PRENATAL AND POSTNATAL INGESTION OF FLUORIDES — FOURTEEN YEARS OF INVESTIGATION — FINAL REPORT*

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INTRODUCTION

In previous publications[1, 2] evidence was presented showing that the ingestion of fluorides during the formative stages of amelogenesis did, in fact, have an effect on the developing dentition, that the element was retained in blood and certain soft tissues and that a small percentage of patients manifested adverse systemic reactions. The data presented in this report confirm and extend the findings in a larger number of subjects.

METHOD

Three different sources of fluorides were used in this study. The tablets containing 1.0 mgm. fluorine ion from CaF_2; 1.2 mgm. fluorine ion, from NaF and 0.825 mgm. fluorine ion from Na_2PO_3F, each. These values were chosen so that each tablet would contain approximately the same amount of the ion and to supply an optimum amount of daily dietary supplement.

The measured doses of these salts were ingested by gravid women and by children through their eighth year of life, or during the periods of dental enamel formation. These tablets could be dissolved in the mouth, dissolved in any liquid or could be chewed, depending on the individual's preference or ability. One tablet daily was prescribed.

There was no selection of the patients included in this study, they were patients utilizing the facilities of the hospital, coming from all walks of life and all ethnic groups. The controls were patients chosen at random from the above group who received no known supplemental fluoride. The water in the study area is fluoride free.

In the analytical phase of this study, the fluoride was first isolated from these tissues by the Willard-Winter procedure[3] and then determined by the Williams titration[4] as modified by Smith and Gardner.[5]

This report on the analytical section presents the findings obtained from prenatal cases in which analysis were made of placental tissue from 332 study cases with 251 controls (tables I and III) and of cord blood from 361 cases with 240 controls, (tables I and II) followed by the clinical findings from 672 cases with 461 controls (table IV).

RESULTS

The storage of fluoride occurring in the soft tissue examined in this study varies over a wide range. This is shown in table I in which the concentration of fluoride is expressed in micrograms fluorine ion per 100 grams or 100 millilitres of tissue.

The data extending over so wide a range compelled us to determine in more detail the concentration found in each analysis. This is shown in tables II and III in which the fluoride concentration found in 100 millilitres of blood and in 100 grams of tissue is shown.

Three placentas were obtained at random and analysed completely for their fluoride content. The results are represented diagrammatically in Figs. I, II, and III.

The effects of the ingestion of dietary fluoride supplement given at varied ages of life on the incidence of dental caries is shown in table IV. Table V shows the results reported in another tablet study[6] and in three fluoridated water areas which, compared with our results shown in table IV demonstrate the efficacy of early dietary fluoride supplementation.

DISCUSSION

The average fetal blood fluoride concentration (table I) in the tablet study group was: in the CaF_2 group, 44.8 mcg/100cc; NaF

* This study made possible in part by grant D-70, C-4, United States Public Health Service, Dept. of Health Education and Welfare, Washington 25, D.C.

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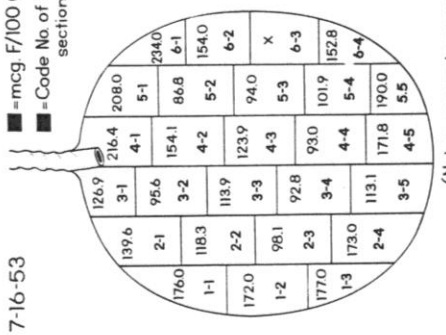
FIGURE II
WHOLE PLACENTAS
(Control)

J.G., 7-16-53

■ = mcg. F/100 Gm. tissue
■ = Code No. of tissue section



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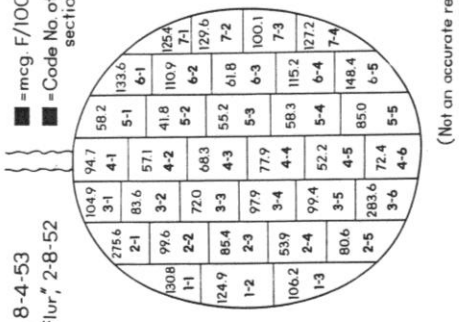
Weight: 612.23 Gm.
Average: 141.1 mcg. F/100 Gm. placenta

FIGURE I
WHOLE PLACENTAS

T.B., 8-4-53
"Enziflur", 2-8-52

■ = mcg. F/100 Gm. tissue
■ = Code No. of tissue section



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Weight: 667.45 Gm.
Average: 102.1 mcg. F/100 Gm. placenta

group 32.68 mcg/100cc and the Na_2PO_3F group, 26.85 mcg/100cc. In the controls, 12.9 mcg/100cc.

