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FLUORINE CONTENT IN THE URINE AND SERUM OF HYDROFLUORIC ACID OPERATORS

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ABSTRACT

Studies were made on the usefulness of measuring the fluorine content in the urine and serum as an index for the health care of hydrofluoric acid operators in the electronic industry, particularly those working within exposure to relatively low concentrations.

The fluorine concentration values in the urine and serum of operators irregularly exposed to 1–3 ppm hydrofluoric acid in their working environment increased to 1.15 ± 0.59 ppm and 19 ± 12 ppb respectively, as compared with the normal values 0.72 ± 0.46 ppm and 12 ± 8 ppb respectively. However, in the evaluation of exposure to a relatively low concentration of hydrofluoric acid, the food-oriented effect of fluorine has to be considered. The authors have confirmed the effect in the subjects both statistically and experimentally.

Recently more industries have been using fluorides. This means that operators in such industries as aluminium smelter, phosphatic fertilizer and fluorine-oriented chemical industries are faced with greater risks of exposure to fluorides. Among various fluorides produced and used in fluorine-oriented chemical industries, hydrofluoric acid is an essential chemical compound. This material has a wide application in the washing of silicon. In fact, recent progress in the electronic industry shows a trend towards using increasing amounts of hydrofluoric acid for this purpose.

The authors have studied the significance of the amount of fluorine in the urine and serum as an index for the health care of operators working in hydrofluoric acid processes in the electronic industry, particularly with exposure to low concentrations of hydrofluoric acid.

Since the normal values of these biological fluids have not yet been established for the Japanese, particularly as regards the serum, the authors have clarified the values prior to taking measurements on hydrofluoric acid operators. Furthermore, since the Japanese are fond of green tea, black tea and marine products which contain a high amount of fluorine, the authors have taken into consideration the influence of fluorides in these foodstuffs on the normal values.

SUBJECTS AND METHODS

Measurements were made on about 300 male operators aged 16 to 59 (average 29 years) working with hydrofluoric acid for washing glass bulbs for TV picture tubes and etching semiconductors in a Japanese electronic industry. As a control group, 1500 operators working with non-hydrofluoric-acid--oriented processes were subjected to the measurements under the same conditions. The amount of fluorine in the urine and serum was measured for the operators on a fasting program and on a non-fasting program at different time intervals during the spring season (average temperature 25 °C). For measuring the amount of fluorine in the urine, spot urine was used, with a correction of the specific gravity to 1.024.

The influence of fluorine-containing food intake on the normal values was statistically observed in the control group. Additional observations were made on several normal volunteers who consumed tea and marine products containing much fluorine: subsequent variations in the amount of fluorine in their urine and serum were observed.

For measuring the amount of fluorine in the urine and serum, fluoride ion--specific electrodes as described below were employed: Fluoride ion--specific electrodes: Orion, Type 96–09, Matsushita, Type pF. IE 510102; reference electrode: Orion, Type 90–10; digital ion analyzer: Orion, digital pH meter, Type 701A; recorder: Shimadzu, Type R-12; total ion strength urinary buffer (TISUB, Neefus and co-workers[6] 1970); serous buffer; acetate buffer.

RESULTS

The time necessary for the stabilization of the electrode potential in the measurement of specimens was determined by means of the pattern in which the electrode analog signal had been recorded.

As shown in Figure 1, generally about three minutes and twelve minutes were necessary for the urine and serum, respectively.

The distribution of the amount of fluorine in the urine of the control group showed a skew as illustrated in Figure 2; the mode was 0.6 ppm and the range 0.05–2.8 ppm. In this case, by converting the fluorine concentration into a logarithm, it can be confirmed that it gives a logarithmic normal distribution as the shape of its distribution indicates. Similarly, the distribution of the fluorine concentration in the serum gave a mode of 12 ppb and a range of 3–135 ppb, with a trend towards a logarithmic normal distribution as shown in Figure 3.

Table 1 shows the fluorine concentration in the urine and serum specimens as statistically processed normal values. The arithmetic mean and S.D. of fluorine in the urine and serum were 0.72 ± 0.46 ppm and 12 ± 8 ppb, respectively. In this case, the geometric mean ± 3 S.D. showed a tendency towards good agreement with the range observed as was anticipated from the shape of distribution.

