Effect of different exposure compounds on urinary kinetics of aluminium and fluoride in industrially exposed workers

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Abstract

Objective—To conduct a field study to obtain information on the urinary concentrations of aluminium (Al) and fluoride (F⁻) depending on the different compounds exposed to in the aluminium industry.

Methods—16 workers from one plant that produced aluminium fluoride (AlF₃), and from two plants that produced aluminium electrolytically by two different processes participated in the study for one working week. Pollutants were monitored by eight hour personal sampling every day, and urine samples were collected during the week. Al and F⁻ were analysed in both atmospheric and urine samples by atomic absorption spectrometry and an ion selective electrode.

Results—The principal results show different characteristics of kinetic curves of Al and F⁻ excretion in workers with different exposures. Some characteristics of excretory peaks were linked to specific exposures—for instance, after exposure to AlF₃ there was one delayed Al peak associated with one delayed F⁻ peak about eight hours after the end of the daily shift, and after mixed exposure to HF and AlF₃, two F⁻ peaks were noted, one fast peak at the end of the shift and another delayed peak at 10 hours synchronised with an Al peak. In one of the electrolysis plants, the exposure to Al and F⁻ compounds led to the simultaneous excretion of Al and F⁻ peaks, either as a single peak or two individual ones depending on the type of technology used on site (open or enclosed potlines). The average estimated half life of Al was 7.5 hours, and of F⁻ about nine hours. Quantitative relations between excretion and exposure showed an association between the F⁻ atmospheric limit value of 2.5 mg/m³ with a urinary F⁻ concentration of 6.4 mg/g creatinine at the end of the shift, a peak of 7.4 mg/g creatinine, and 7.4 mg excreted a day. For Al, the exposure to 1.36 mg/m³ during the shift corresponded to a urinary concentration at the end of the shift of 200 µg/g creatinine. Daily excretion of 200 µg corresponded to an exposure to 0.28 mg/m³.

Conclusion—Particular differences in the behaviour of Al and F⁻ in urine depended upon the original molecular form in the pollutant. These results reinforce the principle that, in biological monitoring, the sampling strategy and the choice of

limit value should be dependent on kinetic data that take the exposure compound of the element in question into account.

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Aluminium (Al) is one of the most common elements and was long considered to be harmless. Recently, considerable toxic effects of aluminium have been found. Increasing research has been directed towards understanding diseases occurring in patients with impaired renal function on long term haemodialysis.¹ It was recognised that the main pathology, dialytic encephalopathy, was caused by the use of solutions containing Al.^{2,3} Other studies examined its toxic effects on bone and mineral metabolism.⁴

Exposure to Al, and metal compounds containing Al is common in metal and metal processing industries. Certain studies on the health of workers in the Al production industry have identified several adverse effects. Some of these are related to exposure to fluoride (F⁻), but pulmonary diseases (fibrosis)^{5,8} and suspected neurological disorders^{9,10} were also reported.

Occupational exposure to dusts containing Al can increase intake through the respiratory tract. In workers thus exposed, increased Al concentrations were found in serum and urine.¹¹⁻¹⁶ Few studies have been carried out on the biological monitoring of workers exposed to Al.¹¹⁻¹⁷ One reason for this is the difficulty inherent in the analysis of Al. Also, recent interest in the toxicology of Al has focused on Al soluble in water.

The biological monitoring of F⁻ has been studied in greater depth.¹⁸⁻²⁵

The purpose of our study was to investigate the relation between occupational exposure and the variations of Al and F⁻ concentrations in the urine of exposed workers. The survey was conducted in the French aluminium industry among workers exposed to different Al compounds varying both chemically and in occupational exposure characteristics.