The average placental tissue fluoride concentration in the tablet study group was: NaF group, 149.2 mcg/100 gms; CaF_2 group, 109.1 mcg/100 gms and Na_2PO_3F group, 107.8 mcg/100 gms. In the controls, 105.8 mcg/100 gms.

In the tablet study group, the average cord blood concentration and the average placental tissue concentration was higher than in the controls. Examination of tables II and III reveals the wide spread in the data. There is a marked difference in the F- concentration between study and control cases in the cord blood (table II), the difference in the placental tissue is not as marked except in the NaF cases (table III).

Of interest is the finding that in no case was a fluoride concentration in placental tissue below 25 mcg/100 gms in either the CaF_2 or NaF cases.

The recovery of high F- concentrations in control placenta tissue analysis puzzled us for a period of time. As a result, microdeterminations of fluoride content of pharmaceuticals prescribed as prenatal medication were done. Thirty nine prescription items were obtained and analysed. It was found that an occult supply of fluoride was being used, there being no mention made of fluoride content as a constituent on the labels of many of the products.[7]

Six samples of placental tissue were inadvertently left out of the refrigerator in Morristown, an artificially fluoridated city (tables II and III). Upon analysis, it was found that the fluoride, had, to a marked degree left the tissue. It was found in the liquid resulting from the autolysis. This, although on a small number of cases, 6 in number, causes us to surmise that fluoride may be a function of intracellular activity.

The data presented demonstrates that fluoride is present in the placenta, reaching that tissue via the metabolic process, it is stored there with the higher concentrations in the periphery and

TABLE 1
AVERAGES AND RANGES

SOURCE OF FLUORIDE	BLOOD (mcg. F/100 Ml.)	PLACENTA (mcg. F/100 Gm. Tissue)
Na_2PO_3F	Range: 4.7-131.6 Average: 26.85	Range: 18.6-340.8 Average: 107.8
CaF_2	Range: 23.2-90.4 Average: 44.8	Range: 37.2-197.6 Average: 109.1
NaF	Range: 4.4-225.6 Average: 32.68	Range: 26.4-784.0 Average: 149.2
CONTROLS	Range: 0.34-292.0 Average: 12.9	Range: 15.9-764.0 Average: 105.8

TABLE 2
FLUORIDE CONCENTRATION IN MCG. F/100 ML. IN CORD BLOOD

SOURCE OF FLUORIDE	NO. OF CASES	RANGE 0-10	10-25	25-50	50-75	75-100	100-150	150-200	200-400	OVER 400	
NaF	162	30	63	45	9	0*	9	0	6	0	Range: 4.4-225.6 Average: 32.68
CaF_2	100	0	29	41	8	22	0	0	0	0	Range: 23.2-90.4 Average: 44.8
Na_2PO_3F	99	21	39	12	13	13	1	0	0	0	Range: 4.7-131.6 Average: 26.85
CONTROLS	240	94	104	29	6	2	3	1	1	0	Range: 0.34-292.0 Average: 12.9
MORRISTOWN WATER	19	5	5	3	3	1	1	1	0	0	Range: 4.4-127.0 Average: 34.0
CONTROLS	9	2	3	3	1	0	0	0	0	0	Range: 8.4-38.2 Average: 24.7
WATER AUTOLYSED	6	1	1	3	1	0	0	0	0	0	Range: 5.9-45.9 Average: 28.8

that it passes the placental barrier to enter the foetal blood supply. From the foetal blood supply it enters into the enamel complex of the forming teeth, in a manner as yet not known.