As shown in Figure 4, the relationship between age and the amount of fluorine in the urine showed a tendency towards a proportional increase with

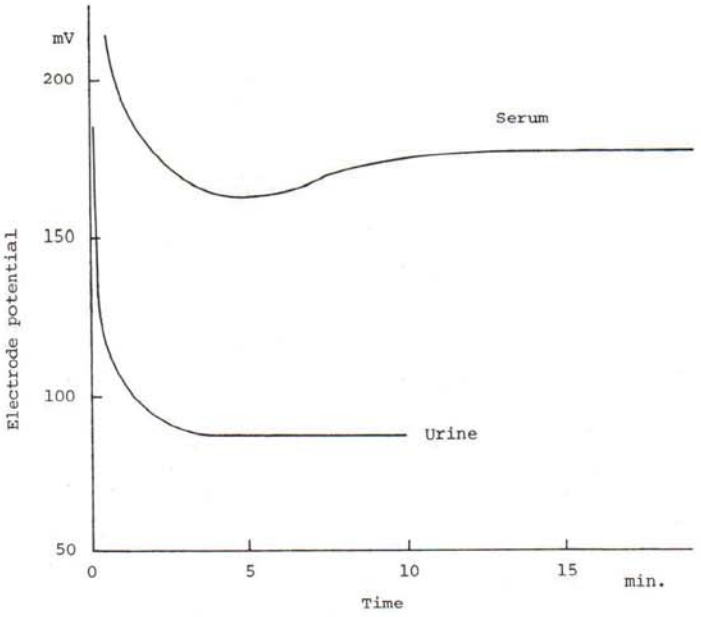

FIG. 1 – Electrode potential and stabilization time.

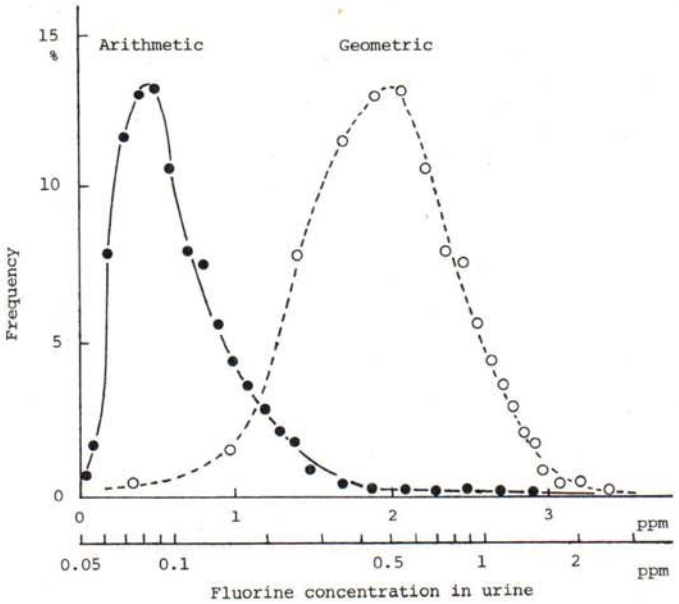

FIG. 2 – Arithmetic and geometric distribution of urinary fluoride.