Subjects and methods

POPULATIONS AND OCCUPATIONAL EXPOSURES
The study was carried out on 16 male workers exposed to Al compounds in two different industrial processes:

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(1) Production of aluminium fluoride (AlF_3) in plant A was with a dry process that used alumina (Al_2O_3) and hydrofluoric acid (HF). Two workers (A_1 and A_2) were followed up. A_1 was 28 years old and had been mainly exposed to AlF_3 dust for two months while working in the bagging section of the plant. A_2 was 37 years old and had been exposed to AlF_3 , HF, and Al_2O_3 for 14 years while involved in the production of AlF_3 . These two volunteers worked eight hours a day (5 00 am to 1 00 pm) for five days after two days rest.

(2) Electrolytic production of Al occurred in two selected plants (B and C), and the workers studied were located in the potroom where alumina is reduced to Al by electrolysis with cells connected in series called potlines. Prebaked anodes were used. Workers were exposed to a mixture of pollutants, mainly compounds with Al and F identified as: NaAlF_4 , Na_2AlF_5 , NaF, $\text{Na}_2\text{Al}_2\text{F}_8$, HF, Al_2O_3 , AlF_3 , and Na_3AlF_6 .

In plant B, where potlines were enclosed and equipped with a pot fume collection, nine potroom workers were followed up. Five of them (aged 34, 41, 35, 32, and 35 years with exposure durations of 9, 13, 9, 7, and 20 years, respectively) worked an eight hour shift (5 00 am to 1 00 pm) for three days after two days rest. The four other workers (aged 45, 31, 28, and 46; durations of exposure 11, 7, 3, and 19 years, respectively) worked a shift of eight hours (1 00 pm to 9 00 pm) for three days after two days rest.

In plant C, where the potlines were open, five workers in the potroom participated in the study (aged: 40, 57, 44, 49, and 46 years with exposures of 9, 10, 8, 1, and 14 years, respectively). They worked eight hours a day (1 00 pm to 9 00 pm) for four days after two days rest.

Each volunteer was informed of the purpose of the study and was supposed to be representative of Al exposure in each type of task. This was confirmed by the occupational physician and the technical staff of each plant.

The home tap water of each worker was analysed. In plant A, the mean (range) Al content of the volunteers' home tap water was 54 (10 to 92) $\mu\text{g/l}$. The concentration of Al in the factory water was 34 $\mu\text{g/l}$. In plant B, Al concentrations of home tap water was 15 (6 to 20) $\mu\text{g/l}$. The concentration of Al in the plant water was 33 $\mu\text{g/l}$. In plant C, the concentration of Al in home tap water was 18 (9 to 22) $\mu\text{g/l}$ and in the Al plant was 17 $\mu\text{g/l}$.

AIR SAMPLES

Airborne particulate sampling was performed on quartz microfibre filters (Whatman QM-A, diameter 37 mm) in Millipore filter holders. The cassettes were clipped to the collar of the work clothes, near the breathing zone of the subjects. Sampling was continued for the entire duration of a shift, divided into two periods if possible when dust pollution was significant. Membrane filter pumps (Dupont model P2500) were used at a flow rate of 1 l/min. The filter holders were in closed face configuration allowing the selective sampling of inspirable particles.

In the case of exposure to fluoride (in the production of AlF_3 and in electrolytic production of Al) both particulate and gaseous F^- compounds were collected with 37 mm closed face filter holders (Millipore) containing one DM800 metricel membrane (Gelman) for particles, and one Na_2CO_3 impregnated paper filter (Durieux) for gas.

ANALYSIS OF AIR SAMPLES

The reagents used for analysis of Al were 65% nitric acid (RP Normapur Prolabo), 40% HF (Prolabo, Merck), and Al (1 g/l titrisol (Merck)). The aluminium content of the samples was analysed by the method developed by the French National Research and Institut for Occupational Health (INRS)^{26, 27} which takes into account particles deposited both on the filter and on the inner walls of the filter holder. The soluble fraction was obtained by dissolving the dusts in 10 ml of distilled water inside the holder. After mechanical stirring for 30 minutes, the solution was filtered through the quartz fibre filter and diluted to 20 ml. To determine the insoluble fraction, HF (3 ml) and nitric acid (2 ml) were added directly to the cassette to dissolve both filter and particles. The solution was then diluted to 20 ml. Both soluble and insoluble fractions of Al were evaluated with DCP-OES (direct current plasma—optical emission spectrometry) with a Spectrametrics Spectraspan III B, at 396.1 nm. Standards were prepared from Al (1.0 g/l) titrisol grade solution (Merck). The matrices of the standards and the samples were matched.