The data presented in table IV shows the effects of prenatal fluoride ingestion as compared to the postnatal dietary flouride ingestion as well as the lack of it in controls. Shown is the effect on the dental caries incidence in 228 cases where the fluoride was ingested prenatally and postnatally, 162 cases where it was ingested prenatally but not postnatally, 282 cases where it was instituted at various starting ages as compared with 461 controls.

At seven years of age, dental caries is nonexistant in cases where the mother and child both ingested the supplement. At nine years of age, the deciduous dentition was afflicted with .2 def and the permanent dentition over 80% caries free. Incidentally, caries, when it appeared, involved posterior teeth only and either the occlusal or buccal surfaces. Rarely, in these cases have we observed compound cavities.

In those cases where the child had no supplemental fluoride postnatally, but did, prenatally, more caries occurred than in those who ingested it prenatally and postnatally, as can be seen in the table IV, but much less than in the controls.

The same picture is seen when the fluoride is administered postnatally, at various ages, but the earlier begun, the fewer the caries experience.

The question of the insolubility of CaF_2 is of interest. CaF_2 is 16 PPM soluble in water. That it dissociates is demonstrated by the fact the bone meal products and phosphates given in infant feedings cause dental fluorosis. My own children are so affected. We obtained gastric juice from six cases, maintained it at 37°C, added CaF_2 and analysed it. It was found that in gastric juice, with its low pH, that CaF_2 was 50 PPM soluble.

We have encountered a few cases of dental fluorosis, questionable to very mild, according to Dean & Arnolds' classification[8] in the per-

manent and deciduous dentition. As a result of this occurrence in the permanent dentition we do not give supplementary dietary fluoride to infants whose mothers ingested fluorides during pregnancy until the end of the 6th month of life. We have also reduced the dosage given to children up to the end of their second year of life to 0.5 mgm F/day. This has resulted in the elimination of the incidence of this affliction.

Within a period of six weeks after the institution of the fluoride tablet therapy, a noticeable elimination occurs of the materia alba attached to the teeth of the children. We advise that when the child is old enough to understand and cooperate that the tablet be dissolved in the mouth or chewed, thus giving a topical as well as systemic effect to the therapy.

One percent of our cases reacted adversely to the fluoride. By the use of placebos, it was definitely established that the fluoride and not the binder was the causative agent. These reactions, occurring in gravid women and in children of all ages in the study group affected the dermatologic, gastro-intestinal and neurological systems. Eczema, atopic dermatitis, urticaria, epigastric distress, emesis, and headache have all occurred with the use of fluoride and disappeared upon the use of placebo tablets, only to recur when the fluoride tablet was, unknowingly to the patient, given again. When adverse reactions occur, the therapy can be readily discontinued and the patient or parent advised of the fact that sensitivity exists and the element is to be avoided as much as possible.

With regular frequency, families with varied numbers of children are seen where the mother took a fluoride dietary supplement during pregnancies with some children and did not with others. The clinical findings are the same as shown in table IV.

The results of our study compared with the data in table V are readily observable. The prenatal value is readily discernable as well as is the benefit to be derived from early supplementation.

TABLE 3
FLUORIDE CONCENTRATION IN MCG. F/100 GM. IN PLACENTAL TISSUE

SOURCE OF FLUORIDE	NO. OF CASES	RANGE									
		0-10	10-25	25-50	50-75	75-100	100-150	150-200	200-400	OVER 400	
NaF	141	0	0	33	30	12	27	9	21	9	Range 26.4-784 Average 149.2
CaF_2	91	0	0	31	19	20	11	10	0	0	Range 37.2-197.6 Average 109.1
Na_2PO_3F	100	0	5	21	34	14	9	11	6	0	Range 18.6-340.8 Average 107.8
CONTROLS	251	1	22	74	67	29	17	20	16	5	Range 15.9-764 Average 105.8
MORRISTOWN WATER	19	0	0	5	6	4	1	2	1	0	Range 33.6-358 Average 90.7
CONTROLS	8	0	1	1	2	4	0	0	0	0	Range 15.9-91.6 Average 76.2
AUTOLYSED	6	0	1	3	1	1	0	0	0	0	Range 18.9-75.2 Average 39.5