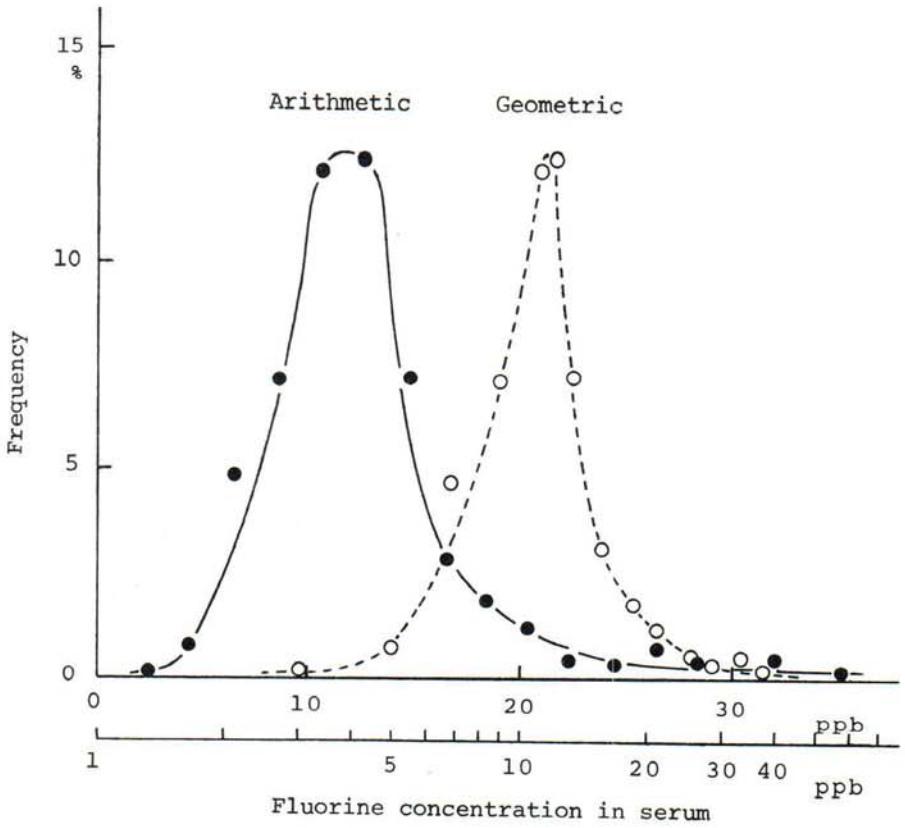

FIG. 3 – Arithmetic and geometric distribution of fluoride in serum.

TABLE 1
Fluoride ion levels in biological fluids as statistically processed normal values.

Sample	N	Calculation	Fluorine concentration in ppm			
			Mean	S.D.	Range estimated ± 3 S.D.	Range observed
Urine	1436	Arithmetic	0.72	0.46	0–2.10	0.04 –3.55
		Geometric	0.60		0.10–3.63	
Serum	2911	Arithmetic	0.012	0.008	0–0.036	0.003–0.240
		Geometric	0.011		0.003–0.044	

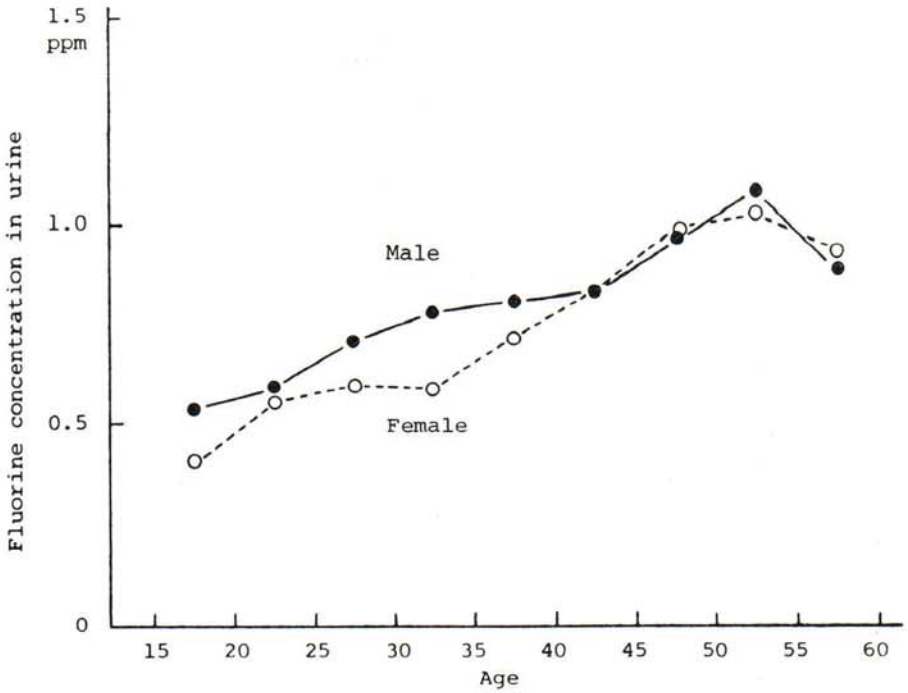

FIG. 4 – Relation between age and urinary fluoride levels.

increasing age. The regression equation expressing this relationship differed between the two sexes giving a slightly lower value for women as compared with men. The equations were for men ($N = 859$): $Y = 0.011\ X + 0.37$ and for women ($N = 577$) $Y = 0.015\ X + 0.17$ [Y = ppm fluorine, X = age in years (15–60)].

