BIOLOGICAL MODEL FOR CHARACTERIZATION OF FLUORINE TOXICOKINETICS

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One of the basic criteria with hygienic-toxicological characterization of a given production presents the determination of the degree of exposition. According to Shedivetz (1978), exposition tests are based on determination of alien substances in biological media in order to assure harmless labour-hygienic conditions for the workers and prevention of occupational intoxications. Spasovski et al. (1980) define biologically utmost permitted concentrations those quantities of toxic substances in biological media which correlate to utmost permitted concentrations in the air of the working medium.

However, we could not find any data clarifying the kinetics of urinary fluorine elimination in case of hydrogen fluoride exposition (HF) within hygienic permitted levels in the literature available. That is why we decided to carry out toxicokinetic investigations of volunteers exposed to HF at the levle of utmost permitted concentrations.

Material and methods

Five individuals (volunteers) were placed in a special chamber to be exposed to HF within the Bulgarian utmost permitted concentration (1 mg/m^3) for 8 hours. HF was obtained after the reaction between chemically pure ammonium fluoride and sulphur acid (96 per cent). HF was stored in polyethylene banks of 1 l and introduced into the chamber by a plastic pipe by means of liquid paraffin at different speed: between 120 and 600 cm^3/h. Parallelly to air HF level estimation, fluoride concentrations in 6-hour urine as well as in 2-hour sample (during the last two hours of 8-hour exposition) for 5 successive days and after a 64-hour rest were measured. 6-hour diuresis was also measured. All the results from urinary fluorine analysis were then corrected according to: specific urine weight, creatinine, body weight and height of volunteers, and minute pulmonary ventilation (MPV). Analogous examinations were performed of a control group of individuals without occupational contact with fluorine.

Potentiometric methods with fluorine-sensitive electrode «Radelkis» were used to determine the concentrations of air HF and of urinary fluorine (3, 4). Data obtained were processesd by the methods of variation and correlation analyses.

Results and discussion

Table 1 shows that mean HF concentrations in the air of the chamber vary between 0.90 and 1.05 mg/m³ during the experiment and thus correspond to the level of HF and fluorine compounds in the air of the occupational medium approved in Bulgaria (i. e. of 1 mg/m³) when between 10 and 14 samples were

Table 1

Mean HF concentrations in the air of the chamber

Days	Samples n	Mean HF concentration in mg/m³	Standard deviation S	Variation coefficient V%
I[st]	14	0.90	0.19	19.8
II[nd]	12	1.01	0.21	20.8
III[rd]	11	1.04	0.16	15.3
IV[th]	13	1.05	0.14	13.4
V[th]	10	0.99	0.16	16.0

daily taken. Variation coefficients are below 30 per cent, i. e. in concordanc with the requirements of the Bulgarian State Standard No 12430—74 (1).

Data demonstrate that in the experimental chamber conditions for HF exposition of volunteers at the level of utmost permitted concentrations have been created, indeed.

Our results obtained indicate an outlined tendency towards urinary fluorine content increase during the experiment not only for the first 6 hours but also for the last two hours of the whole 8-hour exposition reaching maximal levels at the end of the trial — at the average of 0.0085 mmol for 6 h and of 0.0041 mmol for 2 h (fig. 1). Higher urinary fluorine levels are due to its accumulation in the organism in the course of exposition for every successive day. (We have previously established that fluorine accumulation in the organism varies from 5.3 per cent at the beginning up to 42.1 per cent at the end of the experiment). In comparison with the data from the control group analysis it is found out that there is a statistically significant increase of fluorine eliminated by urine when both intervals are concerned ($p < 0.05$).

Concerning the speed of urinary fluorine elimination it is to be noted that this speed is greater for the last 2 hours than that for the first 6 ones (fig. 2). It stresses that elimination speed increases during the five experimental days reaching maximal levels at the end of the assay — at the average of $1.42 \cdot 10^{-3}$ mmol/h for the first 6 hours and $2.05 \cdot 10^{-3}$ mmol/h for the last 2 ones. It can be assumed that excretion acceleration within the last 2 hours as well as during the experiment as a whole is directed towards liberation from the organism of fluorine accumulated in the course of exposition. Fluorine elimination rate is statistically significantly higher ($p < 0.05$) than that of the persons of the control group.

On fig. 3 different kinds of corrections (a total of 7 ones) of urinary fluorine content are presented. Regression lines restrict the area where 95 per cent of the results obtained can be found. According to Shedivetz (1978) the smaller the angle between regression lines determining the limit of 95 per cent reliability of the results, the greater the accuracy of exposition test. Angle dimension depends mainly on the kind of the units representing the toxic substance in the biological material.

