attempt to swallow the feed without allowing it to come in contact with the molar teeth. No noticeable effort was made to chew the feed. The same animals were reluctant to drink cold water. It was also found that sows reared and maintained on high-fluorine rations did not consume sufficient feed for good lactation or to prevent them from becoming unthrifty.

DISCUSSION

From the results of these experiments, it is evident that excessive fluorine in the ration exerts definite physiological effects upon swine. These effects, in general, were the same whether the fluorine was derived from rock phosphate or sodium fluoride. The only difference noted was the effect that liberal amounts of rock phosphate (1 per cent or more of the ration) exerted on the kidneys. Equivalent or even higher levels of fluorine, in the form of sodium fluoride, had no such effect. Two explanations present themselves as to the cause of this discrepancy. Either the naturally occurring product must contain some substance or material, other than fluorine, which causes a pathological change in the kidney, or the fluorine in rock phosphate is present in a more toxic form than in sodium fluoride.

The increased water consumption of the pigs on the high-fluorine levels may in part be accounted for by the results of Gottlieb and Grant (*12*). These investigators recently reported that the intravenous injection of sodium fluoride into dogs caused a marked diuresis. Although no urinary volume determinations were attempted in the present experiments, it was noted that the litter in the pens of the high-fluorine-fed pigs was much more soiled with urine than that in the other pens. A marked increase in urine volume must therefore be accompanied by an increased water intake in order to avoid a serious dehydration of the body tissues.

The outstanding effect of fluorine on the femurs of pigs, noted in these investigations, was the decrease in breaking strength of these bones. Although the bones of the animals which received the larger amounts of fluorine were larger in diameter and contained approximately the same percentage of ash, their tensile strength was significantly less than bones from those in the low-fluorine lots. Obviously, the breaking strength of a bone is influenced by factors other than ash content. The close correlation between the amount of ash per unit volume of bone and its breaking strength suggest that the ash to volume ratio is a better criterion of the tensile strength of a bone than is the percentage of ash. The fact that the weakest bones possessed the greatest diameter and contained the least ash per unit of volume, suggests that fluorine may cause some change in the cellular structure of the bones.

The results of the effects of fluorine ingestion on the inorganic composition of the femurs substantiate the findings of Forbes and his associates (*9*), that the weak bones caused by rock-phosphate feeding are characterized by maximum magnesium and minimum carbon dioxide percentages, but are in disagreement with the report of the same investigators that the proportions of calcium and phosphorus are also changed. It is of interest that the high magnesium and low carbonate percentages were independent of the magnesium or carbonate contents of the rations, the source of calcium and phosphorus in the rations, and the form in which fluorine was ingested. This shows that excessive fluorine intake alters the inorganic composition of the bone. Whether this change in composition as a result of excessive fluorine ingestion is due, in part, to a partial replacement of the carbonate by the fluoride, or an actual shift in the percentages of the different bone salts normally present to compensate for the increased fluorine content, requires further detailed study.

The mandibles of pigs which had been fed toxic amounts of fluorine showed changes similar to those described by Huffman and Reed (*17*) in the case of dairy cattle fed rock phosphate. On cross section, it was observed that the marrow cavities were greatly enlarged without noticeable increase in the thickness of the bone wall. A marked difference was also noted between the types of bone marrow in the high-fluorine and the low-fluorine lots. The marrow of the low-fluorine lots was red, while that from the high-fluorine lots was pale yellow and appeared to have a decided increase in fatty material. The difference in the size of the marrow cavity and color and texture of the marrow was particularly evident in animals that were fed sodium fluoride or rock phosphate for an extended period.

It was evident that fluorine exerted a definite effect on tooth structure in swine. This fact was especially noticeable in animals fed fluorine for two or more years. These tooth changes were similar to those reported by Huffman and Reed (*17*) in the case of dairy cattle fed rock phosphate. The chemical analysis of the teeth did not reveal any striking differences in their inorganic composition, aside from the increase in the percentage of fluorine, the increase being directly correlated with the fluorine content of the ration, which substantiates the work of Sonntag (*34*) with dogs.