A similar trend was observed as regards the amount of fluorine in the serum. The proportional increase with increasing age was lower (about 60%) than that in the urine.

Investigations were made as regards variations in the amount of fluorine in the urine and serum, when foodstuffs containing much fluorine such as green tea, black tea or marine products were consumed. When green tea or black tea were taken for breakfast, the fluorine concentration in the urine after 2–4 hours increased as compared with the control group without tea intake; the difference was statistically significant (Table 2).

Figures 5 and 6 show the amount of fluorine in biological fluids as a function of time after intake when the volunteers took green tea, or black tea and oiled sardines. The analysis of the amount of fluorine in the foodstuffs, necessary for this experiment, was performed using a combination of Willard-Winter's steam distillation and the electrode method. Table 3 shows the result.

TABLE 2
Effect of tea intake on urinary level of fluoride ion.

Intake	Subjects	N	Concentration of fluoride (ppm) Mean ± S.D.
Fasting	Men	51	0.53 ± 0.22
	Women	18	0.50 ± 0.28
Breakfast without tea	Men	59	0.63 ± 0.27
	Women	23	0.59 ± 0.26
Breakfast with black tea	Men	65	1.09 ± 0.60
	Women	14	0.86 ± 0.41
Breakfast with green tea	Men	99	0.99 ± 0.51
	Women	26	0.97 ± 0.51

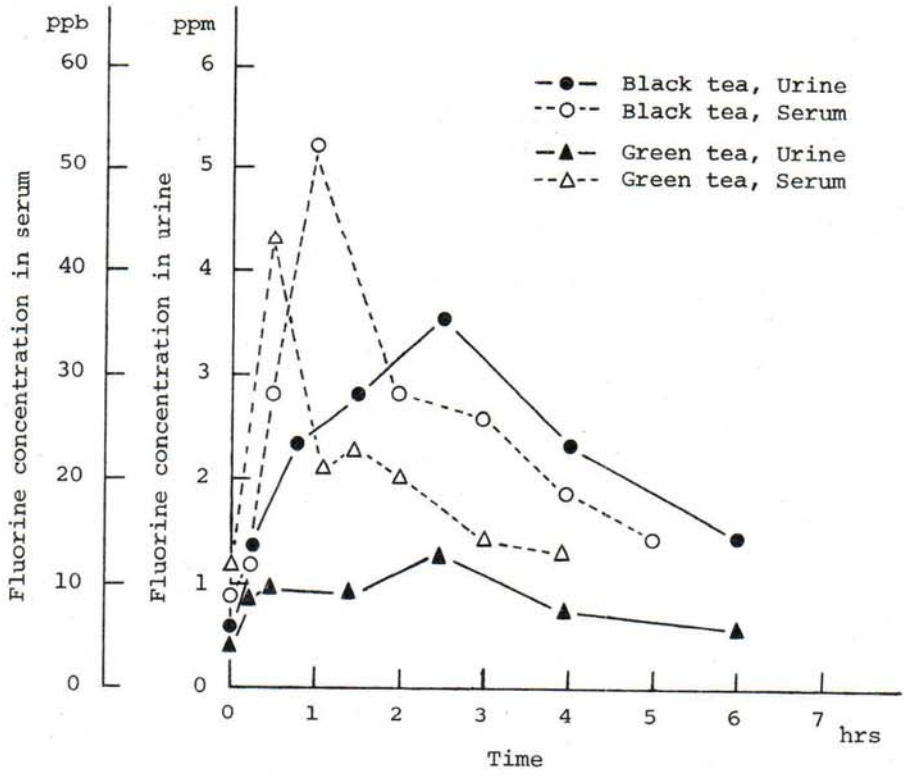

FIG. 5 – Effects of black tea (1.40 mg F) and green tea (0.23 mg F) intake on fluoride ion levels in biological fluids.