It is evident that result presentation in mmol/dm³ causes the greatest dispersing and that the unit mmol/ventilation is the most appropriate one because

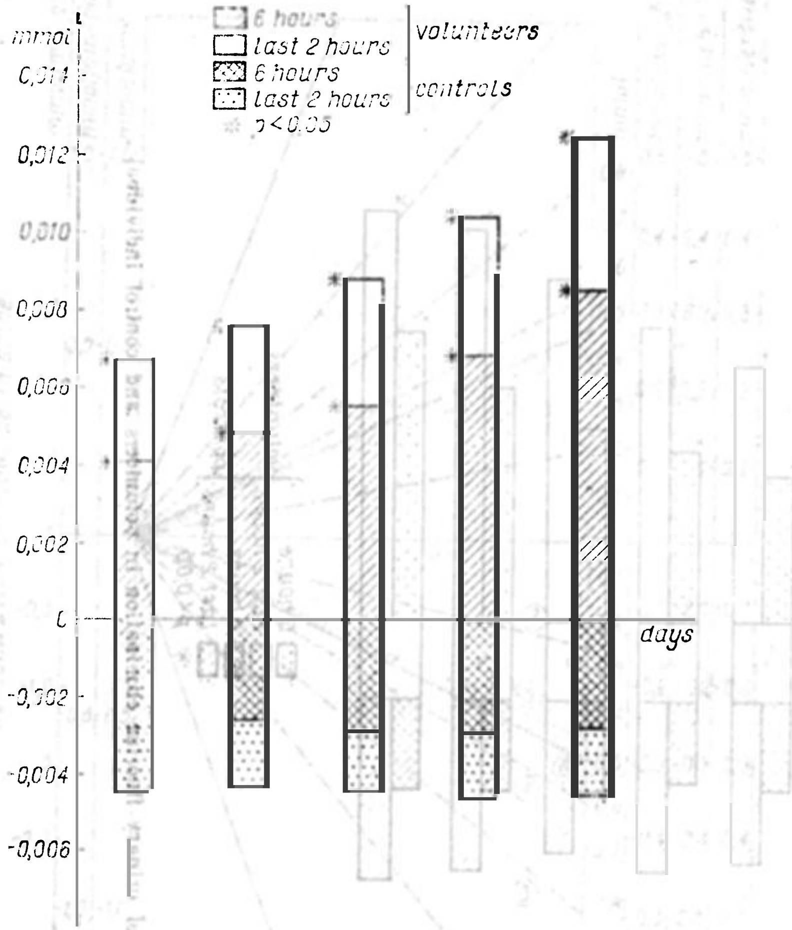

Fig. 1. Urinary fluorine concentration in volunteers and control individuals.

the angle between regression lines is the smallest one. The usage of the units: mmol/kg and mmol/height—100, i. e. correction accoring to the so-called ideal body weight of volunteers leads also to very good results.

As previously reported, in investigations of workers the unit mmol/ventilation is replaced by mmol/vital capacity (VC) (fig. 4). On this figure one can see that this unit is appropriate to presentation of the results from urinary fluorine analyses, too, as the angle between lines is the smallest one.

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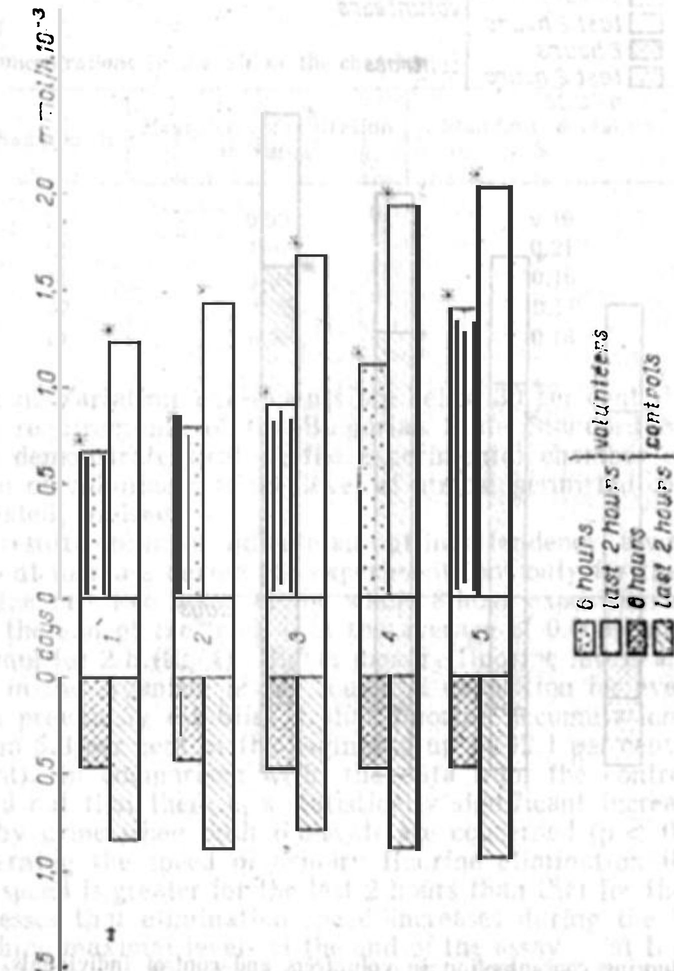

Fig. 2. Speed of urinary fluorine elimination in volunteers and control individuals.