The results are in agreement with the work of other investigators with different species of animals, in that excessive fluorine in the ration decreases growth and feed consumption, and the efficiency with which the feed is utilized. The data, in general, show that when more than approximately 0.03 per cent fluorine is included in the ration the normal performance of the pig is retarded. This is especially true in case of long-continued fluorine feeding. Under these conditions, the feed consumption is impaired to such an extent in sows suckling pigs that lactation is adversely affected, and frequently the animals become so unthrifty that it is impossible to bring them back to good condition on the same feed.

It should be pointed out that the average daily calcium and phosphorus intake of the pigs in the different lots in the same experiment were not always uniform, for the reason that the percentages of these elements in the rations between lots varied, or the daily feed intake between lots was not the same. The authors are of the opinion that these variations in calcium and phosphorus intake do not detract from the significance of the results obtained, in that the minimum requirements for these elements were amply satisfied in all instances. Forbes and his associates (*9*) and McClure and Mitchell (*20*) obtained good results with pigs on a daily intake of 5 to 7 g of calcium. In the experiments herein reported, the daily calcium intake was from 2 to 3 times that fed by the above-mentioned investigators, and in all probability the requirements of the pigs for calcium and phosphorus were not limiting factors in the results secured.

SUMMARY

The feeding to pigs of rations containing approximately 0.03 per cent or more of fluorine derived from rock phosphate or sodium fluoride impaired growth and feed consumption and lessened the efficiency with which the rations were utilized. The femurs of the pigs were characterized by an increase in the diameter of the shaft, a loss of normal color and luster, the presence of exostoses, and a decreased breaking strength. These changes became more pronounced as the fluorine content of the ration increased.

The bones weakened by fluorine feeding contained normal percentages of ash, calcium, and phosphorus, increased amounts of magnesium and fluorine, and decreased percentages of carbon dioxide. The increased magnesium and fluorine contents and the decreased carbonate content were directly correlated with the percentage of fluorine in the ration. The feeding of fluorine caused an increase in the size of the rami of the mandibles. This enlargement was due to an increase in the size of the marrow cavity rather than to an increase in the thickness of the wall. The type of marrow in the cavity was also changed.

Excessive amounts of fluorine in the ration when fed over long periods softened the teeth of pigs. The percentages of ash, calcium, phosphorus, magnesium, and carbon dioxide in the teeth were not significantly affected by fluorine feeding; however, the fluorine content was directly proportional to the amount fed.

The fluorine from rock phosphate and sodium fluoride exerted the same physiological effects on swine, with the exception that rock phosphate caused certain pathological changes in the kidneys. A nephritis with resulting induration of the kidney occurred in varying degrees in all pigs fed approximately 1 per cent or more of rock phosphate in their ration.

LITERATURE CITED

(1) ANONYMOUS.
1932. FLUORIDES IN WATER SUPPLIES. Jour. Amer. Med. Assoc. 99: 395.

(2) BALDWIN, H. B.
1899. THE TOXIC ACTION OF SODIUM FLUORIDE. Jour. Amer. Chem. Soc. 21: 517–521.

(3) BERGARA, C.
1927. ALTÉRATIONS DENTAIRES ET OSSEUSES DANS L'INTOXICATION CHRONIQUE PAR LES FLUORURES. Compt. Rend. Soc. Biol. [Paris] 97: 600–602, illus.

(4) BETHKE, R. M., KICK, C. H., HILL, T. J., and CHASE, S. W.
1933. THE EFFECTS OF DIETS CONTAINING FLUORINE ON THE JAWS AND TEETH OF SWINE AND RATS. Jour. Dental Research (accepted for publication).

(5) BLAIZOT, [L.]
1893. TOXICITÉ ET EMPLOI THÉRAPEUTIQUE DE FLUORURE DE SODIUM. Compt. Rend. Soc. Biol. [Paris] 45: 316–319.

(6) BRANDL, J., and TAPPEINER, H.
1891. UEBER DIE ABLAGERUNG VON FLUORVERBINDUNGEN IM ORGANISMUS NACH FÜTTERUNG MIT FLUORNATRIUM. Ztschr. Biol. 28: [518]–539.