TABLE 3
Fluoride ion levels in food.

Food	N	Fluoride ion (ppm)	
		Mean	Range
Black tea (India, Ceylon) – infusion	5	2.00	1.42 – 2.37
Black tea (Tanzania) – infusion	1	4.75	
Black tea (tea bag) – infusion	5	1.08	1.02 – 1.19
Green tea (domestics) – infusion	5	1.51	0.74 – 2.77
Coffee – infusion	5	0.24	0.15 – 0.34
Coffee – instant	5	0.02	< 0.01 – 0.04
Milk	3	0.07	0.04 – 0.09
Grape fruit juice	3	0.02	0.02 – 0.03
Oiled sardine (with bone)	5	5.23	5.13 – 5.44
Salted salmon (fillets)	5	0.92	0.85 – 1.08
Sea bream (fillets)	3	1.24	1.00 – 1.66
Sea eel (with small bone)	3	3.43	3.29 – 3.64
Prawn	6	1.11	0.90 – 1.50
Beef	3	0.16	0.10 – 0.24
Pork	3	0.28	0.16 – 0.34

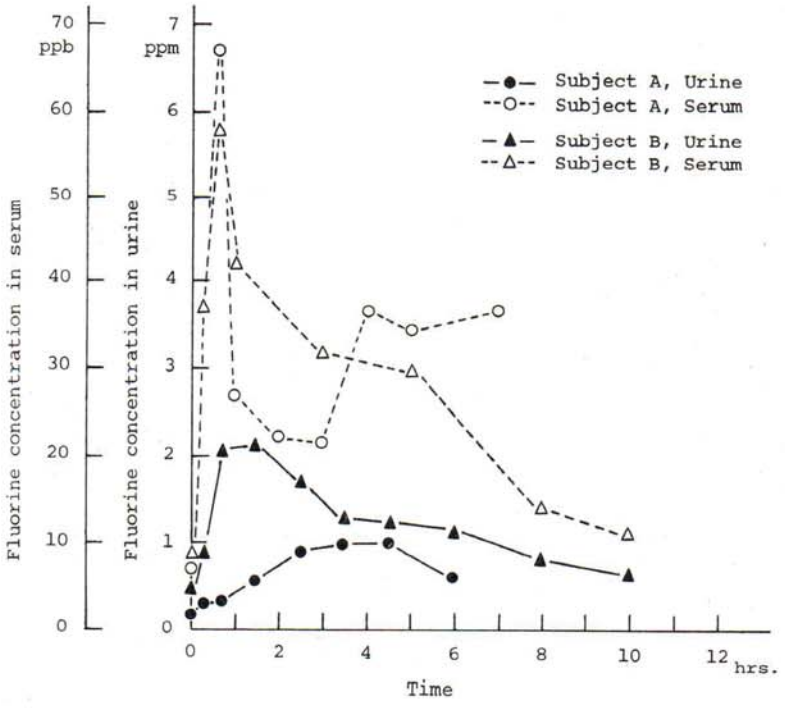

FIG. 6 – Effect of oiled sardine intake (0.52 mg F) on fluoride ion levels in biological fluids.

The intake of black tea produced a relatively sharp increase in the concentration of fluorine in the serum, reaching the maximum value after 0.5–1.0 hour. The fluorine concentration in the urine showed a relatively flatter curve, reaching the maximum value after 1–2 hours. In these cases, the amounts of fluorine in the serum and urine were 5.8 and 6.2 times higher when compared with the normal values. In the case of green tea intake, a similar trend was observed. Similar phenomena were observed in the case of the intake of oiled sardines, as an example of marine products.

The fluorine concentration in the serum largely varied within a short period of time after the intake of foodstuffs containing a high amount of fluorine. Therefore, an evaluation of exposure to environmental fluorides is to be performed, in some cases, in subjects on a fasting program under the condition of a limited intake of foodstuffs containing a high amount of fluorine.

