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THE EFFECT OF FLUORINE ON BLOOD AND RESPIRATION

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Much interest has been manifested in fluorine during the past few years. This is due to two reasons: first, fluorine is found in several phosphatic mineral supplements, which are fed to farm animals; and, second, fluorine has been found in drinking waters in this and many other countries of the world. The interest of the authors in fluorine dates from the discovery by Ostrem, Nelson, Greenwood, and Wilhelm (1) of fluorine in the drinking waters of communities in the State of Iowa, with the resulting production of mottled enamel of the teeth. There can be no question that fluorine in excessive amounts in water causes damage to the teeth. Smith, Lantz, and Smith (2) have produced considerable evidence that the presence of excessive fluorine in the drinking water will cause mottled enamel in man. The question naturally arises as to whether fluorine in water produces other harmful effects or pathological changes in the body, aside from the disturbance to the teeth.

The work in this paper relates to the effect of fluorine on respiration, blood pressure, hemoglobin, blood calcium, blood phosphorus, and coagulation of blood. Little has been done on these phases of the subject. Sollmann (3) refers to the work of Tappeiner and states that in mammals NaF causes salivation, gastroenteritis, dyspnea, muscular weakness and tremors, epileptic convulsions, fall of blood pressure, and stoppage of respiration and heart. Schulz (4) observed results similar to Tappeiner. Gerschmann (5) reports that injection of 30 mg. NaF per kg. body weight reduces blood Ca in 24 hours. Stuber and Lang (6) observed a number of hemophilic patients with high amounts of F in the blood, and they are inclined to accept the idea that a high F content of blood accompanies a long clotting period. Schwyzer (7), however, observed a very high degree of coagulability of the blood of rabbits, dogs, and pigeons which received F. Hauck, Steenbock, Lowe, and Halpin (8) have reported a few analyses of the calcium and phosphorus content of the blood of chickens receiving fluorides, but they admit that their data are insufficient to draw any definite conclusions. Phillips (9) summarized concisely the

status of this problem when he stated, "Very little work is reported dealing with the influence of fluorine on blood composition."

Experimental

All of the experiments were performed on dogs. A total of 7 dogs, 5 females and 2 males, was employed in studies on respiration and blood pressure. They weighed from 6 to 26.8 kg. The remainder of the experiments were performed on puppies — 13 in number, 5 males and 8 females. Nembutal in distilled water was used as the anesthetic. In general it was administered intraperitoneally at the rate of 30 mg. per kilo body weight. NaF was injected into the femoral vein. Blood pressure records were taken from the central (heart) end of a ligated carotid artery with a mercury manometer writing on a long paper kymograph. Eight per cent citrate solution was used to prevent clots in the cannulae and tubes. Respiratory tracings were made with a Becker air tambour connected to a pneumograph tied around the chest. Newcomer's method was used in the determination of hemoglobin. The Brodie-Russell-Boggs coagulometer was used in studying the time of coagulation of blood. Calcium was determined in the blood plasma by the Clark and Collip modification of the Kramer Tisdall method and acid soluble inorganic phosphorus by the Youngberg method.

Table I summarizes the results obtained on respiration and blood pressure; the data show that intravenous injection of 1.5 to 5.3 mg. of F as NaF per kilo of body weight produces a detectable effect on respiration. The average respirations increased from 15 per minute to 22 per minute, by injecting from 1.5 to 5.3 mg. of F as NaF per kilo of body weight. Furthermore, the data reveal that intravenous injection of 16 to 31.7 mg. of F as NaF per kilo of body weight causes a perceptible lowering of blood pressure. The average blood pressure was lowered from 170 mm. Hg. pressure to 135.6 mm. Hg. pressure, by increasing the concentration of F as NaF from 0 mg. per kilo body weight to a level of 16 to 31.7 mg. of F as NaF per kilo body weight. The above amounts of NaF were the initial doses. At intervals following the initial dose larger amounts of NaF were injected into the femoral vein. Following increased doses, respiration increased to as high as 150 per minute, and blood pressure fell to as low as 40 mm. Hg. In all cases there was respiratory paralysis before stoppage of the heart. Two dogs received orally per kilo of body weight 20 times the amount of F as NaF ordinarily consumed daily by human beings in the Ankeny area, without causing any noticeable effect on respiration and

Table I — Effect of Intravenous Injection of Fluorine as Sodium Fluoride on Respiration and Blood Pressure

Dog No.	Respirations per minute before injection of F	Mg. F per kilo body wt. required to produce detectable change in respiration	Respirations per minute after injection of F	Blood pressure in mm. Hg before injection of F	Mg. F per kilo body wt. required to produce detectable change in blood pressure	Blood pressure in mm. Hg after injection of F	Mg. F per kilo body wt. which caused death of animal
1	+			145	31.7	120	92.6
2	12	5.3	16	150	20.4	114	47.5
3	++			200	23.8	164	32.5
4	12	1.5	20	180	22.7	120	30.4
7	22	2.0	32	175	16.0	160	31.9
Averages	15.3	2.9	22.6	170	22.9	135.6	47.0

+ Artificial respiration was used during the first part of the experiment.
++ Artificial respiration was used throughout experiment.

blood pressure. The dogs received orally 4.5 mg. F as NaF per kilo of body weight, which was followed in a few minutes by 9 mg. of F as NaF and then up to higher doses at intervals of a few minutes. When the oral dosage of F reached 22.6 mg. per kilo of body weight, a detectable effect on respiration and blood pressure resulted. At the higher levels vomiting and salivation occurred which prevented accurate determinations. Autopsy of these dogs showed gastroenteritis and congestion of the kidneys. Dr. A. E. Merkel of Ankeny has made blood pressure studies on 65 school children who received fluorine water and exhibited mottled enamel, and he has observed that there is no significant variation in blood pressure from the normal.

Determinations of hemoglobin, coagulation time of blood, blood calcium, and blood phosphorus were made every 2 weeks for 18 weeks. The analyses were made on 13 dogs (5 to 9 months of age) receiving the following amounts of F in mgs. per kilo body weight: 0.0, 0.45, 0.90, 2.26, and 4.52. The average values of hemoglobin, expressed in gms. per 100 cc. of blood, were: 11.86, 12.37, 12.26, 11.96, and 12.18 respectively; and the coagulation times of blood in seconds were: 84.0, 72.5, 85.3, 95.4, and 91.4 respectively. The average values for calcium, expressed as mg. calcium per 100 cc. of blood plasma, were: 12.17, 12.05, 12.0, 12.15, and 12.07; and the results, obtained on acid soluble inorganic phosphorus, expressed as mg. P per 100 cc. blood plasma, were: 5.58, 5.48, 5.29, 5.24, and 5.13 respectively. The results show no significant changes in hemoglobin, blood coagulation, blood calcium, or acid soluble inorganic phosphorus at the levels of F administered. The fluorine was given orally as NaF.

SUMMARY

Fluorine as NaF when injected intravenously at levels from 1.5 to 5.3 mg. per kilo of body weight causes a detectable effect on respiration in dogs.

Intravenous injection of 16 to 31.7 mg. of F as NaF per kilo of body weight in dogs causes a detectable lowering of blood pressure.

Oral administration of 0.45 mg. to 4.5 mg. F as NaF caused no effect on total calcium, acid soluble inorganic phosphorus, hemoglobin, or coagulation time of blood.

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