TABLE 4-A

def and DMF RATES IN 618 STUDY CASES AS COMPARED WITH RATES FOUND IN 461 CONTROLS

NO. CASES	STARTING AGE	AVERAGE def and DMF AT AGES 3-12										
		3	4	5	6	7	8	9	10	11	12	
46	under 3	0 -	0 -	0 -	.04 0	.09 0	0.2 0	0.38 0.5	- 1.1	- 1.35	- 1.7	def/child DMF/child
39	3	0.1 -	0.14 -	0.2 -	0.2 0	0.25 0	0.27 0.2	0.5 0.7	- 1.2	- 1.5	- 1.8	def DMF
38	4	• -	0.45 -	0.47 -	0.44 0.1	0.66 0.21	0.91 0.29	1.03 0.36	- 1.8	- 2.0	- 2.4	def DMF
47	5	-	- -	1.2 -	1.33 0.4	1.54 1.0	0.99 1.0	1.09 1.4	- 1.9	- 2.49	- 2.6	def DMF
38	6	- -	- -	- -	2.1 .5	2.6 .8	2.9 1.2	2.7 1.7	- 2.2	- 2.5	- 2.65	def DMF
39	7	- -	- -	- -	- -	3.2 1.0	3.5 1.46	2.9 2.0	- 2.4	- 2.9	- 3.2	def DMF
35	8	- -	- -	- -	- -	- -	3.9 1.9	3.7 2.1	- 2.5	- 2.9	- 3.3	def DMF

TABLE 4-B

def and DMF RATES IN 618 STUDY CASES AS COMPARED WITH RATES FOUND IN 461 CONTROLS

	AVERAGE def and DMF AT AGES 3-12										
AGE:	3	4	5	6	7	8	9	10	11	12	
PRENATAL NOT POSTNATAL 162 CASES	0 -	0 -	0 -	0.2 0.1	0.5 0.9	1.0 1.3	1.5 1.7	0.5 2.0	0.3 2.6	0.3 2.9	def DMF
PRENATAL AND POSTNATAL 228 CASES	0 -	0 -	0 -	0 0	0 0	.09 0	.2 .12	.03 .19	.03 .24	.01 .38	def DMF
CONTROLS 461 CASES	33	29	39	51	49	49	54	52	46	59	
	2.	4.0	4.1	4.5	4.7	5.4	6.3	3.4	2.0	1.4	def
	3.	7.6	7.1	7.8	8.6	10.0	10.3	5.1	3.8	2.0	defs
	-	-		2.0	2.5	3.2	4.0	4.6	4.9	5.8	DMF
	-	-	-	2.0	3.5	3.8	6.4	7.0	7.2	9.4	DMFS

In prenatal cases, where the ingestion of dietary fluorides is begun during the first two trimesters of pregnancy, the favorable effect on the incidence of dental caries is quite evident; whereas when it is begun during the last trimester, the effects are not as pronounced.

This may be due to the fact that the element has not been in intimate association with the forming teeth to become a part of the calcifying structures that form early, and which are in the areas of more susceptibility to caries, normally the occlusal surfaces and contact points of the deciduous teeth and the beginnings of the occlusal surfaces of the 1st permanent molars.

Exfoliated teeth and teeth lost through accidents have been analysed for their fluorapatite contents. Those examined at Indiana University[9] have not demonstrated its presence. Reports on others sent out for analysis to determine the presence of fluorapatite have not, as yet, been received. Theoretically, calcium fluorapatite should be an end product of fluoride ingestion during the formative periods of amelogenesis. All methods for its determination that are available to Dr. Muhler have failed to reveal its presence in any of the specimens available from this study. Clinically, a visible difference in the appearance of the enamel is apparent. The teeth are opalescent, highly glistening somewhat like the inside of an oyster shell, with shallow, well fused grooves and fissures that resist to a marked degree the forces causing dental caries. It may be inferred that the fluoride influences the pituitary in a favorable manner since this gland is related to normal tooth morphology.[10]

Abortions have been examined microscopically for possible aberrations to the developing dental structures during embryonal and foetal development. None have shown any abnormalities.

Blood studies comparing the red blood count, white blood count and differential, hemaglobin, bleeding and clotting time have revealed no unusual effects or differences between study cases and controls in 250 examinations.