For analysis of gaseous F^- , the impregnated filter was leached with distilled water, an equivalent volume of total ionic strength adjustment buffer (TISAB/ORION) was added to the solution, and the F^- concentration was measured with an Orion selective electrode (94-09). For analysis of particulate F^- , the membrane was heated in an Na_2CO_3 mixture to dissolve the insoluble particles. After cooling, the mixture was dissolved in distilled water and the solution was filtered after precipitation of interfering ions. The F^- content of the solution was determined by the same method as used for gaseous F^- .

URINE SAMPLES

For each subject, 24 hour urine was collected with generally six samples a day for four to seven days. Sample times were chosen to collect urine just before the shift, at midshift, and at the end of the shift. The other samples were taken at subjects' homes with an attempt to keep the sampling intervals as regularly spaced as possible. Collection started at home on the morning of the first day before work and was continued until after the last day of the two day rest period.

During the working day, samples were collected at the electrolysis plant and at the AlF_3 production site only after the workers had taken a shower. In the third plant, sampling was performed in a clean room without work clothes and after hands had been washed.

Urine was collected in polyethylene bottles

(500 ml). Bottles, caps, and seals were carefully cleaned beforehand in acid and rinsed with distilled water. Collection time was noted, specific gravity, temperature, and volume were measured. One sample was preserved for the assessment of creatinine. Nitric acid was added to the sample used in the analysis of Al (65% Suprapure Merck equivalent to 1% of the sample volume) and the solution was stored at -20°C until analysis.

ANALYSIS OF URINARY CREATININE

Creatinine concentration was measured by photometry (test, combination creatinine, Boehringer) on a Cobas-Bio analyser (Roche).

ANALYSIS OF URINARY Al

The main analytical difficulties in the measurement of Al concentrations were potential problems of contamination during urine sampling, transport, storage, and sample treatment. Sampling and sample preparation were therefore performed under strictly controlled conditions. Clean receptacles and tested reagents were used. Analytical procedures required a quality control scheme.

Urinary Al concentration was evaluated by electrothermal atomic absorption spectrometry with a Perkin Elmer 3030/Zeeman device, equipped with an HGA 600 furnace and an AS 60 autosampler. Analysis was performed with pyrolytic graphite tubes at 309.3 nm by a direct method derived from Oster.²⁸

The urine sample was diluted (1/5) with an original diluent (Triton X 100 (0.5%), HNO_3 (0.02 M), and EDTA (0.5%)). Standard addition was used for calibration. The detection limit calculated (by the formula: mean blank value + 3 SDs) with results from three months was $3.8 \mu\text{g/l}$.

The between run coefficient of variation varied routinely by 4.2% over three months at

a concentration of $80 \mu\text{g/l}$. Quality control samples provided by Nymcomed (Oslo, Norway batch 108) were included in each analytical series. The external quality control was performed by participating in the French inter-laboratory quality control programme for aluminium in dialysis fluids. Urinary Al and F^- concentrations were expressed per g creatinine. Only samples containing between 0.5 and 3.0 g creatinine/l were taken into account for correction of urinary results.

ANALYSIS OF URINARY F

In the case of coexposure to F^- compounds (gas or dust), the F^- concentration was determined just after collection in fresh urine at room temperature by means of a selective ion electrode (Orion 94-09), with the analytical technique described by Tusl.²⁹

The external quality control was assumed by participating to an international programme between laboratories (Centre de Toxicologie Québec).