(7) CHANELES, J.
1928. ACTION DE L'IODE SUR LA FLUOROSE CHRONIQUE. Compt. Rend. Soc. Biol. [Paris] 102: 863.

(8) [CHRISTENSEN, C. L.]
1932. STUDY BEING MADE OF SAFE LIMITS FOR ROCK PHOSPHATE AS A MINERAL FEED. Wis. Agr. Expt. Sta. Bul. 421 (Ann. Rpt. 1930–31): 104–107, illus.

(9) FORBES, E. B., HALVERSON, J. A., MORGAN, L. E., SCHULZ, J. A., WELLS, E. B., HUNT, C. H., and WINTER, A. R.
1921. THE UTILIZATION OF CALCIUM COMPOUNDS IN ANIMAL NUTRITION. Ohio Agr. Expt. Sta. Bul. 347, 99 p., illus.

(10) GAUTIER, A.
1914. SUR LE RÔLE ET L'ÉTAT DU FLOUR DANS L'ÉCONOMIE ANIMALE. Compt. Rend. Acad. Sci. [Paris] 158: 159–166.

(11) GOLDEMBERG, L.
1927. ACTION BIOLOGIQUE DU FLUOR. Jour. Physiol. et Path. Gén. 25: [65]–72, illus.

(12) GOTTLIEB, L., and GRANT, S. B.
1932. DIURETIC ACTION OF SODIUM FLUORIDE. Soc. Expt. Biol. and Med. Proc. 29: 1293–1294.

(13) GRÜTZNER, P.
1853. UEBER CHEMISCHE REIZUNG MOTORISCHE NERVEN. Pflüger's Arch. Physiol. 53: 83–139.

(14) HARMES, H.
1899. BEITRÄGE ZUR FLUORFRAGE DER ZAHN- UND KNOCHENASCHEN. Ztschr. Biol. 38: [487]–498.

(15) HART, E. B., MCCOLLUM, E. V., and FULLER, J. G.
1909. THE RÔLE OF INORGANIC PHOSPHORUS IN THE NUTRITION OF ANIMALS. Wis. Agr. Expt. Sta. Research Bul. 1, 38 p., illus.

(16) HEIDENHAIN, H.
1899. NEUE VERSUCHE ÜBER DIE AUFSAUGUNG IM DÜNNDARM. Pflüger's Arch. Physiol. 56: 579–631.

(17) HUFFMAN, C. F., and REED, O. E.
1930. RESULTS OF A LONG TIME MINERAL FEEDING EXPERIMENT WITH DAIRY CATTLE. Mich. Agr. Expt. Sta. Circ. Bul. 129, 11 p., illus.

(18) JODLBAUER, [A.]
1901. ÜBER DEN FLUORGEHALT DER ZÄHNE UND KNOCKEN. Ztschr. Biol. 41: [487]–492.

(19) MCCLURE, F. J., and MITCHELL, H. H.
1931. THE EFFECT OF FLUORINE ON THE CALCIUM METABOLISM OF ALBINO RATS AND THE COMPOSITION OF THE BONES. Jour. Biol. Chem. 90: 297–320, illus.

(20) ——— and MITCHELL, H. H.
1931. THE EFFECT OF CALCIUM FLUORIDE AND PHOSPHATE ROCK ON THE CALCIUM RETENTION OF YOUNG GROWING PIGS. Jour. Agr. Research 42: 363–373, illus.

(21) MCCOLLUM, E. V., SIMMONDS, N., BECKER, J. E., and BUNTING, R. M.
1925. THE EFFECT OF THE ADDITIONS OF FLUORINE TO THE DIET OF THE RAT ON THE QUALITY OF THE TEETH. Jour. Biol. Chem. 63: 553–562, illus.

(22) MCCRUDDEN, F. H.
1910. THE QUANTITATIVE SEPARATION OF CALCIUM AND MAGNESIUM IN THE PRESENCE OF PHOSPHATES AND SMALL AMOUNTS OF IRON, DEVISED ESPECIALLY FOR THE ANALYSIS OF FOODS, URINE, AND FECES. Jour. Biol. Chem. 7: 83–100.