The mode of action by Fluoride on teeth is unknown. That benefits are derived from its ingestion during the period of tooth formation is quite evident. To attribute all of the benefits as shown in this study to it alone would be erroneous. Patients interested in the dental well being of their children utilize other measures, such as the reduction in refined sugar and carbohydrate intake, use of oral hygiene measures and regular visits to their dentists.

There being a delay in the eruption of the teeth, in some cases by as much as a year from the accepted eruption dates, this may be a factor in the lesser incidence of decay. The teeth delayed in eruption have the opportunity to mature more prior to becoming exposed to the forces that trigger the caries mechanism. Becks and Baume[11] and De Eds[13] report that fluoride is a thyroid inhibitor and that hypothyroidism delays the eruption of the teeth.[12, 13]

From the data reported in this paper and in reports by others, it is evident that much investigation is needed on the biological effects of ingested fluorides.

TABLE 5

MEAN NUMBER OF DMF AND def TEETH OF CHILDREN WHO INGESTED NaF TABLETS AND DATA REPORTED FROM OTHER STUDIES, AFTER TEN YEARS OF FLUORIDATION AND AFTER USE OF A NATURAL FLUORIDE WATER*

AGE GROUPS	NaF TABLETS		AURORA, ILLINOIS*		GRAND RAPIDS, MICHIGAN†				BRANTFORD, ONTARIO†	
					Base Line		10 yrs. of F			
	def ± SE	DMF ± SE	def	DMF	def	DMF	def	DMF	def	DMF
4- 5.....	1.2 ± 0.6	.....	2.7	.....	5.2	.....	2.5	.....	2.6	.....
6- 9.....	1.8 ± 0.4	0.6 ± 0.2	3.4	0.8	5.8	2.3	3.1	1.0	3.4	0.9
10-12.....	0.9 ± 0.3	2.2 ± 0.5	1.3	2.5	1.5	6.5	1.6	2.9	1.4	2.8
13-15.....	.....	4.5 ± 0.9‡	.....	3.8	.....	11.0	.....	6.7	.....	5.0

* Aurora = a natural fluoride water.
† Grand Rapids and Brantford = fluoridated water.
‡ Five of this group were caries-free.

SUMMARY

Data is presented showing that fluoride ingested by gravid women enters the maternal circulation, is stored in the placenta and passes through the placental barrier to enter the foetal blood supply.

Evidence is presented that the fluoride in the foetal blood supply affects the developing teeth to make them more resistant to dental caries.

No unusual effects have been observed on the blood pictures of children who ingested fluoride.

One percent of our cases presented evidence of undesirable side effects from fluoride therapy. It is pointed out that if a patient is affected by the fluoride, by this method, the allergen or intoxicant can be removed readily from

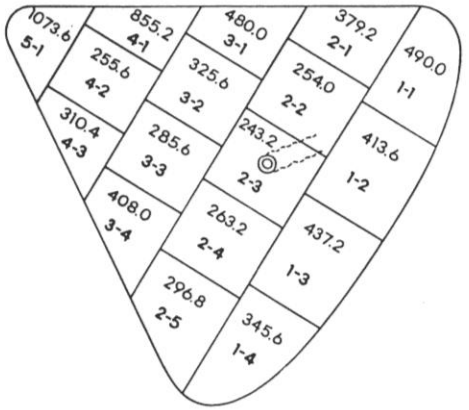
FIGURE III

WHOLE PLACENTAS

(Sodium Fluoride)

G.L., 12-19-53 ■ = mcg. F/100 Gm. tissue

■ = Code No. of tissue section



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Weight: 427.55 Gm.

Average: 418.6 mcg. F/100 Gm. placenta

the diet by discontinuance of the dietary supplement.

Beneficial results to the dentition are demonstrated. Dental fluorosis has been observed and eliminated by adjusting the dosage. Fluorides ingested during the first or second trimester of pregnancy produce benefits as seen in the incidence of dental caries, and have been found of no value if begun in the third trimester.

The mode of action of fluoride is unknown.

A delay in the eruption of the teeth occurs.

It is pointed out that much more study on the Biological effects of ingested Fluoride is necessary.

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