STATISTICAL ANALYSIS

Version IV of the Statgraphics computer software package (Manugistics) was used for descriptive statistics and estimation of linear regression models.

Half lives of Al and F^- in urine were estimated by graphic analysis of decreasing rates v time.³⁰

Results

To clarify the presentation and to avoid a loss of information, only individual kinetics curves are shown here.

EXPOSURE TO AlF_3

Figure 1 shows the urinary Al and F^- concentrations /g creatinine plotted against time (each point is located at the time when urine was sampled). It corresponds to a subject (A_1)

Figure 1 Atmospheric and urinary Al and F^- concentrations in worker A_1 (bagging worker in AlF_3 production). Air concentrations of Al and F^- correspond to the soluble part.

who regularly bagged AlF_3 powder in the AlF_3 production plant (A). The only modification of his task was the additional bagging of cryolite (Na_3AlF_6) on the Thursday shift.

The urinary concentrations of Al from individual workers showed a daily rhythm: each day shift was followed by an increase in urinary Al excretion with maximal concentration at a regular interval after the end of exposure. The Thursday peak was higher, which seemed to be related to the exposure to cryolite.

It seems that the kinetics of urinary F^- and Al were similar each day, with synchronisation of peaks. Surprisingly, the highest daily F^- concentration was not at the end of the exposure time, as would be expected. This finding is even more surprising when one considers that the subject's workload was more intensive at the beginning of his shift. The effective end of the work (jobbing work) did not correspond to the official end of the shift.

The Thursday peaks with a shorter delay showed a relative difference in the Al/ F^- ratio attributed to the handling of cryolite.

EXPOSURE TO HF AND AlF_3

In the case of simultaneous exposure to HF and AlF_3 during production of AlF_3 (subject A_2) the F^- curve had a double peak each day (fig 2). One started during the shift and peaked at the end of exposure, the other one peaked after a delay of about 10 hours. The second peak was narrower than the first, and was located on its decreasing slope. The corresponding results of each day's personal air samples are shown on the same graph. The pollution consisted of gaseous HF, and particulate AlF_3 . The ratio between gaseous and particulate varied from day to day.

The urinary Al concentrations for Tuesday, Wednesday, Thursday, and Friday, showed a single peak at about the same time after the end of exposure as occurred in volunteer A_1 exposed to AlF_3 . It was found that the Al peak

corresponded exactly to the second daily peak for F^- .

The difference in the exposures between the two workers was the exposure to HF of volunteer A_2 . It is possible that the first F^- peak corresponded to the excretion of F^- coming from HF and the second one from AlF_3 . This result reinforced the hypothesis of a linkage between the exposure to particulate F^- from AlF_3 and the existence of a second F^- peak.

The volunteer A_2 worked throughout the whole shift, unlike A_1 who accomplished his task rapidly in the first half of the shift. The delay between the end of the time of exposure and the end of the normal shift could be four hours. This delay could explain the different positions of the Al peaks in A_2 and A_1 , which were different by one urine sample.

EXPOSURE TO POTROOM POLLUTANTS

Figure 3 shows the curves of urinary Al and F^- in the aluminium smelters of plant B and C.

In plant B, with enclosed potlines, nine workers were followed up. The curves of all nine workers show the same characteristics. Figure 3 shows the curves of two of these workers (B_1 and B_2). They show a single Al and F^- peak daily, at about the time of the sample taken after the shift, or in the next sample. The position of these peaks close to the end of the daily exposure was not consistent with the previous results in several ways: both Al and F^- curves were synchronous; their peaks were close to the end of the shift; the Al peaks were not positioned as in the case of exposure to AlF_3 (figs 1 and 2); the F^- peak seemed to correspond to that of exposure to HF.