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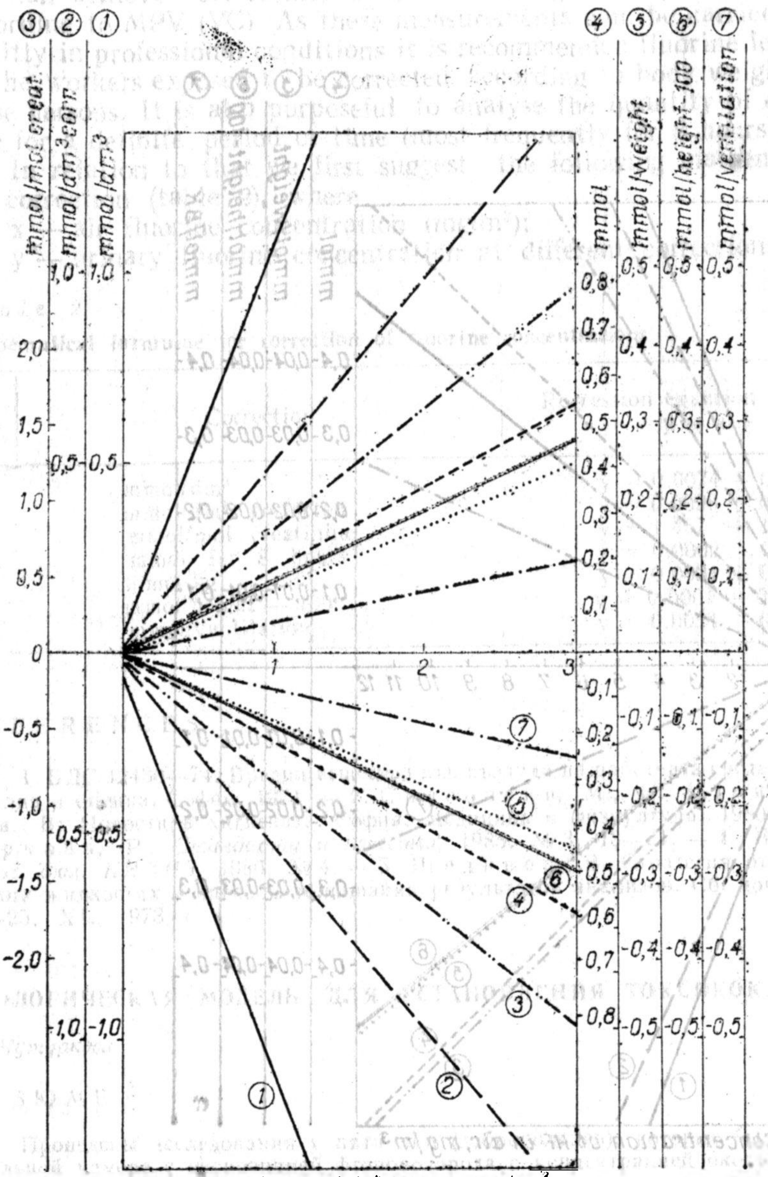

Fig. 3. Corrections for urinary fluorine concentration in volunteers.