(23) ———
1911. THE DETERMINATION OF CALCIUM IN THE PRESENCE OF MAGNESIUM AND PHOSPHATES: THE DETERMINATION OF CALCIUM IN URINE. Jour. Biol. Chem. 10: 187–199.

(24) McNally, W. D.
1923. four deaths caused by sodium fluoride. Jour. Amer. Med. Assoc. 81: 811–813.

(25) Marcovitch, S.
1928. studies on toxicity of fluorine compounds. Tenn. Agr. Expt. Sta. Bul. 139, 48 p., illus.

(26) Maumené, E.
1854. expérience pour déterminer l'action des fluorures sur l'économie animale. Compt. Rend. Acad. Sci. [Paris] 39: 538–540.

(27) Pitotti, G.
1893. dell'influenza che esercita il fluoruro di sodio sui vari organi e sugli elementi dei tessuti dell'organismo animale. Bol. Sci. Med. Bologna (7) 4: 5–22. [Abstract in Jahresber. Fortschr. Tier -Chem. 23: 103. 1904.]

(28) Reed, O. E., and Huffman, C. F.
1930. the results of a five-year mineral feeding investigation with dairy cattle. Mich. Agr. Expt. Sta. Tech. Bul. 105, 63 p., illus.

(29) Reynolds, D. S., Ross, W. H., and Jacob, K. D.
1928. volatilization method for the determination of fluorine with special reference to the analysis of phosphate rock. Jour. Assoc. Off. Agr. Chem. 11: 225–236, illus.

(30) Schulz, J. A., and Lamb, A. R.
1925. the effect of fluorine as sodium fluoride on the growth and reproduction of albino rats. Science (n. s.) 61: 93–94.

(31) Siegfried, A.
1901. ein beitrag zur kenntnis des physiologisch-chemischen und pharmokologischen verhaltens des kieselsauren natriums, des kieselfluornatriums und des fluornatriums. Arch. Internatl. Pharmacodyn. et Ther. 9: [225]–284.

(32) Smith, M. C., Lantz, E. M., and Smith, H. V.
1931. the cause of mottled enamel, a defect of human teeth. Ariz. Agr. Expt. Sta. Tech. Bul. 32, p. [253]–282, illus.

(33) Sollmann, T., Schettler, O. H., and Wetzel, N. C.
1921. studies of chronic intoxications of albino rats. iv. fluorid, chlorid, and calcium (including sodium fluorid, sodium chlorid, "phosphate rock," calcium phosphate (precipitated), and calcium carbonate (precipitated). iv. Jour. Pharmacol. and Expt. Ther. 17: 197–225, illus.

(34) Sonntag, G.
1917. über ein verfahren zur bestimmung des fluorgehalts von knocken und zähnen normaler und mit fluoriden gefütterter hunde. Arb. K. Gsndhtsamt. (1915–1917) 50: [307]–336.

(35) Taylor, G. E.
1929. effect of fluorine in dairy cattle ration. Mich. Agr. Expt. Sta. Quart. Bul. 11: 101–104, illus.

(36) Tolle, C., and Maynard, L. A.
1931. a study of phosphatic limestone as a mineral supplement. N. Y. (Cornell) Agr. Expt. Sta. Bul. 530, 27 p., illus.

(37) Van Slyke, D. D.
1918. the determination of carbon dioxide in carbonates. Jour. Biol. Chem. 36: 351–354, illus.

(38) Weinland, G.
1894. ueber chemische reizung des flimmerepithels. Pflüger's Arch. Physiol. 58: 105–132, illus.

(39) Wieland, H., and Kurtzahn, G.
1923. zur kenntnis der fluorwirkung. Arch. Expt. Path. u. Pharmakol. 97: [489–498], illus.

(40) Wramplemeyer, E.
1893. ueber den fluorgehalt der zahne. Ztschr. Analyt. Chem. 32: 550–553.

(41) Zdarek, E.
1910. über die verteilung des fluors im den einzelnen organen des menschen. Hoppe-Seyler's Ztschr. Physiol. Chem. 69: [127]–137.