In plant C, with open potlines, urinary excretion of Al and F^- seemed slightly different (fig 4, workers C_1 and C_2). It was possible to discriminate a broad peak for Al that corresponded to a broad peak for F^- every day. The wide peak could have been the combination of

Figure 2 Atmospheric and urinary Al and F^- concentrations in worker A_2 (in AlF_3 production). Air concentrations of Al and F^- correspond to the soluble part.

Figure 3 Atmospheric and urinary Al and F concentrations in potroom workers (plant B enclosed potlines). (A) worker B₁, (B) worker B₂. Air concentrations of Al and F correspond to the soluble part. No atmospheric F data on Sunday and Monday were available.

Figure 4 Atmospheric and urinary Al and F concentrations in potroom workers (plant C open potlines). (A) worker C₁, (B) worker C₂. Air concentrations of Al and F correspond to the soluble part.

two peaks. We found that the second peaks of both Al and F⁻ occurred at a sampling time after the end of exposure as in the case of exposure to AlF₃ (fig 1). The positions of the first daily Al and F⁻ peaks (fig 4) were similar to those of F⁻ and Al for potroom exposure in the aluminium production plant B (fig 3).

Technological differences existed between plants B and C. In plant B, the important air pollutants were collected from enclosed potlines, and the atmospheric concentrations of AlF₃ and Al₂O₃, which were fed automatically into the cell bath, were not very high. Enclosed potlines and automatic feeding could account for the discrepancies in the air pollutants and in their biological behaviour between the subjects in plants B and C. An example of this type of biologically different response was found between workers C₁ and C₂ (fig 4). Worker C₂'s job was performed in the potroom, but he was less exposed to dust because he did not do exactly the same task as C₁. Worker C₁ often restored the surface of the electrolytic bath for a series of potlines by sweeping away the bath powder found on the floor around the cells. This operation was more dusty. The curves for Al and F⁻ for worker C₂ (fig 4) showed a main daily peak for both elements; only a slight, but systematic deformation in the decreasing slopes marked the position of the second peak. This curve could be considered as intermediate between those of B₁, B₂ (fig 3), and C₁ (fig 4). The exposure was more uniform in plant B that had the new potroom technology because the tasks were less diverse.

In several cases (figs 1, 2, 3, and 4) we noted a supplementary peak of Al excretion during the day after the last exposure. This Al peak in the rest day existed in all exposed subjects followed up in plant B. No equivalent tendency was found for F⁻ excretion in the same cases.

Finally, in this study we noted some specific characteristics in the peaks of the urinary excretion of Al and F⁻ attributable to different exposures: for exposure to AlF₃ (A₁, fig 1): one delayed Al peak (delay ≈ 8 hours) associated with one delayed F⁻ peak. For exposure to HF + AlF₃ (A₂, fig 2): one isolated fast F⁻ peak and one delayed Al peak synchronised with one delayed F⁻ peak (delay ≈ 10 or 11 hours). For exposure to Al and F⁻ in potroom plant B (nine workers, B₁ and B₂, fig 3): one fast Al peak associated with one fast F⁻ peak. For exposure to Al and F⁻ in potroom plant C (five workers, C₁ and C₂, fig 4): one fast Al peak associated with one fast F⁻ peak and one delayed Al peak (delay 12/13 hours) associated with one delayed F⁻ peak (delay ≈ 10 hours).

HALF LIFE

The mean (range) half life of Al in urinary excretion (n = 7) was 7.5 (5–9) hours. For F⁻ (n = 8) the mean (range) value was about 9 (6.5–13.5) hours. For subjects C₂ and C₁, a second F⁻ half life could be identified at 18 and 15 hours.