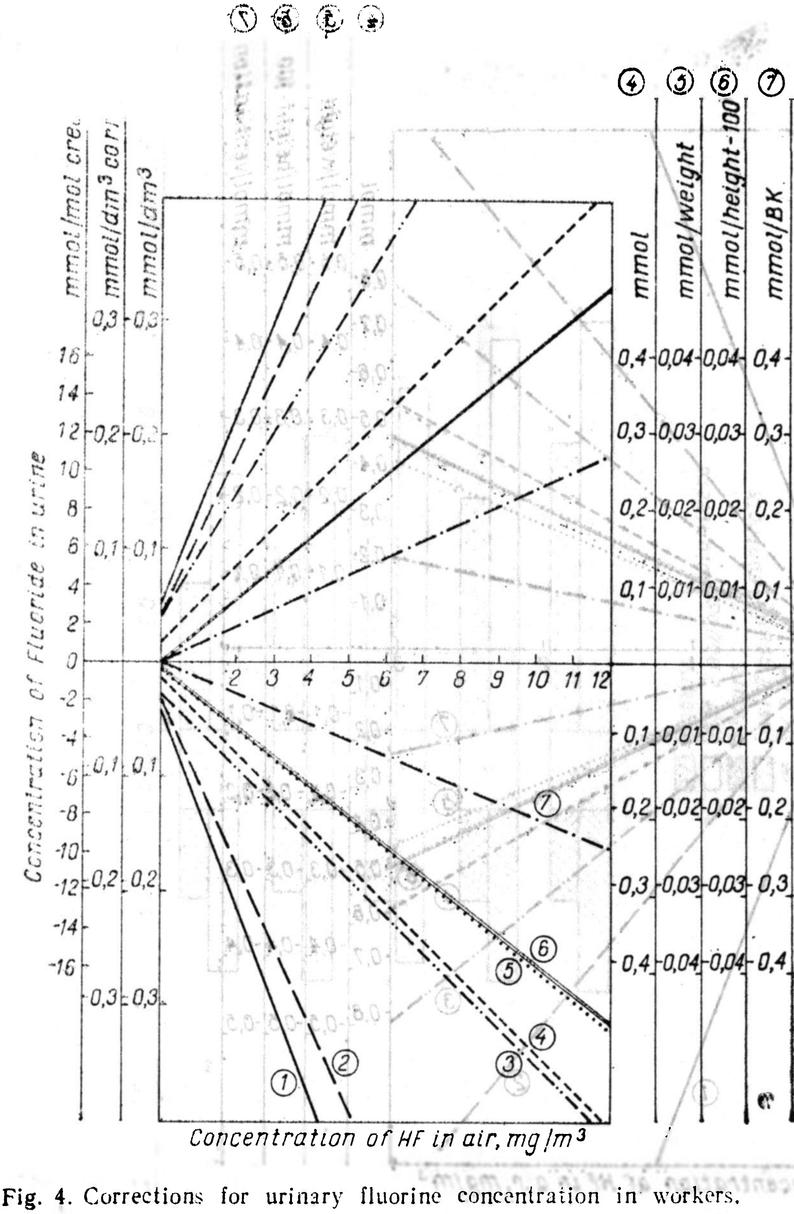

Fig. 4. Corrections for urinary fluorine concentration in workers.

lation of eliminated fluorine is clarified for the first time. It is proved that one can achieve best results when correcting urinary fluorine concentration according to MPV (VC). As these measurements can be carried out rather difficultly in professional conditions it is recommended fluorine levels in the urine of the workers exposed to be corrected according to body weight and height of these persons. It is also purposeful to analyse the quantity of eliminated fluorine for a definite period of time (most frequently for 8 hours).

In relation to that we first suggest the following mathematical formulae for correction (table 2), where

x — air fluorine concentration (mg/m^3);

y — urinary fluorine concentration at different corrections.

Table 2

Mathematical formulae for correction of fluorine concentrations

No.	Correction	Regression equation general formula: $y = a + b . x$
1.	mmol/dm^3	$y = 0.0074 + 0.0242 . x$
2.	mmol/dm^3 corrected	$y = 0.0098 + 0.0267 . x$
3.	mmol/mol creatinine	$y = 1.457 + 1.874 . x$
4.	mmol for 8 hours	$y = 0.0062 + 0.074 . x$
5.	mmol/kg	$y = 0.0001 + 0.0001 . x$
6.	mmol/height — 100	$y = 0.0001 + 0.0001 . x$
7.	mmol/ventilation	$y = 0.0024 + 0.0019 . x$

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БИОЛОГИЧЕСКАЯ МОДЕЛЬ ДЛЯ УСТАНОВЛЕНИЯ ТОКСИКОКИНЕТИКИ ФТОРА

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РЕЗЮМЕ

Проведены исследования у пяти лиц (добровольцев), которые были помещены в специальной камере с экспозицией фтороводорода с концентрацией около болгарской ПДК (1 mg/m^3). Параллельно с определением концентрации фтороводорода в воздухе, измерялось содержание фторидов в моче: на шестой час с начала экспозиции, последние два часа и в восьмичасовой моче в течение пяти последовательных дней. Результаты корригировались по: стандартному удельному весу мочи, креатинину весу тела и росту добровольцев и минутной легочной вентиляции. Для определения концентрации ионов фтора в моче и в воздухе использовались потенциометрические методы с фтор-селективным электродом.

Установлена повышенная скорость элиминирования фтора с мочой в последние 2 часа по сравнению с стоимостями, установленными на шестой час, а также по сравнению со стоимостями в течение пятидневного эксперимента. Данные относительно корреляции содержания фтора в моче показывают, что рассеивание в наиболее ниской степени получается при корригировании минутной легочной вентиляции.