TABLE 4
Fluoride ion levels in biological fluids of hydrofluoric acid operators.

Workers	Concentration of fluoride in:		
	Air (ppm)	Urine (ppm)	Serum (ppb)
TV picture tube bulb washing	3.0–0.3	1.15 ± 0.59*	19 ± 12
Semiconductor etching	under 0.2	0.76 ± 0.42**	
Control		0.72 ± 0.46	12 ± 8

* N = 82
**N = 196

The hydrofluoric acid operators were divided into two groups. One group consisted of operators washing TV picture tube bulbs; these operators were exposed irregularly (average 1–2 hours/day) to 1–3 ppm of hydrogen fluoride in the air. The other group consisted of operators doing semiconductor etching; these operators were exposed to a low concentration of hydrogen fluoride (below 0.2 ppm, average 4 hours/day).

In the case of these operators, the serum was tested under fasting program conditions, and the urine under non-fasting program conditions. The fluorine concentration values in the urine and serum of operators washing TV picture tube bulbs were 1.15 ± 0.59 ppm and 19 ± 12 ppb, respectively. In comparison with the control group, significant differences were observed. In the case of the semiconductor etching operators, the amount of fluorine in the urine was 0.76 ± 0.42 ppm; in comparison with normal subjects, no differences were observed (Table 4). These results varied depending on the time of the collection

of specimens. In other words, as compared with the work-starting time, an increase of about 100% in the value was observed within one day. However, no day-to-day or week-to-week variations were observed. In this case, the fact should be considered that the normal values also vary due to the influence of the food intake.

DISCUSSION

The fluorine ion-specific electrodes developed by Frant and Ross[2] have made the quantitative analysis of fluorine in biological fluids easier and quicker. Thus the quantitative analysis of fluorine in biological fluids by means of this method has become the standard practice for the evaluation of the influence of exposure to environmental fluorides.

Since many specimens have to be treated, it is important to know the stabilization of the electrode potential at an early stage for the sake of measurement accuracy and time-saving.

The stabilization time for each measurement should be determined by means of the recording method employed in the current studies, since the stabilization time is strongly influenced by the concentration in the preceding measurement.

The fluorine concentration in the urine of Japanese subjects obtained as a normal value was slightly higher than the result obtained by Zipkin[9], and as published by National Academy of Sciences[5]. Since water fluoridation is not practiced in Japan, it seems that this fact is due to the special characteristics of Japanese dietary habits. For fluorine concentration in the serum, a value of 10–70 ppb has been published[3,4,7,8]. As in the case of urine, this value is influenced by dietary habits and the time of the collection of specimens. The results obtained by the current studies seem to come nearest to the values of Husdan and co-workers[3].

The intake of tea and marine products having bones or shells which contain much fluorine obviously influences the fluorine concentration levels in biological fluids. Therefore, when judging the effect of environmental fluorides of relatively low concentrations on the living body as in the current studies, it is desirable to make the evaluation under the condition of a limited intake of these foodstuffs or on a fasting program.

In the exposure to environmental hydrofluoric acid of low concentration, the fluorine concentration in the urine and serum reflected well its average exposure. This means that even in the case when the exposure time and the concentration of environmental fluorides are irregular, with variations as in the current studies, testing the amount of fluorine in biological fluids is considered to be an appropriate means for evaluating the status of exposure. However, the collection of the serum and the measurement of the fluorine concentration in the serum are often much more difficult to carry out than in the case of urine. For this reason it is considered possible to evaluate the influence of environmental fluorides as routine work by measuring only the fluorine content in the urine. In the meantime, as Carlson's work suggests[1], it seems that the level of fluorine

concentration in the serum varies as a result of a long-term load. Thus it may be stated that the fluorine concentration in the serum could possibly serve as an index for the prevention of chronic fluorine poisoning.

The effect of exposure to a relatively low concentration of hydrofluoric acid can be monitored by determining the fluorine concentration in the urine and serum, making adjustments for the influence of the food intake. However, fluorine concentration in the serum is very low, while the cellection of samples often proves difficult.

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