RELATION TO EXPOSURE

The atmospheric concentrations of Al are

Table 1 Eight hour TWA concentrations of Al and F⁻ in air during the survey and quantities excreted during several days of exposure by workers of plants A, B, and C

Worker	Days (n)	Soluble Al (mg/m ³)	Insoluble Al (mg/m ³)	Total urinary* Al (μg)	Daily mean Al (μg)	Gaseous soluble F ⁻ (mg/m ³)	Particulate soluble F ⁻ (mg/m ³)	Total soluble F ⁻ (mg/m ³)	Total urinary* F ⁻ (mg)	Daily mean F ⁻ (mg)	Molecular ratio F ⁻ /Al (soluble part) air	Molecular ratio F ⁻ /Al urine
A ₁	5	0.29	4.79	180	36	0.08	< 0.1	0.08	10.2	2.0	0.4	80.6
A ₂	5	0.03	0.33	99	20	0.25	< 0.1	0.25	7.3	1.5	11.8	105.8
B ₁	3	0.22	0.35	210	70	0.36	0.54	0.90	17.3	5.8	5.8	116.7
B ₂	3	0.25	0.53	257	86	—	—	—	10.6	3.5	—	58.6
B ₃	3	0.15	0.29	104	35	0.14	0.44	0.58	4.8	1.6	5.5	64.9
B ₄	3	0.20	0.41	180	60	0.28	0.52	0.80	10.3	3.4	5.7	81.9
B ₅	3	0.18	0.29	165	55	0.41	0.82	1.23	7	2.3	9.7	60.7
B ₆	3	0.14	0.32	176	59	0.12	0.44	0.56	9.4	3.1	5.7	76.6
B ₇	3	0.23	0.62	224	75	—	—	—	12.7	4.2	—	80.5
B ₈	3	0.16	0.40	110	37	—	—	—	6.2	2.1	—	80.8
B ₉	3	0.18	0.33	165	55	—	—	—	15.9	5.3	—	137.0
C ₁	4	0.56	0.76	393	98	0.98	0.91	1.89	27.3	6.8	4.8	98.3
C ₂	4	0.31	0.10	473	118	0.58	0.43	1.01	24.6	6.1	4.6	73.9
C ₃	4	0.11	—	321	80	0.53	0.26	0.79	7.7	1.9	10.2	34.3
C ₄	4	0.21	0.19	130	32	0.76	0.46	1.22	5.5	1.4	8.2	60.2
C ₅	4	0.22	0.32	312	78	0.76	0.65	1.41	10.9	2.7	9.1	49.9

*Amount excreted in urine over n days.

reported in terms of insoluble and soluble Al. Likewise, F⁻ was evaluated as soluble gaseous F⁻, soluble particulate F⁻, and total soluble F⁻ (table 1). The quantities of urinary Al and F⁻ excreted each day of the survey were calculated for each subject. These daily amounts varied regularly around a mean value for each worker. These 16 workers excreted in their urine between 20 and 118 μg of Al and between 1.4 and 6.8 mg of F⁻ during each working day. The individual molecular ratios of F⁻/Al ranged between 34 and 137 (10 values in the 58–82 range). In comparison the same molecular ratio in air (table 1), ranged from 4.6 to 11.8 (with the exception of the value of 0.4 for subject A₁, exposed only to AlF₃). Excretion of F⁻ exceeded Al excretion by an average factor of 80, compared with the mean ratio of between seven and eight for soluble Al and F⁻ in air. The relation between urinary F⁻ and Al was calculated on a molecular basis from all the individual daily amounts excreted. This showed a significant correlation between them ($r = 0.776$, $n = 67$, $P < 0.0001$). Assuming a linear relation, 5 μmol of Al eliminated corresponded to 346 μmol of F⁻ ($Y = 67.6 X + 7.8$).

Three relations between the exposure and the urinary excretion in electrolytic plants B and C were examined for Al and for F⁻ with individual daily data (time weighted averages (TWA) soluble concentration of Al and F⁻ for atmospheric and urinary data).

The first relation between urinary Al concentration at the end of the daily work period and the airborne soluble Al concentration was calculated with a linear regression model as follows:

$$Y1 = 0.127 X + 27.1$$

$$(r = 0.411; df = 15; P < 0.005)$$

where Y1 is the urinary concentration of Al at the end of the shift (units μg/g creatinine) and X is the atmospheric concentration of soluble Al (units: μg/m³). An atmospheric Al concentration of 500 μg/m³ corresponds to a urinary excretion of 90 μg/g creatinine.

The second relation corresponded to the regression model:

$$Y2 = 0.153 X + 27.8$$

$$(r = 0.464; df = 43; P < 0.0015)$$

where Y2 is the peak concentration of Al in urine. With this model, the same atmospheric Al concentration of 500 μg/m³ corresponded to a urinary excretion of 105 μg/g creatinine.

The third relation between exposure and concentrations excreted in urine during 24 hours was also calculated:

$$Y3 = 0.615 X + 28$$

$$(r = 0.649; df = 15; P < 0.006)$$

where Y3 is the amount of Al excreted a day. The same atmospheric Al TWA of 500 μg/m³ corresponded to 110.5 μg Al excreted a day.

For F⁻, the regression models are expressed in the same way as for aluminium:

$$Y4 = 2.24 X2 + 0.77 \text{ for urinary F}^- \text{ (end of shift)}$$

$$(r = 0.490; df = 29; P < 0.006)$$

$$Y5 = 2.27 X2 + 1.72$$

for urinary F⁻ (peak) ($r = 0.412$; $df = 29$; $P < 0.02$) where X2 is the soluble atmospheric concentration in mg/m³ and Y3 and Y4 are the urinary F⁻ concentration (mg/g creatinine) for the end of the shift and the peak values, respectively. At the end of shift, urinary F⁻ reached 6.4 mg/g creatinine for 2.5 mg/m³ of atmospheric F⁻. In the second situation, the peak value reached 7.4 mg/g creatinine.

For the net amounts of F⁻, the model was:

$$Y6 = 2.5 X2 + 1.12$$

$$(r = 0.586; df = 11; P < 0.04).$$

With this relation, the amount of F⁻ excreted a day, Y6, after exposure to 2.5 mg/m³ of atmospheric F⁻ during one shift was estimated to be 7.4 mg of F⁻.

Discussion

Our study shows some characteristics of the urinary excretion of Al and F⁻ related to the compounds of exposure. We have shown the individual curves to illustrate the characteristics of the urinary excretion. One could argue that generalisations cannot be made from individual curves but several interesting points

emerge: some cases of simple and combined exposure were studied with good urinary responses from the 418 samples collected from the 16 subjects; they clearly showed a coherent and homogeneous urinary pattern for both elements between days for a given subject and between subjects in the same working conditions. Both of these points underline the representativeness of the observed data.

The results provide a better understanding of the kinetics of excretion of Al and F⁻. From these kinetic properties we noted that:

- (1) simultaneous associated peaks of Al and F⁻ when these elements were found together in the compound of exposure (AlF₃).
- (2) Specific time of excretion of the element for a specific compound of exposure. For Al F₃ this corresponded to one delayed peak after the end of the shift.
- (3) A two step excretion of one element when exposure was to two different compounds (F⁻ in AlF₃ and HF).
- (4) The change in the molecular ratio between F⁻ and Al in air (soluble part) and in urine.

Some biological limit values, such as the United States biological exposure indices (BEI) from the American Conference of Governmental Industrial Hygienists (ACGIH),³¹ are established based on the principle that they are equivalent to atmospheric limit values. We have therefore developed several relations with different biological values corresponding to the atmospheric limit values, each of which can be justified. It seems that the most effective of these is the relation between the atmospheric concentration and the quantities excreted daily in the urine. In practice, however, it is not easy to collect daily urine samples in occupational medicine.

Table 2 shows the comparison of our results (F⁻) with the data of BEIs³¹ and Biologische Arbeitstoleranzwerte (BAT)³² for the urine samples at the end of a shift with a TWA exposure to F⁻ of 2.5 mg/m³.

In a study dealing with workers exposed essentially to HF, Högstedt³³ found a relation between exposure and F⁻ in samples of urine after a shift ($Y = 1.4 + 4.6 X$), and between exposure and total F⁻ excretion in 24 hour urine samples ($Y = 0.6 + 3.2 X$). With one exposure to 2.5 mg/m³ of F⁻, the equivalent urinary values were 12.9 mg/l (after the shift) and 8.6 mg/24 hours (daily excretion). The differences between our and Högstedt's results after a shift may be due to the difference in exposures—that is, essentially limited to HF in Högstedt's case and consisting of a mixture of compounds in our situation.

In contrast, our results do not differ significantly from those of Steinegger and Schlatter, which were also obtained in Al smelters.¹⁸ They found a good relation between 7 mg/l of F⁻ in urine and an exposure to 2.5 mg/m³ of F⁻ ($Y = 1.08 X + 2.31$). We found a similar correlation with our data from samples from the end of a shift and the daily quantities. These conclusions only concern the exposures in aluminium smelting plants.

The F⁻ half life of nine hours, calculated here from urinary excretion rates, can be compared with Ekstrand and Ehrnebo's value of 5.1 hours.²² In that study the pharmacokinetic data were obtained from volunteers after an intake of 10 mg of Na F.

For Al, the BAT value is 200 µg/l in urine at the end of a shift.³² Sjögren *et al*¹³ found a relation between the urinary concentration after a shift and the corresponding air concentration of Al:

$$\text{urinary Al } (\mu\text{g/l}) = 34.7 \times \text{air Al } (\text{mg/m}^3) + 24.5$$

Mussi found a similar equation³⁴:

$$\text{urinary Al } (\mu\text{g/l}) = 36 \times \text{air Al}(\text{mg/m}^3) - 16.$$

In these two studies the exposed workers were Al welders.

With our model the corresponding exposure value for excretion of 200 µg/g creatinine after a shift is 1.36 mg/m³ (near to the BAT value). If we consider the quantities excreted in place of concentrations, amounts of 200 µg and 400 µg of Al eliminated daily correspond to exposures of 0.280 mg/m³ and 0.600 mg/m³ of soluble Al, respectively.

The Al elimination half life in our study was calculated to be about 7.5 hours, a value equivalent to that of Sjögren *et al*, who found it to be eight hours. The calculation of these half lives in our volunteers was accurate, with slight variations between subjects.

These results pointed out the existence of significant differences in the behaviour of a xenobiotic in urine depending on its original molecular form during exposure. The typical example in this study was that of a worker exposed to AlF₃ (A₁). The Al and F⁻ curves (fig 1) show their maxima several hours after the end of the shift, for Al the end of the shift corresponded to the minimum excretion. Consequently, the end of the shift seems to be an unsuitable time to take samples in practice. This is highly important in occupational hygiene as it has a direct bearing on the setting of a limit value, depending upon the monitoring strategy.

An important characteristic taken into account in the development of a sampling strategy is the elimination half life, and the classic approach in the determination of a biological limit value is the statistical validation of a relation between exposure concentrations and the concentrations at the end of the shift. This is an unsatisfactory method when a delay exists in the urinary excretion of the substance, and this discrepancy is reinforced in the case of double peaks as shown here. For

Table 2 F⁻: biological values corresponding to an exposure of 2.5 mg/m³

	BEI end of shift	BAT end of shift	Our results		
			End of shift	Peak	Daily amount mg/day
Urinary fluoride (mg/g creatinine)	10	7	6.4	7.4	7.4

example, in the plant C, where broad urinary peaks were found (fig 4), the concentrations of F^- and Al showed two peaks or one large peak that led to a higher concentration at the beginning of the next day than was found with a single peak. A second consequence of this delay is a cumulative effect due to the lack of time between exposure periods for sufficient elimination. This has the same effect as a longer half life. This also leads to a modified relation between the excretion (measured as concentration) and the exposure concentration.

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